(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
26 July 2018 (26.07.2018)

WIPO | PCT

(10) International Publication Number
WO 2018/136823 A1

(51) International Patent Classification:
A01K 67/027 (2006.01) *C07K 16/00* (2006.01)

(21) International Application Number:
PCT/US2018/014568

(22) International Filing Date:
19 January 2018 (19.01.2018)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/448,317 19 January 2017 (19.01.2017) US

(71) Applicant: **OPEN MONOCLONAL TECHNOLOGY, INC.** [US/US]; 3911 Sorrento Valley Boulevard, Suite 110, San Diego, CA 92121 (US).

(72) Inventors: **BUELOW, Roland**; 2747 Ross Road, Palo Alto, CA 94303 (US). **BRUGGEMANN, Marianne**; 2 Station Road, Fexton, Cambridge CB22 6SA (GB). **MA, Biao**; Top Floor Flat, 99 Hills Road, Cambridge CB2 1PG (GB). **OSBORN, Michael, J.**; Jasmine Cottage, Sturmer, Haverhill, Suffolk CB9 7XF (GB).

(74) Agent: **LORENZ, Todd, A.** et al.; Arnold & Porter Kaye Scholer Llp, Three Embarcadero Center, 10th Floor, San Francisco, CA 94111 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report (Art. 21(3))*
— *with sequence listing part of description (Rule 5.2(a))*

(54) Title: HUMAN ANTIBODIES FROM TRANSGENIC RODENTS WITH MULTIPLE HEAVY CHAIN IMMUNOGLOBULIN LOCI

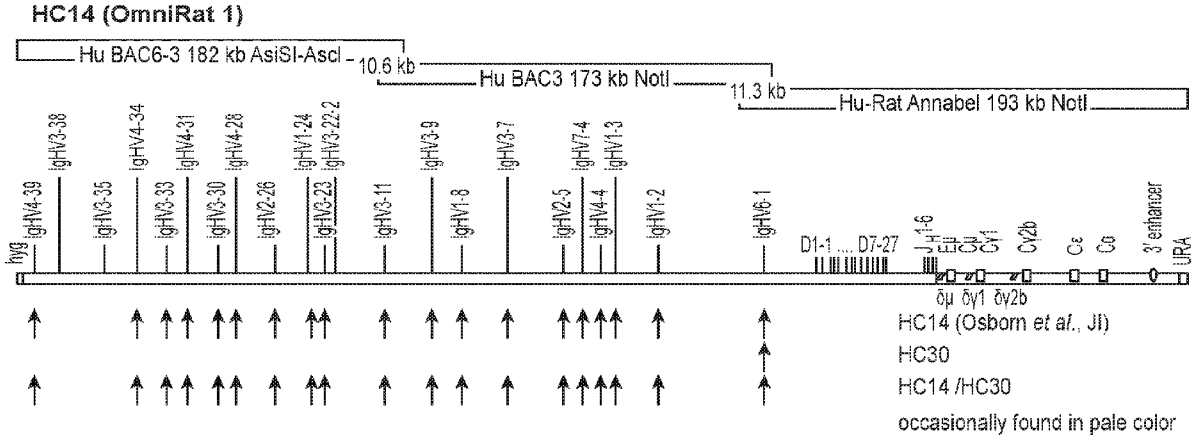


FIG. 1A

(57) Abstract: The invention relates to transgenic animals useful for optimal production of functional immunoglobulins with human idiotypes.

WO 2018/136823 A1

HUMAN ANTIBODIES FROM TRANSGENIC RODENTS WITH MULTIPLE HEAVY CHAIN IMMUNOGLOBULIN LOCI

FIELD OF INVENTION

[1] The invention relates to transgenic animals useful for the production of immunoglobulins with human idiotypes in rodents, and methods for making the same. The invention further relates to compositions and methods for the production of humanized and fully human antibodies using polynucleotides derived from modified large regions on bacterial artificial chromosomes and their combined tandem integration. Crossbreeding of independently obtained transgenic animals allowed the expression of highly diverse human antibody repertoires using many different, potentially all, human VH, D and JH segments. Expression is managed *in vivo* by regulating separate integration sites in unison such as to obtain VH gene diversity and choice without interference.

BACKGROUND OF THE INVENTION

[2] Human monoclonal antibodies have proven to be invaluable in therapeutic applications, either as IgG of conventional size, single chains or domain modules (Chan & Carter *Nature reviews. Immunology* **10**, 301-316 (2010); Enever et al. *Current opinion in biotechnology* **20**, 405-411 (2009)). Despite the successes there are still major shortcomings in their production, which relies either on specificity selection of available human material and subsequent modification of individual products, or the immunization of the limited availability of transgenic animals (Brüggemann et al. Part I: Selecting and shaping the antibody molecule, Selection Strategies III: Transgenic mice, in Handbook of Therapeutic Antibodies. Ed. Dübel, S. *Wiley-VHC*, 69-93 (2007)).

[3] DNA rearrangement and expression of human immunoglobulin (Ig) genes in transgenic animals was pioneered over 20 years ago by stably inserting heavy-chain genes in germline configuration (Bruggemann, M. et al. *PNAS* **86**, 6709-6713 (1989)). One problem associated with the therapeutic application of non-human immunoglobulins is the potential immunogenicity of the same in human patients. In order to reduce the immunogenicity of such preparations, various strategies for the production of chimeric, partially human (humanized) and fully human antibodies have been developed. Chimeric antibodies comprise a human constant region and a binding region encoded by non-human V-genes. The ability to produce transgenic antibodies having a human idiotype in non-human animals is particularly desirable as antigen binding determinants lie within the idiotype region,

and non-human idiotypes are thought to contribute to the immunogenicity of current antibody therapeutics. Human idiotype is an especially important consideration in respect of monoclonal antibody therapeutics, which consist of a single idiotype delivered at relatively high concentration as opposed to the variety of idiotypes delivered at lower concentrations by a polyclonal antibody mixture.

[4] Major improvements resulting in higher expression levels and exclusive production of human Ig, combined two new strategies: gene knock-out in embryonic stem (ES) cells (Kitamura et al. *Nature* **350**, 423-426 (1991)) and locus extension on artificial chromosomes (Davies et al. *Nucleic acids research* **21**, 767-768 (1993)). Silencing of the endogenous Ig genes by gene targeting in ES cells produced several inactive mouse lines without the ability to rearrange their IgH and lgL locus or without producing fully functional IgH, IgK or IgL products. More recently zinc finger nucleases (ZFNs) were designed to generate site-specific double-strand breaks in Ig genes, which allowed gene disruption by deletion and non-homologous DNA repair. Injection of ZFN plasmids into fertilized eggs produced Ig silenced rats and rabbits with IgH and IgL disruptions(Geurts, A.M. et al. *Science* **325**, 433 (2009); Menoret, S. et al. *European journal of immunology* **40**, 2932-2941 (2010); Flisikowska, T. et al. *PloS one* **6**, e21045 (2011)).

[5] A significant technical challenge encountered with many prior art approaches to producing humanized transgenic antibodies in non-human animals relates to the apparent competition between duplicate Ig loci in the same animal, *e.g*, an existing or endogenous Ig locus and an exogenous or artificial locus introduced into the transgenic animal. Historically, in the absence of effective knock-out the endogenous locus out-competes the exogenous locus for antibody production, such that the duplicate locus is effectively silenced (Lonberg et al., *Nat Bio*, **23**, 1117, 2005; Nicholson et al. *J Immunol*, **163**, 6898, 1999; Brüggemann et al., *AITE* **63**, 101, 2015). In this regard, therefore, the prior art does not address or resolve whether duplicate Ig loci integrated at different chromosomal sites can act cooperatively in the production of transgenic antibodies in the same host animal, and in fact would reasonably suggest to the skilled artisan that the opposite is true.

[6] Another technical challenge encountered with the production of transgenic antibodies having a human idiotype in non-human animals is the difficulty with providing the full complement of human immunoglobulin VDJ or VJ gene-segments used to generate the human antibodies. Some have attempted to address the problem by

introducing megabase-sized fragments from the human heavy and kappa light chain loci. However, this approach has only proven successful with roughly 80% of the human immunoglobin gene included in the germ-line configuration and has relied on the use of protoplasts to deliver the large fragments of the relevant chromosomes with a yeast artificial chromosome (YAC) system (US 5,939,598).

[7] While integration of extensive overlapping V_H D J_H regions, such as to maintain the full functionality of the IgH locus and essential for DNA rearrangement, have been utilized in transgenic animals in order to maximize antibody diversity, the overlapping integration had primarily been reported for much smaller regions (<100 kb) (Wagner et al. *Genomics* **35**, 405-414 (1996); Bruggemann et al. *European journal of immunology* **21**, 1323-1326 (1991)) or with larger regions but still having a limited repertoire at a single integration site (WO2014/093908; Bruggemann et al.). At the time of filing, the common understanding in the art was that spreading or multiple integration of BAC or YAC mixtures were rare and would be a disadvantage for breeding to homozygosity. Moreover, laborious integration of large YACs into stem cells and subsequent animal derivation therefrom was more commonly performed (Mendez et al. *Nature genetics* **15**, 146-156 (1997); Davies et al. *Biotechnology (N Y)* **11**, 911-914 (1993)).

[8] Optimal production of immunoglobulins or antibodies maximizing the diversity of antibodies with human idiotypes using transgenic animals with the full complement of human V-genes remains a challenge for the generation of novel specificities for therapeutic applications in a broad range of disease areas.

SUMMARY OF INVENTION

[9] The current invention resolves the foregoing uncertainties in the art with the provision of a transgenic animal comprising a plurality of artificial Ig heavy chain loci comprising duplicate/overlapping human immunoglobulin VDJ or VJ gene segments integrated at different chromosomal sites, and lacking the capacity to produce endogenous immunoglobulin. The method used to generate these transgenic animals comprising the insertion of two different loci in two different locations on two different chromosomes surprisingly produced functional B cells that advantageously avoids allelic exclusion and provides increased antibody diversity as a result of the full complement of human

immunoglobulin VDJ heavy chain gene segments integrated into the genome of the transgenic animal.

[10] In one aspect of the invention, novel polynucleotides are disclosed comprising nucleic acid sequences encoding chimeric immunoglobulin chains, particularly chimeric heavy chains for use in creating transgenic animals. The polynucleotides of the present invention advantageously provide optimal expression due, at least in part, to the inclusion of a 3' enhancer since transloci lacking this 3' enhancer result in impaired isotype switching and low lgG expression. Accordingly, in preferred embodiments the invention provides chimeric polynucleotides comprising a rat 3' enhancer sequence, an Ig constant region gene and at least one human immunoglubulin (Ig) joining (J) region gene. In a preferred embodiment, the rat 3' enhancer sequence comprises the sequence set forth as SEQ ID NO:1, or a portion thereof.

[11] In one embodiment, the chimeric polynucleotides set forth herein may further comprise at least one human variable (V) gene, at least one diversity (D) gene, or a combination thereof. In one embodiment, the constant region gene of the chimeric polynucleotide is selected from the group consisting of a human constant region gene and a rat constant region gene. In a preferred embodiment, the constant region gene is a rat constant region gene. In another preferred embodiment, the constant region gene is selected from the group consisting of Cμ and Cγ.

[12] In one embodiment, the chimeric polynucleotide comprises a nucleic acid sequence substantially homologous to the bacterial artificial chromosome (BAC) Annabel disclosed herein (e.g., SEQ ID NO:10, or a portion thereof), and may optionally further comprise at least one human variable Ig gene isolatable from a BAC6-V_H3-11 and BAC3 construct and/or from a BAC9 and BAC14/5 construct. In a preferred embodiment, the chimeric polynucleotides contemplated herein comprise nucleic acid sequences (a) and (b) in 5' to 3' order: (a) a human Ig variable region comprising human V genes in natural configuration isolatable from a BAC6-V_H3-11 and BAC3 construct and/or a BAC9 and BAC14/5 construct, and (b) a human Ig joining region comprising human J genes in natural configuration isolatable from the BAC Annabel. In another embodiment, each of the human Ig variable region, human Ig diversity region, human Ig joining region, the Ig constant region and the rat 3' enhancer region of a chimeric polynucleotide as disclosed

herein are in the relative positions as shown in FIG. 1a. In another embodiment, a chimeric polynucleotide as disclosed has a sequence comprising or substantially homologous to the sequence set forth as SEQ ID NO:2 or a portion thereof. In another embodiment, a chimeric polynucleotide as disclosed has a sequence comprising or substantially homologous to the sequence set forth as SEQ ID NO:11, or a portion thereof. In a further embodiment, a chimeric polynucleotide as disclosed herein comprises a rearranged V-D-J regions, wherein said rearranged V-D-J regions encode a heavy chain variable domain exon.

[13] In one embodiment, the transgenic animal further comprises a chimeric polynucleotide wherein said human Ig V region comprises at least one human V region gene isolatable from BAC9 and/or BAC14/5. In a preferred embodiment, the chimeric polynucleotides comprise nucleic acid sequences (a) and (b) in 5' to 3' order: (a) a human Ig variable region comprising human V region genes in natural configuration used (or rearranged) from BAC9 and/or BAC14/5; and (b) a human Ig joining region comprising human J region genes in natural configuration used (or rearranged) from the bacterial artificial chromosome (BAC) Annabel. In another embodiment, each of the human immunoglobulin variable region (gene), the human immunoglobulin diversity region (segment), the human immunoglobulin joining region (segment), the immunoglobulin constant region gene, and the rat 3' enhancer are in the positions shown in FIG. 1b. In another embodiment, a chimeric polynucleotide as disclosed has a sequence comprising or substantially homologous to the sequence set forth in FIG. 6. In another embodiment, a chimeric polynucleotide as disclosed has a sequence comprising or substantially homologous to the sequence set forth in FIG. 7, or a portion thereof. In a further embodiment, chimeric polynucleotides as disclosed herein may comprise rearranged V-D-J, wherein said rearranged gene segments are derived from the above SEQ ID NOs and Figures.

[14] Also disclosed herein are polynucleotides encoding human kappa light chain genes. In one embodiment, a polynucleotide as disclosed herein has a nucleic acid sequence comprising or substantially homologous to a nucleic acid sequence selected from the group consisting of RP11-1156D9 (set forth as SEQ ID NO:3) and RP11-1134E24 (set forth as SEQ ID NO:4). In another embodiment, the isolated polynucleotide comprises nucleic acid sequences (a) and (b) in 5' to 3' order: (a) a human Ig variable

region comprising human V genes in natural configuration isolatable from bacterial artificial chromosomes (BAC) RP11-156D9 and/or RP11-1134E24; (b) a human Ig joining region comprising human J genes in natural configuration isolatable from the bacterial artificial chromosomes (BAC) RP11-1134E24 and/or RP11-344F17 (set forth as SEQ ID NO:5). In a preferred embodiment, each of the human Ig variable region, the human Ig joining region, and the human Ig constant region are in relative position as shown in FIG. 2. In another embodiment, a chimeric polynucleotide as disclosed has a sequence comprising or substantially homologous to the sequence set forth as SEQ ID NO:6 or a portion thereof.

[15] Also provided herein is a rodent cell comprising one or more polynucleotides of the invention. For example, provided herein is a rodent cell comprising a polynucleotide as disclosed herein, preferably comprising a nucleic acid sequence encoding for a chimeric heavy chain, e.g., a nucleic acid sequence encoding a rat 3' enhancer sequence, an Ig constant region gene and at least one human J region gene, and optionally, comprising a nucleic acid sequence substantially homologous to the nucleic acid sequence selected from the group consisting of RP11-1156D9, RP11-1134E24 and portions thereof. The rodent cell contemplated herein may further comprise a polynucleotide encoding a functional light chain, e.g., having a nucleic acid sequence comprising or substantially homologous to a nucleic acid sequence selected from the group consisting of the sequence shown in FIG. 2a (set forth as SEQ ID NO:6), the sequence shown in FIG. 2b (set forth as SEQ ID NO:7), and portions thereof. In one embodiment, one or more of the polynucleotides are integrated into the rodent cell genome.

[16] In another aspect of the invention, a transgenic animal is provided which comprises at least one inactivated endogenous Ig locus and a plurality of artificial transgenic Ig heavy chain loci integrated in the animal's genome at different chromosomal sites. In one embodiment, the transgenic animal having a plurality of artificial Ig heavy chain loci comprises (i) a V-region having at least one human V gene segment encoding a germline or hypermutated human V-region amino acid sequence; (ii) one or more J gene segments; and (iii) one or more constant region gene segments, wherein said artificial Ig heavy chain loci are functional and capable of undergoing gene rearrangement and act cooperatively to produce a repertoire of artificial immunoglobulins. In another embodiment, the transgenic animal comprises the full complement of human variable heavy chain regions. In other

various embodiments, the transgenic animal i) has an artificial heavy chain loci which comprises overlapping heavy chain gene segments, ii) lacks a functional endogenous Ig light chain locus and/or iii) lacks a functional endogenous Ig heavy chain locus. In yet another embodiment, the transgenic animal expresses a diverse repertoire of antibodies encoded by V-genes from transgenic immunoglobulin loci located at different chromosomal sites.

[17] In some embodiments, the transgenic animal lacks a functional Ig light chain locus and is capable of producing heavy chain-only antibodies.

[18] In another embodiment, the transgenic animal with at least two artificial Ig heavy chain loci has at least one artificial Ig heavy chain loci which comprises at least one human immunoglobulin (Ig) joining (J) region gene, an Ig constant region gene, and a rat 3' enhancer. In these transgenic animals the rat 3' enhancer may comprise the sequence set forth as SEQ ID NO:1. The transgenic animal described in the above embodiments which may further comprise at least one human Ig variable (V) region gene and/or a human Ig diversity (D) region gene. In other embodiments of the invention the constant region gene is selected from the group consisting of a human constant region gene and a rat constant region gene. In certain embodiments the constant region gene comprises a constant region gene selected from the group consisting of Cμ and Cγ. In various embodiments the transgenic animal comprises a nucleic acid sequence substantially homologous to bacterial artificial chromosome (BAC) Annabel, or a portion thereof.

[19] In certain embodiments, the human Ig V region of the transgenic animal comprises at least one human V region gene isolatable from BAC6-V_H3-11 and/or BAC3. In a specific embodiment the transgenic animal comprises nucleic acids with (a) a human Ig variable region comprising human V region genes in natural configuration isolatable from BAC6-V_H3-11 and/or BAC3; and (b) a human Ig joining region comprising human J region genes in natural configuration isolatable from the bacterial artificial chromosome (BAC) Annabel, in 5' to 3' order. In one embodiment each of the human immunoglobulin variable region, the human immunoglobulin diversity region, the human immunoglobulin joining region, the immunoglobulin constant region, and the rat 3' enhancer are in the relative positions shown in FIG. 1a. In another embodiment the transgenic animal has a nucleic acid sequence substantially homologous to the nucleic acid sequence set forth as SEQ ID NO:2. In yet another embodiment he transgenic animal has a nucleic acid sequence substantially homologous to the nucleic acid sequence set forth as SEQ ID NO:11. In some embodiments

he transgenic animal has V-D-J regions which are rearranged and form a complete exon encoding a heavy chain variable domain.

[20] In certain other embodiments, the transgenic animal has an human Ig V region which comprises at least one human V region gene isolatable from BAC9-V_H3-53 and/or BAC14/5. In a specific embodiment these transgenic animals comprises nucleic acids with (a) a human Ig variable region comprising human V region genes in natural configuration isolatable from BAC9-V_H3-53 and/or BAC14/5; and (b) a human Ig joining region comprising human J region genes in natural configuration isolatable from the bacterial artificial chromosome (BAC) Annabel, in 5' to 3' order. In one embodiment each of the human immunoglobulin variable region, the human immunoglobulin diversity region, the human immunoglobulin joining region, the immunoglobulin constant region, and the rat 3' enhancer are in the relative positions shown in FIG. 1b. In another embodiment the transgenic animal has a nucleic acid sequence substantially homologous to the nucleic acid sequence set forth in FIG. 6. In yet another embodiment he transgenic animal has a nucleic acid sequence substantially homologous to the nucleic acid sequence set forth in FIG. 7.

[21] In another aspect of the invention, a method for producing antibodies is provided which comprises immunizing the transgenic animal as described above with an immunogen. In one embodiment a polyclonal antisera composition is produced wherein said antisera comprise antigen-specific antibodies encoded by V-genes encoded by transgenic immunoglobulin loci located at different chromosomal sites. In another embodiment the method for producing a monoclonal antibody comprises (i) immunizing the transgenic animal described above with an immunogen, (ii) isolating a monoclonal antibody producing cell from said transgenic animal wherein said monoclonal antibody producing cell produces a monoclonal antibody that specifically binds to said immunogen; and (iii) using said monoclonal antibody producing cell to produce said monoclonal antibody that specifically binds to said immunogen, or using said monoclonal antibody producing cell to produce a hybridoma cell that produces said monoclonal antibody and using said hybridoma cell to produce said monoclonal antibody.

[22] In another embodiment, the method for producing a monoclonal antibody, comprises (i) immunizing the transgenic animal as described above with an immunogen, (ii) isolating a monoclonal antibody producing cell from said transgenic animal wherein said monoclonal antibody producing cell produces a monoclonal antibody that specifically binds

to said immunogen; (iii) isolating from said monoclonal antibody producing cell a monoclonal antibody nucleic acid which encodes said monoclonal antibody that specifically binds to said immunogen; and (iv) using said monoclonal antibody nucleic acid to produce said monoclonal antibody that specifically binds to said immunogen. In certain embodiment the monoclonal antibody has a human idiotype.

[23] In yet another embodiment the method for producing a fully human monoclonal antibody comprises (i) immunizing the transgenic animal as described above with an immunogen, (ii) isolating a monoclonal antibody producing cell from said transgenic animal wherein said monoclonal antibody producing cell produces a monoclonal antibody that specifically binds to said immunogen; (iii) isolating from said monoclonal antibody producing cell a monoclonal antibody nucleic acid which encodes said monoclonal antibody that specifically binds to said immunogen; (iv) modifying said monoclonal antibody nucleic acid to produce a recombinant nucleic acid encoding a fully human monoclonal antibody; and (v) using said recombinant nucleic acid encoding a fully human monoclonal antibody to produce the encoded fully human monoclonal antibody.

[24] Another aspect of the present invention is a monoclonal antibody produced by the method described above.

[25] In yet another aspect a method for neutralizing an antigenic entity in a human body component is provided which comprises contacting said body component with a polyclonal antisera composition as described above, wherein said polyclonal antisera composition comprises immunoglobulin molecules that specifically bind and neutralize said antigenic entity. In one embodiment the method for neutralizing an antigenic entity in a human body component comprises contacting a body component with the monoclonal antibody according to the above, wherein said monoclonal antibody specifically binds to and neutralizes said antigenic entity.

BRIEF DESCRIPTION OF THE DRAWINGS

[26] FIG. 1: A summary of the integrated chimeric (human, rat) and fully human Ig loci. The 2 chimeric human-rat IgH regions (HC14 and HC30) contain each 3 overlapping BACs with ≥22 different and potentially functional human V_H segments. In HC14 BAC6-3 has been extended with V_H3-11 to provide a 10.6 kb overlap to BAC3, which

overlaps 11.3 kb via V_H6-1 with the C region BAC Hu-Rat Annabel (A) and in HC30 BAC9 provides an overlap of 4.6 kb to BAC14/5, which was extended by adding VH3-43 followed by part of BAC5 and equipped with an overlap of 6.1 kb to Hu-Rat Annabel (B). The latter is chimeric and contains all human D and J_H segments followed by the rat C region with full enhancer sequences. Arrows indicate the VH gene usage in HC14, HC30 and HC14/HC30 combined. Fainter bands indicate less frequently expressed VH genes. Sequences were obtained by unbiased RT-PCR and NGS.

[27] FIG. 2: **(A)** The human Igk BACs with 12 Vks and all Jks provide a ~14 kb overlap in the Vk region and ~40 kb in Ck to include the KDE. **(B)** The human Igl region with 17 Vls and all J-Cls, including the 3' enhancer, is from a YAC (Vincent-Fabert, C. et al. *Blood* **116**, 1895-1898 (2010)).

[28] FIG. 3: Depicts HC14 locus integration into chromosome 6 and HC30 locus integration into chromosome 15.

[29] FIG. 4: Analysis by ELISA of IgM and IgG concentration in serum from HC30 and HC14/HC30 animals. Each dot (HC30) or square (HC14/HC30) represents the titre (μg/ml) of one animal. IgG is further analysed for the content of IgG1 and IgG2b.

[30] FIG. 5: Analysis by ELISA of anti-β-gal specific antibodies from HC30 and HC14/HC30. Each dot (HC30) or square (HC14/HC30) represents the serum titre (in comparative dilution) from one animal.

[31] FIG. 6: BAC 9 sequence.

[32] FIG. 7: BAC 14/5 sequence.

DETAILED DESCRIPTION

[33] Provided herein are chimeric polynucleotides encoding a recombinant or artificial immunoglobulin chain or loci. As described above, the chimeric polynucleotides disclosed herein are useful for the transformation of rodents to include human Ig genes and for the production of immunoglobulins or antibodies having human idiotypes using such

rodents. As further provided herein, transgenic animals are generated that comprise at least three distinct transgene constructs harboring the full complement of human immunoglobulin VDJ heavy chain gene segments tandemly integrated into the genome of the transgenic animal, thereby ensuring the availability of the entire human immunoglobulin genes in germ-line configuration in a background of complete inactivation of endogenous immunoglobulin genes or locus. Unexpectedly, as demonstrated herein for the first time, a plurality of transgenic loci comprising different V-genes can act cooperatively in the expression of humanized and fully human transgenic antibodies.

DEFINITIONS

[34] Immunoglobulin refers to a protein consisting of one or more polypeptides substantially encoded by immunoglobulin genes. The recognized human immunoglobulin genes include the kappa, lambda, alpha (IgA1 and IgA2), gamma (IgG1, IgG2, IgG3, IgG4), delta, epsilon and mu constant region genes, as well as the myriad immunoglobulin variable region genes. Full-length immunoglobulin "light chains" (about 25 Kd, or 214 amino acids) generally comprise a variable domain encoded by an exon comprising one or more variable region gene(s) and one or more joining region gene(s) at the NH_2-terminus (about 110 amino acids) and constant domain encoded by a kappa or lambda constant region gene at the COOH-terminus. Full-length immunoglobulin "heavy chains" (about 50 Kd, or 446 amino acids), similarly comprise (1) a variable domain (about 116 amino acids) encoded by an exon comprising one or more variable region genes, one or more diversity region genes and one or more joining region genes, and (2) one of the aforementioned constant domains comprising one or more constant region genes, e.g., alpha, gamma, delta, epsilon or mu (encoding about 330 amino acids). The immunoglobulin heavy chain constant region genes encode for the antibody class, i.e., isotype (e.g., IgM or IgG1).

[35] As used herein, the term "antibody" refers to a protein comprising at least one, and preferably two, heavy (H) chain variable domains (abbreviated herein as VH), and at least one and preferably two light (L) chain variable domains (abbreviated herein as VL). An ordinarily skilled artisan will recognize that the variable domain of an immunological chain is encoded in gene segments that must first undergo somatic recombination to form a complete exon encoding the variable domain. There are three types of regions or gene segments that undergo rearrangement to form the variable domain: the variable region comprising variable genes, the diversity region comprising diversity genes (in the case of an immunoglobulin

heavy chain), and the joining region comprising joining genes. The VH and VL domains can be further subdivided into regions of hypervariability, termed "complementarity determining regions" ("CDRs") interspersed with regions that are more conserved, termed "framework regions" ("FRs"). The extent of the FRs and CDRs has been precisely defined (see, Kabat et al. (1991) Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242; and Chothia et al. (1987) *J. Mol. Biol.* **196**:901-17, which are hereby incorporated by reference). Each VH and VL domain is generally composed of three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. The antigen binding fragment of an antibody (or simply "antibody portion," or "fragment"), as used herein, refers to one or more fragments of a full-length antibody that retain the ability to specifically bind to an antigen (e.g., CD3).

[36] Examples of binding fragments encompassed within the term "antigen binding fragment" of an antibody include (i) an Fab fragment, a monovalent fragment consisting of the VL, VH, CL and CH1 domains; (ii) an $F(ab')_2$ fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; (iii) an Fd fragment consisting of the VH and CH1 domains; (iv) an Fv fragment consisting of the VL and VH domains of a single arm of an antibody, (v) a dAb fragment (Ward et al. (1989) *Nature* **341**:544-46), which consists of a VH domain; and (vi) an isolated complementarity determining region (CDR). Furthermore, although the two domains of the Fv fragment, VL and VH, are coded for by separate genes, they may be joined, using recombinant methods, by a synthetic linker that enables them to be made as a single protein chain in which the VL and VH regions pair to form monovalent molecules (known as single chain Fv (scFv); see, e.g., Bird et al. (1988) *Science* **242**:423-26; and Huston et al. (1988) *Proc. Natl. Acad. Sci. USA* **85**:5879-83). Such single chain antibodies are also intended to be encompassed within the term "antigen binding fragment" of an antibody. These antibody fragments are obtained using conventional techniques known to those skilled in the art, and the fragments are screened for utility in the same manner as are intact antibodies.

[37] An antibody may further include a heavy and/or light chain constant domain to thereby form a heavy and light immunoglobulin chain, respectively. In one embodiment, the antibody is a tetramer of two heavy immunoglobulin chains and two light immunoglobulin chains, wherein the heavy and light immunoglobulin chains are interconnected, e.g., by

disulfide bonds. The heavy chain constant domain is comprised of three gene segments, CH1, CH2 and CH3. The light chain constant domain is comprised of one gene, CL. The variable domains of the heavy and/or light chains contain a binding domain that interacts with an antigen. The constant domains of the antibodies typically mediate the binding of the antibody to host tissues or factors, including various cells of the immune system (e.g., effector cells) and the first component (C1q) of the classical complement system.

[38] By polynucleotide encoding an artificial immunoglobulin locus or artificial immunoglobulin chain is meant an recombinant polynucleotide comprising multiple immunoglobulin regions, e.g., a variable (V) region or gene segment comprising V genes, a joining (J) gene region or gene segment comprising J genes, a diversity (D) region or gene segment comprising D genes in the case of a heavy chain locus and/or at least one constant (C) region comprising at least one C gene. Preferably, each region of the variable domain, e.g., V, D, or J region, comprises or spans at least two genes of the same type. For example a variable region as used herein comprises at least two variable genes, a joining region comprises at least two joining genes and a diversity region comprises two diversity genes. A constant region may comprise only one constant gene, e.g. a κ gene or λ gene, or multiple genes, e.g., CH1, CH2, and CH3.

[39] "Enhancer sequences" or "enhancer" as used herein refers to sequences that have been identified near many active genes by nuclease digest and hypersensitivity to degradation. Hypersensitive sites may precede promoter sequences and the strength of their activity was correlated with the DNA sequence. Linkage to reporter genes showed elevated transcription if enhancer function was present (Mundt *et al.*, *J. Immunol.*, **166**, 3315[2001]). In the IgH locus two important transcription or expression regulators have been identified, Eμ and the 3'E at the end of the locus (Pettersson *et al.*, *Nature*, **344**, 165 [1990]). In the mouse the removal of the whole 3' regulatory region (containing hs3a, hs1,2, hs3b and hs4) allows normal early B-cell development but abrogates class-switch recombination (Vincent-Fabert *et al.*, *Blood*, **116**, 1895 [2010]) and possibly prevents the optimization of somatic hypermutation (Pruzina *et al.*, *Protein Engineering, Design and Selection*, **1**, [2011]). The regulatory function to achieve optimal isotype expression is particularly desirable when transgenic human IgH genes are being used. Transgene constructs with incomplete 3'E region, usually only providing the hs1,2 element, led to disappointing expression levels in transgenic mice even when the endogenous IgH locus was knocked-out. As a consequence,

only few antigen-specific fully human IgGs have been isolated from constructs produced in the last 20 years (Lonberg *et al.*, *Nature* **368**, 856 [1994]; Nicholson *et al.*, *J. Immunol.*, **163**, 6898 [1999]; Davis *et al.*, *Cancer Metastasis Rev.* **18**, 421 [1999]; Pruzina *et al.*, *Protein Engineering, Design and Selection*, **1**, [2011]). In the rat IgH locus, the 3'E region has only been poorly analyzed. A comparison of mouse and rat sequences did not allow identification of hs4, the crucial 4th element with additional important regulatory sequences further downstream (Chatterjee *et al.*, *J. Biol. Chem.*, **286**,29303 [2011]). The polynucleotides of the present invention advantageously provide optimal expression due, at least in part, to the inclusion of a rat 3' enhancer since chimeric polynucleotides lacking this 3' enhancer result in impaired isotype switching and low IgG expression. In one embodiment, the rat 3' enhancer has a sequence comprising or substantially homologous to the sequence set forth as SEQ ID NO:1 or a portion thereof.

[40] As used herein, a polynucleotide having a sequence comprising or substantially homologous to a portion, e.g., less than the entirety, of second sequence (e.g., SEQ ID NO:1, SEQ ID NO:2, etc.) preferably retains the biological activity of the second sequence (e.g., retains the biological activity of a 3' enhancer to provide optimal expression and/or isotype switching of immunoglobulins, is capable of rearrangement to provide a humanized chimeric heavy chain, etc.) . In one embodiment, a nucleic acid comprising a sequence comprising or substantially homologous to a portion of SEQ ID NO:1 comprise at least 8 kB, preferably at least 10 kB of continuous nucleic acids that are substantially homologous to SEQ ID NO:1. In another embodiment, a second nucleic acid comprising a sequence comprising or substantially homologous to a portion of SEQ ID NOs:59 or 60 comprise at least 8 kB, preferably at least 10 kB of continuous nucleic acids that are substantially homologous to SEQ ID NOs:59 or 60.

[41] "Artificial Ig locus" as used herein may refer to polynucleotides that (e.g., a sequence comprising V-,D-, and/or J regions in the case of heavy chain, or V- and/or J regions in the case of light chain, and optionally a constant region for either or both a heavy and light chain) that are unrearranged, partially rearranged, or rearranged. Artificial Ig loci include artificial Ig light chain loci and artificial Ig heavy chain loci. In one embodiment, an artificial immunoglobulin locus of the invention is functional and capable of rearrangement and producing a repertoire of immunoglobulin chains. In a preferred embodiment, the variable domain or portion thereof of a polynucleotide disclosed herein comprises genes in

natural configuration, i.e., naturally occurring sequences of an human Ig gene segment, degenerate forms of naturally occurring sequences of a human Ig gene segment, as well as synthetic sequences that encode a polypeptide sequence substantially identical to the polypeptide encoded by a naturally occurring sequence of a human Ig gene segment. In another preferred embodiment, the polynucleotide comprises a variable domain or portion thereof in a natural configuration found in humans. For example, a polynucleotide encoding an artificial Ig heavy chain as disclosed herein may comprise in natural configuration at least two human V genes, at least two D genes, at least two J genes or a combination thereof.

[42] In a preferred embodiment, an artificial Ig locus comprises a non-human C region gene and is capable of producing a repertoire of immunoglobulins including chimeric immunoglobulins having a non-human C region. In one embodiment, an artificial Ig locus comprises a human C region gene and is capable of producing a repertoire of immunoglobulins including immunoglobulins having a human C region. In one embodiment, an artificial Ig locus comprises an "artificial constant region gene", by which is meant a constant region gene comprising nucleotide sequences derived from human and non-human constant regions genes. For example, an exemplary artificial C constant region gene is a constant region gene encoding a human IgG CH1 domain and rat IgG CH2 and CH3 domain.

[43] In some embodiments, an artificial Ig heavy chain locus lacks CH1, or an equivalent sequence that allows the resultant immunoglobulin to circumvent the typical immunoglobulin: chaperone association. Such artificial loci provide for the production of heavy chain-only antibodies in transgenic animals which lack a functional Ig light chain locus and hence do not express functional Ig light chain. Such artificial Ig heavy chain loci are used in methods contemplated herein to produce transgenic animals lacking a functional Ig light chain locus, and comprising an artificial Ig heavy chain locus, which animals are capable of producing heavy chain-only antibodies. Alternatively, an artificial Ig locus may be manipulated in situ to disrupt CH1 or an equivalent region and generate an artificial Ig heavy chain locus that provides for the production of heavy chain-only antibodies. Regarding the production of heavy chain-only antibodies in light chain-deficient mice, see for example Zou et al., *JEM*, **204**:3271-3283, 2007.

[44] By "human idiotype" is meant a polypeptide sequence present on a human antibody encoded by an immunoglobulin V-gene segment. The term "human idiotype" as

used herein includes both naturally occurring sequences of a human antibody, as well as synthetic sequences substantially identical to the polypeptide found in naturally occurring human antibodies. By "substantially" is meant that the degree of amino acid sequence identity is at least about 85%-95%. Preferably, the degree of amino acid sequence identity is greater than 90%, more preferably greater than 95%.

[45] By a "chimeric antibody" or a "chimeric immunoglobulin" is meant an immunoglobulin molecule comprising a portion of a human immunoglobulin polypeptide sequence (or a polypeptide sequence encoded by a human Ig gene segment) and a portion of a non-human immunoglobulin polypeptide sequence. The chimeric immunoglobulin molecules of the present invention are immunoglobulins with non-human Fc-regions or artificial Fc-regions, and human idiotypes. Such immunoglobulins can be isolated from animals of the invention that have been engineered to produce chimeric immunoglobulin molecules.

[46] By "artificial Fc-region" is meant an Fc-region encoded by an artificial constant region gene.

[47] The term "Ig gene segment" as used herein refers to regions of DNA encoding various portions of an Ig molecule, which are present in the germline of non-human animals and humans, and which are brought together in B cells to form rearranged Ig genes. Thus, Ig gene segments as used herein include V gene segments, D gene segments, J gene segments and C gene segments.

[48] The term "human Ig gene segment" as used herein includes both naturally occurring sequences of a human Ig gene segment, degenerate forms of naturally occurring sequences of a human Ig gene segment, as well as synthetic sequences that encode a polypeptide sequence substantially identical to the polypeptide encoded by a naturally occurring sequence of a human Ig gene segment. By "substantially" is meant that the degree of amino acid sequence identity is at least about 85%-95%. Preferably, the degree of amino acid sequence identity is greater than 90%, more preferably greater than 95%

[49] Polynucleotides related to the present invention may comprise DNA or RNA and may be wholly or partially synthetic. Reference to a nucleotide sequence as set out herein

encompasses a DNA molecule with the specified sequence, and encompasses an RNA molecule with the specified sequence in which U is substituted for T, unless context requires otherwise.

[50] Calculations of "homology" or "sequence identity" between two sequences (the terms are used interchangeably herein) are performed as follows. The sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment and non-homologous sequences can be disregarded for comparison purposes). In a preferred embodiment, the length of a reference sequence aligned for comparison purposes is at least 30%, preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, and even more preferably at least 70%, 80%, 90%, 100% of the length of the reference sequence. The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position (as used herein amino acid or nucleic acid "identity" is equivalent to amino acid or nucleic acid "homology"). The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences.

[51] The comparison of sequences and determination of percent sequence identity between two sequences may be accomplished using a mathematical algorithm. In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch ((1970) *J. Mol. Biol.* **48**:444-53) algorithm, which has been incorporated into the GAP program in the GCG software package (available online at gcg.com), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (available at www.gcg.com), using a NWSgapdna. CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. A particularly preferred set of parameters (and the one that should be used if the practitioner is uncertain about what parameters should be applied to determine if a molecule is within a sequence identity or homology limitation of the invention) is a Blossum

62 scoring matrix with a gap penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5. The percent identity between two amino acid or nucleotide sequences can also be determined using the algorithm of Meyers and Miller ((1989) *CABIOS* **4**:11-17), which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

ARTIFICIAL Ig LOCI

[52] The present invention is further directed to artificial Ig loci and their use in making transgenic animals capable of producing immunoglobulins having a human idiotype. Each artificial Ig locus comprises multiple immunoglobulin gene segments, which include at least one V region gene segment, one or more J gene segments, one or more D gene segments in the case of a heavy chain locus, and one or more constant region genes. In the present invention, at least one of the V gene segments encodes a germline or hypermutated human V-region amino acid sequence. Accordingly, such transgenic animals have the capacity to produce a diversified repertoire of immunoglobulin molecules, which include antibodies having a human idiotype. In heavy chain loci human or non-human-derived D-gene segments may be included in the artificial Ig loci. The gene segments in such loci are juxtaposed with respect to each other in an unrearranged configuration (or "the germline configuration"), or in a partially or fully rearranged configuration. The artificial Ig loci have the capacity to undergo gene rearrangement (if the gene segments are not fully rearranged) in the subject animal thereby producing a diversified repertoire of immunoglobulins having human idiotypes.

[53] Regulatory elements, like promoters, enhancers, switch regions, recombination signals, and the like, may be of human or non-human origin. What is required is that the elements be operable in the animal species concerned, in order to render the artificial loci functional. Preferred regulatory elements are described in more detail herein.

[54] In one aspect, the invention provides transgenic constructs containing an artificial heavy chain locus capable of undergoing gene rearrangement in the host animal thereby producing a diversified repertoire of heavy chains having human idiotypes. An artificial heavy chain locus of the transgene contains a V-region with at least one human V gene segment. Preferably, the V-region includes at least about 5-100 human heavy chain V

(or "VH") gene segments. In a preferred embodiments, the V-region includes greater than 20, greater than 25, greater than 30, greater than 35, or greater than 40 VH gene segments. As described above, a human VH segment encompasses naturally occurring sequences of a human VH gene segment, degenerate forms of naturally occurring sequences of a human VH gene segment, as well as synthetic sequences that encode a polypeptide sequence substantially (i.e., at least about 85%-95%) identical to a human heavy chain V domain polypeptide.

[55] In a preferred embodiment, the artificial heavy chain locus contains at least one or several rat constant region genes, e.g., Cδ, Cμ and Cγ (including any of the Cγ subclasses).

[56] In another preferred embodiment, the artificial heavy chain locus contains artificial constant region genes. In a preferred embodiment, such artificial constant region genes encode a human CH1 domain and rat CH2 CH3 domains, or a human CH1 and rat CH2, CH3 and CH4 domains. A hybrid heavy chain with a human CH1 domain pairs effectively with a fully human light chain.

[57] In a preferred embodiment, an artificial Ig locus comprises 3' enhancer sequences, including hs1,2, hs3a, hs3b and sequences between rat Calpha and 3'hs3b.

[58] In another preferred embodiment, the artificial heavy chain locus contains artificial constant region genes lacking CH1 domains In a preferred embodiment, such artificial constant region genes encode truncated IgM and/or IgG lacking the CH1 domain but comprising CH2, and CH3, or CH1, CH2, CH3 and CH4 domains. Heavy chains lacking CH1 domains cannot pair effectively with Ig light chains and form heavy chain only antibodies.

[59] In another aspect, the invention provides transgenic constructs containing an artificial light chain locus capable of undergoing gene rearrangement in the host animal thereby producing a diversified repertoire of light chains having human idiotypes. An artificial light chain locus of the transgene contains a V-region with at least one human V gene segment, e.g., a V-region having at least one human VL gene and/or at least one rearranged human VJ segment. Preferably, the V-region includes at least about 5-100 human

light chain V (or "VL") gene segments. Consistently, a human VL segment encompasses naturally occurring sequences of a human VL gene segment, degenerate forms of naturally occurring sequences of a human VL gene segment, as well as synthetic sequences that encode a polypeptide sequence substantially (i.e., at least about 85%-95%) identical to a human light chain V domain polypeptide. In one embodiment, the artificial light chain Ig locus has a C-region having at least one rat C gene (e.g., rat Cλ or Cκ).

[60] Another aspect of the present invention is directed to methods of making a transgenic vector containing an artificial Ig locus. Such methods involve isolating Ig loci or fragments thereof, and combining the same, with one or several DNA fragments comprising sequences encoding human V region elements. The Ig gene segment(s) are inserted into the artificial Ig locus or a portion thereof by ligation or homologous recombination in such a way as to retain the capacity of the locus to undergo effective gene rearrangement in the subject animal.

[61] Preferably, a non-human Ig locus is isolated by screening a library of plasmids, cosmids, YACs or BACs, and the like, prepared from the genomic DNA of the same. YAC clones can carry DNA fragments of up to 2 megabases, thus an entire animal heavy chain locus or a large portion thereof can be isolated in one YAC clone, or reconstructed to be contained in one YAC clone. BAC clones are capable of carrying DNA fragments of smaller sizes (about 50-500 kb). However, multiple BAC clones containing overlapping fragments of an Ig locus can be separately altered and subsequently injected together into an animal recipient cell, wherein the overlapping fragments recombine in the recipient animal cell to generate a continuous Ig locus.

[62] Human Ig gene segments can be integrated into the Ig locus on a vector (e.g., a BAC clone) by a variety of methods, including ligation of DNA fragments, or insertion of DNA fragments by homologous recombination. Integration of the human Ig gene segments is done in such a way that the human Ig gene segment is operably linked to the host animal sequence in the transgene to produce a functional humanized Ig locus, i.e., an Ig locus capable of gene rearrangement which lead to the production of a diversified repertoire of antibodies with human idiotypes. Homologous recombination can be performed in bacteria, yeast and other cells with a high frequency of homologous recombination events. Engineered

YACs and BACs can be readily isolated from the cells and used in making transgenic animals

Transgenic animals comprising artificial Ig loci and capable of producing antibodies having human idiotypes

[63] In one aspect, the invention provides transgenic animals capable of producing immunoglobulins having human idiotypes, as well as methods of making the same. The transgenic animals used are selected from rodents (e.g., rats, hamsters, mice and guinea pigs).

[64] The transgenic animals used for humanized antibody production in the invention carry germline mutations in endogenous Ig loci. In a preferred embodiment, the transgenic animals are homozygous for mutated endogenous Ig heavy chain and/or endogenous Ig light chain genes. Further, these animals carry at least two artificial heavy chain loc Ig loci that are functional and capable of producing a repertoire of immunoglobulin molecules in the transgenic animal. The artificial Ig loci used in the invention include at least one human V gene segment.

[65] In a preferred embodiment, the transgenic animals carry at least two artificial Ig heavy chain locus and at least one artificial Ig light chain locus that are each functional and capable of producing a repertoire of immunoglobulin molecules in the transgenic animal, which repertoire of immunoglobulin molecules includes antibodies having a human idiotype. In one embodiment, artificial loci including at least one non-human C gene are used, and animals capable of producing chimeric antibodies having a human idiotype and non-human constant region are provided. In one embodiment, artificial loci including at least one human C gene are used, and animals capable of producing antibodies having a human idiotype and human constant region are provided.

[66] In another preferred embodiment, the transgenic animals carry at least two artificial Ig heavy chain loci, and lack a functional Ig light chain locus. Such animals find use in the production of heavy chain–only antibodies.

[67] Production of such transgenic animals involves the integration of at least two artificial heavy chain Ig loci and one or more artificial light chain Ig loci into the genome of a

transgenic animal having at least one endogenous Ig locus that has been or will be inactivated by the action of one or more meganucleases. Preferably, the transgenic animals are nullizygous for endogenous Ig heavy chain and/or endogenous Ig light chain and, accordingly, incapable of producing endogenous immunoglobulins. Regardless of the chromosomal location, an artificial Ig locus of the present invention has the capacity to undergo gene rearrangement and thereby produce a diversified repertoire of immunoglobulin molecules. An Ig locus having the capacity to undergo gene rearrangement is also referred to herein as a "functional" Ig locus, and the antibodies with a diversity generated by a functional Ig locus are also referred to herein as "functional" antibodies or a "functional" repertoire of antibodies.

[68] The artificial loci used to generate such transgenic animals each include multiple immunoglobulin gene segments, which include at least one V region gene segment, one or more J gene segments, one or more D gene segments in the case of a heavy chain locus, and one or more constant region genes. In the present invention, at least one of the V gene segments encodes a germline or hypermutated human V-region amino acid sequence. Accordingly, such transgenic animals have the capacity to produce a diversified repertoire of immunoglobulin molecules, which include antibodies having a human idiotype.

[69] In one embodiment, the artificial loci used comprise at least one non-human C region gene segment. Accordingly, such transgenic animals have the capacity to produce a diversified repertoire of immunoglobulin molecules, which include chimeric antibodies having a human idiotype.

[70] In one embodiment, the artificial loci used comprise at least one human C region gene segment. Accordingly, such transgenic animals have the capacity to produce a diversified repertoire of immunoglobulin molecules, which include antibodies having a human idiotype and a human constant region.

[71] In one embodiment, the artificial loci used comprise at least one artificial constant region gene. For example, an exemplary artificial C constant region gene is a constant region gene encoding a human IgG CH1 domain and rat IgG CH2 and CH3 domain. Accordingly, such transgenic animals have the capacity to produce a diversified repertoire of

immunoglobulin molecules, which include antibodies having a human idiotype and an artificial constant region comprising both human and non-human components.

[72] The transgenic vector containing an artificial Ig locus is introduced into the recipient cell or cells and then integrated into the genome of the recipient cell or cells by random integration or by targeted integration.

[73] For random integration, a transgenic vector containing an artificial Ig locus can be introduced into a recipient cell by standard transgenic technology. For example, a transgenic vector can be directly injected into the pronucleus of a fertilized oocyte. A transgenic vector can also be introduced by co-incubation of sperm with the transgenic vector before fertilization of the oocyte. Transgenic animals can be developed from fertilized oocytes. Another way to introduce a transgenic vector is by transfecting embryonic stem cells or other pluripotent cells (for example primordial germ cells) and subsequently injecting the genetically modified cells into developing embryos. Alternatively, a transgenic vector (naked or in combination with facilitating reagents) can be directly injected into a developing embryo. Ultimately, chimeric transgenic animals are produced from the embryos which contain the artificial Ig transgene integrated in the genome of at least some somatic cells of the transgenic animal. In another embodiment, the transgenic vector is introduced into the genome of a cell and an animal is derived from the transfected cell by nuclear transfer cloning.

[74] In a preferred embodiment, a transgene containing an artificial Ig locus is randomly integrated into the genome of recipient cells (such as fertilized oocyte or developing embryos). In a preferred embodiment, offspring that are nullizygous for endogenous Ig heavy chain and/or Ig light chain and, accordingly, incapable of producing endogenous immunoglobulins and capable of producing transgenic immunoglobulins are obtained.

[75] For targeted integration, a transgenic vector can be introduced into appropriate recipient cells such as embryonic stem cells, other pluripotent cells or already differentiated somatic cells. Afterwards, cells in which the transgene has integrated into the animal genome can be selected by standard methods. The selected cells may then be fused with enucleated nuclear transfer unit cells, e.g. oocytes or embryonic stem cells, cells which are totipotent and

capable of forming a functional neonate. Fusion is performed in accordance with conventional techniques which are well established. See, for example, Cibelli et al., *Science* (1998) **280**:1256; Zhou et al. *Science* (2003) **301**: 1179. Enucleation of oocytes and nuclear transfer can also be performed by microsurgery using injection pipettes. (See, for example, Wakayama et al., *Nature* (1998) **394**:369.) The resulting cells are then cultivated in an appropriate medium, and transferred into synchronized recipients for generating transgenic animals. Alternatively, the selected genetically modified cells can be injected into developing embryos which are subsequently developed into chimeric animals.

[76] In one embodiment, a meganuclease is used to increase the frequency of homologous recombination at a target site through double-strand DNA cleavage. For integration into a specific site, a site specific meganuclease may be used. In one embodiment, a meganuclease targeting an endogenous Ig locus is used to increase the frequency of homologous recombination and replacement of an endogenous Ig locus, or parts thereof with an artificial Ig locus, or parts thereof. In one embodiment, the transgenic animal lacks a functional Ig light chain locus and comprises an artificial Ig heavy chain locus.

[77] The preferred embodiments for integration of the human Ig gene segments using YACs and BACs, and interchanging between the two, has the advantage of both, speed and the ability to check integrity when making constructs of large regions by overlapping homology. The tandem integration of the constructs with overlapping regions have the ability to integrate, such as to maintain the full functionality, which is essential for DNA rearrangement. The preferred embodiments of the invention not only have the desired integration by homology but also produce tandem integration as a frequent event. This eases the transgenic technology substantially as no laborious integration of large YACs into stem cells and subsequent animal derivation therefrom has to be performed. In addition, ZFN technology, also performed via DNA injection (Geurts et al. *Science* **325**, 433 (2009); Menoret et al. *European journal of immunology* **40**, 2932-2941 (2010)), produced Ig KO strains easily and may well be the future technology of choice for gene disruptions and replacement. Silenced endogenous Ig gene expression in OmniRats™, containing human-rat IgH and human IgL loci, has the advantage that no interfering or undesired rat Ig could give rise to mixed products.

[78] In the mouse an enhancer region downstream of Cα plays a vital role in class-switch recombination (Vincent-Fabert et al. *Blood* **116**, 1895-1898 (2010)) and it is likely that elements in that region may facilitate hypermutation (Pruzina et al. *Protein engineering, design & selection : PEDS* **24**, 791-799 (2011)). This may be the reason why immune responses and generation of diverse hybridomas at high frequency may be difficult in mice carrying even a large fully human locus (Davis et al. *Cancer metastasis reviews* **18**, 421-425 (1999); Lonberg *Current opinion in immunology* **20**, 450-459 (2008)). As the chimeric human-rat IgH locus facilitates near wt differentiation and expression levels in OmniRats, it can be concluded that the endogenous rat C region and indeed the ~30 kb enhancer sequence 3' of Cα are providing optimal locus control to express and mature human V_H genes. Another region, Cδ with its 3' control motif cluster (Mundt et al. *J Immunol* **166**, 3315-3323 (2001)), has been removed from the chimeric C-region BAC since silencing or a lack of IgD did not appear to reduce immune function (Chen *Immunol Rev* **237**, 160-179 (2010)). Normally, mature IgM^+IgD^+ B-cells down-regulate IgD upon antigen contact, which initiates class-switch recombination (Id). Thus, switching may be increased without IgD control, which is supported by our finding that IgG transcripts and serum levels are significantly lower when the Cδ region is retained in transgenic constructs (data not shown).

[79] The production of specific IgG in OmniRats™ is particularly encouraging as we found that in various immunizations mAbs with diversity in sequence and epitope, comparable to what was produced in wt controls, could be isolated via spleen and lymph node fusion. V-gene, D and J diversity was as expected and nearly all segments were found to be used productively as predicted (Lefranc & Lefranc The immunoglobulin factsbook. *FactsBook Series, Academic Press, GB*, 45-68 (2001)). This was in stark contrast to mice carrying fully human transloci where clonal expansion from a few precursor B-cells produced little diversity (Pruzina et al. *Protein engineering, design & selection : PEDS* **24**, 791-799 (2011)). Since the number of transplanted V-genes is only about half of what is used in humans we anticipated to find restricted immune responses and limited diversity when comparing OmniRats with wt animals. However, this was not the case and a comparison of CDR3 diversity in over 1000 clones (sequences can be provided) revealed the same extensive junctional differences in OmniRats as in wt animals. The few identical gene-segment combinations were further diversified by N-sequence additions or deletion at the V_H to D and/or D to J_H junctions and also by hypermutation. Thus, it is clear that the rat C region

sequence is highly efficient in controlling DNA rearrangement and expression of human V_HDJ_H. Extensive diversity was also seen for the introduced human Igκ and Igλ loci, similar to what has previously been shown in mice (Nicholson et al. *J Immunol* **163**, 6898-6906 (1999); Pruzina et al. *Protein engineering, design & selection : PEDS* **24**, 791-799 (2011); Popov et al. *The Journal of experimental medicine* **189**, 1611-1620 (1999)). Hence, substantially reduced efficiency in the production of human antibodies from mice (Lonberg, N. *Nature biotechnology* **23**, 1117-1125 (2005)) has been overcome in OmniRats™, which diversify rearranged H-chains reliably and extensively by class-switch and hypermutation to yield high affinity antibodies in bulk rather than occasionally. The yield of transgenic IgG and the level of hypermutation, impressively utilized in antigen-specific mAbs, showed that clonal diversification and production level are similar between OmniRats™ and wt animals. Routine generation of high affinity specificities in the subnanomolar range was even accomplished by different single immunizations and again compares favorably with wt animals; results that have not been shown in transgenic mice producing human antibody repertoires from entirely human loci (Mendez et al. *Nature genetics* **15**, 146-156 (1997)).

[80] In summary, to maximize human antibody production an IgH locus that uses human genes for antibody specificity but rodent genes for control of differentiation and high expression should be regarded essential. L-chain flexibility is a bonus as it permits highly efficient human IgH/IgL assembly even when wt Ig is present. For therapeutic applications chimeric H-chains can be easily converted into fully human Abs by C-gene replacement without compromising the specificity.

Immunoglobulins having a human idiotype

[81] Once a transgenic animal capable of producing immunoglobulins having a human idiotype is made, immunoglobulins and antibody preparations against an antigen can be readily obtained by immunizing the animal with the antigen. "Polyclonal antisera composition" as used herein includes affinity purified polyclonal antibody preparations.

[82] A variety of antigens can be used to immunize a transgenic animal. Such antigens include but are not limited to, microorganisms, e.g. viruses and unicellular organisms (such as bacteria and fungi), alive, attenuated or dead, fragments of the microorganisms, or antigenic molecules isolated from the microorganisms.

[83] Preferred bacterial antigens for use in immunizing an animal include purified antigens from Staphylococcus aureus such as capsular polysaccharides type 5 and 8, recombinant versions of virulence factors such as alpha-toxin, adhesin binding proteins, collagen binding proteins, and fibronectin binding proteins. Preferred bacterial antigens also include an attenuated version of *S. aureus, Pseudomonas aeruginosa, enterococcus, enterobacter,* and *Klebsiella pneumoniae*, or culture supernatant from these bacteria cells. Other bacterial antigens which can be used in immunization include purified lipopolysaccharide (LPS), capsular antigens, capsular polysaccharides and/or recombinant versions of the outer membrane proteins, fibronectin binding proteins, endotoxin, and exotoxin from *Pseudomonas aeruginosa, enterococcus, enterobacter,* and *Klebsiella pneumoniae*.

[84] Preferred antigens for the generation of antibodies against fungi include attenuated version of fungi or outer membrane proteins thereof, which fungi include, but are not limited to, *Candida albicans, Candida parapsilosis, Candida tropicalis,* and *Cryptococcus neoformans*.

[85] Preferred antigens for use in immunization in order to generate antibodies against viruses include the envelop proteins and attenuated versions of viruses which include, but are not limited to respiratory synctial virus (RSV) (particularly the F-Protein), Hepatitis C virus (HCV), Hepatits B virus (HBV), cytomegalovirus (CMV), EBV, and HSV.

[86] Antibodies specific for cancer can be generated by immunizing transgenic animals with isolated tumor cells or tumor cell lines as well as tumor-associated antigens which include, but are not limited to, Her-2-neu antigen (antibodies against which are useful for the treatment of breast cancer); CD20, CD22 and CD53 antigens (antibodies against which are useful for the treatment of B cell lymphomas), prostate specific membrane antigen (PMSA) (antibodies against which are useful for the treatment of prostate cancer), and 17-1A molecule (antibodies against which are useful for the treatment of colon cancer).

[87] The antigens can be administered to a transgenic animal in any convenient manner, with or without an adjuvant, and can be administered in accordance with a predetermined schedule.

[88] For making a monoclonal antibody, spleen cells are isolated from the immunized transgenic animal and used either in cell fusion with transformed cell lines for the production of hybridomas, or cDNAs encoding antibodies are cloned by standard molecular biology techniques and expressed in transfected cells. The procedures for making monoclonal antibodies are well established in the art. See, e.g., European Patent Application 0 583 980 A1 ("Method For Generating Monoclonal Antibodies From Rabbits"), U.S. Patent No. 4,977,081 ("Stable Rabbit-Mouse Hybridomas And Secretion Products Thereof"), WO 97/16537 ("Stable Chicken B-cell Line And Method of Use Thereof"), and EP 0 491 057 B1 ("Hybridoma Which Produces Avian Specific Immunoglobulin G"), the disclosures of which are incorporated herein by reference. In vitro production of monoclonal antibodies from cloned cDNA molecules has been described by Andris-Widhopf et al. *J Immunol Methods* **242**:159 (2000), and by Burton *Immunotechnology* **1**:87 (1995).

[89] Once chimeric monoclonal antibodies with human idiotypes have been generated, such chimeric antibodies can be easily converted into fully human antibodies using standard molecular biology techniques. Fully human monoclonal antibodies are not immunogenic in humans and are appropriate for use in the therapeutic treatment of human subjects.

Antibodies of the invention include heavy chain-only antibodies

[90] In one embodiment, transgenic animals which lack a functional Ig light chain locus, and comprising at least two artificial heavy chain loci, are immunized with antigen to produce heavy chain-only antibodies that specifically bind to antigen.

[91] In one embodiment, the invention provides monoclonal antibody producing cells derived from such animals, as well as nucleic acids derived therefrom. Also provided are hybridomas derived therefrom. Also provided are fully human heavy chain-only antibodies, as well as encoding nucleic acids, derived therefrom.

[92] Teachings on heavy chain-only antibodies are found in the art. For example, see PCT publications WO02085944, WO02085945, WO2006008548, and WO2007096779.

See also US 5,840,526; US 5,874,541; US 6,005,079; US 6,765,087; US 5,800,988; EP 1589107; WO 9734103; and US 6,015,695.

Pharmaceutical Compositions

[93] In a further embodiment of the present invention, purified monoclonal or polyclonal antibodies are admixed with an appropriate pharmaceutical carrier suitable for administration to patients, to provide pharmaceutical compositions.

[94] Patients treated with the pharmaceutical compositions of the invention are preferably mammals, more preferably humans, though veterinary uses are also contemplated.

[95] Pharmaceutically acceptable carriers which can be employed in the present pharmaceutical compositions can be any and all solvents, dispersion media, isotonic agents and the like. Except insofar as any conventional media, agent, diluent or carrier is detrimental to the recipient or to the therapeutic effectiveness of the antibodies contained therein, its use in the pharmaceutical compositions of the present invention is appropriate.

[96] The carrier can be liquid, semi-solid, e.g. pastes, or solid carriers. Examples of carriers include oils, water, saline solutions, alcohol, sugar, gel, lipids, liposomes, resins, porous matrices, binders, fillers, coatings, preservatives and the like, or combinations thereof.

Methods of Treatment

[97] In a further aspect of the present invention, methods are provided for treating a disease in a vertebrate, preferably a mammal, preferably a primate, with human subjects being an especially preferred embodiment, by administering a purified antibody composition of the invention desirable for treating such disease.

[98] The antibody compositions can be used to bind and neutralize or modulate an antigenic entity in human body tissues that causes or contributes to disease or that elicits undesired or abnormal immune responses. An "antigenic entity" is herein defined to encompass any soluble or cell surface bound molecules including proteins, as well as cells or

infectious disease-causing organisms or agents that are at least capable of binding to an antibody and preferably are also capable of stimulating an immune response.

[99] Administration of an antibody composition against an infectious agent as a monotherapy or in combination with chemotherapy results in elimination of infectious particles. A single administration of antibodies decreases the number of infectious particles generally 10 to 100 fold, more commonly more than 1000-fold. Similarly, antibody therapy in patients with a malignant disease employed as a monotherapy or in combination with chemotherapy reduces the number of malignant cells generally 10 to 100 fold, or more than 1000-fold. Therapy may be repeated over an extended amount of time to assure the complete elimination of infectious particles, malignant cells, etc. In some instances, therapy with antibody preparations will be continued for extended periods of time in the absence of detectable amounts of infectious particles or undesirable cells.

[100] Similarly, the use of antibody therapy for the modulation of immune responses may consist of single or multiple administrations of therapeutic antibodies. Therapy may be continued for extended periods of time in the absence of any disease symptoms.

[101] The subject treatment may be employed in conjunction with chemotherapy at dosages sufficient to inhibit infectious disease or malignancies. In autoimmune disease patients or transplant recipients, antibody therapy may be employed in conjunction with immunosuppressive therapy at dosages sufficient to inhibit immune reactions.

EXAMPLES

[102] In mice transgenic for human immunoglobulin (Ig) loci, suboptimal efficacy in delivery of fully human antibodies has been attributed to imperfect interaction between the constant regions of human membrane IgH chains and the mouse cellular signaling machinery. To obviate this problem, we here describe a humanized rat strain (OmniRat™) carrying chimeric human/rat IgH loci [comprising 22 human V_Hs, all human D and J_H segments with germline gene spacing but linked to the rat C_H locus] together with fully human light-chain loci [12 Vκs linked to Jκ-Cκ and 16 Vλs linked to Jλ-Cλ]. The endogenous rat Ig loci were silenced by designer zinc finger nucleases. Following immunization, OmniRats perform as efficiently as normal rats in yielding high affinity serum IgG. Monoclonal antibodies,

comprising fully human variable regions with sub-nanomolar antigen affinity and carrying extensive somatic mutations, are readily obtainable – similarly to the yield of conventional antibodies from normal rats.

MATERIALS AND METHODS

Construction of modified human Ig loci on YACs and BACs

a) IgH loci

[103] The human IgH V genes were covered by 2 BACs: BAC6-VH3-11 containing the authentic region spanning from VH4-39 to VH3-23 followed by VH3-11 (modified from a commercially available BAC clone 3054M17 CITB) and BAC3 containing the authentic region spanning from VH3-11 to VH6-1 (811L16 RPCI-11). A BAC termed Annabel was constructed by joining rat CH region genes immediately downstream of the human VH6-1-Ds-JHs region (Figure 1). All BAC clones containing part of the human or rat IgH locus were purchased from Invitrogen.

[104] Both BAC6-VH3-11 and Annabel were initially constructed in S. cerevisiae as circular YACs (cYACs) and further checked and maintained in E. coli as BACs. .

[105] Unlike YACs, BAC plasmid preps yield large quantities of the desired DNA. To convert a linear YAC into a cYAC or to assemble DNA fragments with overlapping ends into a single cYAC in *S. cerevisiae*, which can also be maintained as a BAC in E. coli, two self-replicating S. cerevisiae/E. coli shuttle vectors, pBelo-CEN-URA, and pBelo-CEN-HYG were constructed. Briefly, S. cerevisiae CEN4 was cut out as an AvrII fragment from pYAC-RC (Marchuk & Collins *Nucleic acids research* **16**, 7743 (1988)) and ligated to *SpeI* – linearised pAP599 (Kaur & Cormack *PNAS* **104**, 7628-7633 (2007)). The resulting plasmid contains CEN4 cloned in between S. cerevisiae URA3 and a hygromycin-resistance expression cassette (HygR). From this plasmid, an ApaLI–BamHI fragment containing URA3 followed by CEN4 or a PmlI–SphI fragment containing CEN4 followed by HygR was cut out, and ligated to ApaLI and BamHI or HpaI and SphI doubly digested pBACBelo11 (New England Biolabs) to yield pBelo-CEN-URA and pBelo-CEN-HYG.

[106] To construct BAC6-VH3-11, initially two fragments, a 115 kb NotI-PmeI and a 110 kb RsrII-SgrAI, were cut out from the BAC clone 3054M17 CITB. The 3' end of the former fragment overlaps 22 kb with the 5' end of the latter. The NotI-PmeI fragment was

ligated to a NotI-BamHI YAC arm containing S. cerevisiae CEN4 as well as TRP1/ARS1 from pYAC-RC, and the RsrII-SgrAI fragment was ligated to a SgrAI-BamHI YAC arm containing S. cerevisiae URA3, also from pYAC-RC. Subsequently, the ligation mixture was transformed into *S. cerevisiae* AB1380 cells via spheroplast transformation[41], and URA+TRP+ yeast clones were selected. Clones, termed YAC6, containing the linear region from human VH4-39 to VH3-23 were confirmed by Southern blot analysis. YAC6 was further extended by addition of a 10.6 kb fragment 3' of VH3-23, and conversion to a cYAC. The 10.6 kb extension contains the human VH3-11 and also occurs at the 5' end of BAC3. We constructed pBeloHYG-YAC6+BAC3(5') for the modification of YAC6. Briefly, 3 fragments with overlapping ends were prepared by PCR: 1) a 'stuff' fragment containing S. cerevisiae TRP1-ARS1 flanked by HpaI sites with 5' tail matching the sequence upstream of VH4-39 and 3' tail matching downstream of VH3-23 in YAC6 (using long oligoes 561 and 562, and pYAC-RC as template), 2) the 10.6 kb extension fragment with a 5' tail matching the sequence downstream of VH3-23 as described above and a unique AscI site at its 3' end (using long oligoes 570 and 412, and human genomic DNA as template), and 3) pBelo-CEN-HYG vector with the CEN4 joined downstream with a homology tail matching the 3' end of the 10.6 extension fragment and the HygR joined upstream with a tail matching the sequence upstream of VH4-39 as described above (using long oligoes 414 and 566, and pBelo-CEN-HYG as template). Subsequently, the 3 PCR fragments were assembled into a small cYAC conferring HYGR and TRP+ in S. cerevisiae via homologous recombination associated with spheroplast transformation, and this cYAC was further converted into the BAC pBeloHYG-YAC6+BAC3(5'). Finally, the HpaI-digested pBeloHYG-YAC6+BAC3(5') was used to transform yeast cells carrying YAC6, and through homologous recombination cYAC BAC6-VH3-11 conferring only HYGR was generated. Via transformation, see below, this cYAC was introduced as a BAC in E. coli. The human VH genes in BAC6-VH3-11 were cut out as a ~ 182 kb AsiSI (occurring naturally in the HygR) – AscI fragment, and the VH genes in BAC3 were cut out as a ~173 kb NotI- fragment (Figure 1 top).

[107] A self-replicating shuttle vector, termed pCAU, efficiently working in both *Saccharomyces cerevisiae* and *E. coli*, was constructed based on pBelo-CEN-URA published previously. (Osborn et al. *J Immunol* 2013; **190**:1481-1490) In brief, *ARSH4* was amplified from *S. cerevisiae* genomic DNA using primers 878 and 879 (all primer sequences are listed below), with an *ApaL*I site followed by *AsiS*I and a *SexA*I introduced into either end. The fragment was digested with *ApaL*I and *SexA*I, and ligated with pBelo-CEN-URA digested

with the same restriction enzymes to yield pCAU. This vector contains *S. cerevisiae CEN4*, *URA3* and *ARSH4* in the pBeloBAC11 backbone (New England BioLabs).

[108] Three BACs derived from human chromosome 14 - CTD-2011A5 (BAC9), CTD-3148C6 (BAC14), CTD-2548B8 (BAC5) were purchased from Invitrogen/Thermo Fisher. The human genomic region encompassing IgHV3-74 to IgHV1-58 in BAC9 was isolated as a 185 kb *Not*I – fragment. BAC(14+5) was constructed from BAC14 and BAC5. The combined genomic regions in this BAC was isolated as a 210 kb *Bsi*wI - fragment including from 5' to 3': a 90.6 kb region derived from BAC14 containing 4.6 kb sequence overlapping with the 3' of the *Not*I –fragment from BAC9 followed by a 86 kb region encompassing IgHV5-51 to IgHV1-45, a 1.7 kb synthetic region joining BAC14 and BAC5 with IgHV3-43 located in the centre, a 111.7 kb region derived from BAC5 encompassing IgHV3-21 to IgHV3-13, and a 6.1 kb region providing an overlap with the 5' of Anabel (the BAC carrying human Ig constant regions).

[109] BAC(14+5, also referenced as 14/5) was constructed in three steps all involving generating a circular YAC (cYAC) via homologous recombination in yeast and converting the cYAC to BAC as described previously. Firstly, a BAC vector - pCAU+GAP-BAC14,5, was generated by assembling the following 3 overlapping fragments in yeast: a 1.9 kb synthetic DNA (ordered from ThermoFisher) containing from 5' to 3': 116 bp sequence overlapping with the 5' as well as 3' end of the desired region in BAC14 with an unique *Rsr*II site in the centre, 1.6 kb IgHV3-43 gene [including 1.0 kb 5' untranslated region (UTR) and 0.2 kb 3' UTR], 106 bp sequence overlapping with the 5' as well as 3' end of the desired region in BAC5 with an unique *Pme*I site in the centre, and 38 bp sequence overlapping with the 5' end of Anabel, a 6.1 kb PCR fragment corresponding to the 5' of Anabel using primers 383 and 384, and an amplified pCAU vector using primers 1066 and 1088. Secondly, the pCAU+GAP-BAC14,5 vector was linearized with *Pme*I, and co-transformed with a 154 kb *Not*I – fragment isolated from BAC5 into yeast strain AB1380. The resulting BAC (~ 128 kb in length) had the desired region of BAC5 incorporated into the BAC vector via homologous recombination mediated by the homology ends to BAC5 exposed in the *Pme*I – linearized vector. Thirdly, the BAC carrying BAC5 from the second step was linearized with *Rsr*II to expose the homology ends to the desired region in BAC14, and co-transformed with a 114 kb *Sna*BI – fragment isolated from BAC14 to yield BAC(14+5).

[110] For the assembly of the C region with the VH overlap, the human VH6-1-Ds-JHs region had to be joined with the rat genomic sequence immediately downstream of the last JH followed by rat Cs to yield a cYAC/BAC. To achieve this, 5 overlapping restriction as well as PCR fragments were prepared; a 6.1 kb fragment 5' of human VH6-1 (using oligos 383 and 384, and human genomic DNA as template), an ~78 kb PvuI-PacI fragment containing the human VH6-1-Ds-JHs region cut out from BAC1 (RP11645E6), a 8.7 kb fragment joining the human JH6 with the rat genomic sequence immediately downstream of the last JH and containing part of rat μ coding sequence (using oligos 488 and 346, and rat genomic DNA as template), an ~ 52 kb NotI-PmeI fragment containing the authentic rat μ, δ and γ2c region cut out from BAC M5 (CH230-408M5) and the pBelo-CEN-URA vector with the URA3 joined downstream with a homology tail matching the 3' end of the rat γ2c region and the CEN4 joined upstream with a tail matching the 5' region of human VH6-1 as described (using long oligoes 385 and 550, and pBelo-CEN-URA as template). Correct assembly via homologous recombination in S. cerevisiae was analyzed by PCR and purified cYAC from the correct clones was converted into a BAC in E. coli.

[111] For the assembly of Annabel parts of the above cYAC/BAC containing humanVH6-1-Ds-JHs followed by the authentic rat μ, δ and γ2c region, as well as PCR fragments were used. Five overlapping fragments contained the 6.1 kb fragment at the 5' end of human VH6-1 as described above, an ~83 kb SpeI fragment comprising human VH6-1-Ds-JHs immediately followed by the rat genomic sequence downstream of the last JH and containing part of rat Cμ, a 5.2 kb fragment joining the 3' end of rat μ with the 5' end of rat γ1 (using oligos 490 and 534, and rat genomic DNA as template), an ~118 kb NotI-SgrAI fragment containing the authentic rat γ1, γ2b, ε, α and 3'E IgH enhancer region cut out from BAC I8 (CH230-162I08), and the pBelo-CEN-URA vector with the URA3 joined downstream with a homology tail matching the 3' end of rat 3'E and the CEN4 joined upstream with a tail matching the 5' end of human VH6-1 as described above. There is a 10.3 kb overlap between the human VH6-1 regions in both the BAC3 and Annabel. The human VH6-1 -Ds - JHs followed by the rat CH region together with the S. cerevisiae URA3 in Annabel can be cut out as a single ~183 kb NotI-fragment (see Figure 1).

[112] BAC6-VH3-11, BAC3, BAC9 and BAC (14+5) and Annabel were checked extensively by restriction analysis and partial sequencing for their authenticity.

b) IgL loci

[113] The human Igλ locus on a ~410 kb YAC was obtained by recombination assembly of a Vλ YAC with 3 Cλ containing cosmids (Popov et al. *Gene* **177**, 195-201 (1996)). Rearrangement and expression was verified in transgenic mice derived from ES cells containing one copy of a complete human Igλ YAC (Popov et al. *The Journal of experimental medicine* **189**, 1611-1620 (1999)). This Igλ YAC was shortened by the generation of a circular YAC removing ~100kb of the region 5' of Vλ3-27. The vector pYAC-RC was digested with ClaI and BspEI to remove URA3 and ligated with a ClaI/NgoMIV fragment from pAP 599 containing HYG. PCR of the region containing the yeast centromere and hygromycin marker gene from the new vector (pYAC-RC-HYG) was carried out with primers with 5' ends homologous to a region 5' of Vλ3-27 (primer 276) and within the ADE2 marker gene in the YAC arm (primer 275). The PCR fragment (3.8 kb) was integrated into the Igλ YAC using a high efficiency lithium acetate transformation method (Gietz & Woods *Methods in Microbiology* **26**, 53-66 (1998)) and selection on hygromycin containing YPD plates. DNA was prepared from the clones (Epicentre MasterPure Yeast DNA purification kit) and analysed for the correct junctions by PCR using the following oligos: 243 + 278 and Hyg end R + 238. Plugs were made (Peterson *Nature protocols* **2**, 3009-3015 (2007)) and yeast chromosomes removed by PFGE (0.8% agarose (PFC) (Biorad) gel [6V/cm, pulse times of 60s for 10hr and 10s for 10hr, 8°C) leaving the circular yeast artificial chromosome caught in the agarose block (Beverly, *Nucleic acids research* **16**, 925-939 (1988)). The blocks were removed and digested with NruI. Briefly, blocks were preincubated with restriction enzyme buffer in excess at a 1X final concentration for 1 hr on ice. Excess buffer was removed leaving just enough to cover the plugs, restriction enzyme was added to a final concentration of 100U/ml and the tube incubated at 37°C for 4-5hrs. The linearized YAC was ran out of the blocks by PFGE, cut out from the gel as a strip and purified as described below.

[114] For the human Igκ locus 3 BACs were chosen (RP11-344F17, RP11-1134E24 and RP11-156D9, Invitrogen), which covered a region over 300 kb from 5' Vκ1-17 to 3' KDE (Kawasaki et al. *European journal of immunology* **31**, 1017-1028 (2001)). In digests and sequence analyses three overlapping fragments were identified: from Vκ1-17 to Vκ3-7 (150 kb NotI with ~14 kb overlap), from Vκ3-7 to 3' of Cκ (158 kb NotI with ~40 kb overlap) and from Cκ to 3' of the KDE (55 kb PacI with 40 kb overlap). Overlapping regions

may generally favour joint integration when co-injected into oocytes (Wagner et al. *Genomics* **35**, 405-414 (1996)).

Gel analyses and DNA purification

[115] Purified YAC and BAC DNA was analysed by restriction digest and separation on conventional 0.7% agarose gels (Sambrook & Russell Molecular Cloning. A laboratory Manual. . *Cold Spring Harbor Laboratory Press, NY* (2001)). Larger fragments, 50-200 kb, were separated by PFGE (Biorad Chef MapperTM) at 80C, using 0.8% PFC Agaraose in 0.5% TBE, at 2-20 sec switch time for 16 h, 6V/cm, 10mA. Purification allowed a direct comparison of the resulting fragments with the predicted size obtained from the sequence analysis. Alterations were analysed by PCR and sequencing.

[116] Linear YACs, circular YACs and BAC fragments after digests, were purified by electro-elution using ElutrapTM (Schleicher and Schuell) (Gu et al. *Journal of biochemical and biophysical methods* **24**, 45-50 (1992)) from strips cut from 0.8% agarose gels run conventionally or from pulsed-field-gel electrophoresis (PFGE). The DNA concentration was usually several ng/µl in a volume of ~100µl. For fragments up to ~200 kb the DNA was precipitated and re-dissolved in micro-injection buffer (10 mM Tris-HCl pH 7.5, 100 mM EDTA pH 8 and 100 mM NaCl but without Spermine/Spermidine) to the desired concentration.

[117] The purification of circular YACs from yeast was carried out using Nucleobond AX silica-based anion-exchange resin (Macherey-Nagel, Germany). Briefly, spheroplasts were made using zymolyase or lyticase and pelleted (Davies et al. Human antibody repertoires in transgenic mice: Manipulation and transfer of YACs. . *IRL Oxford*, 59-76 (1996)). The cells then underwent alkaline lysis, binding to AX100 column and elution as described in the Nucleobond method for a low-copy plasmid. Contaminating yeast chromosomal DNA was hydolyzed using Plamid –Safe™ ATP-Dependent DNase (Epicentre Biotechnologies) followed by a final cleanup step using SureClean (Bioline). An aliquot of DH10 electrocompetent cells (Invitrogen) was then transformed with the circular YAC to obtain BAC colonies. For microinjection, the insert DNA (150-200 kb), was separated from BAC vector DNA(~10 kb) using a filtration step with sepharose 4B-CL (Yang et al. *Nature biotechnology* **15**, 859-865 (1997)).

Derivation of rats and breeding

[118] Purified DNA encoding recombinant immunoglobulin loci was resuspended in microinjection buffer with 10 mM Spermine and 10 mM Spermidine. The DNA was injected into fertilized oocytes at various concentrations from 0.5 to 3 ng/μl.

[119] Plasmid DNA or mRNA encoding ZFNs specific for rat immunoglobulin genes were injected into fertilized oocytes at various concentrations from 0.5 to 10 ng/ul.

[120] Microinjections were performed at Caliper Life Sciences facility. Outbred SD/Hsd (WT) strain animals were housed in standard microisolator cages under approved animal care protocols in animal facility that is accredited by the Association for the Assessment and Accreditation for Laboratory Animal Care (AAALAC). The rats were maintained on a 14-10 h light/dark cycle with ad libitum access to food and water. Four to five week old SD/Hsd female rats were injected with 20-25 IU PMSG (Sigma-Aldrich) followed 48 hours later with 20-25 IU hCG (Sigma-Aldrich) before breeding to outbred SD/Hsd males. Fertilized 1-cell stage embryos were collected for subsequent microinjection. Manipulated embryos were transferred to pseudopregnant SD/Hsd female rats to be carried to parturition.

[121] Multi-feature human Ig rats (human IgH, Igκ and Igλ in combination with rat J KO, κ KO and λ KO) and WT, as control, were analyzed at 10–18 weeks of age. The animals were bred at Charles River under specific pathogen-free conditions.

[122] The procedure of introducing multiple different V_H region on separate loci can be implemented through the insertion of these different loci into separate transgenic rats (preferably with a defective rat IgH locus) as described in the example above. These separate loci are used to generate separate transgenic rat lines, which are subsequently crossed to obtain double transgenic rats that would have all of the VHregions used available for the recombination process. Crossing these rats to homozygosity for both loci would double the number of VH regions available for recombination (see FIG. 3 karyogram with one locus integrated on chromosome 6 and

one locus on chromosome 15). Having multiple copies of an integrated locus would increase this number yet further.

[123] The procedure of introducing distinct loci separately, by the transfer of multiple different V_H regions in conjunction with one constant region array, allowed unconnected and multiple translocus integration. This was followed by breeding to generate an animal that expresses antibodies from both separately integrated loci.

[124] The same procedure is also applied for the light chains, where one line of animals is made with a kappa locus and another line is made with a lambda locus. The loci are combined in animals by crossbreeding.

PCR and RT-PCR

[125] Transgenic rats were identified by PCR from tail or ear clip DNA using a Genomic DNA Mini Kid (Bioline). For IgH PCRs < 1kb GoTaq Green Master mix was used (Promega) under the following conditions: 94°C 2 mins, 32 x (94°C 30 secs, 54-67°C (see **Table 1** for primers and specific annealing temperatures) 30 secs, 72°C 1 min), 72°C 2 mins. For IgH PCRs >1kb KOD polymerase (Novagen) was used under the following conditions: 95°C 2 mins, 32 x (95°C 20 secs, 56-62°C, Table 1) 20 secs, 70°C 90 secs), 70°C 2 mins. For Igκ and Igλ PCR, all <1kb, the above condition were used except extension at 72°C for 50 secs.

[126] RNA was extracted from Blood using the RiboPure Blood Kit (Ambion) and RNA extraction from spleen, bone marrow or lymph nodes used RNASpin mini kit. (GE Healthcare). cDNA was made using Oligo dT and Promega Reverse Transcriptase at 42°C for 1 hour. GAPDH PCR reactions (oligos 429-430) determined the concentration.

[127] RT-PCRs were set up using VH leader primers with rat μCH2 or rat γCH2 primers (**Table 2**). Amplification with GoTaq Green Master mix were 94°C 2 mins, 34 x (94°C 30 secs, 55-65oC 30 secs, 72°C 50-60 secs), 72°C 2 mins. PCR products of the expected size were either purified by gel or QuickClean (Bioline) and sequenced directly or cloned into pGemT (Promega).

[128] The sequences of the primers used in the PCR and RT-PCR assays to detect human IgH and IgL integration and expression are provided in **Table 3**.

Characterization of antibodies in immunized OmniRat animals by next generation sequencing

[129] A total of 6 OmniRat2 animals were immunized with beta-gal and B-cells were isolated from draining lymph nodes. After pelleting the B-cells and removing supernatant, total RNA was prepared from lymph node derived B-cells. RNA was reverse transcribed, and the resulting cDNA was used as template to amplify the full variable region of the Ig heavy chain rearranged locus (the VH region). This amplified product was then prepared for next-generation sequencing (NGS) and the full VH repertoire of each animal was determined by NGS.

[130] After post-processing and quality control of the raw NGS reads, the V-gene usage of each animal was determined by aligning each unique VH sequence to the germline V-gene reference sequence. The percent V-gene usage was calculated as the number of VH sequences using a particular V-gene divided by the total number of VH sequences in that animal.

Protein purification

[131] IgM was purified on anti-IgM affinity matrix (BAC B.V., Netherlands, CaptureSelect #2890.05) as described in the protocol. Similarly, human Igκ and Igλ was purified on anti-L chain affinity matrix (CaptureSelect anti-Igκ #0833 and anti-Igλ # 0849) according to the protocol.

[132] For rat IgG purification (Bruggemann et al. *J Immunol* **142**, 3145-3150 (1989)) protein A and protein G agarose was used (Innova, Cambridge, UK, #851-0024 and #895-0024). Serum was incubated with the resin and binding facilitated at 0.1 M sodium phosphate pH 7 for protein G and pH 8 for protein A under gentle mixing. Poly-prep columns (Bio-Rad) were packed with the mixture and washed extensively with PBS pH7.4. Elution buffer was 0.1 M Sodium Citrate pH 2.5 and neutralization buffer was 1 M Tris-HCl pH 9.

[133] Electrophoresis was performed on 4-15% SDS-PAGE and Coomassie brilliant blue was used for staining. MW standards were HyperPage Prestained Protein Marker (#BIO-33066, Bioline).

Flow cytometry analysis and FISH

[134] Cell suspensions were washed and adjusted to 5x105 cells/100 µl in PBS-1% BSA-0.1% Azide. Different B-cell subsets were identified using mouse anti-rat IgM FITC-labelled mAb (MARM 4, Jackson Immunoresearch Laboratories) in combination with anti-B cell CD45R (rat B220)-PE-conjugated mAb (His 24, BD biosciences) or anti-IgD-PE-conjugated mAb (MARD-3, Abd Serotec). A FACS CantoII flow cytometer and FlowJo software (Becton Dickinson, Pont de Claix, France) was used for the analysis.

[135] Fluorescence in situ hybridisation was carried out on fixed blood lymphocytes using purified IgH and IgL C-region BACs as described. (Meisner & Johnson *Methods* **45**, 133-141 (2008))

Immunization, cell fusion and affinity measurement

[136] Immunizations were performed with 125 µg PG in CFA, 150 µg hGHR in CFA, 200 µg Tau/KLH in CFA, 150 µg HEL in CFA, 150 µg OVA in CFA at the base of the tail and medial iliac lymph node cells were fused with mouse P3X63Ag8.653 myeloma cells 22 days later as described (Kishiro et al. *Cell structure and function* **20**, 151-156 (1995)). For multiple immunizations protein, 125 µg PG or HEL, or 100 µg hGHR or CD14 in GERBU adjuvant (www.Gerbu.com), was administered intraperitoneally as follows: day 0, day 14, day 28 and day 41 without adjuvant, followed by spleen cell fusion with P3x63Ag8.653 cells 4 days later (Meisner & Johnson *Methods* **45**, 133-141 (2008)).

[137] Binding kinetics were analyzed by surface Plasmon resonance using a Biacore 2000 with the antigens directly immobilized as described (Pruzina et al. *Protein engineering, design & selection : PEDS* **24**, 791-799 (2011)).

Detection of antigen-specific antibodies by ELISA

[138] Rat serum samples were analysed for B-Gal IgG and IgM antibody and antigen titers using an antigen-coat, anti-IgG or IgM reporter ELISA. 96-well plates were coated with B-Gal overnight at 2-6 °C, blocked with PBS-Casein-Blocker/Diluent 1 X, washed with ELISA Wash Buffer, incubated with serum, washed with ELISA Wash Buffer, incubated with either a mixture of goat anti-rat IgG1-HRP, goat anti-rat IgG2a-HRP, and goat anti-rat IgG2b-HRP (each at a 1/5,000 dilution) or goat anti-rat IgM (1/5,000 dilution), washed with ELISA Wash Buffer, incubated with TMB Substrate Solution for 30 minutes and ELISA Stop Solution was added to the wells. Absorbance in the plate wells was measured at 450 nm. Except where noted above, incubations were for 1.5 to 2 hours at ambient temperature.

Determination of IgM and IgG concentration in rat serum.

[139] Rat serum samples were also analysed for the concentration of Total Rat IgG1, Rat IgG2b, and Rat IgM using a Double Antibody ELISA Sandwich assay format. Total Rat IgG1, Rat IgG2b, and Rat IgM concentrations were calculated using standard curves generated individually for each isotype. 96-well plated were coated with the respective isotype specific capture antibody (either mouse anti-rat IgG1, mouse anti-rat IgG2b, or goat anti-rat IgM) overnight at 2-6 °C, blocked with PBS-Casein-Blocker/Diluent 1 X, washed with ELISA Wash Buffer, incubated with serum, washed with ELISA Wash Buffer, incubated with the respective detecting antibody (either mouse anti-rat IgG or goat anti-rat IgM), washed with ELISA Wash Buffer, incubated with TMB Substrate Solution for 30 minutes and ELISA Stop Solution was added to the wells. Absorbance in the plate wells was measured at 450 nm. Except where noted above, incubations were for 1.5 to 2 hours at ambient temperature.

Table 1
PCR* conditions to detect human IgH and IgL integration and expression

IgH	Primers	Annealing Temp (Tm-5)	Fragment size
Hyg (5' BAC6)	Hyg 3' F - 459	54°C	~400bp
V4-34 (BAC6)	205-206	65°C	~1kb
V4-28 (BAC6)	203-204	65°C	~1kb
V3-11 (overlap BAC6-BAC3)	448-461	60°C	~500bp
V1-8 (BAC3)	371-372	60°C	~300bp
V4-4 (BAC3)	393-396	60°C	~750bp
V6-1 (BAC3-Annabel)	359-360	65°C	~350bp
JH (Annabel)	368-369	62°C	~250bp
μ-γ1 (Annabel)	583-535	62°C	~3kb
Ura (3' Annabel)	241-253	56°C	~3kb

Igκ	Primers	Annealing Temp (Tm-5)	Fragment size
KDE	313-314	66°C	~600bp
cKappa	307-308	64°C	~600bp
V4-1	333-334	60°C	~300bp
V1-5	329-330	64°C	~400bp
V1-6	331-332	60°C	~300bp
V3-7	309-310	66°C	~700bp
V3-15	311-312	66°C	~500bp

Igλ	Primers	Annealing Temp (Tm-5)	Fragment size
V3-27	215-216	67°C	~400bp
V3-19	213-214	67°C	~700bp
V2-14	211-212	67°C	~400bp
V middle	168-169	65°C	~500bp
JLambda	162-163	67°C	~800bp
cLambda	170-171	67°C	~500bp
Enhancer	172-173	67°C	~400bp

*For DNA extraction from ear and tail clips the Genomic DNA Mini Kit (Bioline) was used. For PCRs 1kb or less in size GoTaq Green Master mix (Promega) was used under the following conditions: 94°C 2 mins, 32 x (94°C 30 secs, Tm-5 (below) 30 secs, 72°C 1 min [50 sec for Igκ/λ]), 72°C 2 mins. Annealing temperatures were set at the lowest primer Tm– 5^0C (www.sigmagenosys.com/calc/DNACalc.asp). For PCRs >1kb KOD polymerase (Novagen) was used under the following conditions: 95°C 2 mins, 32 x (95°C 20 secs, Tm-5 20 secs, 70°C 90 secs), 70°C 2mins.

Table 2
RT-PCR conditions to detect human IgH and IgL integration and expression**

IgH	Primer	Annealing Temp (Tm-5)	Fragment size
VH1 Leader	390	65°C	↓
VH2 Leader	391	65°C	↓
VH3 Leader	392	65°C	↓
VH4 Leader	393	60°C	↓
VH6 Leader	394	65°C	↓
VH4-39 Leader	761	55°C	↓
Rat μCH2	345	↑	~1kb
Rat γCH2	682	↑	~800bp

Igκ	Primer	Annealing Temp (Tm-5)	Fragment size
HuVK1 Leader	400/474	63°C	↓
HuVK3 Leader	401/475	63°C	↓
HuVK4 Leader	476	63°C	↓
HuVK5 Leader	477	63°C	↓
Hu κ C region	402	↑	~600bp

Igλ	Primer	Annealing Temp (Tm-5)	Fragment size
HuVL2 Leader	388/478	58°C	↓
HuVL3 Leader	398/479/480/482/483/481/484	58°C	↓
HuVL4 Leader	485	58°C	↓
Hu λ C region	387	↑	~600bp

**RNA was extracted from Blood using the RiboPure Blood Kit (Ambion). RNA extracted from spleen, bone marrow or lymph nodes used the RNASpin mini kit (GE Healthcare). cDNA was made using Oligo dT and Promega Reverse Transcriptase at 42°C 1 hour. PCRs using the GoTaq Green Master mix were set up as follows: 94°C 2 mins, 34 x (94°C 30 secs, Tm-5 30 secs, 72°C 1 min [50 sec for Igκ/λ]), 72°C 2 mins.

Table 3
Primer Sequences

Number	Oligonucleotide sequence 5'-3'
162	GGGGCCAAGGCCCCGAGAGATCTCAGG
163	CACTGGGTTCAGGGTTCTTTCCACC
168	GTGGTACAGAAGTTAGAGGGGATGTTGTTCC
169	TCTTCTACAAGCCCTTCTAAGAACACCTGG
170	AGCACAATGCTGAGGATGTTGCTCC
171	ACTGACCCTGATCCTGACCCTACTGC
172	AAACACCCCTCTTCTCCCACCAGC
173	CGCTCATGGTGAACCAGTGCTCTG
203	GCTATTTAAGACCCACTCCCTGGCA
204	AAAACCTGCAGCAAGGATGTGAGG
205	GCTCCTTCAGCACATTTCCTACCTGGA
206	CCATATATGGCAAAATGAGTCATGCAGG
211	CTCTGCTGCTCCTCACCCTCCTCACTCAGG
212	GAGAGTGCTGCTGCTTGTATATGAGCTGCA
213	TGGCTCACTCTCCTCACTCTTTGCATAGGTT
214	GATGGTTACCACTGCTGTCCCGGGAGTTAC
215	ATCCCTCTCCTGCTCCCCCTCCTCATTCTCTG
216	TGATGGTCAAGGTGACTGTGGTCCCTGAGCTG
238	AACAAGTGCGTGGAGCAG
241	GTACTGTTGACATTGCGAAGAGC
243	TGGTTGACATGCTGGCTAGTC
253	TGTCTGGCTGGAATACACTC
275	AAATGAGCTTCAAATTGAGAAGTGACGCAAGCATCAATGGTATAATGTCCAGAGTTGTGAGGC CTTGGGGACTGTGTGCCGAACATGCTC
276	CCAGCACTGTTCAATCACAGTATGATGAGCCTAATGGGAATCCCACTAGGCTAGTCTAGTCACC ACATTAAAGCACGTGGCCTCTTATCG
278	TGACCATTGCTTCCAAGTCC

Number	Oligonucleotide sequence 5'-3'
307	GAGGAAAGAGAGAAACCACAGGTGC
308	CACCCAAGGGCAGAACTTTGTTACT
309	TGTCCAGGTATGTTGAAGAATGTCCTCC
310	TGGACTCTGTTCAACTGAGGCACCAG
311	GGCCTTCATGCTGTGTGCAGACTA
312	CAGGTCGCACTGATTCAAGAAGTGAGT
313	TTCAGGCAGGCTCTTACCAGGACTCA
314	TGCTCTGACCTCTGAGGACCTGTCTGTA
329	TCACGTGACTGTGATCCCTAGAA
330	CACTGTTATGCCAACTGAACAGC
331	CGTAGCAGTCCCCATCTGTAATC
332	ATGTCAGAGGAGCAGGAGAGAGA
333	CACGCCTCACATCCAATATGTTA
334	ATACCCTCCTGACATCTGGTGAA
345	GCTTTCAGTGATGGTCAGTGTGCTTATGAC
346	TGGAAGACCAGGAGATATTCAGGGTGTC
359	TTGCTTAACTCCACACCTGCTCCTG
360	TGCTTGGAACTGGATCAGGCAGTC
368	CACCCTGGTCACCGTCTCC
369	AGACAGTGACCAGGGTGCCAC
371	TGAGGAACGGATCCTGGTTCAGTC
372	ATCTCCTCAGCCCAGCACAGC
383	CCTCCCATGATTCCAACACTG
384	CTCACCGTCCACCACTGCTG
385	CTGTGCCACAAACATGCAAAGATAAGTTCCATGTGACAAGTCTGAACTCAGTGTTGGAATCATG GGAGGCGGCCGCGTTATCTATGCTGTCTCACCATAG
387	TGCTCAGGCGTCAGGCTCAG
388	TGCTCAGGCGTCAGGCTCAG
390	ATGGACTGGACCTGGAGGATCC
391	TCCACGCTCCTGCTGCTGAC
392	ATGGAGTTTGGGCTGAGCTGG

Number	Oligonucleotide sequence 5'-3'
393	TGAAACACCTGTGGTTCTTCC
394	TCATCTTCCTGCCCGTGCTGG
396	GACTCGACTCTTGAGGGACG
398	ATGTGGCCACAGGCTAGCTC
400	ATGAGGGTCCCCGCTCAG
401	ATGGAAGCCCCAGCTCAGC
402	CCTGGGAGTTACCCGATTGG
412	GGCGCGCCAAGCATCATGTCCTACCTGGCTG
414	CAAAGTACGTGGCACCTCCCTCGTCTTTCTTCCTCCTGCTCCAGCCAGGTAGGACATGATGCTTG GCGCGCCGTTATCTATGCTGTCTCACCATAG
429	CAGTGCCAGCCTCGTCTCAT
430	AGGGGCCATCCACAGTCTTC
448	CTTCACTGTGTGTTCTTGGGATAC
459	GTGTAATGCTTTGGACGGTGTGTTAGTCTC
461	GCATAGCGGCGCGCCAAGCATCATGTCCTACCTGGCTG
474	GACATGAGAGTCCTCGCTCAGC
475	AAGCCCCAGCGCAGCTTC
476	ATGGTGTTGCAGACCCAGGTC
477	GTCCCAGGTTCACCTCCTCAG
478	TCCTCASYCTCCTCACTCAGG
479	CGTCCTTGCTTACTGCACAG
480	AGCCTCCTTGCTCACTTTACAG
481	CCTCCTCAYTYTCTGCACAG
482	GCTCACTCTCCTCACTCTTTGC
483	CCTCCTCTCTCACTGCACAG
484	GCCACACTCCTGCTCCCACT
485	ATGGCCTGGGTCTCCTTCTAC
488	ATTACTACTACTACTACTACATGGACGTCTGGGGCAAAGGGACCACGGTCACCGTCTCCTCAGG AAGAATGGCCTCTCCAGGTC
490	CTGTCGTTGAGATGAACCCCAATGTGAG
534	GGAACTGATGTGATCTCAGTCACACAGCTAATGCAAAGGTCAGCAGGCTGTTTACTGCCTGGAG

Number	Oligonucleotide sequence 5'-3'
	GTTCATCGCCCAATTCCAAAGTCAC
535	CTAGTCTGCATGGGTCTCCGCAAAC
550	CTGGTATAATCATAAGTCTCCACTTAATAGTTCTGTAGACAGAATCTTCATTTAGACTTACAGAC
	CGCGGCCGCACCGCAGGGTAATAACTG
561	GCAACCCTTCTTGCCACTCATGTCCCAGCTCTCACCATGTGACATAGCCTGTTAACAATTCGGTCG
	AAAAAAGAAAAGGAGAG
562	AATGTTCTTAGTATATATAAACAAGCTACTCCCAATTCATAGTCAACTAAGTTAACATTCCACATG
	TTAAAATAGTGAAGGAG
566	TTAACAGGCTATGTCACATGGTGAGAGCTGGGACATGAGTGGCAAGAAGGGTTGCCAGACTCCCC
	CTTTACCTCTATATCGTGTTC
570	CTTAGTTGACTATGAATTGGGAGTAGCTTGTTTATATATACTAAGAACATTTGTCAGAAGCTCTTT
	CTTGTTTATTCCCAGTTTGC
583	CATGTCCGTATGTTGCATCTGC
682	GGGAAGATGAAGACAGATG
761	TGGAGTGGATTGGGAGT
878	GCGATCGCAAAGACGAAAGGGCCTCGTG
879	ACCTGGTGATCGCCAACAAATACTACC
1066	GCGGTGGGTCTCCCACGGGGGCAAACAGCAGTGGTGGACGGTGAGCGTACGGTTATCTATGCTGTCTCACCATAG
1088	CTGTCAGCTGGAAGCAGTTAAGGTTGGCCTTTGTCTGTATTCGTACGCACACGCTTTTCAATTCAATTCATC

RESULTS

The human IgH and IgL loci

[140] Construction of the human Ig loci employed established technologies to assemble large DNA segments using YACs and BACs (Davies et al. *Nucleic acids research* **20**, 2693-2698 (1992); Davies et al. *Biotechnology (N Y)* **11**, 911-914 (1993); Wagner et al. *Genomics* **35**, 405-414 (1996); Popov et al. *Gene* **177**, 195-201 (1996); Mundt et al. *J Immunol* **166**, 3315-3323 (2001)). As multiple BAC modifications in *E. coli* frequently deleted repetitive regions such as switch sequences and enhancers, a method was developed to assemble sequences with overlapping ends in *S. cerevisiae* as circular YAC (cYAC) and, subsequently, converting such a cYAC into a BAC. Advantages of YACs include their large size, the ease of homologous alterations in the yeast host and the sequence stability, while BACs propagated in E. coli offer the advantages of easy preparation and large yield. Additionally, detailed restriction mapping and sequencing analysis can be better achieved in BACs than in YACs.

[141] Sequence analysis and digests identified gene clusters of interest and ensured locus integrity and functionality to secure DNA rearrangement and switching over a wide region as shown in Figure 1. As shown previously, overlapping regions may generally favor joint integration when co-injected into oocytes (Wagner et al. *Genomics* **35**, 405-414 (1996)). Thereby, insertion of BAC6-VH3-11, a 182 kb AsiSI-AscI fragment, with BAC3, a 173 kb NotI fragment, and BAC3-1N12M5I8 (Hu-Rat Annabel), a 193 kb NotI fragment, led to the reconstitution of a fully functional transgenic IgH locus (HC14) in the rat genome. Similarly, injection of BAC9, BAC (14+5) and BAC3-1N12M5I8**,** led to the reconstitution of a fully functional transgenic IgH locus (HC30) in the rat genome.

[142] Similarly, the human Igκ locus was integrated by homologous overlaps. The human Igλ locus was isolated intact as a ~300 kb YAC and also fully inserted into a rat chromosome. The integration success was identified by transcript analysis which showed V(D)J-C recombinations from the most 5' to the most 3' end of the locus injected. Multiple copies were identified by qPCR (not shown) and it is likely that head to tail integrations occurred. In all cases, transgenic animals with single-site integrations were generated by breeding.

Breeding to homozygosity

[143] The derivation of transgenic rats by DNA microinjection into oocytes, their breeding and immunization is comparable to the mouse. However, ZFN technology to obtain gene knock-outs has only been reported recently (Geurts et al. *Science* **325**, 433 (2009); Flisikowska et al. *PloS one* **6**, e21045 (2011)). Silencing of the rat IgH locus by J_H deletion using ZFN KO technology has been described (Menoret et al. *European journal of immunology* **40**, 2932-2941 (2010)) and a manuscript describing silencing of the rat IgL loci, targeting of Cκ and deletion of J-Cλ genes, is in preparation. We derived multiple founders with integrated human Ig loci and silenced endogenous Ig production; all analyzed by PCR and FISH with complete trans-locus integration selected and interbred (**Table 4**). Several founder rats carried low translocus copy numbers; with the rat C-gene BAC in OmniRat™ likely to be fully integrated in 5 copies as determined by qPCR of Cμ and Cα products (not shown). Identification by FISH of single position insertion in many lines confirmed that spreading or multiple integration of BAC mixtures were rare; an advantage for breeding to homozygosity, which was achieved.

Table 4: Generated rat lines: transgenic integration, knock-out and gene usage

	human V_H	rat C_H	human Igk	human Igl	ZFN KO			FISH
rat line	VH BACs about 400 kb	(Annabel) 193 kb	BACs 300 kb	Igl YAC 300 kb	J_H KO	Igκ KO	Igγ KO	rat chromosome
HC14	√	√						5q22
HC30	√	√						15q24
OmniRat	√	√	√	√	√	√	√	**homozygous KOs**
LC#79			√					17
LC#6.2				√				6q23
#117					√			6q32
#23						√		4
#35							√	11

[144] Rats carrying the individual human transloci - IgH, Igκ and Igλ - were crossbred successfully to homozygosity with Ig locus KO rats. This produced a highly efficient new multi-feature line (OmniRats™) with human V_H-D-J_H regions of over 400 kb

containing 22 functional V_Hs and a rat C region of ~116 kb. DNA rearrangement, expression levels, class-switching and hypermutation was very similar between the different founders and comparable to wt rats. This is probably the result of the associated rat constant region accommodating several Cs and with the 3'E (enhancer control) region in authentic configuration. OmniRat animals carrying the HC14 heavy chain locus were bred with OmniRat animals carrying the HC30 locus to generate OmniRat2. OmniRat2 animals contain two heavy chain loci containing 43 functional VHs.

B-cell development in the knock-out background

[145] To assess whether the introduced human Ig loci were capable of reconstituting normal B-cell development flow cytometric analyses were performed. Particular differentiation stages were analyzed in spleen and bone marrow lymphocytes (Osborn et al. *J Immunol* 2013; **190**:1481-1490), which previously showed a lack of B-cell development in JKO/JKO rats (Menoret et al. *European journal of immunology* **40**, 2932-2941 (2010)), and no corresponding IgL expression in κKO/κKO as well as in λKO/λKO animals (data not shown). Most striking was the complete recovery of B-cell development in OmniRats compared to wt animals, with similar numbers of B220(CD45R)$^+$ lymphocytes in bone marrow and spleen. IgM expression in a large proportion of CD45R$^+$ B-cells marked a fully reconstituted immune system. Size and shape separation of spleen cells was indistinguishable between OmniRats™ and wt animals and thus successfully restored in the transgenic rats expressing human idiotypes with rat C region. Moreover, the small sIgG$^+$ lymphocyte population was present in OmniRats (Osborn et al. *J Immunol* 2013; **190**:1481-1490).

[146] The analysis of other OmniRat lymphocyte tissues showed that they were indistinguishable from wt controls and, for example, T-cell subsets were fully retained (data not shown), which further supports the notion that optimal immune function has been completely restored.

Ig levels in serum

[147] To gain unambiguous information about antibody production we compared quality and quantity of serum Ig from HC30 and HC14/HC30 animals (FIG. 4) The results demonstrated that animals with one Ig locus (HC30) expressed similar amounts of IgM and IgG in serum compared to animals with two heavy chain loci (HC14 and HC30).

[148] ELISA analysis of serum from immunized OmniRat animals with one HC locus (HC30) or two HC loci (HC14 and HC30) revealed similar titers of anti-beta gal IgM and IgG in such animals (FIG. 5).

Diverse human H- and L-chain transcripts

[149] Extensive transcriptional analysis was carried out using blood lymphocytes or spleen cells from transgenic rats with functional endogenous Ig loci. RT-PCR from specific human V_H group forward to Cμ or Cγ reverse primers, showed human V_HDJ_H usage. For L-chain analysis group specific human Vκ or Vλ forward primers were used with Cκ or Cλ reverse primers.

[150] In addition, B-cells from animals were collected, RNA was prepared and reverse transcribed, and the resulting cDNA was used as template to amplify the full variable region of the Ig heavy chain rearranged locus (the VH region). This amplified product was then prepared for next-generation sequencing (NGS) and the full VH repertoire of each animal was determined by NGS. After post-processing and quality control of the raw NGS reads, the V-gene usage of each animal was determined by aligning each unique VH sequence to the germline V-gene reference sequence. The percent V-gene usage was calculated as the number of VH sequences using a particular V-gene divided by the total number of VH sequences in that animal. Of the 43 total human V-genes introduced on the transgenes in OmniRat2, we detect 33 V-genes expressed at a level greater than 0.1% in a rearranged IgG transcript.

[151] The results of the RT-PCR VH-gene expression analysis and NGS repertoire analysis are summarized in Figure 1. These result showed the use of all integrated human V_H genes regarded as functional (Lefranc & Lefranc The immunoglobulin factsbook. *FactsBook Series, Academic Press, GB*, 45-68 (2001)) in combination with diverse use of D segments and all J_H segments.

[152] The results clearly demonstrate that addition of more variable regions provided by the two loci (HC14+HC30) leads to an even broader antibody repertoire. In conclusion, we have demonstrated that antigen specific high affinity Abs of potentially any class can be produced in transgenic animals with one or two Ig heavy chain loci. This technology will allow the production of fully human Abs of any class or fragments thereof in response to antigen challenge for use as therapeutic or diagnostic agents in man. By using different loci our technology also allows for the production of high affinity matured antibodies from rodents for use as reagents, diagnostics or for the treatment of humans.

DISCUSSION

[153] A combination of human and rat genes to assemble a novel IgH locus has resulted in highly efficient near normal expression of antibodies with human idiotypes. Moreover, integration of the human Igκ and Igγ loci revealed that chimeric Ig with fully human specificity is readily produced and that association of rat C-regions with human L-chains is not detrimental. Advantages of using part of the rat IgH locus are that species-specific C regions and enhancer control elements are kept in their natural configuration, with essentially only the diverse human V_H D J_H region being transplanted. Furthermore, expression of antibodies with rat Fc-regions allow normal B-cell receptor assembly and optimal activation of the downstream signalling pathway essential for the initiation of highly efficient immune responses. In particular, the quality of an immune response to antigen challenge relies on combined actions of many receptor associated signalling and modifier components (see: www.biocarta.com/pathfiles/h bcrpathway.asp).

[154] The approach of using YACs and BACs, and interchanging between the two, has the advantage of both, speed and the ability to check integrity when making constructs of large regions by overlapping homology. Several founder rats carried low translocus copy numbers; with the rat C-gene BAC in OmniRat likely to be fully integrated in 5 copies as determined by qPCR of Cμ and Cα products (not shown). Identification by FISH of single position insertion in many lines confirmed that spreading or multiple integration of BAC mixtures were rare; an advantage for breeding to homozygosity, which was achieved. Little was known whether extensive overlapping regions would integrate, such as to maintain the

full functionality, essential for DNA rearrangement. Previously, overlapping integration has been reported but for much smaller regions (<100 kb) (Wagner et al. *Genomics* **35**, 405-414 (1996); Bruggemann et al. *European journal of immunology* **21**, 1323-1326 (1991)) and our results suggest that desired integration by homology or in tandem is a frequent event. This eases the transgenic technology substantially as no laborious integration of large YACs into stem cells and subsequent animal derivation therefrom has to be performed. (Mendez et al. *Nature genetics* **15**, 146-156 (1997); Davies et al. *Biotechnology* (N Y) **11**, 911-914 (1993)) In addition, ZFN technology, also performed via DNA injection (Geurts et al. *Science* **325**, 433 (2009); Menoret et al. *European journal of immunology* **40**, 2932-2941 (2010)), produced Ig KO strains easily and may well be the future technology of choice for gene disruptions and replacement. Silenced endogenous Ig gene expression in OmniRats, containing human-rat IgH and human IgL loci, has the advantage that no interfering or undesired rat Ig could give rise to mixed products. Interestingly, immunization and hybridoma generation in OmniRats still producing wt Ig revealed that many products were fully human, human-rat IgH and human IgL, despite incomplete Ig KOs. Here, despite the extensive number of wt V genes, it was remarkable that the introduced human genes amplified readily and thus showed to be efficient expression competitors. This is in line with the observation of generally good expression levels of all our integrated transgenes, which favorably compete with the endogenous loci. Previously in mice expressing a human antibody repertoire, Ig KOs were essential as little expression of human products was found when wt Ig is released (Bruggemann et al. *PNAS* **86**, 6709-6713 (1989); Mendez et al. *Nature genetics* **15**, 146-156 (1997)).

[155] It is possible that the production of fully human Ig loci even in Ig KO mice is suboptimal as strain specific cis-acting sequences are required for high-level expression. In the mouse an enhancer region downstream of Cα plays a vital role in class-switch recombination (Vincent-Fabert et al. *Blood* **116**, 1895-1898 (2010)) and it is likely that elements in that region may facilitate hypermutation (Pruzina et al. *Protein engineering, design & selection : PEDS* **24**, 791-799 (2011)). This may be the reason why immune responses and generation of diverse hybridomas at high frequency may be difficult in mice carrying even a large fully human locus (Davis et al. *Cancer metastasis reviews* **18**, 421-425 (1999); Lonberg *Current opinion in immunology* **20,** 450-459 (2008)). As the chimeric human-rat IgH locus facilitates near wt differentiation and expression levels in OmniRats, it

can be concluded that the endogenous rat C region and indeed the —30 kb enhancer sequence 3' of Cα are providing optimal locus control to express and mature human V_H genes. Another region, Cδ with its 3' control motif cluster (Mundt et al. *J Immunol* **166**, 3315-3323 (2001)), has been removed from the chimeric C-region BAC since silencing or a lack of IgD did not appear to reduce immune function 37. Normally, mature IgM^+IgD^+ B-cells down-regulate IgD upon antigen contact, which initiates class-switch recombination (Chen *Immunol Rev* **237**, 160-179 (2010)). Thus, switching may be increased without IgD control, which is supported by our finding that IgG transcripts and serum levels are significantly lower when the Cδ region is retained in transgenic constructs (data not shown).

[156] The production of specific IgG in OmniRats is particularly encouraging as we found that in various immunizations mAbs with diversity in sequence and epitope, comparable to what was produced in wt controls, could be isolated via spleen and lymph node fusion. V-gene, D and J diversity was as expected and nearly all segments were found to be used productively as predicted (Lefranc & Lefranc *The immunoglobulin factsbook. FactsBook Series*, Academic Press, GB, 45-68 (2001)). This was in stark contrast to mice carrying fully human transloci where clonal expansion from a few precursor B-cells produced little diversity (Pruzina et al. *Protein engineering, design & selection : PEDS* **24**, 791-799 (2011)). Since the number of transplanted V-genes is only about half of what is used in humans we anticipated to find restricted immune responses and limited diversity when comparing OmniRats with wt animals. However, this was not the case and a comparison of CDR3 diversity in over 1000 clones revealed the same extensive junctional differences in OmniRats as in wt animals. The few identical gene-segment combinations were further diversified by N-sequence additions or deletion at the V_H to D and/or D to J_H junctions and also by hypermutation. Thus, it is clear that the rat C region sequence is highly efficient in controlling DNA rearrangement and expression of human V_HDJ_H. Extensive diversity was also seen for the introduced human Igκ and Igγ loci, similar to what has previously been shown in mice (Nicholson et al. *J Immunol* **163**, 6898-6906 (1999); Pruzina et al. *Protein engineering, design & selection : PEDS* **24**, 791-799 (2011); Popov et al. *The Journal of experimental medicine* **189**, 1611-1620 (1999)). Hence, substantially reduced efficiency in the production of human antibodies from mice (Lonberg *Nature biotechnology* **23**, 1117-1125 (2005)) has been overcome in OmniRats, which diversify rearranged H-chains reliably and extensively by class-switch and hypermutation to yield high affinity antibodies in bulk rather

than occasionally. The yield of transgenic IgG and the level of hypermutation, impressively utilized in antigen-specific mAbs, showed that clonal diversification and production level are similar between OmniRats and wt animals. Routine generation of high affinity specificities in the subnanomolar range was even accomplished by different single immunizations and again compares favorably with wt animals; results that have not been shown in transgenic mice producing human antibody repertoires from entirely human loci. (Mendez et al. *Nature genetics* **15**, 146-156 (1997))

[157] In summary, to maximize human antibody production an IgH locus that uses human genes for antibody specificity but rodent genes for control of differentiation and high expression should be regarded essential. L-chain flexibility is a bonus as it permits highly efficient human IgH/IgL assembly even when wt Ig is present. For therapeutic applications chimeric H-chains can be easily converted into fully human Abs by C-gene replacement without compromising the specificity.

[158] All patents and patent publications referred to herein are hereby incorporated by reference.

[159] Certain modifications and improvements will occur to those skilled in the art upon a reading of the foregoing description. It should be understood that all such modifications and improvements have been deleted herein for the sake of conciseness and readability but are properly within the scope of the following claims.

Claims:

1. A transgenic animal comprising at least one inactivated endogenous Ig locus and a plurality of artificial transgenic Ig heavy chain loci integrated in the animal's genome at different chromosomal sites.

2. The transgenic animal according to claim 1, wherein the plurality of artificial Ig heavy chain loci comprise (i) a V-region having at least one human V gene segment encoding a germline or hypermutated human V-region amino acid sequence; (ii) one or more J gene segments; and (iii) one or more constant region gene segments, wherein said artificial Ig heavy chain loci are functional and capable of undergoing gene rearrangement and act cooperatively to produce a repertoire of artificial immunoglobulins.

3. The transgenic animal of claim 2, wherein the at least two artificial Ig heavy chain loci comprise the full complement of human variable heavy chain regions between them.

4. The transgenic animal of claim 1, wherein said artificial heavy chain loci comprise overlapping heavy chain gene segments.

5. The transgenic animal according to claim 1, wherein said transgenic animal lacks a functional endogenous Ig light chain locus.

6. The transgenic animal according to claim 1, wherein said transgenic animal lacks a functional endogenous Ig heavy chain locus.

7. The transgenic animal according to claim 1, wherein said transgenic animal expresses a diverse repertoire of antibodies encoded by V-genes from transgenic immunoglobulin loci located at different chromosomal sites.

8. The transgenic animal of claim 7, wherein said transgenic animal lacks a functional Ig light chain locus and is capable of producing heavy chain-only antibodies.

9. The transgenic animal of claim 2, wherein at least one of the artificial Ig heavy chain loci comprises at least one human immunoglobulin (Ig) joining (J) region gene, an Ig constant region gene, and a rat 3' enhancer.

10. The transgenic animal of claim 9, wherein said rat 3' enhancer comprises the sequence set forth as SEQ ID NO:1.

11. The transgenic animal as in any of the preceding claims, further comprising at least one human Ig variable (V) region gene and/or a human Ig diversity (D) region gene.

12. The transgenic animal of claim 2 or 9, wherein the constant region gene is selected from the group consisting of a human constant region gene and a rat constant region gene.

13. The transgenic animal of claim 12, wherein the constant region gene comprises a rat constant region gene.

14. The transgenic animal of claim 2 or 9, wherein the constant region gene comprises a constant region gene selected from the group consisting of Cμ and Cγ.

15. The transgenic animal as in any of the preceding claims, comprising a nucleic acid sequence substantially homologous to bacterial artificial chromosome (BAC) Annabel, or a portion thereof.

16. The transgenic animal as in any of claims 11-15 wherein said human Ig V region comprises at least one human V region gene isolatable from BAC6-V_H3-11 and/or BAC3.

17. The transgenic animal as in any of the preceding claims comprising nucleic acid sequences (a) and (b) in 5' to 3' order:

(a) a human Ig variable region comprising human V region genes in natural configuration isolatable from BAC6-V_H3-11 and/or BAC3; and

(b) a human Ig joining region comprising human J region genes in natural configuration isolatable from the bacterial artificial chromosome (BAC) Annabel.

18. The transgenic animal as in any of claims 11-17, wherein each of the human immunoglobulin variable region, the human immunoglobulin diversity region, the human immunoglobulin joining region, the immunoglobulin constant region, and the rat 3' enhancer are in the relative positions shown in FIG. 1a.

19. The transgenic animal as in claim 18, comprising a nucleic acid sequence substantially homologous to the nucleic acid sequence set forth as SEQ ID NO:2.

20. The transgenic animal as in claim 18, comprising a nucleic acid sequence substantially homologous to the nucleic acid sequence set forth as SEQ ID NO:11.

21. The transgenic animal as in any of claims 11-18, wherein said V-D-J regions are rearranged and form a complete exon encoding a heavy chain variable domain.

22. The transgenic animal as in any of claims 11-15 wherein said human Ig V region comprises at least one human V region gene isolatable from BAC9-V_H3-53 and/or BAC14/5.

23. The transgenic animal as in any of the preceding claims comprising nucleic acid sequences (a) and (b) in 5' to 3' order:

(a) a human Ig variable region comprising human V region genes in natural configuration isolatable from BAC9-V_H3-53 and/or BAC14/5; and

(b) a human Ig joining region comprising human J region genes in natural configuration isolatable from the bacterial artificial chromosome (BAC) Annabel.

24. The transgenic animal of claim 22 or 23, wherein each of the human immunoglobulin variable region, the human immunoglobulin diversity region, the human immunoglobulin joining region, the immunoglobulin constant region, and the rat 3' enhancer are in the relative positions shown in FIG. 1b.

25. The transgenic animal as in claim 24, comprising a nucleic acid sequence substantially homologous to the nucleic acid sequence set forth in Figure 6.

26. The transgenic animal as in claim 24, comprising a nucleic acid sequence substantially homologous to the nucleic acid sequence set forth in Figure 7.

27. A method for producing antibodies, comprising immunizing the transgenic animal as in any of the preceding claims with an immunogen.

28. A polyclonal antisera composition produced by the method of claim 27 wherein said antisera comprise antigen-specific antibodies encoded by V-genes encoded by transgenic immunoglobulin loci located at different chromosomal sites.

29. A method for producing a monoclonal antibody, comprising (i) immunizing the transgenic animal as in any of claims 1-26 with an immunogen, (ii) isolating a monoclonal antibody producing cell from said transgenic animal wherein said monoclonal antibody producing cell produces a monoclonal antibody that specifically binds to said immunogen; and (iii) using said monoclonal antibody producing cell to produce said monoclonal antibody

that specifically binds to said immunogen, or using said monoclonal antibody producing cell to produce a hybridoma cell that produces said monoclonal antibody and using said hybridoma cell to produce said monoclonal antibody.

30. A method for producing a monoclonal antibody, comprising (i) immunizing the transgenic animal as in any of claims 1-26 with an immunogen, (ii) isolating a monoclonal antibody producing cell from said transgenic animal wherein said monoclonal antibody producing cell produces a monoclonal antibody that specifically binds to said immunogen; (iii) isolating from said monoclonal antibody producing cell a monoclonal antibody nucleic acid which encodes said monoclonal antibody that specifically binds to said immunogen; and (iv) using said monoclonal antibody nucleic acid to produce said monoclonal antibody that specifically binds to said immunogen.

31. The method according to claim 29 or 30, wherein said monoclonal antibody has a human idiotype.

32. A method for producing a fully human monoclonal antibody, comprising (i) immunizing the transgenic animal as in any of claims 1-26 with an immunogen, (ii) isolating a monoclonal antibody producing cell from said transgenic animal wherein said monoclonal antibody producing cell produces a monoclonal antibody that specifically binds to said immunogen; (iii) isolating from said monoclonal antibody producing cell a monoclonal antibody nucleic acid which encodes said monoclonal antibody that specifically binds to said immunogen; (iv) modifying said monoclonal antibody nucleic acid to produce a recombinant nucleic acid encoding a fully human monoclonal antibody; and (v) using said recombinant nucleic acid encoding a fully human monoclonal antibody to produce the encoded fully human monoclonal antibody.

33. A monoclonal antibody produced by the method according to any one of claims 29-32.

34. A method for neutralizing an antigenic entity in a human body component, said method comprising contacting said body component with a polyclonal antisera composition according to claim 28, wherein said polyclonal antisera composition comprises immunoglobulin molecules that specifically bind and neutralize said antigenic entity.

35. A method for neutralizing an antigenic entity in a human body component, said method comprising contacting said body component with the monoclonal antibody according to claim 33, wherein said monoclonal antibody specifically binds to and neutralizes said antigenic entity.

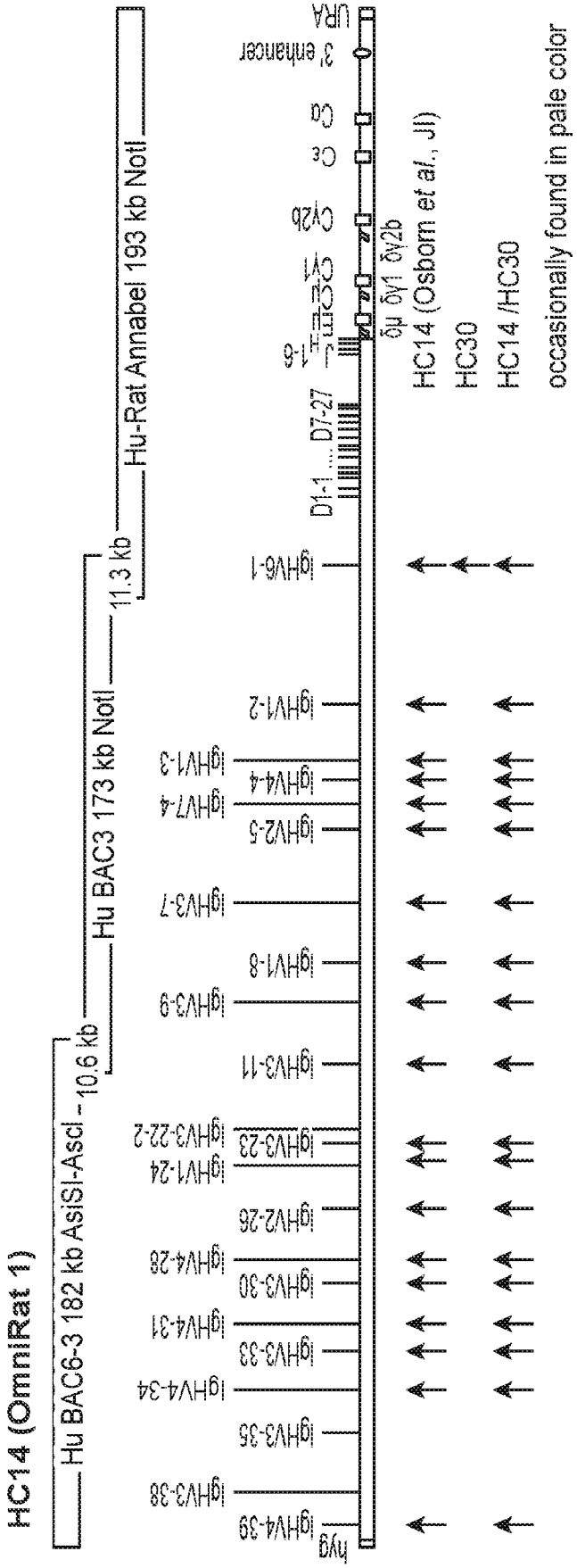

HC14 (OmniRat 1)
Hu BAC6-3 182 kb AsiSI-AscI
10.6 kb
Hu BAC3 173 kb NotI
11.3 kb
Hu-Rat Annabel 193 kb NotI
hγ9
IgHV4-39
IgHV3-38
IgHV3-35
IgHV4-34
IgHV3-33
IgHV4-31
IgHV3-30
IgHV4-28
IgHV2-26
IgHV1-24
IgHV3-22-2
IgHV3-23
IgHV3-11
IgHV3-9
IgHV1-8
IgHV3-7
IgHV2-5
IgHV7-4
IgHV4-4
IgHV1-3
IgHV1-2
IgHV6-1
D1-1 ... D7-27
JH1-6
δμ δγ1 δγ2b
Cγ2b
Cε
Cα
3' enhancer
ULRA
HC14 (Osborn et al., JI)
HC30
HC14 /HC30
occasionally found in pale color

FIG. 1A

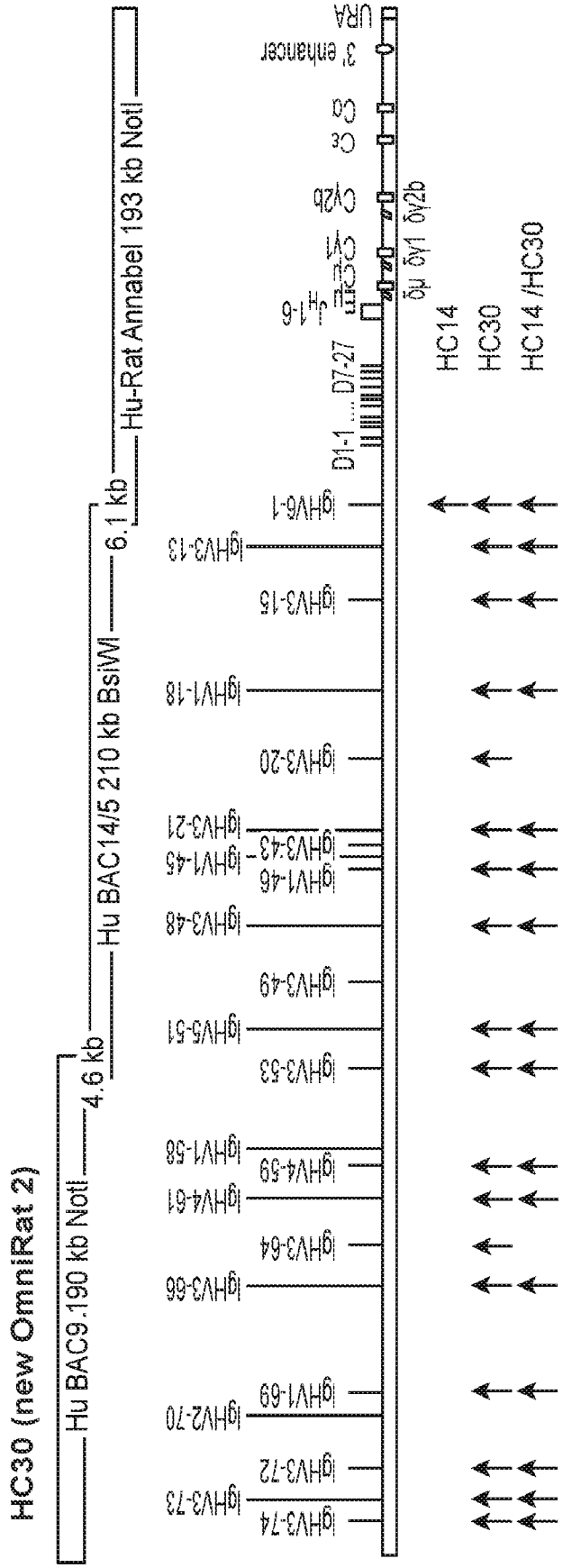

HC30 (new OmniRat 2)
Hu BAC9.190 kb NotI
4.6 kb
Hu BAC14/5 210 kb BsiWI
6.1 kb
Hu-Rat Annabel 193 kb NotI
IgHV3-73
IgHV3-72
IgHV2-70
IgHV1-69
IgHV3-66
IgHV3-64
IgHV4-61
IgHV4-59
IgHV1-58
IgHV3-53
IgHV5-51
IgHV3-49
IgHV3-48
IgHV1-46
IgHV1-45
IgHV3-43
IgHV3-21
IgHV3-20
IgHV1-18
IgHV3-15
IgHV3-13
IgHV6-1
D1-1 .... D7-27
JH1-6
Cμ
Cγ1
Cγ2b
Cε
Cα
3' enhancer
URA
δμ δγ1 δγ2b
HC14
HC30
HC14 /HC30

FIG. 1B

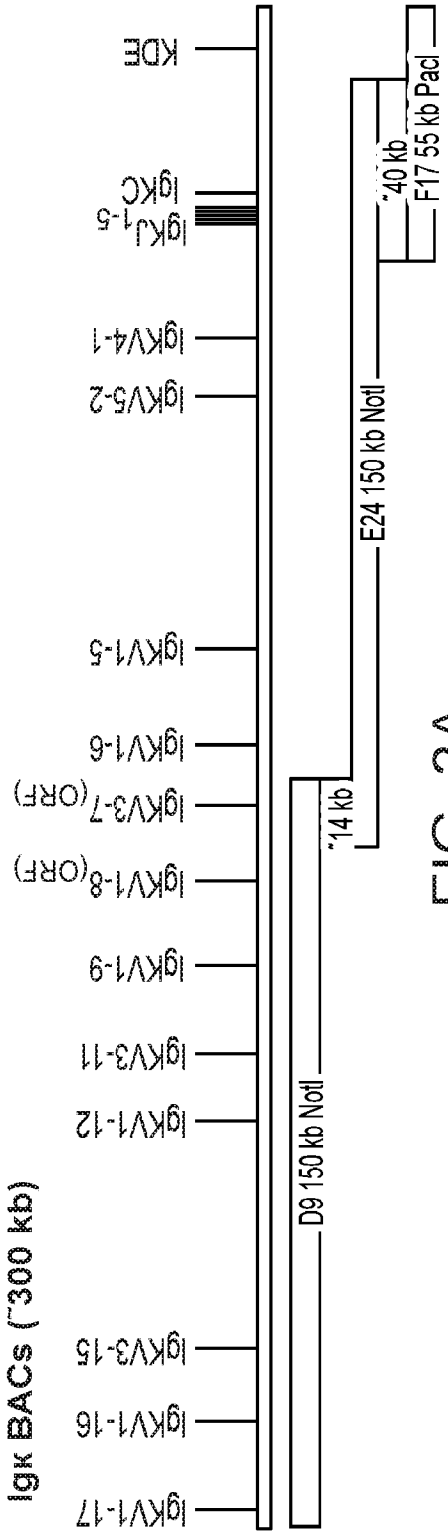

Igκ BACs (~300 kb)
IgκV1-17
IgκV1-16
IgκV3-15
IgκV1-12
IgκV3-11
IgκV1-9
IgκV1-8(ORF)
IgκV3-7(ORF)
IgκV1-6
IgκV1-5
IgκV5-2
IgκV4-1
IgκJ1-5
IgκC
KDE
D9 150 kb NotI
~14 kb
E24 150 kb NotI
~40 kb
F17 55 kb PacI

FIG. 2A

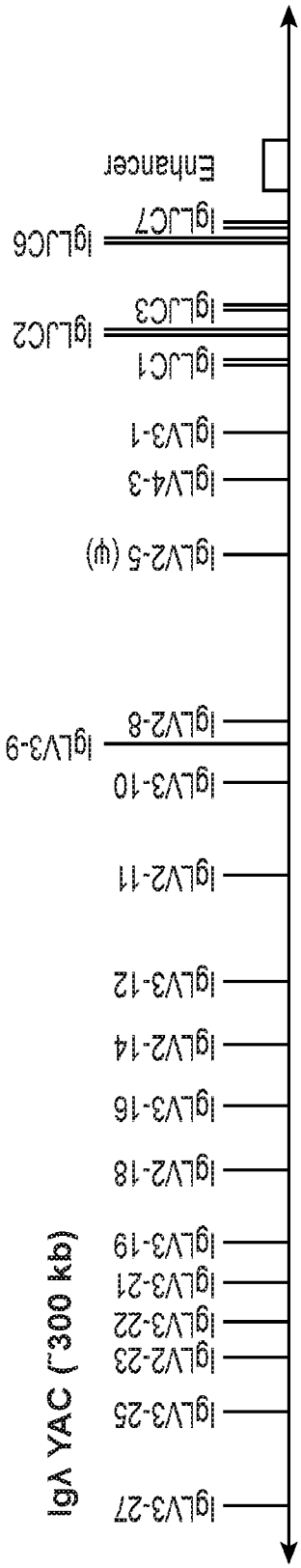

Igλ YAC (~300 kb)
IgLV3-27
IgLV3-25
IgLV2-23
IgLV3-22
IgLV3-21
IgLV3-19
IgLV2-18
IgLV3-16
IgLV2-14
IgLV3-12
IgLV2-11
IgLV3-10
IgLV2-8
IgLV3-9
IgLV2-5 (ψ)
IgLV4-3
IgLV3-1
IgLJC1
IgLJC2
IgLJC3
IgLJC6
IgLJC7
Enhancer

FIG. 2B

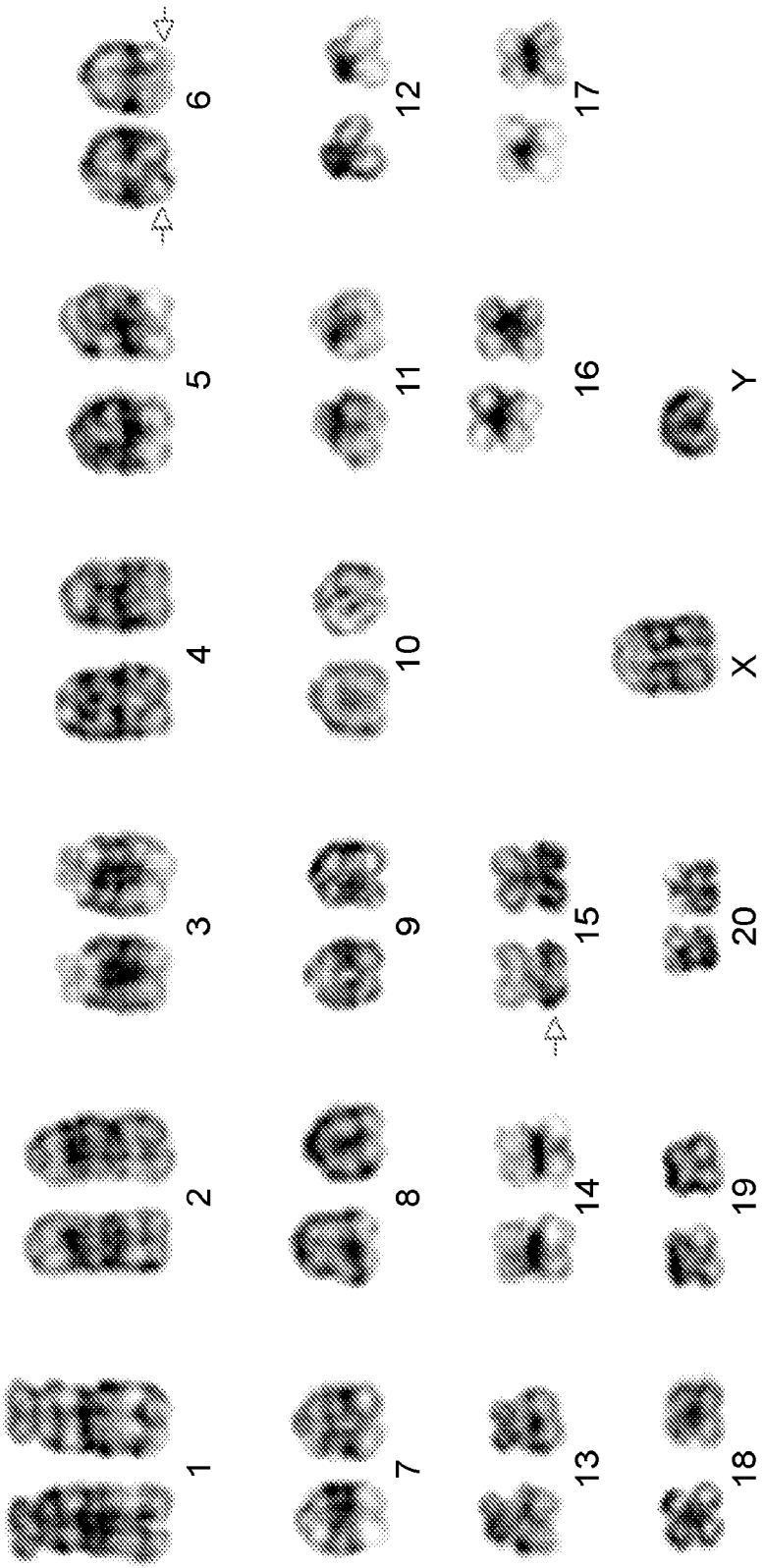


FIG. 3

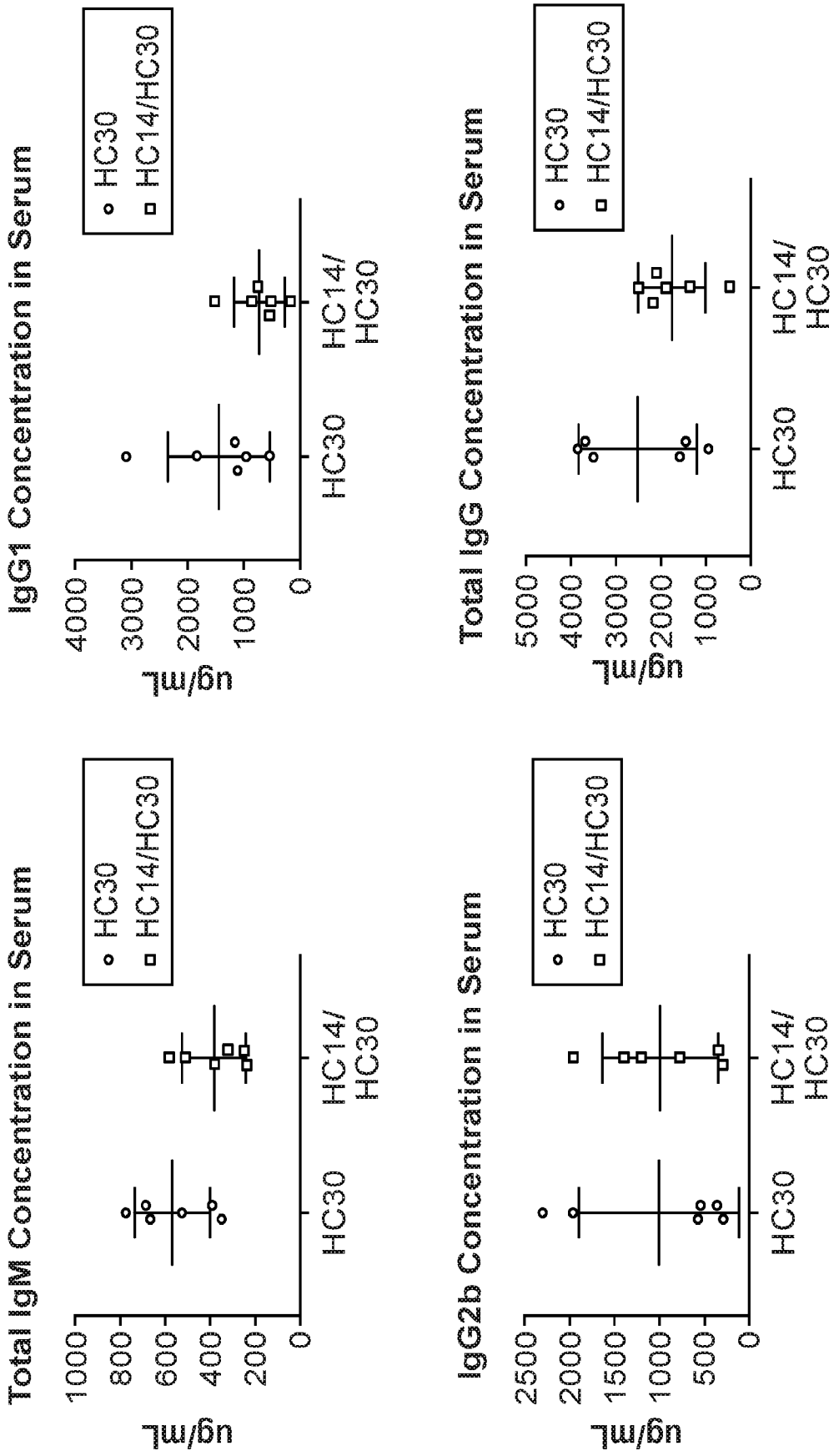
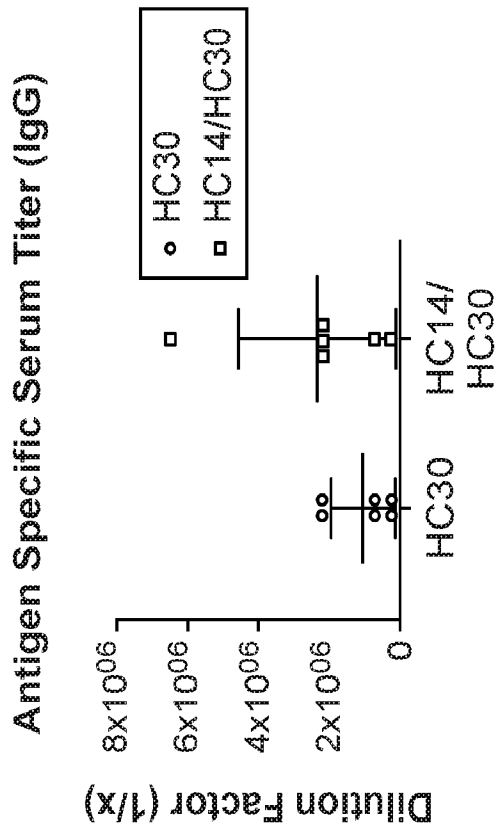

IgG1 Concentration in Serum
ug/mL
4000
3000
2000
1000
0
HC30
HC14/HC30
HC30
HC14/
HC30
Total IgG Concentration in Serum
ug/mL
5000
4000
3000
2000
1000
0
HC30
HC14/HC30
HC30
HC14/
HC30
Total IgM Concentration in Serum
ug/mL
1000
800
600
400
200
0
HC30
HC14/HC30
HC30
HC14/
HC30
IgG2b Concentration in Serum
ug/mL
2500
2000
1500
1000
500
0
HC30
HC14/HC30
HC30
HC14/
HC30

FIG. 4


Antigen Specific Serum Titer (IgG)
Dilution Factor (1/x)
8x10^06
6x10^06
4x10^06
2x10^06
0
HC30
HC14/
HC30
HC30
HC14/HC30

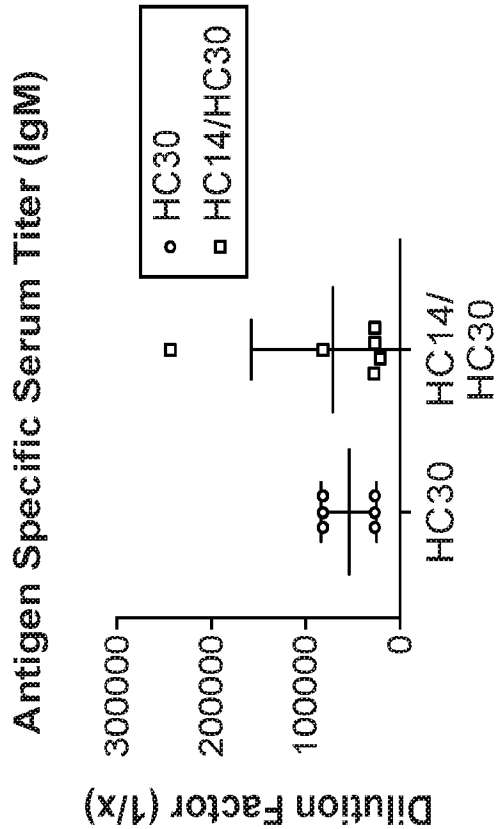

Antigen Specific Serum Titer (IgM)
Dilution Factor (1/x)
300000
200000
100000
0
HC30
HC14/
HC30
HC30
HC14/HC30

FIG. 5

Predicted BAC9 (CTD-2011A5) sequence

- [Human VH3-74 → VH3-53] is cloned as a ~184 kb *Hind*III - fragment into pBeloBAC11.
- The entire human sequence flanked by short stretches of vector sequence can be cut out as a single 185 kb NotI- fragment. The NotI sites are in red font and boxed.
- The vector sequence is highlighted in grey.

Primer 1053 [redacted]
Primer 1054 gcatctgctttatcacatgcagacacagc

AAGCTTGTTTGGTGAGAGTGAAACGTGACTGTGGAATTGATTCTTTGTTGTGCAAACCAGAAGAAATTTTGAATTTTGTCAGA
ATCAAAACGGAGTCACTTTTGTTAAAACTTTTGCAAATGGGACTGGGAAAGGCCATAGAAGCAGGGTTCTCATACACTTACAC
TTGGTAACAAGAACTACCACAAATAGAGCCTAAAAAACACAACCTTGCACAAAATCCACCACAACTTTAGGAAAAAGCTACCC
CCACAAGGATATGTCCTCATGTACTGTGAGTCCAACTTTCCACTGTTGCCACCCTTGTTATTAATCTTTGCAGCCCAGGAAAA
TTGTCTCAAAGCAACTTAGCAACTTACTTAGCCCTTCTTATTTTAACTTTAACTGCCTAAGAATTTATACCGTGAAGTAATTG
CTTCATTTAGTGTTAATATTAATGCCCTTTTGACAATCTTTGAAGCTCTTTTTTTCTGATATTTCTTCCAACATAAAGAATGG
GAGCTTTTTCACCATATAAAGAATTTTTAGGAAGATATGATGGAAAGGGAAACTCAATGTATTGTTCAGTGTTTCTGCCTAAC
ACATCAATCTCTTAAAATATTTT[redacted]TAACACTGGAGATAAAAGAAAAAAATGCACA
GACCTTCCACATTCCAAATCATAAAGTGGTACTGGATGTGTTTCTGATGAAGTGAACCATGGGTCATAAGTGCTAGTGCAAGT
AGCTTTGGAAAATGGAGTTCATAGCTTCTTAAAGTTTTGCTAGTTTTAATTTAAGAATGTTATTTACTATTTCTTTTTAGTAC
AAGCTTTCCAGAAGATTCTTGATGGTAATGGAAGTGTCGCATTTAAGAATTACAAATGACTCACAGAGTTACTTTGTAATTTT
TTCTGTAGGGTGTACATGTCAGTCACTTGACATAAAAGCTCATATGTCACAGATAGAAAAATGAAAATTGAGCCAATTTTAAT
AACTGCAGTGGAAATAGTTTTTGGCAATGAGTGCTTCAAGACAACCACAAAATAAATCGGCAAAATATTAAAATACAGCAGGA
ATCTGATCTCAGTTTCTCTGCCTTATAAGAACAAGGCTGTCCCACATCAAAATTATTATTCAAGCTCTAGGAAAAAATACACT
TTTGGATTCTGGAAGCTAAAAGCTCTCTCCTTAGATAGTGCTAAAGTACTTGTGAAATGCAGAGTTGTGTTCATGAAAAAGAT
GACTTTATTGTGATTTTTTTTTTTTTTTTTTGCCTGTTGACAACTCACCAATCTGTCTCAGATGTAAAGCCCTGCTCTATGGG
TTGAATGTGGTTGCACATGACTGGCAGAGACTGATTATTCATAACTCCAGGTGCCCTGTCTTTGGAGCAGCTACAGGAGTCAG
GCCCAGACTAGAAGAGCCCACACTGACCTTCTGCATCACTTATGCTCTCTCTGGCCACTACATCACAAACAGTGCTTATGACT
GGGCCTGAATCTGCCAGCCCAGGAAAGGGCTGGAATGGATGGGGTGCATTGGTAGTGATGGTGGGGGTCCTACTAGCCTGTGG
CAAATGGAAGCATCTCTTTTTTTATCAGACTGAATAATATTGTAGTGTTTTCTTATACCACATTTACTTCATCCCTTTGTGCAT
TAACACTTAGGTTGTTTTTATATATTGGCTGCCATAAATAGAGCTGCAATTAATATAAGAGCACAGGTGTCTTTACAAGTTCA
TGATTTTATTTCCTTTCCCTGTATTTCCAGAGAAGCGTTTGCTGAGTCATATTGTATTTCCATTTTTGATTTATTTATGAGCT
GCTATACTGTTTTTCATAATGGTGCAACTAAAAAATGGTGTAGTCATCATGAAAAACAGTTTTAGTTTTTGACATAATCCAAA
CACAATGTTTGAATCTGGTTATCTATAGGAGTTTCTAGTAAAATTGGTGAATGTAAATTAAAAAGCAGTAAGAAAAATCTGCA
ATTCAGAAATAGTGTACCCAGATGGTCTTTCTCTCCGAAATGAAAGAGAAATAAACTATTTCTCAGGTGAGATAAACTAAGAT
ATTTTCTTCACACTTGACCAGTCATACAAGAAATATTCAAGGGAATTTTTGTATAAAAGCCAGCATATGAAAACCATCAGCTT
GGAAAAAAACACACAAAACCTATATTTCAATGGTAGAAACAATTAAAAAAGGAGAAAAGAAACAAACATTATTACTACAAAAC
AACATCAAATCATAAAACCAAACAGAAAGAGAATAAACAAAGATAGAGATATATACATATATACAAACAATCATAAAACAATA
AAGAAAATAATTTGAGTAAATACTTATAAATAATAACCTTATGTAATAAAATTCCTCAATTAAAAATACAGTATAAAAATTGA
TTTTATTAAAGTCCCAACTCTATGCTGCTTACAAGAGACTCAAATCATCTGAGAATCTACACACAGACTGAAAGTGAGTGGGT
GGAAAAAAGATATGCTACAAAAATAGAAACCAACAGCACAAATAGCTCTACTTATATCAGACACAAATTTTAAGTCAAATGCT
GTAAAGGGAGACCAAAATGGACATTATATAATAAAAAATGATCAATGTAGCAAGAATACGTAACAACTGTAAATATACATATA
TACATATATGTTATATATATGTAACAAGAACACATAATTGTATATATATACATATATACACACACACATATATACATATGTAC
CCACACCTGAGAACTCAAATATGTAAAGCAAATCTATTACATAGTAAGGGATAGATACTAACCTTATACAATTATAGTTGGAG
AATTTAACACGTTATTTAGCATTGGATATGTTACCTAGCCAAAAATTAACAGACAAACATTGGATTTAAACTGCACTATATTC
CAAATGGACCTGAATTTACAGACCATTGCACCAAACAACTTCAGAACACATATTCTTTTTTTTTTAAAAATTAAATGGATGTG
TTTATTTATCTTTTTTTATTATTATTATACTTTAAGTTTTAGGGTACATGTGCACAATGTGCAGGTTAGTTACATATGTATAC
ATGTGCCATGCTGGTGTGCTGCACCCATCAACTCGTCATTTAGCATTAGGTATATCTCCTAAAGCTATCCCTCCCCTCTCCCC
CCACCCCACAACAGTCCCCAGAGTGTGATGTTCCCCTCCTGTGTCCATGTGTTCTCATTGTTCAATTCCCACCTGTGAGTGAG
AATATGTTTGGTTTTTTGTTCTTGCGATAGTTTACTGAGAATGATGATTTCCAGTTTCATCCATGTCCCTACAAAGGACATGA
ACTCATCATTTTTTGTGGCTGCATAGTATTCCATGGTGTATATGTGCCACATTTTCTTAATCCAGTCTATCATTGTTGGACAT
GTGAGTTGGTTCCAAGTCTTTGCTATTGTGAATAGTGCCGCAATAAACATACGTGTGCATGTGTCTTTATAGCAGCATGATTT
ATAGTCCTTTGGGTATATACCCAGTAATGGGATGGCTGGGTCAAATGGTATTTCCAGTTCTAGATCCCTGAGGAATGGCCACA
CTGACTTCCACAATGGTTGAACTAGTTTACAGTCCCACCAACAGTGTCAAAGTGTTCCTATTTCTCCACATCCTCTCCAGCAC
CTGTTGTTTCCTGACTTTTTAATGATTGCCATTCTAACTGGTGTGAGATGGTATCTCATTGTGGTTTTGATTCGCATTTCTCT
GGTGGCCAGTGATGGTGAGCATTTTTTCATGCAGAACACATATTCTTTTCTTCAGCGCATGTGATACTCTTCAGAGTTGATCA
TATATTAATACAGAAAATGTATCAAAAAATTTAAATAAAATTATACCGACGTTTTATCTGACTAAGATAGAGTCAAAGATGGA
ATCAAACTAAACATCAGTAACTGGAGGAACTTCTTTTTTTTTTTTTTTGAGATAGACTCTTTCTCTGTATCCCAGGCTGGAGT
GCAGTGACAGAATCTCGGCTCACTACAACCTCCACCTTCCGAGTTCAAACCATTCTCCTGCCTCAGCCTCCTGATAAGCTGAA
ATTACAGGCACCTGCCACCACTCCTGGCTAATTTTGGTATGTTTAGTAGAGAGGGGGTTTCACCATGTTGGCCAGGCTGGTCT
TGAAATCCTGACCTAAAGTCATCCACCAGCCTCGGCCTCCAAAGTGCCGGGACTACAGGCATGAGCCACCACCCAGCCTGGAG
AAAATTTCAAAAAAATATAAACACAAAAATTAAACAAATCACTCTTACATGGCCAATGGGTGAAAGAAGACATTAAGAAGAAA
ATAAAAAATGTATGAAACAAACAAAGAAACACAACATACCAAATCTTATGGCGTTTAGTCAAATCACTATTATGAGGCAAGTT

FIG. 6

TAGAGCAATAAATGCCCACATCAAAAAGTAGAAATATCTTAATTAATCAAAATAACAATGCATGTTAGAGAACTTGAAGAACA
AGAAAAAGCTAAATTCAAAATTATTTTTAAAAACAATAAAGAGCAGATTAGATATAAATGGAATTAAGACTAAAAATACCAGA
AAATATTAAAATAGCAATAGTCTTTTTAAAAAAGATAAGCAAAATTGAAAGCCATTAGCTGGGCTAACAAAAAAATATAAAG
AGCTAAGACATGAATAAATGAGGTAGAAACAGAAGATGTCTCAACTGATATCCCAGAATTAAAATAAATTAGGAAATACTATA
ATAAATTATGTGATAAATGTGAAAACCTAGAGGAATTGGATACATTCCTGGCCATATACTACCTAACAAGATTGAAAAAGGAA
AAAATAGAAAGCCTTAACAGACCAATAAAAAGTAATGAGAGGGACTCACTTAAAAAATCTATATCCTATTGAACATAAATAAA
AAAACCCAAATTACTAGCACAGCAAATCAAACAGCATTTAAATACTAATACTAATACTAATACAGCATGACAAAGTAGAATTC
AACCCAGGGATTCAATTATGCTTTAATATACACAAGTGAATAAACATGATATATCACGTATATACGACAAGGATGAAAAACAT
ATTTTTACTTTAATAGATGCAGAATAAGTACTTTATAAAACTCAAAACCTCTTCATGAAAAAAACTCTCAATTATGTGTAGAA
AGAACAACACAATAAGACCACATGACAAGTTCATAGCTAACATCATACTTAACAGAAAAAAGTTTAATGCTTTTCTTCTGAA
AACTGGAAAAGACAAGGAAGCCAACTCTCAGCACTTATTCAACACAGTACTGAAGGTACTAGCCAGAGCAGTTAGACAAGAGA
AAGAAATAAAGGGGATTACAATTAGAAAAAAGGTAGCCAAATTACCTCTAATTTCAGATGACATAATCATATATATACTAAAG
ACTCTTGTAAATGCTCTTAGAGCTGATGAATTTAGTAAAGTTTCAAGATACAATATCAACATAGAAATCTCAGTGGGGTTTCT
ATACACAAACAATAAACTAGGTAAAAAAAATCAAGAAATCCCATTTTCAATAACTACAAAAACTATTAAACACCTAGGAATAC
ATTTCACCAAGGAGGTGAAAATCCGTAAATGAACAAACTATGAAACACTGATATAATTAATTGAATGAGACAAACACAAAATA
AGAAGGACAATCTGTATTCATGAACTGGAATAATTTATATTGTTAGAATGACCATAATGCACATGACAATCTACATATTCAAT
GTCATCTCTATGAAAATACCAATGGCATTATTCACAGAAATATTAAAAAGCATTATTAAAATTTGTATACAATTGAAAATACC
CCAAATGACTAATGCAGTCTTGTGGATAAAAAACAGAGGTGGAGGTATTAACAACCAGATTTCAAAAAAAATTATAAAACTGT
AATAACAAAAACAGCGTAGTGCTGGCATAAAAATCCATGGAAAAAAGTAGAGAAACCAAGACATTAATCCATATATTTATAGA
TAACTTATTTGCAACAGAGGCACCAAAAATATTTATTGTGAAAAGAAAAGTATCCTCAGTAAATTGTGTAGGGAAAAACTGAA
TATCCATATGCAGATGAATGAACTTACATTCCCACATTTAACTGTATATAAAAATGAAATAAAAATAAGTTAAATACTCAAAT
GGAAGACCCAAAACTATAAAGCTGCTCTTAAAAACTTAGAAATAATGCTTCATGAAATCTGTCTGGAAAACAATTTTATAAAT
AAGACCTCAAAAGTACAGTCAACTAAATAAAACACAAACGAATTAAATTTTATCAAACTAAACAGTGTTTACACAGTAAAATA
ATCCAAATATTGAATAGATAACATAAAAGTGGTAAAATGTATTTTAAACTATTAATTAAACAGGCTATTAATATCCAGAATAT
ACCAGAAAAATAAATGTCTCAACCACAAAAATATAAATAATCTTATTTATAACAGACAATTAACCCAAATAAGCAGACGTTT
CTCAAAGAAACACATACAAGATGCCAGAAAATATTTGAGAAAAAATGGTCACCATCGGTAATAATCAGGAAAGCACAAATTTA
AAGTACAATGAAATATTATCTCACCCCAGACAGAATAGCCATATTCAAATACATAAAAATAGTGCTAATGTGGATGAAGATAA
AATGGGACATGTATACACTGTTGATGAGAATGTACACTCATACAGCCACTATGGAGAGACGTATAGAAGTTAGTAAAACCACA
AATGCAACAATCATATGATACAGAAATTTTACGACTGAACATTTGTCCCAAGGACAGGAAATTAATATATTGAAGAGGAAAAT
CAATATTTTGATGAGATTTCTTCACTCCCATGTTTATTGCAGCCCTGTTCACAGTAGCCAAGTAATTGAATCAACCGAAGTGT
TCAATATAAGGTGAGTAGAGAAAGATGATGTGGAATATGTACATAATGGAATTCTACACAGCCATGAAAGATTAAATTGTGTC
ACTCATAGAAACTTGCATGTAACATATAAGACTCTATGTTAATTGAAAGAGCCAGGAACAGAAAGCTAAACACCACATGTTTT
CACTCCCATAAAATAGTCAAGAAATATCCATAAAACATAAATAATTGAAATTGGACATGAACTATAGAAACAATAATTGTCAC
CTGAATATTTATTTTCCTTCAAATAATATATAATTCAATGATAGTAAGAAGAGTCCTGATAAATAAATCATGTTGAGATAAAG
AGCTACTGAATTGTGCATTCCACACTAAATGGAAACAATGCCATAAGATCCAGTGTTGTGTAGGATCTGTTTACCTTTTTACC
TCAAATACTACAAGTCACTCCCTTGTTCTAATCACCCCGCAAAACTGATATTTTGTTGCTTTATGTTATGTCAGTAAAAATGA
TTCCACATTGGAAGCTTCATGTGTTGCTCAGAAATCACCCTGTTGATAAAATGAGCACAACTACAGTTACAACCTTTCTGTAG
ATATTTTCTGCATATGATCCTCACTTTTTATTTGTTGTTTTTGTTCACAGTTTCTTTAAGCACTCAGAGTTATATAGCATATT
TTCAGCATATTTTAATTATTTTCCATTGTTATGGTCAGTGCTCCTGTGGGCTCAAGAGTCAGGTGTTGTGTGACTGCCAGTTG
ACTTCACTGCCACCTTTACCTACACAAAACACTGCAAGATGAACCATGATGTGTAAGAACCCATCCACAAAGTGCTTCAAATA
AAGACAAGGTGACTTGTGTATAGATTTAGTGAGACTGGGGAACAGTTCACGGTGTTATGTTACAGAGGAGCAGAAAGGTGAAT
CTCTCTCGGAGTTATTGAGGGTGTAAGAGCTGCAGTTTTGGAGGGTGGTGAAAGGCACTTTTGAGTGGGAAGCCCTAGAGCAT
GTGTGAAAGCTGAAGGAATGATCACCATGCACATGGACGCTGATGAGGCATGTGGTAAGGTCCATTCCCTCCAGATGTTCCTG
GATGGGCGGTTGTAGGATGGCTCATGTATATGAAAATGTGGGCAGGGCTGAAATAGGAACAAGGCCATCATCCCACGGGAATG
CGAGAAAGCAAAACAGAGATGGACACCCATGAAGAGAGCTCATTAGACCTGGTGAAGGAAAGATAGGAATCTCTTCCAAAGGC
TCCGCTGTTCTTGGCTAAATATGAATTGTGGTGATAGACTGAAAATAAGGAGGGGAAGGGAGATATGACTCAAGAGAGGAAAA
ACCCTAAGACAGCATAAACCAAATCTACACAGAACAATCACATGGTAGATGCCAGGGTGGGGCTGAAACAGGAGCTTCAATCT
ACTGGGTACCTAGTTGAGATCCTTTGACATTTCTTGTGAGGTAATTCTAGTGATGATGAATTTCCTCAGTTTTCCTTTGTCTG
GGAAGTATTTCTCTATCCTTCATTTCATAAGAGATGTTTTATCAATTTAGGTTCTTGGTTGGCTGCTTTTTCCCCCCAGAAA
TTTAAATCCAGTTATTTGCTGCATAACAAAGTTTCTGCCAGTAACAGATGGTGGTTCCACGGTGCTATACTTCCTTACTTATC
TATATCTCTTTATGTTTAGATACACAAATAATTACTACTATGTTTCCATGGCCAACAGTATTCACTACGGTTGTTTCTGAGTC
ACTGGGGTGTTGCTTTTTCTGGCCAGAACCCTCTGTGGCCAGTGGCACTTTTGCCTGAGTTCTTGTCCTACATGTGGAAAGAA
TGAAGTATGCAGCCATGTGGAGGGTAAGCAAGACAAAGCCTAGCTTCATTAAGCATTAGAGCATCTCAGAGGAGACCCCCAGT
GAGTAGCTCCTCTCTGTAGGCAGGTAGACTGGTTGAGTGTTCAGCTCTAAGCAGAGAGGGTAGCTCCTCCCTGCAGCCGGTCG
TCCTGTGGTCTTCCCAGTTCTCAGGAGAGAGGGTAGCTCCTCCCTGCAGCTGGTCGTCCTGTGGTCTTCCCATTTCTCAGGAG
AGAGGGTAGCTCCTCCCTGCAGCTGGTCGTCCTGTCGTCTCTCCATCCTCTGTCCTGCTCCAGCTGAGGCCAGGGGTTTTTAC
GGACCTCCGAGGGGAGGAAGTGCAAGCCCATTGGTCCATGGGTGCTCATGGGTGGGCCGTAGGAAGCACCACAAGTCCCGACT
CTGGTCTGAGGATCTGGGAGCCCCGGCCCAGCCTTCAGGCCCTTCCTGGGGACCCGCCCCTGTGCACAGGATCTTCCTGCCTC
CTGTTGTAGTTCATGGTCCCTGGGGCTCCGCCCTGACTTTGCTCCAAGATCAGAGCAGGCACCAGCAGCAGGAAGAAGCCAGG
AAGTGGGAGCAGGCACTTCGGAGCATGCAAGAGCACAGGGCTTTTCCTGGGGACCCCAAGAGTGCAGGGGCGCCTGAGGCCGC
AGCCCCCGGTTTGCGGAGCAGGGCTTCTGCCGGCTTCATGGAGCGAGAGGCCCGTGTCTTCAGCCGCAGTTTGGGAGGCTGCA
GCCACAGCCGGGGAGGCAGGGCTCCTTCCTGTTCCTCGACCTCCAAGAGCACAGAGTCCGAGCCCACTGCCCTGGTTTGCGCA
GCTGGAGCCGCACCTGAGAGATGAGAGCTGCTGCCTGCTCCTGGCTCCCACCGGCTCCGTGGAGCATCAGCCCCTCCACCCCT
CCTTGCAGCCTGGGCAGGGGCTCCTGATCCTCTCTGGGCCCTGGCCGGCGTCCAGGGCAGGAGTGACATCTCCACAAGCTCCC
TGCATTGCCCCGGTGCTCAGGGAGGCCCGGGCAGAGCTGATGACGACCCCGGCCCGTAGTCGGGAGTGGCGGCCTCCATGGTC
ACCCTGACATGCGGCTGAACCCTGGGGACGCGGCCCAAGCAGCCTGCACAGAACCTCCCAAGGCCCAGGAACCCCGCACCCTA

FIG. 6 (Cont. 1)

GGCGGGGTGGGCACAGCGGCTGCTCCGCTGCCCGGGTTTTCAAGGAGGCGCCACTTCCACTTCCCTCCCTGGAACCCCGAAGT
TTGACATGGGGGCTCCTTTCTGCCTTGCTCCGCAGCTCCCCTTCCCCCGGAGTGGAGCCCCCTGTTTCCCTGGCGTTCCCTCC
CACAGCTGCAGTGTTCTCCATCGGTGTCATCACCTTCCAGCTCTGCTGCCCTGCTCTGCAGACTAAGGCTCTGATTCCATAAG
AGAGGGGAGCTGCTTCCCAGTAGAACCTTGCTGGGGAGCTCTGTTCCCATCTCAGTTCCTGAGGGGTTAAACCAGTGCATTTA
GGATACTGGTTTTGGTGGTTTGCCCCTGTTGAGTAATTTCTTAGTTCTCTAGTGGGTGTAAGAGACTTGGCTCTGGAAGCATT
TCAGAAGTGTGGGCTCTGATACACCCCAGACAGACACTTTGGGAAGGGAAGATTTTTGTGACTATTCTCATTATAAGGGAAAG
GCATTCAAAAGAATAGAAAAACTCTCCAGTATGTGGTTCCTGAGAATTTCTCACTAAAAACATGCTTATCACACTCGACTCAA
AACAGTTCAATGTATATTAGTGTATTTTATCTTGTACTAGCCTTTATTGCATTTGGTGAACTCTGCCCCAGTTCAGCTCATAC
TCTAGCTTTGATTCTCCCTACAAAAACTTGTCTCTCTCTAGATTTCAGATTTGTTGATTGTCTTAAAATTTCAATGATCTGAA
GTATTAAAGAAAATTTGCAAAAGTCCATTTTCTCTGATTAACAGTTATTGTTGATTTTATTCTTGTTGTAAAAAAAAGAAATT
CTCATCTATGTACATTTCAAACCTGAATAACAAAATTTTTATTAACACCAAAAATAATAAAAGAATCCAAATATTTATCAGCT
GCCTAATAGAAAAACAAATCATGGTAACATTGTTCGCTGGAATATTACCCATCATTCATAATAAGGGAATGTCTGATACACAA
AATAAGAAGATAAAATTATCAAGTATTTAAATTGAGTAAAATAAGCCAAACAAATAAGAGTATGTATGATTCTATTTTTAAAA
ATTCTGGAAAATGAAAACTGATCTAAAGTAATATAAAGAAGATTAGTAGTTTCCTGGGAATATGTTGGCAGAAGGGAAGGAGA
AAGGATAAGGAAATAGAAATAGGAAGTAGAAGGACAGAAAAGAAGTTGAGGGAATTTCACTTGTCCACCTTCCTTATAATGGT
AATAGTTATGCCATGATTATCAGTTTTACACTTTAAATATGTAAAGTTTATAATCTGTCAATCAAATCTTATAAAATGTATTA
TGAGGAAACAAGTTGAAAATTAGACAATGTAGGAGTGACAGAAAGATAGATATGAGTATGTTGAATGTCAGAGATACCTGAAA
GTTTATCTACCTGAACCCTAGTTCTCTCCATAGTTTAAGGTAAACAGGAGAGTGCAGGAAAATCATCCATATTCTGATTAGGC
AGTGGCTTCTGCAAACCACACTAGGCCTGGCCGGCTGTGTCCTGGAGTTGGCTAAGGGAGGAGTCAGGGCCAGTGGTGAGAAG
TGCAGGCCCAGATACCAGAACTCACTCATCCCAGACATGAGCTCTTAGATACACAGAGAGCCCATCCATGTGTGGATTTATCT
TACATCTGTAAGTAGAGAACATTGACTCTTACAGAACATAATTTACACACATAGGTAAATCTGAAATAAGGTGATCAGTGTGA
AGATTTTATCACAGCACAGTTTCATAATAAGCACAATTTCTCAAATCCCATTGTTGTCACCCATCTTCCTCAGGACACTTTCA
TCTGCCCTGGGTCCTGCTCTTTCTTCAGGTGTCTCACCCCAGAGCTTGATATATAGTAGGAGACATGCAAATAGGGCCCTCAC
TCTGCTGAAGAAAACCAGCCCTGCAGCTCTGGGAGAGGAGCCCCAGCCCTGGGATTCCCAGCTGTTTCTGCTTGCTGATCAGG
ACTGCACACAGAGAACTCACCATGGAGTTTGGGCTGAGCTGGGTTTTCCTTGTTGCTATTTTAAAAGGTGATTCATGGAGAAC
TGGAGATATGGAGTGTGAATGGACATGAGTGAGATAAGCAGTGGATGTGTGGCAGTTTCTGACCAGGGTGTCTCTGTGTTT
GCAGGTGTCCAGTGTGAGGTGCAGCTGGTGGAGTCCGGGGGAGGCTTAGTTCAGCCTGGGGGGTCCCTGAGACTCTCCTGTGC
AGCCTCTGGATTCACCTTCAGTAGCTACTGGATGCACTGGGTCCGCCAAGCTCCAGGGAAGGGGCTGGTGTGGGTCTCACGTA
TTAATAGTGATGGGAGTAGCACAAGCTACGCGGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAACGCCAAGAACACG
CTGTATCTGCAAATGAACAGTCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCAAGAGACACAGTGAGGGGAAGTCAATG
TGAGCCCAGACACAAACCTCGCTGCAGGGGCATCTGAGACCACGAGGGGGTGTCCTGGGCCCTGTGAACTGGGCTGCTCTCCG
TGGCAGCGGCTGGTGGTGCTAAAGGCTGATTTTCTCTCAGCATCTGGGGCTGATTCATCAAGTTTCCTCAGAGACCTTTCAGA
TTACAATTCTGTACTTACGTTTAATGTCTCTGAATGTGACACTTTCCTTCCCTGGTGTGTCTTTGTTTTTGTGACAAGAGGAC
ACATTCTCACCTCCACAGAAGCCCGAGTGTCACTTTGGGGACAGAAATGACCCTGCCCTGGTCACCAGAATCAGAGTCCCGAG
GAAGCCCAGGAGGACCTGGGAAGTGTTTTTCAATCAGACTCAGGGCAGGCGTCTCCGTGGGAATCTCTGATTGGAACAGGCTT
TGGGATTCAGATTGGGACCAAGAGGGAGGCTCACCCAGGGCCAGGGTCCTTAGAATCCTGACAGTTTTCACAGTAACCCCATC
GTCCTTTAAAACTGAACATCTAACTCAGAACTGACCCATTTGGTCCTTTCTCTGTAATCCATTTTCCTTTTCTCTAGGCTTCA
TTCTTACACTTCCCTTTTCACCTTCATTCTGAAAATGGAGGGTGTGCTTCCTGTGGTCTAAACCACAGGCCTCAGATGCATTA
CCTGGAACTCAGGTGTGGCTCTGGCTATGGCTCCTGTGGACCTGGCAGGCTGAGGGATCTTTCTCATTCCCTGGTGCCTGCAT
GCCCCTGCTGTCTTCTATGCGTGGATGCATTTGGGAAATGCAAGTGGACACTCATAGTCGTTTCCTCAAATGGGATACTGTTG
TAGAGGTGATCTTGTGCTTCTCACCCTGTCACAGAGCCCCCACTCTCACTTGTGGATTTTTGGGAGAGCTGAGGATGGACACT
TTATTGGGCTGTGAGCTCTGCATGATGGCAATCGTGAGGTCTGGGTGGGCACAGCCAGAGCCAATGGAGCTGGCCAAAAGGAA
AGACAGGACGGAATTCCTGGGAAGTCCTACAGCTGCTGTCTACCATAGAGTTCCATTGTCTTCTCCTCTGCTAGGATTAAACC
AGACCGACCAAGTTCATCTAGGACAATCTTCCTGACCTAGAGAAGTGATGACAGGCTTTAATAACACCTGTATTATACATCAG
AGCAACACCTAGATTAGTGTTTGATTGAATAATTGAGACTATGTCCTAGTCAAGGTGACACACAAAATCAATTATTACCATGA
TTAATATTTTATATTGATTAATATTTTAATACTAATATTAATCAATGCAATATTGATTTAATATTAATTAATATTTTATATTT
GACAATAGAATCAGACTCATGTTATAAATAATTTTGCAAATATATGTATATTATTATTGGTCTTCTGAGCATAAATCTCCATT
AGCCGATTAAGTGTGCATGCATTGGTCGAAGGAGGGCATCCACCCTTTTGAGGGAAAATGCATGGAGGGTAAATGAGGCTGGG
AAGCTGATGGCATATGATGGAAGCCTGTCCCTGAGTGAAGGAGAGAGGGAGGCAGGATTGGGTGGAACTTTCCTACATTTCTG
TGCTGTGCAAAGAAACTCCAGATTATCACTGAGTCTCCTGCAAGTCAAAGTTGCCCCTCAGGAAACCCCCATCACTCCCAGCA
ATGACTCTGCCCCAGATGAGTGCAAGGCTCACTCTATTCCTGAGAAAGGAGCACAGGATATGGGATTTAGCATGAGCCACGTC
ATGGACGTCAGAGAGCAGGAGCTGGGTGCATGATCCAAGTGCACTGTTCTGCCTGTAGGTGGAGAGAGGAAGGTGCATTCCCA
GAGCTAACACACTGTGGATTTTTATACAGAATACACGTTTTCACCTGATTATTGGAAGGCATATGAAAAAATGTGCAGTCCA
CAAACAATTGTAATTTCCAAATTTACCACAATTGCATTATTTCTTCATTCTGCATGATGTCCTGGAACAGAGTTACATTTTTC
ATGGGTATTGTTTCATGGATTGAGGACATGAATTTCACACCTGCCTTTTTAGCCATGTGCAGAGACCTTGAGTAGAGCATGTC
TGGACCTCATCTACACTATCTCTCATGCCCCAAGGGAAAGAGTGGAGACTTGACTGACTGCAAACTTTGGGGTGGGAGCTGCT
CCTGCACACCTCAGAGGCTGCAGAGACCCCAAGTGCAGTTTTATTGAGTTGGGGTGTCTTTCTATGTGGGGGAATTATGGGCT
GCCCCACTCCTGGTGATTGCTGGTCAGCTCTAAAGACGGGTTCAGAATGAGGTCACCTGGTAACCTTTCTCACTGCAGCTCCA
TTATGTAAATTACCACTACCAGATTCCAGGTAATAATGCAAGCTCTATTTTTGCGACCTCATTTCTTATCTTTTTTGTTCAT
AAGTTTGGTTATAGAAAATGTTACCACCTAGTTTCCTGATTCAAATCCTATAATTTGCTGAACTACTCAGGATGTTTTTTAAT
GTGCCCAGTATTTGGGAAATATAAATGAACAGCCATGTGTGGTTCACTGAGTGGACATAGTCAGTTAAGTACATTAGTAAAAA
CATGATTGCTGAATTGTATAGTGAAACTACAATTAGATTTGCAGAAAATTGCCTCCAGTAATGTCTGAAGGGAGAGCCACCCA
GCCAATCCCGTCTCTGGGCTTGGAGGAAGCTCACTACACAGGCCAGGTCACATGGGTGATATCCAAGGTGCAGCTCCCAGCGT
TACTGTGCTATTTTCCAGGAACCAGACATACAACTTGGCATCTCAGAAGAAGATCTCCAAGATTTCCTTTACCTGGACTTCAT
GGGCAGCACAGGACCAGCAGGAGATGCTCAGAACTCACCCAAGGCAGAACCCCAGGGAAGAGCAGGTGCGGAGAGGAACCAGC
CAGGGAACCTCTGACCACCATCTAGGGTTGCCTTCTTTTCCTTCACAGCATGGAGCCCTCAGGAGACCACCCACTAGGTTGTC

FIG. 6 (Cont. 2)

TGTAACTCACGTCCTTCTTGTCTTGAAGCAAAACAGACATAAATATGAATTTGCAGTTAGCCCCTTGAACCTGGGTCAATTTT
TTCTGAGAATGCCAACTTAATCGTCAACATCATGGGCATTATATCAAAATCGAGATGGATATTTAGTCACCAGGAAGACAGTT
TGTCTCATGGTAGAAGTGCTTATTCAATTAAAAATTACATTTTAATGAAAAGGTCTCTAAGTGAGGACTGTTCAAATAATAAA
GTATTAGTGAAGTATCAGAAAAATAAATGGCACCATTATCTTTGGTATCCAGTTAATCTATAAAGCATATCAATATTCATGTT
GTAAGTGGCCTAGGACAAGTTATGGCAGTATTTAGGCTATAAGGAGACATTGCTTTCCTTCTTAGATAGGAATGTCCTTTTTT
ATCATACTTTAAGTTCTGGGGTACATGTGCAGAATGTGCATGTTTGTTACATAGGTATACAAGTGCCATGGTGGTTTGCTGCA
CTCATCAACCCGTCATCGACATTAGGTATTACTCCTAATGCTATCCCTCCCCTAGCCCCCCACCCCCCAACAGGCCCCAGTGT
GTGATGTTCCCCTCCCTGTGTCCATGTGTTCTCATTCTTCAACTCCCACTTATGAGTGAGAACATGCAGTGTTTGGTTTTCTG
TTCCTGTGTTAGTTTGCTGAGAATGATGGTTTCCAGCTTCATCAATGTCCCTGCAAAGGACATGAACAGGAAATTCCTTCTAA
ATGAACTGTGTTTTGACAAATATTATCCAGTGACTCTTCCTACATGGGGTTTCTACATGATCTATTTTTCTTTTCCAAAAACA
AATCACTCAAGTTTCTCATCTCCTGAGTGAGAAAAATTTTCCCCAAACACAATCTCAGTCTAGGTAGACACCTTCATGAATGA
GCCTTCATTCTCAGACAGGCACACACTGTCCCCATGTGGATGCTTCTCTCAGACAGGCACACATATCCCCACATGGTTGGGAT
CATCTGCTGGGACTTTGCCCCATGGGGATCTCTATTATCACTGGGGCAAGTTAGCACCTCGATCCTCATCCACACTGTGGCCT
TTGATGTCTGTGACCTGCCACACCCTGTCTGTCCCTCAGTGTCTAGAATGGTGAAGTAGTCCACCCCAGGGATGGAGGAAGAT
CCCAGATTTTCCTGTGAAGGAGACAGAATGCCAATCACAGAGATGGAAATCTCTCACATCCCTCCTGGGTCATATTCTGGGCA
GGGTCTCTGAAGTCACCCCTGGATCAGTGTCCTAAGATGTCTCCCTCTATTTCCTTGGGAAGAACCCATAGAAAGACAAATAA
GTTTTTCTATTAGGGCATCGTAGAACTTGTGCTTTCTTGTGTGACAAATATAGGTATTTTGACTATTTTAAAAATTAGATATA
ATATTAAGTCTACCAAATATGTAAATATATAAGCTTTATAATGTATCCCTAGAGGGATGTCTCCTGGAATTGAGAATTGAATA
TATATATATATATATATATATATATATTCCAAGATAAATCTTGGTGAACATTATAAAATTGACTCTAATATTTATGTTCAAGA
TGATCATTTCAAAAAAGTTTTAACAACAGAGACCAGATGTATCTTTCCACCAGAAATAACTGTAAAACACAGTGAAATTTTTT
AAACATGATTTTAAGGTATTTTACATCAAATAACAAGGACAGTGATTGCTGAGGTGGGGAAAATATACAAAAGGAGCCCTCTG
ATGAACGCATGCTTTGCTACTTTTTAAAGAGAGTTTCCAGGCCACAGTGCTGAAGAGGAACCAGGTAGATTTGAAGTTGAGGA
AAAGGAGCTGAGATCCCAGACAGGCCAAGAAGTGTGGAGATCACAGACTAGACAGTGGATAGCAGAACACTGTTCAGAGAGTG
AGCCCCGTAGATGGCCGGAGAGAGACCCAGCCTTGGTAGAGTGTGGATCAGTGTATGGGAACCCTGGAAAGTTGTACATGAGA
ACACACCTTACTCTAGGGGGCTTGCCTTAAAATCTAAAATTACCCTAAAATTTAAACATAATCAGTTACAAATTTTAAAACAT
AAAGAAAGACACCATGTTAAAGAAAGATAAAGGAAAGGTGGATTTGCAATATTAAAATATAAAAAGTGTATTTCTGAACAAAT
GATAATACTGATGAGGGGGGACAAGTTTATTCCATCACGGCAAATGATTTAAGAGAAGAACATTCCAAATGCTTATGGCCCTA
ATGAGGAAGCTTCAATCACGAATATAAATAGAGTTATCTCATTACCAGTGTGATGGTGTGAGAAACTTCAAGATTTCCAAAGA
GACAACCTAATCTGGTAAAAATTATAGAAACCCAACCTGTACTATCAAGGAAAATTATTCTGAGAACACACAGTAAATGAAAT
CCATTGACTGACATAAAGTCCTCCTGTTGACTGAAGGGTTATGACCCCCCACAAGGCATATGTTGGAATCTCAACTCCATCGT
GACGGTGGCAGGAGGTGGGGCCTTTGGTCTCCTTTGAAAGGTGTTGAGGCTCCGTTTCATGAATGGAATCAGCGTCCTGATAC
AATACCCCAGAGAGCTCCCTCTTTCCTTCCACCAGGTGTGGTCACAGTAGGAAGGTGGCAATCTATAAATAAAGAATTGGGAC
ATCACCAGATACCAATCTTTAAGTCATCTTTATCTTGAACTTCCCAGCCTTGAAAATTGGGACAAATGCATTTATGTTATTTC
TGAGCCACCCAGTCCATGATATCCTCTTATAGCAACTCAAACAGTCTTAGCAAGTGCAGTGAGGATCACAATACTTGAGAGAA
GAGCATTACCTCTTCTTTACATCTCAGGATCACAGAATCTTGACCTTGGGCTGAACTGACAAGAAGGTGGTGCTTCCCTCTCC
CCCAGATCTCAGTTGAGGTCATGATGTCAGATCTTTATGGTGGAGACTAAATTCCTGCCTGTGATTTGATGGATGCCTTTCTC
CTCCCAGCCTCACTCACAAGACATAGTTTCCATGTCAGGTGTTATAGACCAAGAACAGGTGGACCCCGATTATTCTCACCCCA
GCTCACTTGTAGGGCAGAGGTTCTGGGAGCTTCCTGGGAGAGGAACAGTGAGATCATACAAGTCCATCACTTCCATGCAGTTT
TCTGTACTTAAAGCAGGAGTGTCCTTCTGAGCTGCTTGAACCCTTTCTTCTGCACCAAGGTAGAGACTTCCATGTTTTTCTAG
TGATACAGTCAGGGCATAAAAACAGTGATAGAAAGCTCTCTCTAAAGGGCGTGACCAGATTTGCAGTAGAATGAGAATAGTTT
CAACCCTAAAGTTCATCTAAAATGTTAGTGGTTTTCATGGTAAGTAATTAATAGAAACCTGACAGCTCCATGACAGCAATATA
GAAATCAATAGTCCACTCATTTTAACAGAGAGAATTAGAAAACCTATAATTTAAGAATAACCAGCTGGGCACTGTGGCTCTGC
CTGCAGTTGAATTTACTTGGGAGTTTGAGGTGAGAGGATCACTTGAGCCCAGGATTTCAAGCGCAGCCTGGAAACATAGCTAG
ACTTAATTTCTTGAAAAAAATCAGTGCTATTTTGGGGTCAGAACAATCCTCAAAAATGGTCCCCGGAAAGAAGCCCAAATTTA
ATTGCACCAGATTGTTGAACGATTTATGCTACAAAACAGTGTCACATGTCAGAAATGAGCACAGTGTAACATCTACATGGTTT
GTTAAGAGACACAAATGGTCAAGTAGAACAATCAGGTAATTAGGCTGTCGAAGGCAACACTGCCAAATGACAGCATTTCCGTG
GAAACTGCGTGTACATCCAGGACTGCACCTGTGAACGATGACATCATACCCTTCACAGTGTCGAGGAAAGAGACATCACTCAA
ACAGACAAGCCAAGGGACTTCAGAAAATATAAGGGGAAATACAGTGTGCAAATATGTAAAAAATGCAATAAGATGATTACTCC
TAAATGAATATCAAGACACAATCACATAATATGAAATTAAATTTTCCTGAATGATAGGATTACTACCAATCACCCCCCAGGAC
ACCCTCATCTACTCTGTGCACAGCCTTCTCGTCAGGCGTCCCAGCCCAGACCTTGCTATGTAGCAGAAGACATGCAAATAAGA
CCCCCCTTTTTGCTGATGAAAAGCAGCCCAGCCCTGACCCTGCAGCTCTGGGAGAGGAGCTCCAGCCTTGGGATTCCCAGCTG
TCTCCACTCGGTGATCGGCACTGAATACAGGACTCACCATGGAGTTTGGGCTGAGCTGGGTTTTCCTTGTTGCTATTTTAA
AAGGTGATTCATGGGGAACTAGAGATACTGAGTGTGAGTGGACATGAGTGAGAGAAACAGTGGACGTGTGTGGCACTTTCTGA
CCAGGGTGTCTCTGTGTTTGCAGGTGTCCAGTGTGAGGTGCAGCTGGTGGAGTCCGGGGGAGGCTTGGTCCAGCCTGGGGGGT
CCCTGAAACTCTCCTGTGCAGCCTCTGGGTTCACCTTCAGTGGCTCTGCTATGCACTGGGTCCGCCAGGCTTCCGGGAAAGGG
CTGGAGTGGGTTGGCCGTATTAGAAGCAAAGCTAACAGTTACGCGACAGCATATGCTGCGTCGGTGAAAGGCAGGTTCACCAT
CTCCAGAGATGATTCAAAGAACACGGCGTATCTGCAAATGAACAGCCTGAAAACCGAGGACACGGCCGTGTATTACTGTACTA
GACACACAGTGAGGGGAGGTCAGTGTGAGCCCGGACACAAACCTCCCTGCAGGGGCGCGCGGGGCTACCAGGGGGCGCTCGGG
ACTCACTGAGGGCGGGACAGGTCCCAGGAACAGGTGCAGCGGTAGGTTTTCTTTCTCCTCAGCTGGAGAAGTCAGGTTTGTGT
TTTCAGAACTCTGGAGTCTTACAGGTTGCTACATTTTCATACAGTTATTAGTATGTATTTATTATCATTGGTATTTAAGTTTT
AATAATTTTAAACCTTTTATGTAGTGTTATTTTTTAAAACTGTTTACTTTCATTTGCAGTTATTCTTCCAGAGTTTCATTAAC
ATCTATTGCTATGAGCAACTACATAGCTATGAGAGCATAAATTTACACCTGTAGACGTAGGTCTAAATGCCACAAACCTGTGC
ATAAATGTATAGTGACTTATATTTAACATTATAATAAGATAATTTTTAAAATATATCCTAAACGATCAAACTTACTGATGAAC
TAAATATAAATTATCAGAGTAATGCATAATTGATTTCAATAATTTTATATTGTTTATATTAATTAATATCTATTTCTTTACTG
AAACATAATATATTGGTCATTTCAAAATAGCTACGATACATTTCAAATGGCCTTGATGCTAATAATGAAAAGATTTTGAGGTG
ATTAATATGCTAATTAGTTATATTTAATTATTCCATATTGTATTAATATATCAAAACATTGCTTTGTACCTCATAAATAGATA

FIG. 6 (Cont. 3)

CAGTCGTAATTTGTCAATTTTCAAGACAGTTATTTAATCCATCCTGGGTCATAATCTTTTTTTCCCCTGTCCATGGCTGATTG
GATTGTCCTGATAAACCCATCCATACGCCTGCCTCCCGCAGGCTTCTGAGACGGGCTCCATGAAGGCCAGAAGCAGGCACCCT
GTGAGAGTCCACACGACCTGGAGCCTCCCTCTCCTTGGATTAGGCCATCTCCTCGGGATCGCAGGGCTCTTCATTATCCTCAC
CCCCTTGTTGTACCAAACAAGCAACATCACACTTTAATTCATCACGCTTTGCTTTAATTTTCCCCCCAAAAATCAAGGTAATA
ATTTTAGCAATAAACATCACAACCTACTATGAGTAAGTCCTTTCCAACGTACTAAGGTTTCTTCTGAGGACTTTACATGTATT
ACACAGTTTAAATTTCTTTATGAAATGAGATACCAATATCTCTATATTAGAGATTGTTTTTCTAAGTCGTTTCTGACAATTAA
TTTGTCCAAGGGCCTGTAAGGATTCTGTTAGAAATCCAGGATAAAATTTGAAATTTCAGCAGTAATATCTGGAAAAACATTGA
GACTATATTTAACTTCGTACACGTGCTCTCAAATATCCTTATTTCCCTAAAGGTTGTTCTCAGTTATTATTTTACACATGATA
TCTATAATTAATACTAATAACACAGGTTAAAATATTATCTCAATTATTTAACGACTTTTGATAATAACAAAATACATATTCCA
CATATTTTTGACCAGTTTGTTTTCTCTATGAAACACGTGTTTATTAACTTATTATTATCAGATGTCACCCTTATCTTTCTGAT
TTCTGGGATTTAATTCTAGCAGGTATCGTTTAGTATATTTTATTAATTCATATTATATTGTTCACATTTTCAGTATGATTTTA
TTATTTGCATTGTTTATTGAATTTGAAACTTTCTTACATAATTTTTTTAATTTTTTATTTTCATGAGATGTAATTTCAATATA
AGTAATAATGCATAGATCTGCAATGTACCATTACAGGATTTCTGGCAAATGTAAACACACTTGTCCCCAACAGCCAAGGTTGG
ATGTAGAGGAGGCCCATTCCCCCAGCACAAGCGACCTTCTCTGTGCTTCCAGTCAGCTCCCACATTTAACACAATGTTTTGAT
TTCTGCCACTGTAGATTCACTGTTCATGTTTTGATTTTCATATAAATGGATTCAAACATTATAGACCCCTTTTCTGGTAAGGG
GCTACTTTTGTTATTTTTGACGTTTATTTATGCTATTTCATATGTAAAATTGCATCTGTATATTGTCATTTATTCACTTAACA
GACTGCCTCTGATATAAAATCTCAAAGTTTTGATATATATGGATAAAGAGAGAGGGAGAGAGAGAGAGGGAGAAATTTTATAC
TTGAGTCAGTGCATTTAACAATAAACGACAGTAAGCTGATCCATTTCCCTGTCAATGCACTTTTAATTTGTTTCTGGTTTATT
AACATCATAAGCAAAGCTGCTGCACATATTTTTTGTTTTTCTATTTACCTTTTCTCATTTTTATTGAGAAAGTATGTGGAAAT
ATCCATTTCTTCATCATAAAAGTAAACTTCATTTGTTCAGCTTTATGGAACTATAATTGACAATAAAATTGTATATATTTGAG
GTGCACCACTTGATATTTTGGTATAAATTGTGAAATTTTCACTATGACCAAGGAGTTAGCATGTCTGTTACCCTACATTTGCC
ATTTTCTTCCTTTAATTTATATGTGTGTGTCCAATGAGAGCACCTGAGATCTATCCCTTTACCAGAGATCAAGTTTGCAATAC
AGTGTTGATAGCTATAGTCCCATTGCTTTACATTAGACCTCCAGAACCCATTCAACCTGCACAACTGAAACTTTATGCCCTTG
ACAAGAATCATTCTATTTCCACTCCTCCCAGCCCTGGGAACCACTTTTCTACTCTCTGCTTCTAAGAATTTGAATATTTAGA
TTCCCCATATAAATGAGATAATGCAGCATTTGTCTTTCTGTGTCTGGCTTATTCCACTTAGCATAATGTTCTCCAGGCCCATC
CATGTTGTTGGAAATGTTATAATTCCTTATTTTTAGAGGTCACATAATATTCCATTGTATGTGTATACATTTGCTTTATACA
CCCATTTACCTACGGTCACTAACTTTAAAAAAATTCTAGGCCATTATGAATAATCTTGTAATAAACATATTTTTTACTTACTG
ATTTTATTTCCTTTGAATACGCAGCCAGAAGTGGGATCACCAGATCACGTAATAGTTTTACTTTCAATTTATAAAATAACTTT
TACTACCACTCCACTGAATAATTCTCTTTTCACCAGCTAACTGTCAGCATTTTGTTATCTTTTGTGTCTGTGATAATAGTCAT
GGTAATGAACGTGAGGTGATATCTCATTGTGGTTTTGATTTGGATTCCCCTGATGATTAGCAATGTGGAACACCTTTCCATGT
CCTGCTGGCCATGCATATGTCTTCCCTTGAATACAATGTCTATGTACAGTTTTGCCCTCTTAAAAATCAGGGGTTTTTTTTGC
TATTGTATGGGTTCTTTACACATTTAGATAGATCCCTTTGTCAGATATATAGCTTCAAGTAATTTATTTGTCTATGATTTTGG
TGTCGAATCCAAATAAATCATTTTCCAGATCAACTCTGGAAAGCTTCTTTTTTCCCTGTTTTCTTCTATGAGTTTACAATTTT
AGATATCATATTATATCCAAGCCTTGAGTACATTTTTAGGTGATTTTTGTATATGAGATGAGATGAGGTCTCATTTTTTTCTG
CATATGGATGCTCAGTTTTTACACCATTTGTTAAAAAGGCAATCTTTTCCTTATTGTGTGTCCTTGGAACAAAAAATCTGGGA
GATACACAAAAGAGGAAAATCTTAGACCAATATTCCTGATGATAGACCTAAAAATCTTCAAGAAAATACTAGGAAATTGAATA
TAGCAGCACATTAAAAAGTTATTACATTATGATCCAGTAGATTTTACTCCTTTCATGCAAGGCTAGTTCAACATACACAAATC
AATAAAGGTGCTCCACCACATAAGCAGAATCAAAAGCAAAAACTATATAATTATCTCAATAGATCCAGAGAAACTTTCAATAA
GATTCAACATTCTTCATGATAAAAACCTTCAACAGACTAGACATCAAAGAAACTTAGCTTAAAATGATAAGAGCCATGTATGA
CAAACCCACAACTGACACCATACTGAATCAACAAAAGCTCAAATCATTCCCCTTCATAACTGGAACAAAACAAGAATACCCAC
TCTCACCACTCCTATTCAACATAGTAGTGGATGTTCTAGCCAGAGAAATCAAACAAGAGAAAGAAATAAAAGGCATCCCCACA
AGTAAATAAGAATTCAAACTATCTATTTTTGCTGTTGATAGGATCCTATGCATAGAAAATTCTATAGACTCTGCCAAAAGAAT
CCTAGAATTGATAAACAACTTTAGTAATGTTTCAGGATACAGAATAAATATACGAAAATCAGTAGCTTTTTTATACACCAACG
ACATCCAGGCATAGAGAAAAATAAATGACACGATCCCACTTACAACATCTACAAAAAAAGAAATACCTAGGAATACAGCTAAC
CAAGGAGGTGAAAGATCTCTACAAGAAGAACTACAACCTCTCCAGCACATGTTGTTTCCTGACTTTTTAATGATCGCCATTCT
AGCTGGTGTGAGATGGTATCTCATTGTGGTTTTGATTTGCATTTCTCTGATGGCGAGTGATGATGAGCAGTTTTTCATGTGTC
TGTTGACTGCATAAATGTCTTCTTTCGAGAAGTGTCTGTTCATATCCTTCACCCACTTTTTGATGGGGTTGTTTGTTTTTTTC
TTGTAAATTTGTTTGAGTTCATTGTAGATTCTGGACATTAGCCCTTTGTCAGATGAGTAGATTGCAAACATTTTCTCCCATTC
GTTAGGTTGCTTGTTCACTCTGTTGGTAGTTTCTTTTGCTGTGCAGAAGCTCTTTAGTTTAATTAGATCCCATTTGTCAATTT
TGGCTTGTGTTGCCATTGCTTTTGGTGTTTTAGACATGAAGTCCTTGCCCATGCTTATGTCCTGAATGGTATTGCCTAGATTT
TCTTCTAGGGTTTCTATGGTTTTAGGTCTAACATTTAAGTTTTTAATCCATCTTGAATTAATTTTTCTATAAGGTGTAAGGAA
GAGATCCAGTTTCAGCTTTCTACATATGGCTAGCCAGTTTTCCCAGCACCATTTATTAAATAGGGAATCCTTTCCCCATTTCT
TGTTTTTGTCAGGTTTGTCAAAGATCAGATAGTTGTAGATATGTGGCATTATTTCTGAGGGCTCTGTTCTGTTCCATTGGTCT
ATATCTCTGGTTTGGTACCAGTACCATGCTGTTTTGGTTACTGTAGCCTTGGAAACAACAGGTAACAACAGGTGCTGGAGAGG
ATGTGGAGAAATAGGAACACTTTTACACTGTTGGTGGGACTGTAAACTAGTTCAAACATTGTGGAAGTCAGTATGGCAATTTC
TCAGGGATCTAGAACTAGAAATACCATTTGACCCAGCCATTCCATTACTGGGTATATACCAAAAGGATTATAAACCATGCTGC
TATAAAAACACATGCACACGTATGTTTATTGTGGCACTATTCACAATAGCAAAGACTTGGAACCAACTCAGATGTCCAACAAT
GATAGACTGGATTAAGAAAATGTGGCACATATACACCATGGAATACTATGCAGCCATAAAAGATGATGAGTTCACGTCCTTTG
TAGGGACATGGATGAAGCTGGAAACCATCATTCTCAGCAAACTATCGCAAGGACAAAAAACCAAACACCGCATATTCTCACTC
ATAGGTGAGAATTGAACAATGAGAACACATGGACACAGGAAGGGGAACATCACACACCGGGGCCTGTTGTGGGGTGGGGGGAG
GAGGGAGGGATAGCATTAGGAGATACACGTAATGCTAAATGATGAGTTAATGGGTGCAGCAGACCAACATGGCACATGTATAC
ATATGTAACACACCTGCACATTGTGCACATGTACCCTAAAACTTAAAGTATAATTAAAAAAAACAATTACAACGAAAATCCTT
AATGTCTCTTGAGTAGGTAGAGAACATATATTTTATCTAAGTAACTTGCTCTAAACTGCAAACCAAAATAAGATGATTCAATA
AAGTATTTTGTAAACTAGTCTTTAGCAAAAAAAAAAAAAGAACTACAAAACACTGCAGAAAGAAATCAGAAAGTAAACAAATA
AATTGAAAAAAAAATTCCATGCTCATGGAATGGGAGAAATAATATTGCAAAAATGGCAATATTATCCTTCAATATTTATCGAT
TCAATGTTATTATCAAAATACCAGTTTTATTCTTCTAGAAATATAAGAAAAGTATTCTAAAATTTGTATGTAACCAAAAAAGA

FIG. 6 (Cont. 4)

ACAAAAACAGCCAAAGTAATCCTCAGCCAAAAGAACAATGCCAGGGACATCACACTATTTGACTTCAAACTCTACTATAAAGC
CACAGTAACAAAAACTGTTTGGTACTTGTACAAGAATAAACACATAGACAAATGAAATAGAATAGAAAACTCAGAAATAAAGC
TGCACACCCACAACCATCTGTTTTTTGACAACCCTGAAAAAAATAAACAAGCAATGGGGAAAAGACAACCTAGTCAATAAATG
GTGCTGGGATAACTTGCTAGCCATATGCAGAAGATGGGAACTTGACTCGTGACTATCACCATATGAAAAAGAAAATTAACTCA
AAATGGATTATAGCTTTAACTAAGACTTCAAACTACAAAAAGCTAGGAAGACAACCTAGGAATACTCTTCTCTGCATTGGCCT
TGGCAAAGAATTACTGGCTCTGAGACCAGGCATTTTTTGTAACAGTGATTTATTTTCTGGGGTACATATCATGGAGTGGGATT
GCTGATTGAACGATAGATCTATTTTAGTTGCTTGATAAGCCTTTACAATTTTTTCACATAGGTTGCACTAATTTACATTACC
AACAACAGTGTATAAATGCATTTTCTCTGAATTCTCATCCATATCTATAATTTTTTGACTTCATAATAATAGGCACTTTGACT
GATGTAAAGTTGTGTCTCACTGTTGTTTTAATATTAATTTATCTAATGATTAATGTTGTTCAGCTTTTTATTTCCATATGCTT
TTTGGCCATTTGAATATCTTCTTCACAAAATGTCTGTTGATGTCTTTTGCCCACATTTTAATGGTGTAATTTATTTATTTGTT
GTTGTTGCTGAGTTGTCTGTGTTCTTGTTAGATTCTAGATGTTAGTTATTTATTGCACAGTAATGTAATAAATCTAAAAGTCA
GGAAACAACAGGTGCTGGAGAGGATGTGGAGAAATAGGAACACTTTTACACTGTTGGTGGGACTGTAAACTAGTTCAACCATT
GTGGAAGTCAGTGTGGCGATTCCTCAGGGATCTAGAACTAGAAATATCATTTGACCCAGCAATCCCATTACTGAGTATATACC
ATCCCATGACTGGGTATATACCCAAAGGATTATAAATCATGCTGCTATAAAGACACATGCACACGTATGTTTATTGTAGCACT
ATTCACAATAGCAAAGACTTGGAACCAACCCAAGTGTCCAACAATGAATAGACTGGATTAAGAAAATGTGGCACATATACCCC
ATGGAATACTATGCAGCCATAAAAGATGATGAGTTCACGTCCTTTGTAGGGACATGGATGAAGCTGGAAACCATCACTCTCAG
CAAACTATCGCAAGGACAAAAAACCAAACACCGCATGTTCTCACTCATAGGTGGGAATTGAACAATGAGAGCACATGGACACA
GGAAGGGGAACATCACACACTGGGGCCTGTTGTGGGGTTGGAGGGGCGGTGGGGAGGGATAGCATTAGGAGAAATACCTAATG
TTAAATGATGAGTTAATGGGTGCAGCACACCAACATGGCACACATATACATATGCAACAAACCTGCACATTGTGCACACATAC
CCTAAAACTTAAAGTGTAATAAAAAAAATAAAATTAAAAAAATCAATTGCAAAAAAACTGTTGAAACTATGAAAATATGAGGT
AATTAAACAACACAATTTTGACCAATCATTGGCTCACCAATAAAATTAAGATATTAATTTTTAAAAATACAAAGAAAAATGAA
GCCACAACATACCAAACCCTCTGAGATACAGGAAGAGCAGTACTAAGAGCTTATAGTTCTAAATGTCTATGAAAAAATAGAAA
GATTATAAACTAGCAATCTATTGATTTACTTCAAGGAACTAGATATTTAGAACAAACCAACCCCAGAGCTAGAAGAAGAAAA
TAAATAAAGATCATGGCAGATTTCAAAAATATTGAAACAAAAAAGCAAAATATAAGGAATCAACAAAACAAAATGTGGTTATT
TTAAAACATGAACACAATTGATAGAGCACTAACTAGGTCAACAAAAAAAAAAAAACAGAAGATTCAAGTTAGCACAAGCAGAAA
TGATAAAGGTGGTATTATAACTGACCCAATGGAAATACAAAAGATTATCAAGACATACTGAATATGTCTATGCTCACAAACTA
GAAAATCTAGAGGAAATCAATAAATTTCTGGAAATATTCAACTACCCCCCAAAATTGAACCAGGAAGGAAAAGAAATCCTAAA
TAGACCAATGCGAGTAATAAGACTGAATCAGAAACTGAAAATCTCCCAACCCCAAAAGCCCAGAACCAGATAAATTCAAGGTC
TAATTTTACCAGATGTACCATTCTTACTGGAACTATTCCAAAGGATTAAAGAGAAGAGATTCTTTCCCACCTTTGTCTAAAAT
ACTCGTATCACCTAATACCAAAATCAGGCAAGGATACAACTACAACAACAAAAAGCTACAGGGAAATATCCCTAATGAACATA
GATACAAAATAGTAAACAGAATACTAGCTAGCTGAAACCAACAGCACAATAAAAGATAATACATCATGACCAATTGGGTTTTA
TTCCAGGGATGCAAAGCTTGTCTAAAATAAACACATCAATAAATATGATTCAACATATAACATAATTAAAAACAGAAAACATA
AGACCATCTCAATGAATGCAAAAAAGTCATTCAATAAAATTCAATATCCCTTCATGAAAAATTCCTCAACAAGCTTAGCATCA
AAGAAACCTACCTCAAAACTATAAAAGCCACATACAACAACCAACAAAAAACTCTTAAATAAATCAATAGAACAGGGATCTTC
TTAAATTTAGTAAAAACCTATGCAACTGATTTATTCAATATGCTGGACTTGGTAGTGAAGAAATGAATGACTTTAACTAAAAA
AAAAAGCCACATATAACAAAACAACATTATATGGAATGAGAAAAAGTTGCAAAAATATTCCTGAAGAACGTGAGCAAGAATGC
ACACTTTCACCACTCCTACTGGACGTATTACTGAAAGTCCTAGCCAGAATAATCAGAAAGGAAAAAAGAAATGTATGTTTCAA
GTTCCAAGCTAAGGAATCCAGGAGTGGCAGACCCAGAGACTTGTTTTTTAATCTATGAATAACATCCAAACCCCTGACCGATC
CCTTGGAACACAGGATTTAGGGGTGATTGAGGCTCTTTCTTTTGGGTTAAATGAAAGTTGCTAGGTGGAGGGTGTTAAGTAAA
AATTACTACATAAGCTGCATAGTTTTGTCAAATGGTTGTAGTTTTCTTGTCCAGCCTGCTGTTCCTGAACCACCCTATATGAA
AGCCCTCAATAAACTATATGTCTTGTTCACTGGTTTGGCCTGTTGTACACGATGCCAGTCCTATTGGAGTCCATATTGGTCTG
GCGTGACATCCAGTCAACCTGGTAAAAGGTCCAAAAAAAATCTCATGAGCACCCAGACAATGGAATCTAAAAAGAGGAGACCC
CTGCAGAAACCTTGGGCAGGCTGTTAATTTCTACGTGGGGCCCAACAGCCGTTATCCATGATGGATGGGGCCCAGTGCCTGAG
TATGGGGATACCGCCACAATGCCAAAAGTTCTGGAAGAACCTCTTCAGTGGGTGCATCTTACAAAGTGAAAGTCAGATGTCCA
GGCTGTTGCATTATCAGGTGAGTGGTTCTTCCTGACTGCACTCTGAGAAGCCACTGAGACAGTGCTCACTGTGTATGCTACAG
TGTGTCAGTCACAAGAAGAGCTACTCCTAGAAAAACATGCCAGACTAGCTCAGACTAATCAGAGACCTTTCTGTCCTGCCTGT
GGAAGCAGAATGGCAAATTGGGGACCGCCGCTTGTGGAGCAGCACATTTGAAGGATTTCTGGCCATCACATGAATTAGTTACG
GCTGTGATGACTAAACTGTCATGGGACCCTAAGACCTAGTTCCCATAAAGAGTTCTAGGGGGAGGAGGATGAAGTTTGGGGTA
AGCCCATGGGGGTTCCTGTCCTCTCTACACATCTGGTGGCTACCACCAAGGTAAAAATGGGCCAACTGCACCAGCAGAGGCGA
GCCCCAGAGACATTTCCCACCTGAAATAAGGAAACACACCACAATGTGGGATTCCACCACTGCGGAATTGCTGACACTTAGAA
ATGGGTTCAGACAGAAGAAGAGAGAGTTGATCACAGGGTGGCTTCTTCATCTGTGAGGCATGCGGGAGGAGGGCATTATACTC
CCTGAACTCAAGATTAGTAAAGTGACATCCATCACAAACCATCTGGGCCTGAGGCAGCACCTCGATGGTGTCAGTCATGGAGA
TTGGACCATCCCTCTCCTTAGCTGGGTGGTTGCAGACTGCAAGGGACCCTGGTGAAACGAGGGAGATGTCCGCTTTATTAGTG
TGTTCTCGTATTGCTAGAAGAAATACCTGAAACTGAGTAATTCACATAGAAAATAGGTTTAATTTACTCATGATTCTGCTGG
CTGTATGGGAAGCATGATGAAAAATCTGTTCAGCTTCTGGAGAGGCCTCAGGAAATTTACAATGATAGTGAAAGGCAAAAGGG
GAGCAGCCACTTTATATGGTGGGAGCAGGAGCAAAGAAAGAGTGAGGGTGGAGGTCCCACACACTGTTAAACAACCAAATCTC
ATGAGAACTCATTTACTATCATAGCAAGGGGACCGTGCTAACCATTATTCATAAATCCGGACCCACGATACAACCACCGGGCC
CCGCCTCAAACATTAGGGAAGCAAAATCACATACAGTTGTTATGACAGGTGGGACATCCTGAAAACCTCTCTAGGCATGTCCC
ACACGGCCCTGGAGCTGTCTCAGGGGAGCAGTCTCCTCCAGTGTTTAGACGCACAGGCACGGATAATAGGGCTAAGTCTGGCC
AGATGTGTGATATTCAACACATTGCACAACTGCTCTGTTCTGTATGTAATTTATCTTCTCTACAAATGTAACATTGATGGTTG
CATTAAATATATTCTGCAAATATGTAAAAATAAAATAAGATGATGATTGCTAAATGATTATCAAGGCACAATCACATAATCCG
AAGTTACAATTTCCTGAGAGATAGGATTACTGCCCATGCTTACCAGGACACTCACATCTGCTCTGGGCACTGCCTTCTCCTCA
GGCGTCCCACCCCAGAGCTTGCTATATAGTAGGAGACATGCAAATAGGGTCCTCCCTCTGCTGATGAAAACCAGCCCAGCCCT
GACCCTGCAGCTCTGAGAGCGGAGCCCCAGCCCCAGAATTCCCAGGTGTTTTCATTTGGTGATCAGCACTGAACACAGAGGAC
TCACCATGGAGTTTGGGCTGAGCTGGGTTTTCCTTGTTGTTATTTACAAGGTGATTTATGGAGAACTAGAGATGTTAAGTGT
GAGTGGACGTGAGTGAGAGAAACAGTGGATTTGTGTGACAGTTTCTGACCAGGGTGTCTCTGTGTTTGCAGGTGTCCAGTGTG

FIG. 6 (Cont. 5)

AGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGAGGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCACC
TTCAGTGACCACTACATGGACTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTGGCCGTACTAGAAACAAAGCTAA
CAGTTACACCACAGAATACGCCGCGTCTGTGAAAGGCAGATTCACCATCTCAAGAGATGATTCAAAGAACTCACTGTATCTGC
AAATGAACAGCCTGAAAACCGAGGACACGGCCGTGTATTACTGTGCTAGAGACACAGCGAGGGGAGGTCAGTGTGAGCCCGGA
CACAAACCTCCCTGCAGGGGCGCGTGGGGCCAACAGGGGCGCGGTCGGGAACCACTGAGGACGGGACAGGTCCCAGGAGCAGGT
GCAGGGGGCGGTTTCCTGTCAGCTGCAGGAGGCGGGTTTGTTTTTGCAGGACTCTGGAGCCTTATGAGGTTGCACTATTTTAT
TATGGTTATTTATCATGTGTTTTTTATTGATATTTGTGTTTTAGTAATTTTTACATTTATATGTAGGGGTATTTTTTAAAAAT
ACATAACTTCAAGAAATAATTCTTCCTAGTAATTTACACCTATTCCTCTAAAGTTTTATTAACACCTGTTGATATCAGCAACT
ACATAGCTATGCAACATTAATTTACATCTATAAACATATGTGTGAATACATGAAACTATGCATACATGTGTAGTCATTTATAT
TTAACATTATAATAAAATAATAAATTAAATAAAATAATTGAATTAAATTAAAAGAATTAAACTTAATGATGAACTAAATATAA
ATTAGAGTAATCCATAATTGATTTCAATCCTTCTCTATGGTTTACATAAATCGATGTCTACTTGTAAGCTTAAGTATAGTGAA
TTGGTCATTTTAAAATAGCCAAGAACAAATTTCAAATGTTCTTGTCACCAAAAAATGATAAGGATTTGAAGATTTGAGGTGAT
ATATATGTCAATTAGCTCGATTCAATTATTCCACATTGCATTCATAAATCATAACATAGCTTTGTACCCCATCAGTATATGGG
GTACAACCAAAATTTCTCAATTTCCAATGAAATTTTAATTATATATTTTTTAATTTGATGCCTCTCTTTGGATCAGGCCACCT
CCTCAGGATTACAGTGCTGTTCAGTTTTCTCAACATGCTGTTGTACCAGATAAGCACAAAACATTTAATTTCATTATGCTTTG
CTTTAGTTTTTCAAAACAACATAAAGGTAATAATTTTCCCAACAAACATATTACAGCCTATTCTATACTTTTTTATTTTTTGT
TTTTATGAGATAAAATTTACATGTAAGAAAAAATTTATAGATCTGAAATGTGTCACTAGAGAGTTTCTGGCAAATGTGAATAC
CCTTGTCCCGAACACCTAAGGTAGACTAAAGAGCAAGTCCATACCCACAACATGCGTCTTTCTCTGTGCCTGCGGTCAACCCC
TACATGGGGAAGTGTTTTGATTTCTGACACCATAGATCCATTTTTTTCTGTTTTGAGCTTTATATAAATGGAATCAAACATTA
TAGACCTTTTTTTTGGTAAGGGACTACTTTGCTATTTTTTAGGTTAATTCATGCTATTTAATGTATGAAATTAGATCATCATAG
TGTCATTTACTCAATTAATGGGCTGACTCTGATATGAAACCTCAAAGTATTCATGTATATATGGAGAGAGAGAGAGGGAGGAA
GGACAGAGATTTTATATCTGAGACAGTCCATTGAGTAAATATATGACAATATATTGATCTATTTGTTGTCGATGGATTTTACA
TTTGTTTCCAGTATATGAATATTATAAGCAAAGCTGTTACAAATACATTAGTGTAAGTTTCTCTATCTATGTTGTCTCAATTT
TGTTGAGAAAATATGAAGTATGTTTTTCTCTATTGTAAGAGGAAGTTTAATTTTTTTCAGTTTTATTGAGGTAAAAATAAAAT
ATTTTTTAAAATGTATAGGTTTAAGGTGCCCCACTTGACGTTTTGATGTTGTATTAGTCCATTCTCACACTGCTATAAAAAAT
GCCTGAGACTGAGTAATTTGAAAAAAAAATATGTTTAATTGGCTCACGGTCTGCAGGCTGTACAGGAAGTGCAGTGGCTTCTC
CTTCTGGGGAGAGTCAGGAAAGTTAGGATCATGGCAGAAGACAAAGGGGAGCAGGTGTGTCACATGGCCAGAGCGGAAGCCAC
AGGAAGCGGACCGGGGTGTGGGGGGACTGCACACTGTTAGACAACTAGATCTTGTGAGAACTCAGGCACTGTAGTGAGAACAG
CACCAGGAGTCGGTGCTGAACCACTCATGAAAGACCCACCCCACGACCCAGTCATCTCCCACCAGGTCCCACCCCAGGACTGA
GGATTATAATATAACATGAGATTTGGTCCAAGACACAGATCCAAACCATATCATATGCACATTGTGAAATGCTCATCATGGTT
AAGGTAATTTGTATATTCATCTTCTCACTATTTTTTGTTTGATTTTTGAGACAGAGTTTTGCTCTTGTCGTCCAGGCTGGAGT
TCAATGTCACCATCTCAGCTCACTGCAACCTCCAACCCCTGGATTCAAGGGATTCTCCTGCCTCAGCTTCCCGAGTAGCTGGG
ATTACAGGAGCTCAACACCACACCCCGCTATTTTTTTTTTTTTTTGGTACTTTTAGTAAAGACAGAGTTTCGCCACGTTGGCC
AGGCTGGCCTCGAACAGCTGACCTCAAGAGATCTGTCCGCCTCGGCCTCCCAAAGTGCTGGGATTACAGATGCAAGCCACAGC
GCCCAGCCAATTTTATTATTTTAAAAATGTACTGCATGTGAGTGTGTGCGTGTGTGTGTTTCATGAGAACACCTAAGATCT
ACCCTTTTAGCAAAAATCACTTTTACAGTACAGTATTAAATACAGGAAAATTGGCGTAGGTTAGATCTCCAGAACTCATTCAC
CCTGCACAGCTGAAACTCTGTACCCTCTGACCAACTTCACCCAATTTCCCTCTCCTCCCAGGTCCTGGGACCCACTATTCTAC
TCTCTGCTTTCAAGAGCTTGAATATTTCAGATCCCACACGTAAATGAGATCATGCAGCATTTGTCTTTCTGCATCTGGCTTAT
TCCACTCAGCGTCATGTCCTCCAGGCCCATCCATGTTGCAAAAGCCAGAACTTCCTTCTTTTCAAAGCTAAATAAAATTCAGT
TTTATGTGTACACATTTTCTTTAAACATTCTTTAATCTATGGTCATTAAACTCTTTCACAAATCTACACTATTATAAAATAATC
TGGCAGTGAACATGTGTTTAACATAATAATTTTATTTCATTTGAATATATAACAAGAAGTGGGATCACCAGATCGTACGATAA
CTTTATTTTTCAATTTATTGAGTAACAAGTCCTACCACACCATATCATGATTTCCTTTCCCAACATTCTTGTGAACACTTGTT
ATATTTTGTCTTGCTGATAATAGTCATTTTAAGTGGTTTGAGGCAATATTTCATCGTGCTTTAGATTTGAATTTCTCTGAAAA
TTAGTAATGTTGGGAACCTTTTTAGGCTCTGTTTTTCATGAGTGGGTTTTCTGAAAAAAAGTCTATCCAGGTTTTTTCCCTTT
TATCAGGTCGTTTGTAATTTGCACATAGTTTTTTTTCCTGTGCTTTTGGTATTAAATTCAAATAAATCATTTCTGAATCAATG
ACAGGAAGTTTTTCCATGCTGTCTATGAGTTTGTGGTTTCAGGTTTTGCTCATTTTTAGTTGATTTTTGTACATGGTGTGAGA
GAAGGTCTAATTTTATTTCTTCTGCATATGGATGTCCAGTTATACATCATTTATTGAGGAGACTGTCTTTCTTCACTGTGTCT
TTTTGGCATACAAAATCAGGAAGAGACATAATTAAAAAAGAAAATATTAGATGAATATTCGTGATGAACATAGACCTAAAAGT
TCTCAACAAAATATTAGCAAATAGAATCCAGAAGCACTTTAAAATGTAACACATCATGATCAAGTGGGCTTTACCCTGGGATG
CAAAGTTCATTCAACATCCACAAATCAATAACTGTGATTCATTGTGTAAGCAGAATAAAAGCAAAAACCATATGTTATCTCAA
TAGATGCTGAGAAAGCTTTTGATATGCTCCAACACTCACTCATAATAAAAACCCTCAGCAAACTAGGCATCAAAAAACATACC
TCAAAATAATAAGAGCCATCTATGACCAACCCACAGTCAACATTATACTGAGTGAGCAAAAGCTCAAACCCCATGAGAATTGG
AACAAGACAAGGATGCCCTCTCACCACTCCTATTGAACATAGCACTGAAAATCCTAGTCAGGGCAACCAGGCAATAGCGAAAA
TAAAACGCAGCCGATATGGTTTGTACTAGTGCCCCATTCAAATTTCATGTCAAATTGTAATTCCCAGGGTTGGGGCTGGGGTC
TGGTGAAGGCTGATTCTATCATGAGGATGGGTCTCCGTCTCTTCTGCTGCTCTCGTGATGGTCCTCAGGAGATCTGGTTTCAA
AGTATGTGTCATCTCCCTCCTCTCTCTTCCTCCTGCTCCTGCCCTGTAAGACATGATGCTTCCCTTTCTGTCATGATTGTCAT
GTTCCTGAGGCCCCCCCAAGAGCCATAATTCCTGTACAGCCTGCAGAACCATAAGACAATTAAAAACCTTTATACATTACACA
GTCTCAGGTGTTTCTTTAGAGTGTGCGAATGGACTAATACAGAATCAAAATAGGAAAAGAAGTCAATGTATCTGTCCAAATTG
ATGATATAATTCTATACCTAGAAAATTCTAAAGACTCTGCCAAAATAATTCTAGAATAGATAAACAACTTTGGTAAAGTGTCG
GGATACAAAATCAATGTACAAAAATCACTAGCATTTGTGTACCCCAACTACATCCAAGCTGAGAGTGAAATCAAGAACACAAT
TCTATCCCACTTACAATATCCACAAAGAAAAGGAAATGCCTGGGAACACAGATAACAAATAAGATGGAAGATCCCTGCAAGAT
GAATGACAAAACACAGCAGAAATAAGTCATAAATGACACAAAAAATGGGAAAACATTTCATGCTCATGATTGGAATAATCAAT
ATTGTAAAAATTGTCATACTGCCAATAGAAATTTACAGATTCAATACTATTCACATAAAACTATCACCATCATTCTTCACAGA
ATTAGAAAAAAAAGTATATATATTCTAAAAGTTATATGGAACCAAAAAGCCCCTGAGTAGCCAAAGCAATTCTAAGCAGAAAG
AACCATGACAGAGGCAACATGATACCTGACTTTAAACTACACCATAAAGTCACAGTAACCAAAACAGCTTGGAAGTGGTACAT
GAGCAGACATGCAGAAAAATGGAACAAGAGAGAAAACAGAAATAAACCTGCACACATAAACCATCTGATATTTGATAAGGCTG

FIG. 6 (Cont. 6)

ACGAAAACAAGCAATGGGGATAAAACTCTGTATTCACTAAACGGTGCTGGGATAACTGGATTCTGTCAGATATACAGAATGCA
AAAGTGAAGGAGGCTGGGCAGCTTCGACTTAGATTTCAGAGGATATGTAGAGGGCCCTGCAGGCCCAGCAGGAGGCCGGCTGC
AGCAGTGCAGCCACCACAGACAGCCTCTACTAGGACAGTGCCAAAGATGGGGAAAGAGAGGGTTGGAGCCCCAATTCACAATC
CCCACTAGGGCATTTTACACTAAAGCTGTGGGAATGTGGCCACGACCCTCAAGGTCCCTGAATGGTAGAACCAAAGGCAGCTT
GCACTCTCAGCCTGGAAAAACTTCTGGTACTCGACTCTAACCTATGAATGCAGGCCAATAAGCTGTGCTCAGCTATAAGGATG
AAAAGCCTGAGGTTTCTGGGACTCCTTCAACCCAGGGTGCCCTGGTTGAAGTACATCAAGTGAAGCGAGATTATTTTGTAGCT
TTAAGATTTAATATCTGCCCAGACAGGCTTTAGGTGTGTGGGGGGCCTATTGGCCATTCCTTTGGACATTTTTTTCCTTTTGT
ATTAACAATATTTAACCAATATCTGTGGCAGTCTTGCATGTTGGAAGTAAATAACTCTTTAAAACATTTTGCCAGCTCATAGC
TGGAGGGAAATTGCCTTAAGACTCGGATAAGACTTTGGAATTTTCAGTTGGAGGTTGACCAAGTTAAGACTTTTGGAAACTAT
TAAAAAAAAAAGATCATTTTGCAACCTCTGAAGGACGTAAGATCAGGGGGCACAAGAGTGAAATGATATAGTTTAGATGATGG
TCCCCTCCAAATCTCATGGCGAAATGTGCTCCACAATATTTGAGGTGGGGCCGACTGGGAGATTTTGGGACATGGGGAAAAAT
CCTTCAGGAATGGCTCAATAACCACCCTATGGCAGTAGGTGAATTATTCCTGTATTAACTACTGGGAGATCTGATTATTAAAA
GGAGTCTGATGACCCTCCTCCCCTCTCACGTCCACCCCTCACCATATGACACCGCCTGCTTCCCCTTTGCCTTCCACCATAAC
TGTAAGCTTCCTGAGGCCCTCACAAGAAGCAGATGCTGGTGCCATGCTCCTCACACAGCCTGCCGAACTCTAAGCCAAATGAG
CCTCTTTTATTTGTAAATTACTTGGCCTCAGGCATTAATTTAGAGCAATGCAAAATAGACTAAAACACACTGCCCAAAGCAAT
ATACAGAGTCAATGCAGTTTCCATCAAATAACCAATATAATTAAGTACATTTTTTTTAAATGTCCTAAAATTTATATGGAAGC
AAAAAAGAGCCTTTTGATTCCATATAATAGCAAAAGCCGTCCTAAGACAAGGAAACAAAGCTGAAAGCCCCACATTCCCTGAC
TTCAAATTATACTACACAGTTATAGGAAGAAAGACAGCACGGTACTGGTACCAAAACAAAACAAAAAATATTAGACCAGGTGT
GCCTGTAATCCCAGCACTTTAGGTGGCAGAAGCTGGTGGATCACCTGAGGTCAGGAGCTCAAGACCAGCCTGACCAACATGGT
GAACCCCTGTCTCTAGTAAAAATATGAAAAACTAGCCAGGCCTAGTGGCCCATACCTGTAATCTCAGCTACATCGGAAGCTGA
GGCAGGAGAATCACTTAAACCCGGGAGGTGGAGGTTTCAGTGAGCTGACATCTTGCCATTGCACTCCAGCCTGGGTGACAAGA
GCAAAACTCCATCTCAAAAAAAAAATTAATGTAACAGAATAGAGAGCCCAGAAAGAAAGCCAAATATCTACAACCAACTATTC
TTTGACAAAACTGACAAAAATATACACTGGAGAAATAGTCCTCTATTCAGTAAGTCGTGCTGGGAAAATTGGATGGCCACTCA
TAGAAGAATAAAACCAGGCTTCTATCTCACCACAGACAAAAAGTAACTGAATATGGATTCAATAATTAAATGTATAAACTGAA
ACTATAAAAATACTTGAAGAAAATGTAGGGAGAATTCTCGGGACATTGGCCTAGGCAGATAAAATATGACTAAGACTTCAAAA
GCAAATGCAACGAAAACAAAAATAGATGAAGAGGACTTAGTTGAACTAAAGATCTTCTGCAGAGAAAAAGAAATAATCAACAT
GGTGAACAAACAGCCTACACAATGGTAGAAGGTATCACTTCATCTCAGTTAAGAAGGCTCTTATCAAAAAAGAAAAAAAACAG
CCAGGCGTGGTGGCTCATGCCTGTAATCCCAGCACTTTGCGAGGCCGAGGCAGGTGGATCACTTGAGATCAGGAGTTTAAGAC
CAACTTGTCCAACATGGCAAAACCCTATCCCTCCTAAAAATGCAAAAATTAGCTGGGCGTGTTGGCCAGCACCTGTAGCCCCA
GCTACTCGGTAGGTTAAGGCAAGATAATCGATTGAACCTGGGAGTTGGAGGTTGCAGTGAGGTGAGATCACGCCACTACACTC
CAGCCTGGGTGACAGGAGTGAAACTCTGTCTCAAAAAGAAGGAAGGAAGGAAGGAAGGAAGGAAGGAAGGAAGGAAGGAAGGA
AGGGAGGGAGGGAGGGAGGGAGGCAGGGAGGGAGGGAGGCAAGGGAAAGAAAGAAAGAAAGAACGAAAGAAAGAAAGAAAGAAA
AAGAAATTAAGAAAGAAAAAAATTAAGAAAGAAAAGAAAGAAAGAAAAAAGAAGGAAAGAGAGAAAAAAGAAAGAGAGAGAGAA
AAAAGGAAGGAAGGATGGAAGGACAGAAGGAGGGATAGAAGGAAGAAAAAGGAAAGGAGAAAGAAAGAAAAAAGAGAAAGAGAT
AAAAAGAAATAAAGAGAGAAAGAAAGAAAACTAACAAATGCTGGTAAGGTTGGGGAGAAGGTAAACTAGTACAGTCAGTCACT
ATGGAGAGCAGCGTGGAGGTACCTCAAAAAACTACAAATACAACTACCAAACGACCCAGCAATTCCACTACTGCAAATGTATC
CAAACGCATGAAAATAATTATATCAGAGATTTCTTACTCCCAGTGTATATGGCAGGACCTTTCACAATGGCCAAGATATGAAA
TCAAACCAGGTGTCAGAGAGCAGATGAATGGTTAAAGATTATGTGGTGCATATACATGATGAGATGCTCATCATCCACAGGAA
AGGAAATCCTGTTGTTTTTGGCAATGAAGACGGAACTGGAGGACATTATGTGAAATGAAATAAACCAGGAACTTCAAGTAATA
CACCTTGTTTTCTCACTCATACGTGGAAGGAAAAAGAAAATTTGTCTCATAGAAATAAATAGTAGAACAGAGGATACTAGAGT
CTGGGAAGTGCAGGGGAAGAGATAGGCAGAGATTTGTGAAGGAATACATTAGAGTTAGGTGGGAGGAATAGATTATAATGTTC
TTTACCACTGTGGGATAAATGTATTTAACAATTATATGTAGTTTCAAACAGTTAGAAGAAGGATATTGAGTGTTCCCAACAAA
AAGAAAATGTTTCAGATGACGGATATATTAATTATCCTTATCTGTCCCCTACACACTGTTTCACAACATCGCTATGTACCTCA
TGAATATTTACAATCATTATTTGTCTATTAAAATTATATTAGAAAACACAAAATTCACTGGAAGTAACATAAATGGAGGCTCT
GGGATAGACCTGGAGATAACGGAGGGTCTGGGATACATTACAGGCCTAGCACTCAATGGTCAGAGGAGCTCCCATTAGCTTTT
TGTATTTGTAGCACTGAGTAAATCTAACATTTCTCAGAGCTTCCCTTTGCAATAGAGACGTGAGGCCTAGGGAGATCTTGCAG
ATAGTCAGATATGCAGAGGGAAGAAGCAGGGGTAGAGGGTTGCTGGCCCATTCAACAATAGTTGGAATGATAATTACGCATGT
AGAGAAGCCAACATTGATTTAAATAAGTTGCATCACTGAAAGCCATGAAAAAAAATCCAAAGGAAATCTTTAAATAAAATTGA
GAGTGAAACTGTTTTGGGTGAAGAAATGTTCACTGAAGTTAGGTGTGCCAGTAAAGCTGTTAAGAACTACAGTAACCACTGGA
TTGGATTCAGCTTTGTCTGAATTCAGTGTGATTATTACTGGCTCAGGCAGGGGTCAGAAATCAACATGGATAGGTGGTAGCAA
CACGAAAAAGCCAGGGACCAGAAAGATTCACAGCCGAATTTTTTCAGATGTATAAAGAAGTGTTGCTACCAATCCTAGTGTAA
CTATTTCCCAAAAATGAGGATAAAGGTCTCCTCCCTAAATTATTCCATGAAGCCAGCATTATTCTGATAACAAAACCTGGCAG
AGACTTAATAAAAAAACATGACTTTAGACCAATATACCTGATGCAAAAATGCTCAATGAAATACTCACAAACTGAATACAGCA
GCACATCAAAAAGCCTAACCTACCAACACTTTGTTCCTGGGATGCAAGGTTGGTTCAACATATGCAAATCAGGAAATGTGATT
CATCACATAAACAGAACGAAAAACAAAAACCATGTTAACCGGCAGGGCACGGTGACTCATGCCTGTAATCCCAGCACTTTGGG
AGGCTGAGGCGGGCGGATCATAAGGTCAGGAGCTCGAGACCATCCTGGTTAACATGGTGAAACCCCGTCTCTACTAAAAATAC
AAAAAAATTAGCTGGGCATGGTGGCGGGCTCCTGTAGTCCCAGCTACTCGGGAGGTTGAGGCAGGAGAATGGCGTGAGTCCAG
GAGGTGGAGCTTGCAGTGAGCCGAGATCACGCCACTGCAGTTCAGCCTGGGCGACAGAGTGAGACTCTGTCTCAAAAAAAAAA
AAAAAAAAGAAAGAAAACGTTAACCATAGACACAGAAAAGGTTTTGAAAAAACTTTAAGATTCTTTCATGTTAAAAACCATCA
ACCAGGCATGAAGGAATACACCACAAAATATAAGGGCCATCTATGACAAACTCACAGCCAACATTATACTGACTGAGCAAAAC
CTGGAAGCATTTTCCCCTGAAAACTAGAACAAGAAAAGGACACCCATTCTAACCACTCCTGTTCATCATTGTCATGGAAGTCC
CAGCCAGAGCATGCAGGCAAGAGAAAGAAATAAAAAGCATCAAGTCAGGAAGAGAGGGTGTCAAACTATCCCTGCAGATGAAA
TGATCACATTCCTGAGTCTGTAGTTTGGTGACTGACATTAATTTAAAATATTGTCAGTCATCATTGTTTAAATATTTCTTCTT
AGCCTTTCTCTATTTTTTTCTATTTCCCATTATGTGCATGTTATACCTCTGTCACTGTCTCACCATTCTTGGGTAAGCTGTTC
TTCTTTTGTATATATGTGTGTGTGTGTATATATATATATGTATATATGTGTGTATATATGTATATATATATGTATATATATGT
GTGTATATATGTATATATGTGTATATATGTATATATGTGTATATATGTGTGTGTGTGTGTCTGTGTGTGTATATTTGTATT

FIG. 6 (Cont. 7)

TGTGTGTTTACTGTTCTAACAATATATTTTTTGTTTTTGCTTTTCAGTTTGGGAAATTTCTATTGAGATAGTTTTAAGTTCAG
ATTTTTGTCCGCAGCTATGCCCCATCTACATATAAGTCCATTGAAAGCATTACTTAATTCTGTTACAAAATTCTTGATATCTA
CTTTTTTTTCCTTTTTTGGAATTTGCTTCATTCTACTTGCATGACACAGCTGTTCCAGCATGCTGTCTGCTTAATTCATTACA
GACCTTAGCATATTAATCACAGTGGTCTTAAATTCTTTGTTTGGTAATTCCAAACTAAATGGCATGGCTGAATCTCATTTTGA
TGCTTGTTTTGTCTTGTCACACTATGATATATTTCTTTTAGTATATATCATGATTTTTATAGGGAGAAATTATGTATCAGGTG
AAAGAAACTGCTGTAAAGAGGCCTTTAGTGATATCATTGTAAGTTGTGGAGAGAAACCTGTTTCATAATCCTCTGGCCATGGC
TTCATCTAGGAAGCTTAAGGCCTTTGAAAATAAATCCTTACATGAACGTGAAAAGATAAGCCACAGATATGGAGAATTTCCTC
ACAAATCAAATATTTGGAAAAGGACTTTTATCAGGAATAATAAAAATTACCTTACAGTTGAATGACAAAACCACATGATCTAA
TTTTAAAATAGACAAAGACCTGTATAGAAAGAAGCCTCATCTAAAAATAAATATAAAAAGTGATCAGCATGATTTTTAGGTAT
ATGTATGTTTAATATTCAAAAAATACTATATCCTGTTAGAATGGGTAAAATACACATTTTAGACAGTACCAAATGGTGATGAG
GAAGTTGAAAAACAGGAACATTCACTCCTTGTGGGTGGGAAGGGGATGCTGAAGAGGCACATACACAACTACAGTTAGTACTT
TATTGTATATTTCAGAATAGCTAGAAGATAAGATTTAGAATGTTCTTAACACAAAGAAGTAATCAGTGATGGAGGTGAGGGAT
ATCCCAGGTATCTGGATTTGATCATTGCAGATAACATGCTTTTATCAAAATATCATGCGTATCCCTTAAAGGTTTTGAACTGT
TATGTATCTATATAAATTAAACATTTTTAAAAAAACGGTGCAGGGGAATCCAGCTAATTGCAGATTCCCATTAGATGGGATGT
GCTGCATAATCTGTAAACTAATCAGAGTCTGTGGGTTTGTAAAGGACTTTAGAAATCAACTGGACTACTTGTTTCTAAAGATA
AGTCTCGCAAGTTTAATTATTTTCTTAATGGGTGGCGATTTTGAACATAGAAGAAATGTTAACAGTTGTTTCTCAAGTTTTCT
TCTAGTTTCAGAAGAAAAGGTTTGCAGGGAGGAATCTGGGACCATCTTTCAAGTCTCAACTTCAATGTGATTATCTCAGTAAA
TATTTTCTGATACCCCTGAGCAGGGTAAGTCTCATATATGTCCTAGAAACTGCAAGTAGAATTCTAGGCACCCCAACTGACTG
AAGGGAACTTTTCTCTTCAACGAGGAGTTCCATGGACACTAGAAAACCTAGTTTAGGCCGTGTCAGAAATGGAGGATCAGAAA
TCCCTCATTATACCCTCCTCCCTTTGGAATTCAAGCACAAGTAACCAGCATTTTCCTTAAAACAGATTTAAGGCTCAGAAAAC
AGATTCCGTGTAGCAGTAAAACACCAAATTCTAACCTGACTCAAGAATAGCATCACATGACAGAGAAAAGGCCTTGGAAGGAA
TCAAAGTCTTTTACCCTAAAATATATGTCTTTGACATATTTTTAAATCACCCTGCACAGTTATCTTTTTGCAAGAGAAATTTA
CATTCTGTAGAGAATCGCTTCCCTTTGAAGGTGTTTGTGTTATACTGAGGTATCGGGGGAAATTCAGCCAGATACTGGGAGAA
ATTCACCCCCGATATTTCACGTAGATTCTTTTCTATTTTCCTTAAGTGTCAGCCGGTCTGAGAAATAAAGGGACAAAGTACAA
AAGAGAGAAATTTTAAAGCTGGGTGTCTGGGGGAGACATCACAGTTCGGCAGGTTCTGTGATGCCCCCTGAGCCGCAAAACCA
GCAGGTTTTTATTAGTGATTTTCAAAAGGGGAGGGAGTGTACGAATAGGGTGTGGGTCACAGAGATCACTGCTTCACAAGGTA
ATAGAATATCACAAGGCCAATGGAGGCAGGGCGAGATCACAGGACCACAGGACCAGGGCGAGATTAAAATTGCTAATGAAGTT
TCAGGCACGCATTGTCATCGATAACATCTTATCAGGAGACAGGGTTTGAGAGCAGACAACCGGTCTGACCAAAATTTATTAGG
CGGGAATTTCCTCGTCCTAATAAGCCTGGGAGCGCTACGGGAGACTGGGGCTTATTTCATCCCCCCGCTGCGACCGTAAAGGA
CAGCCGCCCCCCGAAGCGGCCATTTTAGAGGCGTTTAGAGCGTTTCTGTCTTCTCTCCCAGTTTCTACGAGTTCCTCCAGTGC
CTGTAACACAGAGCTGTTAGTGGCTTTGCCCCTGCCTGTTAATTCTTTGGTCATGTAATGGTGGTGAGGGAGCTGGGTCTGGA
TGCATTTCAGCCACAGCTGCTGTTCCACTTCCCCACACAGAACCATCTCGGGAGGAAGAGGTTGGAGATTTTTCTGATGTGTC
CTCAATCCTGGCAGAAAAGGTTTCAATAGCAATAGGATTCCCTCAGTTGTATGTCCTCTGATAATTTAAACAATAACTTCTTT
ATTATACTCAACTCTAAACGGTCTAAAGAGTATGTCTAAGTTAACCCTGCATTCGCTTATATGACATTTGCTCTACCCCAGAT
AAGGTCATATTCTCTTTCTGTTTGTTCCTGCAAGTCACTGACTTTCACAAGATGTAAGGTCCCTTGTTTGTCCTATAACATCA
ATAATCTGATGTTTTAAAGAAAATATGCTAATTTGCAGCTCAGTAAGTTTAGTTGTAAAAATAATACATTTTTTTCTGAGATG
CCTACATCTCCATGCTGAGTTGGAGCTTTATTTGTAACACTCAGAAACTGGAAATAACAAAAATATTAAGGAGCTTTATAAAT
AGTACGGGCACACTCATTAACTGGAATTCTGTTCCTCATTACAAGGAACATATTCTTTATACACAACCAAACTACTGACTCAC
AAGTAATTGTGCTGAGCAAGAAGCCACACAAATGAAATGGAAACTGTAAGGTTTCACTTTAACCAAATTTTGAAAAATAGACC
TGAAGTAGCAAACATGAGAGACTGACTCAGTGTAGTGAGCGGAAAATGACTGGGAGGCAGGAATTAGAGGAAACTAGGGAAAC
CTTGAAGTGTAATTCATTGTTATCTTGATTGTTATTTTGGATGCACAGGTAAGCACATGTGAAACTGCATTTTTTCCTTTGGA
GACATGGTCTTGCTTTGTCATCCAGGCTGGAGCTCAGTGGTGAGATCATAGCTCTCTGCAGCCTCAGACCCTGCGTCTCCACC
AATCTTCCTCCCTCTGCCATACGTAGCTGGGACTACTGGTATGTAAGACAATACTTGGCTTCAGTGCTTATTAAAATGCACAC
TTTAATTAAGCAGTATTTGTTATACAGCAATCATGCCTCAATAAGAGTATTGCAAATAAGTGGATAGATAATTTGTTCAATAA
AGATTGATGGAAAGATAGATGCTAACATGAGAAAATGCATGACACCCAAGAAAATAACACTGTAGGAAACATGCTTTTCTTTA
CAATTGTTAGGTAATCACAACAGAGCATACACATCACACCATGTTCTCGTTACAGAGAAAAGGTTCTGCAAACCTCACTAGCT
GCAACCCCTGTGTGCTGGGCTTGGTTCAGGGAGAAGTCAGGTCCAGTGGTGAGAAGCACAGGCCCAGATAACCAAGCTCACTC
TGACCGAATGTGAGCCCTGGGTACATTGTACAACCCATCTGTGCTTCTGCTGGTAATTTTTCATCTGTAACATGGAAATGACA
TTGATACTATATACCATGTTTCCTCTGCATATGTAAAAATAAAAGGTGATTGGTGCTAACTTTAAATATACACAGTTTATGTA
CATTGATTGCACCTCAATACAACAGTTTTAAATAGATATTACAACATTATAAGTTTTATAGGTTTAATATTTTATCACAGAAC
AAACTTTCAATAAGAAACCACAATTTCCAAATGCTATCAATATCACAAATCTCCCCCAGGACACTCTCACATGCTCTGAGCCC
CACTCTCTCCTCAGGCGTCCCATCCCAGAGCTTGGCATGTAGTAGGAGACATGCAAATAGAGCCCTCCCTCGGCTTATGAAAA
CCAGCCCAGCCCTGACCCTGCAGCACTGGAAGAGGAGCCCCAGCCCTGGGATTTTCAGGTGTTTTCATTTGGTGATCAGGACT
GAACACAGAGGACTCACCATGGAGTCATGGCTGAGCTGGGTTTTTCTTGCCGCTATTTTAAAAGGTAATTCATTGAGAACTAT
TGAAATTGACTGTGAGTGGATAAGAGTGAGAGAAACAGTGGATTTGTGTGGCAGTTTCTGACCAGGGTTTCTTTTTGTTTGCA
GGTGTCCAGTGTGAGGTGCAGCTGGTGGAGTCCGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAGC
CTCTGGATTCACCTTCAGTGACTACTACATGAGCTGGGTCCGCCAGGCTCCCGGGAAGGGGCTGGAGTGGGTAGGTTTCATTA
GAAACAAAGCTAATGGTGGGACAACAGAATAGACCACGTCTGTGAAAGGCAGATTCACAATCTCAAGAGATGATTCCAAAAGC
ATCACCTATCTGCAAATGAACAGCCTGAGAGCCGAGGACACGGCCGTGTATTACTGTGCGAGAGACACAGTGAGGGGAAGTCA
GTGTGAGCCCGGACACAAACCTCCCTGCAGGGGTCCCCAGGACCACCAGGGGGCGCCAGGGACACTGTGCACGGGGCTGTCTC
CAGGGCAGGTGCAGGTGCTGCTGAGGGCTGGCTTCCTGTGATGGTCTGGGGCTGCCTCATTGTCAAATTTCCCCAGGGAACTT
CTCCAGATTTACAATCCTGTACTAACATTTCATGTCTCTAAATGCAAAACTTTTTTGTTCTTTCTGTATTTTTGTTTTTGTGAA
CAGGAGGACACATTCTCGCCTCCACAGAAGCCACAGTGTCACTTTGGGGGCAGATGATCCTTCTGTAGTCAGCAGGATGAAAG
TGCAGAGGAATCTCAGTGGAACCTGGGAAGTCTTTTCCAGTTAGACTCAGGGCAGAGACCTCCATGGGAATCTCTGATTAGAA
CAGGCTTTGAGTTCTGATAGGAGCCAAGAGAGAGGCTCACCCAGGGTCAGAGTCCTTAAAACCTGACGGTTTTCACAGCTATC
TCACCTCGTCTTGAAAAACTGTGCACATCTGACTCACACTAATTCAGTTGACCTTATTTCTGCTAATCTATTTTCCTTCTCTG

FIG. 6 (Cont. 8)

CAGACTTGATTCTCACAGTTCCCTTTCTTCTTCTCTTGCCTGAAAACAGAGGATGTGTTTTCTGTAGTCAAAATCCCAGAGAT
CAGGTCTGCAGGACCTGGGTAGGCTGAGGGGACTTTCTCACTCACCATAGCCTGGTGACACTCCTGCTGTATTTTGTATGTGG
AGGTGTTTGGAAAACGAAGTGAACATTAGTCATGAAGGGAATAATACTAGTTTTCTCCAAAGGGATGTGGATGTAGAGCTGAT
CTTGTGCTTCTCACACTGTCACAGAATTTATGCTCTCCCCTGTGACTTTAGGAGAGCTGAGGATGGACACTCCATTGTGCTGT
GAGCTCTGGTAATAGTAATTATAGGGTCTCGCTAGGCAGCCTAAGGTCAATACTGCTGGCCTTCGGGAAAGGCAGGCTGGGAT
TCCTAGGAAAACCTGCATCTGCCATCCAGCATGGAGTCCCATCGTCTTCTGTTATGCTCTGATTGAATCAGGCACACCTAGGT
TATCTAGAACACTCTTCGTGACTTGGGAAAAATTAGTGGCAGGCTCTACTAAGACCTGCATTATGCCATGGGAGCAACACCTA
GGCTAGTGTGTGATTGAGTAGGTGAGACTATGGTCTAGTCAAGGTGACAGGGAAAATTGTTGCCATTATTATGTTTTATTTTA
TATTTGGCAATATAGTCATGCTCATATTACAAATATCTTTCTACATTTTTGTGTCAGAAGCTTTTGAACAAGAGCAACTTCA
TCTTGAATAGAGGCTAGGAAAAATAAGACTGAGACCTGCTGGGCTACATTCCCAGTAAGTTAAGGCGTTCTTAGTCACAGGGA
TGAGATAGGAGGTCTGCACACGATCCAGGTTATAAAGACCTTGCTGGTAAAGGTTACAGTAAAGAAGCTGGCCACAGCCCACC
AAAACCAGGATGGCAAAAAAGTGATCTCTGTTCGTCCTCACTGCTCATTATAATGCCTTAACATGCTGAAAGCCACTCCCCTC
AGCGCCATGACGGTTTACACATGCCATGGCAACATCAGGAAGGTTCCCTAGATGGTGTACAAAGGAGGGGAGGACACCTCAGC
TTCGGGAATTGCCCAGGGACTCATGAATAATCCATCCGTTGTGAGAAATACATTCATCCCTTTGAGAGAAAATGCACAGGGGG
TGGAATGAGGCTGGGAAGCCGATGGCACATGGTGGAAGCCTGTCCCTGAGTGAAAGAGAGGGGGAAGCTGGATTGGGTGGAAG
GTCCCTATATTTCTGTGCTGTGCAAGGGAGGGGCAAAATATAATTGAGTCTCTTGTAAGTCAGTGTTTCCTCTCAGGGGATCC
CCATGACTCCCAGAAATAATGGCTCTGCTTAGGAATCCCTGCAGAGTCACTCCTTTCATTAGAGTAGACCACAGGACATGGGC
CTCAGCACACGCCATGCCACAGATGTCAGAAAGCAGCTGCTGGGAACCTGACCCACCTGCATTTTGCTGCCTGTAGGAGGAGG
AGGACGTGCATTCTCAGGGCCAACACACTGTTTTTGGATTTTTATAGAGAACACCTGCTTTTACTTTATTTTTTGGAAAAATA
TATGAACAAATGTGCACCTGCAAACAATTGTAATTTTCACATTTATTTTAATTGCATTTGTTTATAATTGTGCATGAGGTCCT
GGTGCAGAGTTGAGTTTTTCATGGGAATTGTTCCAAGAATCAAGAACATCCATTTTCCACTTTCACTGGTTTTTCCCCATGTG
CAGAGACCTTGAGTAGAGCACATCTGGCCCTTATCCACACTATCTCTTGTGTCCCCGGGAAAGACAGGGATTTGCCTGACTGC
AGAATCTAGGGTAGGAGTCTGCACACGTCTGAGCCTGCAGAGAAGCCCAGTGAAGTTTAATGAAGTCAGAGAGCTTTCCCGTG
TGGGGAACCTCTAGCTTCCTCACTCTCAGAGATTGCTGGTCAGCTGTAATTGAGGGGTTAAGAATTAGAGCACCTGGGAGCCT
GTCTCATCACAGCTCCATTCTGTAACTTACCACCATCAGACTGCAGGTAATAACTCAATCTTGATTTTTCTGACCCCATCTTA
TTCATTTGTAAGTTTGGTTATACAAAATGTTACATTTTAGTTCTGATTCAAACCTCAGAATTTTGTGAATTCATCAGGAATA
ATTAAAAATGTGTCCAGTTTTTGGGAAATGTAAATTAATGTCCATACTGTTTATGTGTGTGTGCGTGTGTGTGTGGGGGGATA
TGTCAGTCACTTACACCCCAGTAAAAATGATTCCTTAATTATATAGTCGAACTGCAATTAGATTTGCTGAAAATTGTCTACAG
TAATTTCTGTGAAGCTGACCTTGCCACCTTGCTGTGAGGATGCTCAGTGCACAGGTGAGGTCTCACAGGAGAGATCCAAGGTT
CAGCCCCCAGGACTGGCTGAGCTCCTGGCTTGGAGCCAGACATAGGACTGGGCATCTCAGAAGCAGATCCCCTGGCCCTCCTT
TATCTGGGCTGTATGGGCAGCAGAGGACAAGCAGAAGAAACTCAGAATTCAGCCAAGACAGAGCCCCATTTAGGAGCAGGTGC
ATCAAGGAACCAGCCAGAGAACCTCTGACTACAATCTAGGGTTGTCTTCTTTTGCTTCACAGCATCCAGTCCTAAGGAGACCA
CCCACTATATCATCTGTAACTCAGAACTTTCTTGTTACAAAGGAAAACACAAATGAATATAACTCTGCAGTTAACTTCTTGAA
CCTGGATTGATGAGTTTCCACGGCCTTATGAGCACAGAGACCACATCCAGTGCAGGTGCAGAGCAAGGCTGCAACAGTCAGCC
TGCTGCTCCCTCAGGAGTCTTCCAATTCCCTTGTCCAAAGCATCCGCTCATTCATGGGCTGAGAAAAGGGAAGTCATTCATGC
AGTCTACTCTCTCCACAGAACTGACGGGGCACAAGGACAACATCGATTTTTCATGGAACATGCCTCTAGGAATGCAGCTGTGT
GCACACACACTGCTAAGCACACACTTCTTTACATAATTACTTGTAACTGTATTTTCTTATTTATTCTCTCCAATTTTTTTACA
CAAATTCATCACTTTTCCCCATAATCAAAGAGGATTTTGATCAGAATGCTTGTGGGGAGCCCCTTGCCCCCCAGATGCCCACC
ATCATTATTCTTGAAGGGAGGAGGAACGGCAGCTCTCTTGATTTCTACTCTAATCCTCTAGGACTAAAACCAGAAGGTTGCAT
GTCCGGTGCGGGAGCATCGAAGAAGATCCTGTCTGTAGAAGCAGGAGCGTCAAGACTTGACTGAGAGCCATGGTGCTGAAATG
AGATAGATTCCCTGATGGAGAGCACACGTGGACCCCCACACCTGAGGGCTCACTGCTCCTCACCACAGATGCACTCCCCTACT
GAGTCCTGAGACCTGAGTGCACCCCATAGAGTAGGGCTCAGATGAGGGGATGCAAATCTCCACCAGCTCCACCCTCCCCTGGG
TTCAAAAGACGAGGACAGGGCCTCGCTCAGTGAATCCTGCTCTCCACCATGGACATACTTTGTTCCACGCTCCTGCTACTGAC
TGTCCCGTCCTGTGAGTGCTGTGGTCAGGTAGTACTTCAGAAGCAAAAAATCTATTCTCTCCTTTGTGGGCTTCATCTTCTTA
TGTCTTCTCCACAGGGGTCTTATCCCAGGTCACCTTGAGGGAGTCTGGTCCTGCGCTGGTGAAACCCACACAGACCCTCACAC
TGACCTGCACCTTCTCTGGGTTCTCACTCAGCACTAGTGGAATGTGTGTGAGCTGGATCCGTCAGCCCCCAGGGAAGGCCCTG
GAGTGGCTTGCACTCATTGATTGGGATGATGATAAATACTACAGCACATCTCTGAAGACCAGGCTCACCATCTCCAAGGACAC
CTCCAAAAACCAGGTGGTCCTTACAATGACCAACATGGACCCTGTGGACACAGCCACGTATTATTGTGCACGGATACCACAGA
GACACAGCCCAGGGCGCTTCCTGTACAAGAACCCAGGTGTTTTTCAGTGGTGCTCCCTCCCCACTTCTGCAGAACAGGATAGT
GTGGCTGAGATGCCATTTCCTGCCCAGGGCGTGCGTTTCCCATCCCCATCTGACTCAGAGCCTTGTTTTCCTCCTTTTTCTTT
ACTAATAAATGGCATGTCCCCTGTTAGTGGTTCATGCAAGCAGAAGCTGTATCCTGTTTGACAAAGATTCAGCATGAAAGGTC
CTGCTACCTAAAAAAAAATAGACAGATGAGATTTAATTAACCTAAATAATTTTTTTCACAACAACAGAGTGAATACGCAATTT
ACAGAATGACAGAAAACTTTTGCACACTTTGCCTGTGACAGGGAACTAATATGAAGAATTTGCAAGGAACTCAAACAACTCTA
CAACAACAACAGCAACAAGAACCAAATAACTCCGTTAAAATGAGCAAAGGACATGAGTAGACATTTTCAAAAGAACACATAGA
AATGGATAATAAATATATAAACAATACTCAACATCACTAACCATCAGGGAAATGCAAATTAAAACCACAATAAGATATCATCT
TCCACCAGTCACAATGACTATTACTAAAAACTCAAATAATATCAGATGTTGCTGAGGATGGGAAATGAAGGCAACTCTTAGAC
ATTGTTGATGAGGATGTAGATGAGTACAACCTCTGTGGAAAATGGTATGGAGATTTCCCAGAAAACTAGAAATAGAACTGTCA
TTTGGTCCAGCAATCCCACTACTGGGTAACTACCCAAAGGAAAATAAACTATTATTTCAAAAAGATACCCACCTTCTATGCTT
ACCATAAAACTACTCTCAATAGCACATATGTCAAACTGAGTGTCTGCCAACCGATGATTTTATAAAAGAATATAGCATGTATG
CACAATTCAATACTAGTCAGCCACAATAAGGAATGAAACTGTGTCTTTTGCAGCAAGATGCATAGAAGTGGGGGACAATATAA
TTAGTGAACTAACTCACAAACAGAATGTCACATGTCACACATTATTACTTGTAAGTGGGAGGTAAACAGCGTGTACACAAGGA
TTTGTAGAGAGAAATTACACACATTGGAGACTTACAAGGATGGGCGGGCAGAAGGTGGGAGCATGATGAGTCATTACATAACA
GGCACAATATAAAATAATTAAGAATTGACCAATGATCTTAAAATTAAAATGTAGAATATGATCAATAAATGAACTTGATATTA
GTTGACCTCATTAAATTTAAAAACTTTTTCTACTCAAATGACTGTAAGAAAATGAATGCCCGGTTACAGATGAGAAACTGTTT
GCGAGTCAAATAACCACCAATGTAACTATAATAAGAAACTTCAGAACTCAACTGTGAATAAAAAAGAAACAACTGATGGATAA
ATTAGGCAAGGGTTTCTACAGACATTTCGTCAAAGAAGATGTGCAGATGACACTGAAGCATATAAACAGGATCTCAACAGGAT

FIG. 6 (Cont. 9)

TTTCCGTTAGAGAAATTCAAATCAAGCCCGCAAAGAGACACCACTGTACACTTTTTAAAATGGCTGAAATTAAGAAGAAATAC
AGATAACATCAATGCTGGTGAGCATACCAGGTTGCTAGAGGCTAAAACATTGCTAACAGGAATGCAAAATGAAACAGATACTC
AGGAAAATAATTTTTAGTTTTCTCTAAAATCAAACATACCCTTAACACCTGAATATTTGCATCAGAGAAAAACAATCTTACAT
TCACGCATAACTTCTATTCAAATATTCAAGATATCGTGTGTATGTGTGTTAGAAAGTAAAAATAACATAAATGTCTCAAAATT
TGAATAGGTGAAGAACTAGGAAGCATCTATAAATTGAATACCACCAGCAATAAAAAAATAACAAGTGACCGATACATAAACTA
TTACAGGTGAACTCCAGACATTGTGCTAAGTGAGAGAAGCCAGTCTCAAAGATCAAAGGGACACAGCTGTAAGCACCACGGTC
ATCCTCAGGTGTCAGTGGTTTGGGCTGGACTTTCTGTGTCTCTTTCCTGACCAGACCCAGATATTGAGCTCCACCACTTGCAG
ATGGAAAATCCTATTTTCAACCATGCAGTGAGGTTTGAACTGCTTCACAGACTGAACGAAACAAACACGGGCTCCTTTGAACA
GCGTCCGGCATTTGTTCCAACCACAAGAGAACGTCCCTCAGCTCTCCCACCTCCTCGGTTCTCTCCTGCAAGCCAGCAGCCCT
GCAGTTTAGCCTGCATCTCCCGTGCATCCACCCATCTCCCTCCAAGCACCTTCCCCCACACCCTCCACTGTTTCTGAGAGCAC
AGGCAGGCTTTGAACTTTTCCGCATTCTGTTGTTATTGAAGTTAGGATGTTTAGGACCAACTTAAGGATCATATTTTATGACT
GAATTCCAGTGCCCCTTCTCTCCTGGGACAGAGTGCATAACCAAGTTTCTGCAGGTGGAGACGAAGTTGAGCTTTTTTCTTCC
TCAGCCTAGGAGATGAGCGCTAATTGGAGGGTTGGCAGAAGCTTCCCACCATCCCAGCACTTTGGTTCTGGTGGGGCGGAATC
GGTGCCATAGGGCAGAGCTAGAAACCGCGGACTGAATGTTCCCAGTGGCACTGGACCCAGGGCAGAGCCTCCATCCACGAGTG
GGGCTCTATGGAAGAAGTGAGTCTCTGGCTCTCAGTAGCTCTCGTCCAGCACTGAACCTCAGCATCATGTGCTGTGTGCAGGG
TCAGAGGGCCAACGTACTGGCCCCTGGGAAAGCGTTTCCTCTGGTGGGAGTTGGTAGAAGGTGTCCTGTCTTCTTGGCTGCAT
CTGTCCGCAGTGGAGTTTACATCATGCTGAGCTGGGATGTGGAAGGAAGGAAGAGCATCTTAGATCAAATATGATGACTGGCC
TTACTGAGTTTTCTAGATTTTCCTGAATAAATGTTTCTTCACTCACTGTGTGCTGTTAGAGTCTTTCCAAACCTGTAATTTCC
CAAAATAATTTTCACTGGTCTCATGAGGGCATGGATTCATTGAGCCCCTCATGCTGTCAAAGAGAAATAGAACTGTTTTTTTT
TTTCACTTCATAGCGAACATCCATGGGTTATCAAATAATGGGCTGGCTTTCTTCCAACACTTTACAGACACCATCAATTTTC
TTCTTGCTTATAAGGTTTTAACCAGAAGAATGCTGTCATGGTCTTTTCTGTTCTTTTGGAAGGAATGCCCCCTCTACTCACCT
CCACTTGTCTGCCTGTATTTCTATTTGTCTTTGGTTTTCAACAATTTTAATAAGATTTACCTAAATGTGTGTGGGGGGAGCAT
GGGGTGTTATTCTGCTGTTCTGTGTTCTCTGAGATGCATGGATTCACCATTTACTCTGTCTCCATTTTTGTGAAAACAATTAG
AAAAAAAGTCAGTATGAGCCCAGAAACAAGCCTCCCTGAAGTGGGCACAGGACCACCTGGGGGCGCTCAGGACCCACTGAACA
CAAGAGCCAGCCCCAGGGCAGGTGCAGATGCGGGTTAAGTTCTGGTTTCCTGTCAACCCTGTGGCTTCCTCTCCATAAAACAG
TTTCCTTTGTGGCATATCTCTGGATTCCTTATCCTGTTCTTCCTGTGAAGTCTCTGAAGAAGAAACATTTGTCGTACAAGAG
AAAAACTTTCTCACATGCACCAAAGGCAGAGTCACCTACAGTCACTTACTCCTGTTTCTCAATGTCAATAAGTTACCAATGCT
TCTGAAGTTAATCAGCTAAATCTATAAAAGGTGCGGTGTTTAACTCAGCATTACAGCCCAGCTCAACAGAACTCCAAAGGTCA
GCCAGCAGCAGCCAGGAAAAAGTGCATGCTGGGCATTGGGGCAGAGGGAGTTACCATCCAGTGCAAGAGAAGAAAGCCCCCGT
GGTGGTCATTGTCAGGACTCCAATCCCACAGTTCCAATTGTAGGTGATGCCAGGCAAAGGAAGAGAGACCCCACCAATGGTTA
GTGTGGATGTCGAGTTTGATGTTTCCACACTCACACTCCAGGTGAATATGAAAAGATTTATTAGCTCTATTTCTGAGGTGTCT
GCTGAGAGCAGCACAGTCCTCTCAAGAAATTACAGATTGGAATTTCCTCAGTAGAGCAGGAAAGGAGGCTGGCTCAGGGCTTT
ATAATGATTTGGTGGTGGGGTCGGCGGGGGGGGGGGGCGTTTCTACTCAGGAGAAGGAGCTTGTGTGATTTAAACCTCACAC
TGACATCACATGAGGGAGCTTCCATGATTTCTTACTAGATTTCCCATGTGTGGGGACAAGGATGAGGGAGAATAAACCTTAA
TTCATCAGCATCAAGGCACCAAAAATAGGACCTGACACTTTATTCTCCCTAGCAGCTTAAGAAAATGAGTGAAAAAGAGAGAT
AAGAGTCCACCCATGTGCTGAAAAGCATAGCTCTTGGTAAAGACGAGAAAAAGGCACTCCTACGAAGAAGGGGTTGGGCAGAA
GCTTTATGCTGAAGGGTTTGGCTAAAGAGACATAATCAACAGGTTACAGGAGGGGCTACTGATGTTCATGGAGGTGGTCCTCA
CACATGCATACTGAACAAACATGTCTGTAACGTATGACCCCTGTTCACTTACCAGTGGAGACTTAGCATTTAAATTCATTCCA
GTCAGGCCCTATGTGCAAACAGCAGAAGCAGAGACACAAAGGTACTCAGGGTGCAGCCTCTGTGAACGGCCAGAGCCAGGCCA
TGGTCAGCGGTCTCGGATTAGGAGAAAGTTCCTGATATCACTGTAGTGTTCAATCAAAGCTGGGGTTATGGTTTGTGGAACAG
GGGTCAGTTCATCAGGGGGTGGGCTGCAATTGTCTTCATAGTGCTTGTCTCAGTGCCGGTGCTTACTGAGCCACTAGAGAAAA
AGGTTTAATTGAGCTTCTTTAAAATCAACATTTTGAATTATTTATCAGACGTTTCAAATATGTCATGTTGTTTAGATTCTATT
GCTGGAGAGTTAAGGTGATATTTGGGGTTTTGTAACTCTGTTTTTTCATACTTCCTGAATTGCTTATCTGTTTGCTTTTCATT
AGCTAAACTATCGCTTCTTCTTATTTTTTAATTCATTCTGATTTTGATGAATATTTAATTCCCTTTAGAATGTGAATATAATG
TACATTGTGTGGGTATTTTGATTTTGGTTCTTGGTTTACTTAGTGGCAAAGACTCTGTAAGAGTTCCTTGTCTATAGATAGCC
ATTATTTAGTGGCTTTCTGAAATGGTGGTTTTAGTACCAAAGTACTGGACTTGTGAGTAGGCTCACTGCCCCCTGCAGGTCCT
AGATAGTGGAGGCCTCAGGAACTGTTTCTCATTTGGAATGCCTTTGTTTCAGCAGATTTTGTGTTGGGTTGTTAAGTTCACCC
TCCACATTAGTAGATGTCCTTACAGATTAGAGCTGACTCTGGTAGAAGCAGTTGAGTGCATGCTTGATATCTGTGCACAGGGA
GAAGCTCTCTGTTGCCTCAGGCGATGGACTGGTCTATGAAATGCACAGTGACCTGAGTTCCCTGCTCAGCCCCTGAGAGGTGG
ACCAAGCTGGACACACATGAGCCACCGAGCCTGGCAAGCAAAAGCGCCAGCCTTGATGGAAATGGCGAGCTGAGCGGCATCTA
CTCAGTGTGGTTTCTTTTGTTATTAAGAGCTTTAGTGTGGTGGCTGTTTCAAATTCCCGTTGTAGTAGTAATATACTGGGTAT
GTGAGCAGGCCCGTGGTCTTTTGCGGGTTGGAATCACCGAAGTAATGAGAAGCTAATCTCATTTTCAACTGCTGTACACTGG
TGGTATTGAGTTTGTATGAGGTCATGCAGTTTGAACGTCAGGCCAGTAGGTGGTGCTCGCAGGTAAGAGCCGGCTATGGTGGC
AGCAGAAGGGTTTATGCTTTACTGGTGATTAAAGTGGGAAACTTGGCGTGTTCCAGATCTTAGAGAAAAGATTTTTAGTTATT
TCTCATTCAACCTGATACTACCTGAAAGTCTCTCGAATGTAACTTTTATTTTGTCGAGATGGGTTCTTTCTATACCCATTTTT
TATGTTTTTTTTTGTGAAAGGATGTTGTTTCATCAAATGCGTTTTCAGCATCAATTGAAAAAAGTTATATGTGGATTAAAGATC
AAAATGTAAAACCTAACACTATAAAACCTCTGGATAATAACATAGGAAACAGAATTTAGGAGGTAAGAACTGACAAAGGTTTT
ATAATGAAAATGCTAGAAGTAGTTGCAACAAAATTGAAAATTGACAAATGGGACCTAAGTAAATTAAAGAACTTCTGTACAGC
AAAAGACACTATCGACAGAGTAAACAGGCAACCTACAGAATGGGAAATAAAATATTTGCAGCCTATACATCTGACAAAGGTCC
GACACTTAGTATATACATGGAAATTTAACAAACATACAAGAAATAAAAAGTGACCAAAGGACATGAAAAGACACTTCAAAAAA
GACCTACATGTGGCCAACAAGCATAGGAAAAAATGCTGAATATCACTATCATTAGAGAAATACATATCAAAACCTCAATGAGG
TACCGTCTCACATCAGTCAGGATGGCTAATCTTAAAAAAAAAAATAACAGATTTTTAAGGTTACAGAAAAAAGGGGAAATTTAT
ACACTTTTGGCGGGAATATAAATGAGTTCAACCATTGTGGAAAGCAGTGTGGTGATCCCTCCAATAACCTAAAACAGAAGTTT
CATTTGACCCAACAATCCTACAACTGGACATATACCTAAAGGAATATAAACATGTAGGTTCACTGCAGCACTATCCACAATAG
CATAGACATGGAATTTACCTAAATCCCCATCACTGGCAGAATGATAGAGAAAAATGTGGTACATACAACCATGGAATACTATG
CAGCTAAGGAAAGAATGAAACTATGTCCTTTGTAGGAACATGATGGAACTGGCAGTCAATACTCTTAGAAAACTAATTCAGGA

FIG. 6 (Cont. 10)

ACAGAAAACCAGATATTATATATTCTCCCTTATTTGTTGGAGATAAATAAAAGCAAATATTCTTCCAGGGCCTGAGTCTTCCT
TATTCAACAAGTCATTCTAAATTAAGTGTTCAGCAAGTTGCTGATACTCATCTAAATATTCTATTTCATCTGGGCCACTTACA
TCACTCAAAAAGCAATGAGAGCTATATTTCTAAGGGGGGTTCTAGGATAATAAATACCTGAATAGTGAGAATATGAAGGATAT
GGAAACTGGGCCACTTATATCACTCAAAAAGGAATGAGAGCTATATTTATAAGGGGGGTTCTAGGATAATAAATACCTGAATA
GTGAGAATATGAAGGATATGGAAACTGGGCCACTTATATCACTCAAAAAGCAATGAAAGCTATATTTACAAGGGGGGTTCTAG
GATAATAAATATCTGAATAGTGAGAATATGAAGGATATGGATGGTTTTTTTTTAACTCAATGGGCACATAACTGTGGGAGATA
CTATATTCCTATGAAGAAGGTATTCAGACTTCAGAGATAAGTAATGTTTCCTACATTGTGCTTGTGACTTGGAAGCAGTGGAT
TGAAGAGTGTGATAAGTGCCCAGACCAAGCAGAACAGAAATCAGCATGTAAAGATGATGATCTATGGATATGATCTAAAACCA
TGTAAATACTTCAAATAATTCTATTTAATGCAGTTTGAAATAAAACACAAACTTATTCAAAATACAAATTACTTGGTAATTAT
TTTGGGAGCTATGAGTTCACCAAGAAACTCAAATTCCTATTTCTATTTCAACCCCTGATTCCTACTGTCAATGGGAGGGAAGT
CTCAGAACCAATCACACATCAGACGGCAAATCTGTCAACCAAGAGTCTTTCCACTGAAGGACCTGGGAGGTCAGGACCCTCAG
GAAAGTGCTGGGGACCCTGTCTTGGGAGTGCCCAGCAGATCTCAGAACTCTCCATGGGTCCTGCTGGACACTCATGTAGGGTA
ACGAGTGGCCACCTTTTCAGTGTTACCAGTGAGCTCTGAGTGTTCCTAATGGGACCAGGATGGGTCTAGGTGCCTGCTCAATG
TCAGAGACAGCAATGGTCCCACAAAAAACCCAGGTAATCTTTAGGCCAATAAAATGTGGGTTCACAGTGAGGAGTGCATCCTG
GGGTTGGGGTTTGTTCTGCAGCGGGAAGAGCGCTGTGCACAGAAAGCTTAGAAATGGGGCAAGAGATGCTTTTCCTCAGGCAG
GATTTAGGGCTTGGTCTCTCAGCATCCCACACTTGTACAGCTGATGTGGCATCTGTGTTTTCTTTCTCATCCTAGATCAGGCT
TTGAGCTGTGAAATACCCTGCCTCATGCATATGCAAATAACCTGAGGTCTTCTGAGATAAATATAGATATATTGGTGCCCTGA
GAGCATCACATAACAACCACATTCCTCCTCTGAAGAAGCCCCTGGGAGCACAGCTCATCACCATGGACTGGACCTGGAGGTTC
CTCTTTGTGGTGGCAGCAGCTACAGGTAAGGGGCTTCCTAGTCCTAAGGCTGAGGAAGGGATCCTGGTTTAGTTAAAGAGGAT
TTTATTCACCCCTGTGTCCTCTCCACAGGTGTCCAGTCCCAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGG
GTCCTCGGTGAAGGTCTCCTGCAAGGCTTCTGGAGGCACCTTCAGCAGCTATGCTATCAGCTGGGTGCGACAGGCCCCTGGAC
AAGGGCTTGAGTGGATGGGAGGGATCATCCCTATCTTTGGTACAGCAAACTACGCACAGAAGTTCCAGGGCAGAGTCACGATT
ACCGCGGACAAATCCACGAGCACAGCCTACATGGAGCTGAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCGAG
AGACACAGTGTGAAAACCCACATCCTGAGAGTGTCAGAAACCCTGAGGGAGAAGGCAGCTGTGCCGGGCTGAGGAGATGACAG
GGGTTATTAGGTTTAAGGCTGTTTACAAAATGGGTTATATATTTGAGAAAAAAAGAACAGTAGAAACAAGTACATACTCTAAT
TTTAAGATAAATATTCCATTCAAGAGTCGTAATATAAGCCAAATTCACAGAGTGGAAAAGGCCACACTCTATAACGTTGATAC
AAACATTCCATGAAGGTGCTACTGTGAACAAGTTTTCAAATTGGATGAATACATGATTTGGAGCAAGGTTATTTGATCATGTG
GTGAGACTAAGAATGATTCTTAAAAAGTGCCAAAAGTTTCCTTCAAATGTTTCTGTCACTCCTTATCATAAAGTTTATTTTAC
AGCAGTTTTAGGATTACAAAGAAATTGCACAGGAGGCGTGAGAATTCCCATGACTCCCTGCCCTACACAGGCACAGCCTCCTC
CACTACGACCATCCTGCACCGCAGTCACAAATCAGTTACAATGGAGGAATCTCCAAGGACGCTTGGTTCTTTCTTTTTCTGGT
GATCTCCTAATATAACAAGCCTAAGTATCTCAAGATTCCACGGTTTTTTCAGTGTTTTCTAGAACTGATATTAGTCAGAGGGA
AAGTGGGTAAGGCTATTACTATTTGAACTCTTTCTTCCAAAATCCACAAAATATATATTAATTTAGAGCTTATCTTACTTCTG
GTTTACAATGCTCCTTCCCAGAGAGTAAGATTTTTAAGCTTTTAGAGGCCAGTTCATGTCTCTAAAAGACCAGAAAGTTCTGG
GGAATCCCATAATGAACATCCTTTCATTGGAATTGGAGACCCTGGCAATGAGAGATTCCATGTATAATGCCCTAGAGTTGGAT
TAGGTGCACTGTGAGCTCTTGGGTGGTGAGTCTGAGTAAGGTGGTTTGTGCAGCAAATGCAAACACATTCATGGGACCCAGGT
AGGAACAAAAGCTTCCCTCTGCAAAGGGAGTGTGCACCTGAAGCAGCCCTCACAGAGGTGGGCACTGCTTGCCCTTGATGAGT
GCACATTAGCCAGAGGCATGATCATGATTGGTCTTGCAGATAAAGAGCACCACTGAGGTCATAGGTTATGAAAATGTTTGTCA
TCCTCCAGCTGAGCAAGTCCATCTGCTTGTTTGTGGGTGTCAACTCCATAGAGGGTGCACTTTGGGAGATGACAAGATGCGCA
CAAACCTGCTCTCACTAATTATCCACTACCACACACTCAAGACCAACCTGTGCTCCGGAAAGGAATACGTGCCTGTGGAAATA
GACAGAGCTTAAGTATTTTGTAACCTGGTGAACATACTGCCCAAAGCCACACGTTTCAGGAAGATTAGCTCAGAAATGTTCAC
CAATTGACTGAAGGGCAGTGGCGGGTGAGGTGATGGGACAGCCTCAGGGCTGCACATGAGGAGGGCTCCCTCCCCCATGCAGG
CTTTTCCTCCAGGAGCTGCATCAGGACCTCAAGGAAGATCAGGGAGAATTCTGAGAACACCCTTCTGTGGAGCTGCCTAGAGA
AGAAGAATAAATATGAAAAAATACAACTCTGAGTAATGCATGGATATTTGTTCATGAAAACTCTCTCTGAAAGCTTGTGAAGG
TCTCGAAATACCCCTGATTAGCTGAAGACAAACATTTAAACCCTCCTTCCACAGGGAGTTCAAGCAGGCTGGATGTGTCCTTC
TATGGATGATCTTCCCCAACCCCTTCCTCTTCCCAGCTCATCCCTGGCTCTCTGTGTAAACAGTTCTCATCAGTGGAATGTGG
TTGATGAAGTGACGTCTTCAATTTCCTCATCTTCTTGGTGGTCATGTTATTTTTTTTCATCTGAGGGTTAAAAACTCACCTGC
ATGCAGCACATGACAGGCTAAAATCTCTTGTGGACAAAACGGTAACAAAGGCACCCACCAGGGTTGAGCATCCGTGTTGCTGA
CAACGACCACCAGGGGTCAACGTCCTCTTCACAATCCTGTGTCAGAGCATCACTGGAATGATTTCATTAGCAACTTCCCAGGA
GAATCAGCTTAAAAAATACTTGTCCCATTTTCCATGCAGATATAACCCATCCCTTTTCCTGAAGAAACAGAGCTCAATACTAA
ATACACTGAATGTTGTTTTTGCTGGTTTTGTAAGTTTGTGACTTTATCACTTTCTAATTTCTGAGTTAGGTGGACCACTCTAC
ATATTTCTCTCATGGGTGTGACCAGCCTTCTGGATGTCAAATATAACTGACTTTGTTCGTGTAAATGTCAACACAAGCTCTTC
ATGGTTTCGGTGCTCACTGACTACTCTAAACTTACACAATGTGTTTCTTTATTAGCTTTGTTTTCTGGTATCTCTACGTGGCT
TATTCATCACGCCCATTTTATGTTACTTGTACAGGTAATTGATTGTTATTTTTAAAATTTACTATTGCTTACTTTAATTAAAT
AAGTAGGCAATAGCTTAGAATAGAAAATAAGGTAAAGTAAAAGTACATGCAGTAATATTTAATATAAGTAAGCAGGCAGCTGA
AAGCAAGGGAAATCTACTCTGCTGTGTAAAAGGGTATGGAGACCTCACAGTATGATGATCTTCTGCAGTTTAATCCATACTGC
TACATAAGTGACAACGTCCACTCTGTTTATATCAGAGCTTCCCCTAATATGTACAATGAAGACTGAGCCCAGGTACCTCCAAC
CAGAATGGCCAGCACCTTTTACCAAGTGCCTGAACTGACAGCAATAGAGATCACGTTTGTCTAAAAAAAAACTCACACTGTAA
GGATACCCACCAGTCATATGGAGACAATTAGAAAAAATTAAAGCCCAAGCCTGATAGGTAGTAATTTGTACTTAGAAGAATTA
ACTTTTATCTCCACATGTTTTTTTTTTAATCATAGAGAAACTACTAGTGGTAGTTCCACTGTCCAAGTTACTGAATATCTTAT
TCCTAGAATGAGACACTGCACAATGTGTTCTGACACGACAGAACGTAGCTGTAGTTAAGGGACAGGAGATGTGATCACGGGAA
CACGAGTCTGCGATCCAGCAGTTCTTGCTCCTTCACATTTGCCCAGAAACAAAGACCCCAGCAGAACAATGGAAGCATTGACT
TAGGTCTCCACAGTCTGATGTGAGATAAACAGCAGGTAGTTTATGCCTCTGTTTTATAGCAGGAAATTTAATCTCTAAAGAAG
GGCCATTTTGGAGATAATACTATTCTCCAGGATGCTTAAATGCCCCCAAACAGAGAGCACTGCAGAGCCCCGTGGCCAGGAGC
TACAACACCTGGGTCTGGAAACCACTGGACAGAAATATGAGATTCTCTTACCACATGTATGATGGAACCTTGAAGAATGTTTC
CTTCCTTCTCCATAATCACAGCCTGCGATGAACTGGAGGTCCCAGTACATAAAAAAACATGTGTCTGCATTGGATACAGAATT
AGTCCCATAAAATAATTGTGCTACTGTGGTGCTCACACTGTTGGACCAGCTGACCAAGAAAGTGTTGTAAGAGCTGCAGTGTC

FIG. 6 (Cont. 11)

TACTGATTCCTACCATATTTGGGGCTACATTCACATCTATCAAGGGAAAGAGAGATAAGAAAATCTCTCTAGGCCGGGCGCGG
TGGCTCACGCCTGTAATCCCAGCACTTTGCGGGGCCAAGGTGGGCGGATCACGAGGTCAGGAGATCCGGACCATCCTGGCCAA
CATGGTGAAACCTCCATCTCTCCTAAAAATACAAAAAATTAGCTGGGCGTGGTGGTGGGCGCCTGTAGTCCCAGCTACTCGGG
AGGCTGAGGCAGGAGAATGGCATGAACCTGGGAGGCGTAGCTTGCAGTGAGCCGAGATTGTGCCACTTCAACTCCAGCCTGGG
GGACAGAGCTAGACTCCATAAAAGAAAGAAAGAAGAAAGAAACAAAGAGAGAGAGAGACAAAGAAAAATAAAGAAAGAAAGAA
AGAAAGAAGAAAGAAAGAAAGAGAAAGAAAGAAAGAAAGAAAGAAAGAAAGAAAGAAAGAAAGAAAGAAAGAAAGAAAGAAAG
AAAGGAAGAAAGAAAGAGAAAGAAAGAAAGAAAAAGGAAATCTGGCCTAGTCTATTGATTTATTTTCATTTCTTCAAAATGAG
GTAAAAAAATCGCATCAACTAAAATGCGGACGATGATGAAGTGATCAAAGACAACAGCCACTCAGTGTTTCAGGTGTGTTTTA
ACCCAAAGTCACACAACATGTGAGAAGCTGAACTCCGGAGCCAGGGGCATCTCTGAGGAGAATGTGGAAGGTGGGCGGGAGGA
AACAGTGATTCATGTCTAGGGAAATTTCAGGGCTGCCTGCTCTAGGGGAAAGGAAAGCCTGAGCCTCTCCCACAGTGTGCTCT
GTTAAAAATTTTGGCTGACTTATTGTATTCTTCGACACAAATATTTTTGTTTCGTCCTCTTTTAAATTTTTTTATCTCTATTA
AAATTCTCACTTTGTTCTTGCATGCTGCCACTAGCTTATTAAACATGTTTCTAATATTTACTTCAAATTTTCTGCCAGGACAT
CCATATGTTTTTTTATTCATTGATGCCAGATTCTGGACCTCTATGTTGTCTGTCTGTTTGGACCATGTTCCCGTGTTTCTTCA
TTTTCCTTGACGGTCTTTCTTGCTATCCGTTCATCATAACAAACAGCTCTTTGCTCATCATAACAAAGAGCCACACTCTTCCA
AGCCTAGGCTCATAGAGACAACCCTCACCAATCACTCCATCAGTGATTGCGGATCTCTCAAAACTTCATAATGACTTCATAAT
ATTCCAACTTCTGTCTCTGTTCTTAGTGGCCCCCAGGTTTAGAGAACGTTGGGTTGTGCCAGGACTCCCAAATAGGAGAGGTA
GAAACTATATACTCAAGTAGCCTCTTGAACAGTGTACCATTAGACACAGTTTTATTATTGAGGTATGATTCATCAAAATAATG
TTAGTTCAAGCGCCTCTCAACCAGTCATCTAACATTGAAATGTTATAATTTCTTATTTGGATCTCTCTGGAGTTTATCTTTTG
AATATTTAGGTAAAATTACAAACTAGTATAAAGCTATTTGGCAAAATTATCTGCTGCAGAAGTTTCATCTTCTGTGTATCTCT
TTTTGCACTTAAATATGTTTTTATTAGTCATGTATCCAGAATATAGAAATATGTCTTAAAGTTCCTTCATTTTTTTAAGGTTA
TGGGGTTTTCAGAAGAGGTGAGAACCTTCTTTATTTATAAAATACCTGATTCCACATTGCTGGATAGTTTCTTCTTTAATTTG
TCTCCTCCTCTCACATTATACTATATTAAGCAAGGAGAAATCAAAACACACCATCCACACTTTGCTTAGAAATCCCCAAAGCT
AAATTTTAAGTATCACTTACTAATTCTAATTTTACCCATTGTAACTTAATTAACATGAAATCTATAACAAGGTTACACATACT
TTCCCGTTCTAATACCATGTTCGTGACAGAAACAAAGCAGGTGTCTTCTCTGCAATGTGGTCATCTGAGGTCTGAGATGAGGG
GTCACACAGGTATTTTATAATATTTAAGGGTTTGGACAACAGTAGTGATAACAATTCTGAACAGCACTGGCTCCTAATTGAAA
GGTTATAGGTAAATTTAATGCTGCAATTTTATATTAACACCTTGTCCGAATGAAGCTCAGAGGAAGATGCCACATCCCAGGTC
ACACAGTGAGGAGGAATGGAGCTGTGCTCTGCTCTCCACACCACCTACAAATCCCAGGCCCCAGCCCAGGTTCCACTGGCGCA
CGGCACCTAGAGCACAGTTCCCAGGGGATGATCTCAGGGCACCTGCTTCCTCGGGCAGGGCGCTGCCTTCTCTCAGTTGTGCA
CTTGCTCCTCCTGCAGGTTCTGTAGTGAGCACTTGCATTGCCGTGATTTATACATGTTCTCTCCCCTAATATGGAAAAAATAT
TTATTAAATTTTCAACTCATTTTCTCTGATGCACACTGCATTAGCAGAAAGGAATAAATCACATTCCTTATCCTCCCATAAAG
CCAAAGATTCCCGAAGACAGAGCTGATGTGATGTACTCATAGGTGGATCTCTGCCCCTCAAGGGAGGCCTTGGTCTTCAAGTT
TCAGTAATTCTAGGAAGCGAAGGACACCTACATCTCCTGCTCCCTGCTCTGTAGCTCACCTGAGAACAGCTTTCTCATTGGAA
TGTCTTGTGTTTAAGGAATAAGAGTCCATGTTTCAGGTTCGGGAGCCCAGGTGCACCTACTGGATGCAGCCCAGGATTGGAGA
CACTTTCCAGAAGACAACATCACCTGAGACATGACCAGTCCCACTGTTTCACTTTCACAATTTCAACTTCCTCAGAAGAAAAT
TAAAATTGCTGAGACTTGTTCATAAGTGTTGTGCCATGTCCTTACTCTGTTTTCTTGCCTGTTCATTTATGTCATACCAGGTG
TCTGTTATATGTAATAAGATCAAAATTCTGCCTCCAGTAACACATCAATGGAGACCTTTGATTGTACTTTTGGTTTATGCACT
GACACATAGATTATGATGTTCATCACATTCATTTTTATGTCAAAGGAAATCTGCATAATCTGAATGCCAATACTTTTTGGAAT
CTGCTAAGTAACTGAAATTGAAAAAAAAATACCCACTCAAGAACCTGGATAGACAGCCATGTCCAGAATGGCAGTTGACACTT
GTTTAACTGGAAGAGAATCTACAGAAGCCACAAGTTGTTGAGGGCACTTACATGATAAGCACTATAGTTGTCTTAAAGACAGA
TGTGGACTCAGTAAATGTGACTGTTCCAGAGGGTCTTATATTTCTATGTTTTATGGACTTTCTCACCAGAAACCTCCAGATTC
TAAAAAATACTATCCAAATACGTTTCTTATTTGTCAGATTGGAGAAGATTAATTACTGAAAAATATTACGGGAGACTTTTTCA
AAAGCTTCTACATGGAAGGACTTTTCGAGAACCTTGTCCTATGTAAAGGAAGACAAATCTCCCATTCCAGATTTCTCTCCCAT
TCTTCCATTATTATAGAAATGAGCAAAGTTAGCCAATAGGGGTAAGATGTAAGTAAATAGTCCAGGGACACTGAAACCACAAA
AGGGAGTAATGGCCAAAGTAGCTTTTCCCCTGGAGATTCCTGGTCAAAGTCACAGCCCAGAAGAGGAAGCCGATCGCATCTCT
AGGTTTCCATTGTCAAAACAGGCAGTGCTTGCCTGCACTGCACAATCCATTCTAACCAGTGTGATAGCTCTGGATTAAAGATG
GAAGTGTGGCAATGCACAGACTCTATGTGAGAAGAACACTGGAAAACTAAAGGACAAAGGCAGAGAGTAGGACAAGGACGACA
AAGCAATCTGAAGCCTCTGACATCACCATTTTTAAGATCAAGGTCTTGGAAACTCCCTCATTGACCTTTAGATCTCTAGGAGA
AAAAAGTCAGATACCTGGGCCTAGTGTCAGTGTAGGAGGAATTTTCTATAGGCTAGGCATTAGGAAGAAGGGAAAATTCTTCC
TTATTAGGAAGTTATTGTTATAGTGTTATAGTGTTATTGGAATAGTGGATATGGAGTGGGCTTTCATCTCGATCAATCTGCAC
CTGCTGGTATTTTCCAATGCTACATTCACCTGCAAGAGCCCAATGAAGAAAGAAGGCACTCCCAAATCTTTTGCAAGTTTTTG
TATTCACTGTGGGTCCACTGCTTAAGTGCATCTGGAGCTTCAGAGAAGGGGCTCTGTCCTGTGTCATAGAACCCTTGCTTTGA
GTCTCACGGCAGAGTTCAATCTGTTTAGTAAAGTTGATCAATTATTTCAAGAGATGGTGTCACCAGCATATGGTGTCACTGAG
GGAGTATTCTACACTAGCACACAGCCATTTCACGCTGGGCTAGAGAAGCTGGGGGGAAATGCTTTGTGAGCCCCAACAGGAAC
CTCCTTGCAAGGCAAGGGCTGGGCGGGAGGGGGCACTCAGGAGCCACTCAGCACGGGTTCCAGCCCTGCAGCTGGTGCACAGG
AGGCTGCTGAGAAGGTTTCCTCTCAGGGGCTGGGTCTTCCTTTGGGAGAAAAAAGCTAAAATTCAATAAGTTGCTGGTGTGCC
CTTAAATATTCTATCACATCTGAGCTGCTCCCACAATTCAAGAGAAGGAGAACTATCTTTTTAAATATTCTATCACATCTGAG
CTGCTCCCACAATTCAAGACAAGGAGAACTATCTTTTTAAAGTCGGCTTCTAAGATTATAAATACCTTAATAGTGAGAATATG
AAGAATAGGGATGGTCTTACTAATTCAATGCAGAGAGAATTATGGGAGTCACTATATTTCCATGAATAATAATTTCAGATTTC
AGGCTGGGGCTGGTGGCTCATGCCTGTAATCCCAGCACTTTGCGAGGCTGAGGTGAGCGGGTCACGAGGTCAGGAGCTGGAGA
CCATCCTGGCTAACACCATGAAACCCTGTCTCTATTCAAAATACAAAAAATTAGCCAGGTGGGGTGGCATGAACCTGTAGTCC
CAGCTACTCGGGAGGCTGAGGCAGGAGATTTAATCCTACAAGACCTACAGCCTCAGACAATGCTGCTGTCAGTGATCGTGGGA
AGCAGAGTTTGCAGTGAGCTGAGATTGTGCCACTGCACTCCAGCTTGGGCAACAAAGCGAGATTCCATCTCCAAAAAAAAAAT
TCAGATTTCAGTGTTAAGTAAAGTTGCCTACATTGTGTGAGTGACAGGGCAGTGGTGGATCCGAGAGTGTGGATCTGAGAGTG
AGTCAGAAATCAGCATGTAAAGATGAGGATCTATGCACATGAACTGAAAGTATGTAAACAGTTCATGAAATTCTAATAAATCC
AGTAGGAAATAAAACCCAAACTTATCCAAAACACAAATTCCCTTGAAATTATTATGGGAGCATGAGTTCATAAAGAACTCCTA
ACTCCTGTTTCAACTTCTGAATCCTAGTGTCCATGACATAAGAAAATCATCTCCAATTATGCATCACAGGGCAAATCTGTAAA

FIG. 6 (Cont. 12)

CTAAGAGTTTTTCTGTTGACGATCCTGGGGAATCAGGACACCAGGAAGGTGCTGGAGAAACTGTCTCAGGAGCGCCCCAGGGA
TCTCAGAGGAACGTGCTGGCACTCACGTGGGACATCAGCGTCACTTGCTCAGAGTCATCAGTGAGCTGTGCTGGTGTCTGACG
GGTCCAGCATAGGGCCAAGGCACCTGCTCTGTGTCATGGACCGAGATGGTCCCCAGAATGATCCAAGTGGTCTCTGTGCTAAT
CTAATGTAGTTTCACAGTGAGAGGCCGTTCTGAGGGGGCTTCTTCTTCAGTGAAAGGACCTCTGTCCACAAATATTCCTAAAT
GGACAGGGGCATGCATTTCCTCAAGCAGGATTAGGGCTTGGACCATCAGCATCTCACTCTTGCAAGGCTGATGTGTCATTTGT
CTTCCCTTTCTTATCATGGATCAGGCTTTGAGCTATGAAATGCCCTGTCTCATGAATATGTAAATACCTGAGATCCACTGAGG
TAAATATGGTCTGTGCCCTGAGAGCTTCACCCAACAATCACATCCCGCCTCTAGAGAATCCCCCGAGAGCATGGCTCCTCACC
ATGGACAGGACCTAGAGCTAATCTTCCTGGTGGCAGCAGCTACAGGTAAGGTGCTCCCAAGTCCCAGTGATGAGAAGGGGATT
GAGTACAGTCAAGGAGGCTTTCATCCACTCCTGTGTCCCACCCTCCAATGGGTGTCTGCTCCCAGGTGCAGCTGGGGCAGTCT
GAGGCTGAGGTAAAGAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCTTCCGGATACACCTTCACTTGCTGCTCCTTGCA
CTGGTTGCAACAGGCCCCTGGACAAGGGCTTGAAAGGATGAGATGGATCACACTTTACAATGGTAACACCAACTATGCAAAGA
AGTTCCAGGGCAGAGTCACCATTACCAGGGACATGTCCCTGAGGACAGCCTACATAGAGCTGAGCAGCCTGAGATCTGAGGAC
TCGGCTGTGTATTACTGGGCAAGATACACGGTGCGAGAACCCACATCCTGAGAGAGTCAGGAACCCCAGGGAGGAGGCAGCTG
TGCTGGCATGGAGGAGATGACAAAGATTATTAGATTGAAGACTTTCTTAGAAAATAGCATTAAGTCATTTACGAAAAGGAACA
ATATAAATGTGTATTTGAGAAATTGTAATTATTTGAGAGATTTCTTATGCAACATTTATTCTGTAAGCAAATTCTAGGGATTG
GAGAATTAATCAAATTAATAAAGCTGACATAGAAATTCCTCTGAAGGTATCTTTGTAAACATCAATTTCTGAATCAGTGTTGT
AAATGTTTTGGAACACAGACACAAGATCACATTTTAACTCTACTTTTGTCTCTATAAAAAATGCCAAAAAGAGTCTCATTTTG
ACCATGTACCTCTTTGAATTCCCACCATCAATGAATGATTGTTCTTGGGTTTCCACATTATATTACCATTTATCATTATGAGA
ATTGTGTGTTTTAACCATTATAATAGGTGAGTAATGGTATCTAATTTTTGCTTAAATGCACATGCCCCTAATAAAATTCATAT
TTAACAATTTTCATATAATTTTTGGTGAGATGCCTCTCCTGATATTTGGTTCATTTTCAATAGCACTGTTTTCTTTTGATTAG
TTGTAAGTTTACTTGCATATTGATTATAAAAGTTAATTAACAAATTAAAAGAATTCATTTAACAAATATGTGACTTGGAAGTT
GCAGGGGTTTGTCCTGCACACCCTGACACAATGACGAATGAATAAAGTGCACTGACACAAAGATATTCTGCTTTGCCAGCTCG
ACTGAGCATCTGGGCCACTTAGTCACAGCCACCGCCTCGATCAGTCAGGGAGACTTACATTTATTCAGTAAAGATTAATTGAC
AAAGGCCGTGAGTAAACACCACTAGAAGGTAATTGACATTGTGGACCTCTTGAGTGGAAAGCAATTAAGCACCCGCGGTAGAT
CAAAGGTTAGTCTTAGGAACACATGAGTAAACAAGCTAGTTAGATAAGCTCCTCACATTCCTTTGTTTCTACTCTACTTTATG
TAACTAAAGGTAAGGGGACTAGGCTGCCTTCAGCCAGATTTATTACCAAAGTTATGCAAACTCACAGGCCTTCCAAGAGGGTT
TGTGGCTATTAGAACTAAAATGTTTCCCACCAGCCTGACTGGACCACCACATCTCCCCATTTTTTGTTTTCTACATCAGGTCT
TTTGGATTGGAGCGTGCAGATATGCGCAGCAACATGTCTGTCAGGTGTGGCAGTCATTGCTCTTATTCTGGCTTTGCATCCTA
GAATTAGCAAATAACATAAAACAATCATGAGTAGAATTAGCAACATTCTTTTCCAGTCAGAGTGACCCCCAGGAGCGGGGTCT
AACCAGGAGAGATGATCTCACACACCCTTCCATATGACTGTTTGTTGGGGGTGTAGATCTATTGCGTGAAGAGATTCTAAAAT
TTTAGTTTGAACTTACTTTACGTCTGCTGTTAAATTGTCATGAAAGGTTCCCCAGAGGTATTGTTTTACCTCATCCTAACTAT
GTATTGATAGATTCCGTGGTAGAGAAGTGATACAGATATGTTCATGTTCCCAGTCACAGTTTAAATGCTGTCAGAATGCCACT
GCATCTTGTCGCTCCCTGACATATTCTAAAGCAGCCTCAAGGGCTAGCAGACGTGTGATAATTTTTTGATCTATACCTTGCTG
TAAGAGAAGTTCATTAGACACATTTTTGGCCAGATTATCTAAAAAGGCAGCAGTTTACACTAAGTCAATAATACATGCAACAG
CAACACTAGCTGTTGCCAGGATGACTATGGCTGAGACTATAAAGGCCATAAGTGTAACTATGAATCTTTTGTGTCTGACCTGG
GACAGGGCACGTTCTAAGGTTGCAAGGGCATAGGAACCTTGCCAATTGCATGCCAGATTGACTGGTAAGAATGCCTCAGATTT
TCTCTTTAATACCATGGCGCTAGTAATTTTTAAGTTAGATATACTGTGATTAGTGATACATGAGGCAAACCAAGCCTGTCCCT
GCATCCAGGTCACAAACGTGGAGTTTTGAGGTGTAATGGAAATGTTAGTTCCCATAAGGAAATCGTATGGATGGGTAGTGCAA
ATTAGGCACTGATCAGTGTGATTATGAATAAAGCTTATAGCATAGTTGCAACGGGAAATATGGTATGTCCCATGCCAGGTGTT
AAGGGAGGTGCTAAGATGTCCCAGACACCATAAAGTACCTTGGGGCGGCATGGACTTTACTTGGGGCCTTGGATATGCCATCC
CCCCTTGGCACAAATTATAGGGGAAAAGACATGGCTATGAAACTGATTGATGCTCTGATGGATGAAGGTATTAGTAAGGCTGC
CCTGCAATCAGCCGCTGGGACTCCAGTCTAAGATGTTATAATTACCTAACTGGAGGCTATGGGCTCGTCTCCCATGACAGACC
TCCCAGCTAAAGTCGAACCGATTACTGTCCCAGCTTTGTTCCTTAGCACAGGAAGGAATGTTTGGGAAAGAAGCAGCGGCATG
GATTGCATTGCTCAGTTTGAGGCTATCTGCAGCTAAGAATGTTAAGGCATTTCCTTTGCTATGATGTAACCATACTTGTTTTT
GGGCAGGTACACAGTAAGGGTTAGAGTCTTTATAACTTACACACACTGGGAGGATAATAGTGGATTGACATATAGTGTTATCT
GCCACCTTAGTCCATTGTGTGCCATTATTGAGGGACCCCACGTGGGGTAAATCTATCCCTCCTAGCCAAGCAGTCACGTTACT
ATAGGCTGGGAAGGGAGTGTCTTCCCATTTGGCAGGGTGAAAGAAAGGTGTGTCTAAGATAGAGGCCCAATAGAGTGTAGCAG
GTACAGGTTGCAGACAAAGTGAGAGCATAAAAAGGATTAATACCCTACATGAGTTGCAATGTACAACAGAAATCATAGCACCA
AACACATTATCTGGAGTAAATGGTGTCTGCATTTGGAGCAGGATTCGTTCAGCCTCCTGAGTTGTCCTTTTCAGTACCCCCCA
GGTAATGTCTGGGGATTGTGTTGTTCACAGAAGCTGCATCGTCCGGGGCTGTAGGTCTTGTAGGGTTAACTCCTTCATTTCTG
GTACTGGGTTGGGTCCTAGCAATGTCCTGGTATGGTTTGATGCGTCGTGCTGGAACCCAAAGACGACCCGAGGGGGTGTGGAT
ACAAGCGTACCCTCTTCCCCACATTAATAATTCACTTGGACCACACCATTCATTACTGTTTACATCTTTCCATAAAACTGCAG
GTTTCATGTATTGGGAAATTTTAGCAAAGTGCTTTTCTACAGCGGATTCAAATTTGTCTTCTAAATTAAAAAAATAAGGTTTG
TGCCAAAAGTGTTGCAGGGTCTGTACCCATACTCCCCTGTTTTTGTTTTTTGTGCATATTTTAAGGGTGGAGTTGGCAAGTTC
TACTATTGCTTGTCCTTGGGGTTTATATGGGATACCTGAGGAATGTCGGATATTCCACGTGTGACAAAATTGTTGAAATTGTG
AGCTGGCCTAACCTGGACAATTATCAGTCTTAATTTTTGCGGGTTGTTCCATAAATGCAAAAGATAAAAGAAGATGTTTAATG
ACATATCGAGTAAACTCTCCAGGCGGAGTATGTGCACTACTTAAATGAGTGTTGATATCAAAGGATACATGTACCTATCTAAG
TTTTCCAAATTCAGGGATGTGTGTAACATCTGTTTGCCACAACAGATTAGGTTCTAGGGTTAATACCTGTTGAAGGAGGAGAC
GTGCCTGTGAGCTGGCGATCTCAGAGACTGTTTAGCCAGTCTCTGTATAAGTTGAGCTGGCGATCTCAGAGACTGTTTAGCCA
GTCTCTATATAAGTTGGAATTGTTTAGATAAGTTTTTCCAATTTTGGTGGAAAAATTGGTGCAATTGGGTGGCTTGGTCAAGC
AGCGATATCATAACTTGAAGGTTGGCTTGATTATTGTCATAAGCTAATGGACCAGGCAGTGAGCTGTGGGCTGGAATGTGTGT
AATAAAATAGGATGTGTACTTTGATTTAGCAATTGCTGAAATCAGAGAAAAAGAGTCCACAGGGCTGGCTCCAGAGTTGACTT
AATTAGGGCTGTAAAAGTTCTCTAGACCCAATATTAAGGACTCAACTTTAGCTTTCTGAGTGCTAGTAAACCCAGATTGAGTG
AATGAATTGTGTGGTGTCCACCAGACTGCTGCTTTTCCATATTTACCAGATCTATCAGTAAACAGTGCTAAAGCATTAAATAT
GGGGGAGTAAACTATTTTTGTAGGTAACACATTAACTAGGCCTTTTGGGAATGATGAAAATGGGTAAATTCTAAGGGCTGTTA
GTAGAATATTACCCATAAAATGAATAATCTTGTAGCCAGGAAACTTTTCCTACTAGGGAGCAAAGCTTGCTTTTAATTGCTC

FIG. 6 (Cont. 13)

CCTAACTAACTTAGGGGCTTTTTGTAATGTCTCTCCCTTTAGAGGTTACTGTTTTACTTAAACTGGATTTGGAGTCATGTTAG
GAATAAGAGAGAGATAACAGTGGCCATTATTAGAAAGAGGTTTCTCAAATTCTTAAATTTTACTTAACTCTTATCATAGAATT
ATAATCTGGGATGTCGCTTGTATACAAAGAACATAACAAATTTGCTTTGGGCCGCCTGCGGAGCCAGAGAGCGGAGCAGGTG
GGTCCCAGGGCGGCTGCGGCTTTGTGCTTGCTTAGAAGCCACTTTTCGCCACCGCGTTTCCTCTGTGCCAGCTCCCTCCCCAC
ACTGCTCAGCAGCTGCTGCCGGCAGAGGGGAGCTTCCTGCACTTGCTCCTGCCCCTAATGCCTTTTCTTAACCCTTCGTGTAC
CTGATTGCCTTGCTGATCTTGCATTACTGGGCAGTCTAAGAGCTCCCCTTTTAATGCTGCTTGTCGAAGACAGGGACATATAG
CTGTAGTGTATTTCCTCTATTTTTTCTATCTATTGAAAGAGGGGGCTCAGGCAAAACCTCCGTTTCCTCTTTGTTATTTTGGG
AAGAGCAGGTGGTAAGGCAAGTGACGTTTCTTCCTCCTTCCCCTTTTTGGGTTCTTCTTTGTATAATGGGACTAAAGCCATCC
CTACTAAAGCCCATAGTGTTAAAGATGATGCTGGGACCCGTTGCGCTTGTGTGTAATGCTGTTCAAGATTTCTCCCTACTTGT
TCCCAGAGCTTTACTTCTAGCTTTCCTTCTTCTGGGACCACAGATTATGTGAGACAACAGTTTTCATTAGGTGCCTTAATTGA
GCCTGCGAAACTGATGCTCCCCTAGCCTTAAGCAACTGTTACAATACTTTCATATGCTGTTTGTGTTGAGCTGATAACTGCTG
TCCCATGATGAAATCTCAGCCTGAACAATCTCCCCTGAACTTGGAGATCCCAAGTGGGCACCAATGACTTACTGTTTTACTGA
CTTGACCACGCAGTCTTCCTCAACCTTCGTTTTCATGGGGTCTGTCACGCTCCCTTTGCAGCGATCCTCACATGGGGCACCGG
CTGTGGGGGTCTGTCCTGCAGGTCCTGACACAACAACGGGTGAATAAAGTACACTGACACACAGATATTCTGCTTTGCCAGCT
TGACTGACCATCCAGGTAGATCAAAGGTGAGTCTTAGGACCACATGAGTGAACAAGCTAGTTAGATAAACTCCCCACATTCTT
TTGTTTCTACTCAAATTTACTAAACTAAAGGTAAGGGGACTAGGCTGCCTTCAGCCAGATTTATTACTGAAGTTATGCAATCT
CTCAAGCCTTCCACGAGGACTTGTGGCTATTATAACTAAAATTTTCCCACGAGCCTGACTGAACCCCACAGGAAGTATTTTC
TCCAAGTCTGTGGTTGCCTTTTACTCCCTTATCAGTAGGTATCGCAGAAAAATGTGTGTGTTTGTGTGTGTGTGTTTGTAC
AAATTTAGATTGAAAACATATATAATTTTATTCATTCATAGATCATGCCTTTGGCATTATATCTGAAGTTTCATTATAAAATA
AACTAATAGTCATTATTTTTTCCATATCTCTAATCTCAGGCCACAATCAACTCATGAGTGTTTAAACTTCACCTGCTTGATTG
GAGGACCATCAATCTAATGTATTTGGAATACTTCTGTAAGGAGATGTGTTCTTCTTCCTATTATTTTTTAATTAATCATCTAT
TAATATCAGTATTGGTTGATGGATGTCCATTTTATACTTTGAAAAAGATCCATGCTACATCATTCATTTAATTGTTCAAAGCA
CCACAGCTTTATTAGGTGCTGGGAGCTCATTTTGTTTGAATCCTGCATCCTTACAGCACACCTCATATTTTTGTTTTTGAACA
CTTGCGTATTTCCTGGTATTACCATAAATTCTAAGCTTGTTTTCTTTATTACCTTTTTTTTACATAGAATCAACCACTTTTATA
AAGATTGCATGTTTCTGATGTTAAAGAATAGTATTAAAATAAAACATTGTGATACTGGCTCTGTGTGTTGTTAATGTGGTATG
AGTACTTCTAGAACCTCTCAAACAATGGTCCCAGTAAACGTGCATGTTTATGTGAACCCAAGTTTATGGACTCATTGAAACTA
TTTATGTATCTAATCTTCTGTAACCATATCACATTAAAAATGAGAACACACTGGTCTCTCCACCCAACTATGTTAGCACATGA
ACCTTTCTAGTCTTCTTTCTTTGCGTTTCCATAACCACCCACTGCAAAGTGAGAAACCCCATTCCACCATATGTAATTTTATT
ACTTAGCTGCACAGTTTCAGGACACATGCATAGCAGTATCAAAAGTGTAAAGCTGTGCCCTTGATGGAACCATGTTTATCTAC
TAGAATAGAGTGCTTATGTGCAGATTTTTTACACATTAAACTTATAGAATTTCTTCGTTTTCTGAGTTGCTTAGGTCAGCAAC
TTCATTTTCCACATTCTTCAATGAAGTCATTTCAATTACATTGTATAATTTCATTTATTTGAAATTCCATAAATGCTTAGACT
ATAGTCAAGTAAACAGACAGAGGATGTTCCAGGAATTTAGAGAGTGGGTATAAAATAAGCAAAAAAAAAAATGTGGTGTTTAG
GAAAAATAAAACTATTTTTAGTGATATGCAATGGTTGAGATATGATATAACTAATTTGTCTAAGCTAATAATTTTGTGATAGA
AAATATAAACTTAAACATATTCAATTAAAAAAATTCAGCAGTTCATTAACCCCAGGATTAAATGCAGACTGTATAAAATTATC
CAATAACTTATTTGGTGAGAGTGGGGATGTTATGAGATACATGCAACAAAGAATGAAGTAATTTTCCCCATTTGCATATACAA
TGTTTCCATTCACTGAAGACCTTTTATTTTAAAAAAATCAATTTTCTACCTTACCCTTGTTTTTAATTCCCGACAAGCAAATA
ACCCAAAGGATTCTTTTCTTTCATTGGTTGAGAAAGATTTTCCCCTAACTTCAGCTTAGTTCAGGCATACGCTGACCTGAATG
GGCATTTACCCTCAGATGGGTACACACCTGTCAATATGTGGACTCTTCTGTCAGACAGACACAGCTTCACTCATGTGGATTCT
TCCCTCAAACACAAATGTCCCCACATGGACTATTTCCTCAGACTACCACATATGTCCTTACATTTACACTTTCCTCAGAAAAC
AGACATTTCCTCATGTGGACTCTTGTCTCAGATAAGCAAACATGTCTCAGTGTGAATGAAGTCTTCACTCAGATAAGTACACA
TATTTCAACACTGACTGTTTCCTGACACAAGCACATATGTCCAATGTTAAACTGTCTTGCGACAAAATGATCTCAAGATAATG
ATAATTATAAACTCCAACCCTGAAAATCTGTAGATCTGCATTTTGTCTATTGTAACATAACTTCATCTCATTGTCAGAAACAG
TCGTTTGCAGCTATAAATGCACTGATTACAGTCAGATTTCCATTTTCTCTGGAAATGTATTTCTTATGTTCTTACTGGACTAA
TTTGTTGATAATGTTTGCTCACATGAAGATACCTGAACAGTGTCCACATTAGAGAATAAAAAAGAGCAATGGGCAGATTAACC
CTGTGCATCCAGACGCAGGAACCATTTGACTCTGCCTTCCCTGAAATGGAGACACAGAGGATGGATGAGCAACGCTGAGTGGT
GCACCTACGACCACAAAGAGAAAGACCTGGAAATATGTCCCATCCCCTCCTCATGAAAGGCAGCTCATCCCCTGTTCCTTCAG
GCCCTGGTGAGGAGCCACCCCATATCTGTGTCTTTCTTCAGTGTTCACACTATGGAGTCTGCACTGATCTGGGTTTCCCTTCT
CATCACCCTCCATATTAGTGTCCCTTGTAAATCAGGTCCAGCTGTGGCTGCTCATAGGGTTGTTCTCAGTCTATTTCCTCTGT
GTTCATAGAAGTCCTGTATGAAGTTCAGTGGTGGAGTCAGAGGGGTAAACGTAGTACAGCCCAGTGGTTCACTGAGACTTTCT
TGCAAAGCGTCTGGATTCACCTTTTCTGGCAACAGCCTGAGGTTGGTCCAGCAGGCTTCACAACAGGGATTGTGGTGGCTGGC
AACAGTGAGTCAACAAGTGGGAGTGCTCAGGTTTACTCTTCATGAGTACAAATAAATTAACTGGTCCAGCGACACCCTTTCAC
GTGCACTCTACCTTACAATGACTAACCTGAAAGCCAAGGACAAGGTTGTGTAATACTGTGAGCTTCACAGGAGAGAGATTATC
TGCACAAGCCCAGACACAAAAATCTGCAGGGAGACAGGAGGGAACTGCATGGTAGATGCTGCTCAGAAGCACCAGGGGGCACT
CAACACAAGGGGGCGCTCAGGACACCAGGCGGCACTCAGGATACAGCTGGGGGCGCTCAGGACACCAGGGGGCCACTCAGGAT
ACAGCGGGGGGTGCTCGGATCCACCAGGGGGCTCTTAGGGCACCAGGGGGCATTCAGGACCACTAGGGAGCCCTCAGGGCCAC
CAGGAGGACCTCAGGACACGTCAGCGTGCTGGAGCCACCGGGGGGGGGGGGGGGGGGCTCTGAGGAAACCAAGAGACGCT
CTGAACCGCGAGGGGAAGGAAGCTCAGGACCACGAGGGGACGCTCAGGACACCAGGGGGCGCTCAGAACACCAGTGGGCACTC
AGAACAGGAAGAATCTCTTAGAAAGCAGCTCCACATCAGGATCCTGGGAGGCTGTGGAGAAATGGGAACACTCATAAACTGTT
GAGCATTTAAATTAGTACAACCACTATAGAGAACAGCTTAGAGTTTCCTCAAAACCTGACGATAGAGTTATCATATAATCTGG
CAATCCTGCTGCTGGTATATACCCCTAAAAAGGAAATGTTTTTGCACTACCATGTCTGTAATAGCACTGTTAAAGCACTGTTC
ACAACAGTCAAAATTTGAAAGCAACCTATGTGCCGATTAACACATGAATGGATAAATAAAATATGGTACATATAGGATATGGG
TTAATATCATGCCATAAAAAAATGAGATTTTGTCATTTGCAGCAACATGGATGAAACTGGAGTTCACTATATTAATTGAAATG
AGCCCAGAACAGAAAGACAAAATTCACATGTTCCCATTTATTTGTGAAAGCTAAAAATTAAGACAATTGAACTCGTGGAGATA
GAGAGGGAAAAGATGGTCACCAGAAGCTGGGAAGGTCTATGGTAGATGGGGATTATTGGGGATGGTCAATGGGTAGAAAAAGT
GATTAGAAATAATAAATAACACATAATATTTTATAACACAACAGAATAAATATAGTCCTCAATAACTTAATTATAGATTTTAA
AATAAAAGTTTATGAATGGAATGTTGGTAACTCTATTAATGCTTGAGAGGATGTATAAAATATTCTTCATGATGTGATTATTA

FIG. 6 (Cont. 14)

TGCAGTTCATGCTGATTCAGAGTCCTGTACCCCATAAATATATACGTGTACTATTTACCCACAAAGATTCAAAATTAAAGTGT
TTATGTGTCTAATATTCTGTAACTATATTACATTAAACCTAAGAACACACTGGCTTTTACACACTACTGTCATCCACATAGAC
ATTCATAGCCTTCTTTCTCTGCTTGTCCATAATCCCACACTCCAAAATGAGAAAACCTCTCCTAAGATATGACATTAATTTAC
TTAGTGCACAATTTCAAAATACACAAATCGTCTTTAGGATTGTTAAACTGACCCTTGTTGAAAATATGTTTATCAACTAGAAT
ACAGTGCTTATGTGGAGCTTATTTATGTTTTACAATCGCAACATCAAATTCTTTCCAAGTCTCTTGTGTCCAATATTTATGCC
CCACCTTCTTCAGTGTAATTAGTTCAAACCTTCTGATTGTTGTTAGATATTTTTATACAGCTGTCTTTTTTTGTGTTTCATGA
CCTGCTAAATACTTTCGAAGTTGTATGCATTTAGGTTAACACTTTGTCTCAAAAAAATATGAGTTTTCAGAAATTCTTTATGCC
ATGTGTCCATCATTGAATATCATAAAAATAGTTTCATTGGCCGGGCGTGTTGGCTCACGCCTGTAATCCCAGCACTTTGGGAG
GCCGAGGTGGGCGGATCACGAGGTCAGGAGATCGAGACCATCCTGGCTAACACAATGAAACCCCATCTCTACTAAAAATACAA
AAATTAGCCGGGAGTGGTGGTGGGCACCTGTAGTCCCAACTACTCGGGAGGCTGAGGCAGGAGAATGGCGCGAACCCGGGAGG
CAGAGCTTGCTATGAGCAGAGATCGCGCCACTGCACTCCAGCCTGGGTGACAGAGCAAGGCTCCCTCTCAAAAAAAAAAAATA
GTTTCATTGGGATTAAAAAGTGTGTGTTTCACCTAATCCACACACCTTCTCCCCACCTTCCTGGGAAACCTCAAATGTTTACT
GGATCTATATTTTTATCTTTGGCAAAACAGCCTGGCTGTTCTCTTAGCCTCTTTTGCAAAGCATCAAGATTCACCTTCACTGA
CTACAGCATAAATTGAGCCCAGATGGCTGGGGGACAGAGGCTGGAGTGGGTGGTAACAGTGATTGATTCAAGTGGAAGTTCTC
AGTGATATTCTGCATCAGCATAATGAAGATTCACAATTCCCAGGGACACCAATTACCAGCACAGTCTCCCTTAAAATAATCTA
CTTGGAAGCTGAGGGGGCTCTCACAGGGGTAGGCAGTGTATTACTGTGAGAGACACAGCGAGGGACATTTCTGTGAGTCCAGA
CAGAAACCTCCCTGCAGGGAGACAAGAGAGGACTTTGTGATAAATGGTGCTTAGGACACCAGGGGGCACTCAGGACAGCAGAG
GGTGCTCAGCAGAGCAGGGTGCGCTCAGGACATGGTGTGTGTTGTAGGGGGCATTGCTCAGGATCACCAGGGGGCTCTCAGAA
CCACCAAGGGTCACTCAGGAAACCAGGGGGCGCTCTGGACACCAGGGGGAGCTCAGAACCACCAGGTGGTACTCAGGACACCA
GGGGGCGCTCATGACCAGCAGGGCATGCTTGGGACTCTATGAGGCATGCAGGAGAAGCAGGCCATGCTCAGGGCAACAGGGGG
CTCACAGAACCACCTGGGGGTGCTCAGAACCACTAGGGGTCACTCAGGACAGCAGCAGGCATTCGGGACACCATGGGGCCCTC
AGGACCTGCAGGGGGCGCTCAGAACACCAGGGGAAGGTCAGAAAGACCTGGGGGCACTTGGAACCACCAGGGGGCACTCAGGA
CAGCAGGGGGCGCTCAGGACCACTAGGGGGCGCTCAGGACCAGCAGGGGGTGCTCAGGACACCATGGGGCATGCAGGAGCAGC
AGGCTGTTCTCAGGGTAACAGGGGGCTCTCAGAACAACCTGGGGGTGCTCAGAACCACCAGGGGGCACCCAGGACATCATGCG
GCCCTCAGAACCTGCAGGGGGCGCTCAGGACACCAGGGGAAGCTCAGAATGACCTGGGGGCACTCAGAACCACCAGGTGGCAC
TCAGGACAGCAGGGGGCGCTCAGTACCACGGGGTGCACTCAGGACAGCAGGGGCGCTCAAGACACAGTGGGATGCTCAGGAC
CAGCAAGAGGCACTCAGGACCACCAGGGGGCACTCGGGGGAGCAGGAGGCACTCAGGACACCAGAAGAGGATCAGAACCACTC
GGGGGCACTCAGAACCACCAGGGGGCGCTCAGGACACTGGGGGCATTCAGAACCACCAGCAGGTTCTCAGGACACCCAGGGAC
ACTCAGGACAGCAGGGGCGCTCAGGACACCAGGGAGGGTGCTCAGGACACCAGGGGGCTCTCAGAAACACCTGGGGGTGACCA
GGACTAGCAGGGGCATGCAGGACACCAGGGAAGGGGCTCAGGACACCAGGGGGTGCTCAGGACAGCAGGGGGCACAGAATCAC
GAGGGTGCATTCCAGACCACCAAGAAATACTCAGGACCAGGGGTAACAGAAACACCTAAAGACACACAAGACCACCAGGAGGC
ACTCACGACTGCTCAGAGTGCTGAGGACACCAGAGCTTCAGGACGAACAGGGGGTGCTCAGGCCACCATGGGGGGCTCAGGAA
CCACCAGGGTATCACTCAGACAACAGGGTTCTCTTAGGAGGCAGCTCCACATCAGGTGCCTGGGGAGGGTCAGATTTGCTTTT
AGACCTTGCTGATCCCTGATCTGGTCAAGCGAAAACCTTCCCAGGATCTCTCACCATTTCTTCCTTGTAACCCATGGTTTCTT
TCACGTACAAATCATTAACTTAGAACAGGAATTCAATTCAACTTTTAACCCTCCATATTTTTAGAATAACACTAGCAGTAATT
GAATGTTTTGATAATAAGAAATTGCGTATGCCTAATTCAAGCTCTGGTTCCATGCATGGGTTTTTGTTTCTTTGCTGTGTCA
GTCACACTATAGTCAATGCTTTTCTACCAATAACTCAGCATAGGCATAGTGTTAAGTTTCTTTTTCTTTCATCTGCCTTTTGT
GGAGATGAAACACCACTTTCAGGGCTCAGTTCCCCCACCTTGGTTGGGTTCTGGTGTTCTGCTCCTCACACTATTTCTCCACC
TTCCCTTCTTCTGTCCAAGCCTTTTGTCTTCCTCAGTCTCCTAGCAAGGAAGCAACAAGTCCCTTTATTTTGCCTCTTCCATG
TCTGGTGAATCTGTTCACTTCTCTTCATGATCATTGAAGTCAACCAAGTTTAGGAGGATAACAGTTCTCCTTAGAATATGCTC
ATCTACCTGCAGACTCTCTGCCTTCCTCACCCCTTTCTAGGGTCCTGCAGACGTCACCTCCACCACATCCACTCCTTTACCTA
AGTACCACAGAATAGTCTCTGCAGCTCCTGCTGCTCTCTGTGTGCTCAGCACTAAGGCTCACTAGTGCTTTGATGATGAAGTT
CAAATCCCTAATGTGTTAGCAATTCTCAGACAACCCTGCCATTGTGAGTGAATTTTGGGGATCCTGGGCTGTTTTCAGTTCCA
TATTACTGGATGTTCTCTAGCATCCAGGAGTACTGGCAAATTAACATCTAGAATTTGTATTGCAAATTTATACAAAATCAATT
GTAGAAAAAAATCCTAATTTCTAAATAAGAACATTTATCCTGACTTTTATAAAAATACAATGTGAATTTAACCAATAATATAA
TACAATTTTAAAAGTGATGTTTATCTTATATGTTATTAAGTTTATTAATAATTGGCTGGTATTTTAAAAGTATACTGATAGCA
AAACTGACAAATAAACCAACACAGATTCTATACATAAATACCATTGTCCATTTAATTAATGTGTTTGGCCAGAATGGCATTTA
CATTCAGTTCTACCGAGGCATGTCTTTAAATGTATTTGTTTATTGGCATTAGGATAGAGAAACACTCACACAGAAAAGCATTA
TTTGGGACTACTACATTATACTATAAAAGAGAGTAAATTCAATTCAATTAAATAAATAAAATAAATTGAATAAATTCATGTTT
TGGTTTGGTATTTGGATAGGTGTTCATTTTTCTATTTTCACATGTATATTTCAGTACTGGGCATATGTGTGTATGTGTATGCA
TGATTATGAACTTCTAAAATACATTACTCCCCTATATAGTTATATAAAATTGAAGTTTTGCATGTTAAGAGACAGTAGAAACCA
CAAAAGGGAAAAGTTATAGAAAGCATTTGGAATACCTAGGGCCTACAGAGGAGTCATATTAAAATGAAAAATAATAGCTGAA
TATTTTGGAAATGACACATGCAGTAAGAAATGTCTATATGAAATTAACAGGATATTGGCACAAAATTTAGAAAAAAATAACAT
GATTATGCCCACTATTGGTCTATGATATGCCTATAATAATAACACATTTTATTTATCATAGAAAATAAAATAATTATACAAAT
AGCACTCTCATTGCTTGATTTTAGTATTAGGTACTTCACTTGTTTTTTGATAGAAATGAACATTTATCATTTTTTGATGATAA
TTTCTATATTATCTTCTAAAATTAATGTCCATAATTATGATTGACATGTTATAATTTCCAGAAACCTATTTTATCAATTGTGA
CTTGTATTTTTATGATAGTATTTTTACATTCATATACATTTGATTCAGAATAATTGTAGATTAACAAAATAATCATAAAGTTA
ATACAGTGTGTTCCCATCTCTAAGTATCTCCTAAGATGAACATCCTCCACAATCATAAAACATGGTGTTAACACATTTACGTT
GATAACTTTAAATATATTCAATACCAGGCCTTATTTGAGATTTACCATTTTTCCAATAATTTCTTTTGTAAACCAAAAATAAA
ATTCTAAGCTTCCTCATCCAACTAAATGAACTCAACTATCAGCCAAAGATATTTTAAAGTAAACTTTAAAACTTGTTCCAGCA
ATAATGGGAAAATGAGAGGTCAGATATGCCTCATTATGTCCTCCTGTCTTTGGAATTAAGGCACCTGTGGCCAGCATTAACAC
TAAAACAAAGACCCTTAGACTGACAAAACTATATTTTTTCTATAAACACTCTTCATAGTGAAAAGATACCAAATTACAATATG
ATTCTAGTATAGCATCACATGACAAACAGCAACGCCTAAAAATCTATTCTCTATGAAGTCTGCTACCTGGAGGTTTCATCTAC
ATAATAACAATTATGAGCTCCACAATCTCGTATCTTAATCCAGATACTCATTTGTAATGAGTGTGTAACATTTCAACCAATTG
CCAATCAGAAAATGTTTGAATTCACGTATGTCCTGGAAGCACTTGAGTAAGCTTATTCTGCCTTTCTGGACTGTGTAAATGGT
ATAGCTCACATGTGTTGATTCATATCTGTCTATACCTTCTGTACCACTAAAATGTATAAAATCAAGCTGTAACCAAACCATTT

FIG. 6 (Cont. 15)

TGGATACGTGTACTCAGGAACTCCTGGAGTTGTGTCATGGGCCTTGGCCACTCATATATATCTCAGAATAAACTGTCTTAAAT
AATTCACGGTTTGTCTCTTTTAGTGGATACTGTCTTTTTCTTTTTTCTTTCTTTTTTTTTTTTTGTTTTTTGAGACAGGATCT
CTCCTTGCTGTTGTTTTTGTATATTTGTTTGTTCCCAGATTCCAACAAGGTCATCACTTTGAATTGAGTTGTCATGTTCCTTT
ATTCTCTTCTGGCAAATCACAGTTTGTGTTTCTGAAGTTTTCTAGTTTAATATTTTATAGATAAAAATTTATCAAGTAGATTG
ATAGTCCTATTTAGGACACTTATATCTTTACTTATTTGAACACTGCTTGTCAATCACAATGAGTGTTGATTTCTCCGTCTTCT
ATACATGTTATTATATTTTCTGTTCCAAATCCATTCATTAAGTATTTTTAAATGTATTTTGGAAAGTTGATCCTATTACTTTA
TGTAATATTTCTCTTGAGTCCCAAAGGTCTTCTTTTTATGATTATTTTGTCTTAAATTAACATAGCTATTTAAGTTTTCTTTT
GGTTTATATTTTCATGATATATATTTTTCCATCTTTATTTTTTCTATTTCTGAATATGTAAAGAAATTTTCTTGGAGATAAAT
AATAGTTGGGTGTTTTTTTTTAGTCAACTATGAAGAATTATTTTTTAATGATGTTACTCTTTTGTCCAATTATTCTTGTTTTA
ATTTGTATTTTTACAATAAAGTTTATTGTTTCTATTAACTTATTATTTAATCATTCTGTGACTAACATTTTATGGGTTACCAT
AAGGATAACAATAAAAAGTTTCTATAATTGAATTCTAATTCAAAAATTTAATTCCCATTCATATATACTACAGAGATATTATA
ACTCTATATATCTAATTCCTCTTTCCTATCCCATGTTTTTTATTTTCTGTTTGTATCTATACATGCTATAAAATGTAATATTG
GCATTTTTATAATTGCTTTCCACACTTACATAATGAACAAAATACAAATGCAAAAACTGTATTTCAACCTCATTTTTCCATTG
TTGACCATCTTCTTTGTGCATATTTTCAGGTGTTGGATCTATGTCACATGGCTATTCATCTAGAGACTCTGCTAAAATGTCTA
CGGAAAGATTCATGTGCTGGAAATAGGTTTTCTCAGGTTTTATTGGTCCGACAGAATATTTATTTGTCTTTGATTTATTGTCT
CCAGAGACAATGTCAAGAATATGCTATATCTGCAAATGGGCGATCTGTAAACCAAGAACACATCAGTATATCACTGTGCAAGA
GGAGCACATGAGGGAAAGCCAGTGTGTGCCCAGACATAAACCTCCAGGGACACATGGGCGAATTAGCTGCAGGGGGAGCTTGG
GACCCACTGATGAGAGTCGACCCCAGAGGGAGGTGCACAGAAAGGTTAAGAACTGCTTTCCTGCCAGTATATTTTTAAAAAAA
CAAAACTTCCATCTGACAGTTTCTCCAGAGAACTTCCCTAATTTTAGCATTCTGTGCCTACCAATGCCATCACTAAATAGGTT
TTTAAAAAATATTGTAATATGAGGACATATTCTCATATGGACAAAACGCAAATTGACATTTACAGAAATGAAAAGTCCTCAAC
CGTGGTCGCTAGAATTGGAGACCTGTAGCAGCTCAGTGGGACCTGTTGAGTCTTCTCCAATCACACTCAGAACAGAGACCTTA
GTGCATCTCCCTGACTAGAATACCCTTTAGGTATCGAGATAACAGCCTAAAGATGGTAAATCATGAGAGTCTCAGATGTCCAG
ATGACAGACATGGGTCTATGGGAATAGTACTGTAACTGACAGTAACTAATTTTCCATACCGCCAGATGTCCTATTCAGGAGCA
GCTACAGCAGTCATGCCTAGGTGTGAAGATCACACACTGACCTCACCCATGCTGTCTCTGGCCACTTCATCACAACCAATGCT
TAATATTGGACGTGGATCTGCCAGTCCCCGGGGAATGGGTTGAATGGATAAAATGCATGGCTAGTGCTGCTGGAAACCCATTC
CTACTGTGGCAAATGGCAGCATCTCTTTTAAAAGGCTAAATAATATTCTATTCTGTATACATACCACATTGCCATTATCCTTT
TTGTTTGTTTGTTTGTTTGTTTGTTTGAGATGGAGATTCACTCACTCTGTCACCCAGGCTGGAGTGCAGTGGCGTGATTTCAG
GTCACTGTAATCCCTGCCTTCTGGGCTCAAACAATTCTCCTGCTTCAGCCTCCGGAGTATCTGGGATTACAGGCATGCACCAC
CACTCCCGGTTAATTTTTGTATTTTTTGTAGAGATGGTGTTTCAACATGTTTGTCAGGCTGGTCTCAAACTGTGACCTCAAAA
AATCAACCCACCTCAGTCTTTGAAAGTGCTCAGATTGCAGGCGTGAGCCATAGCATCCAGCCACTTTTCTGCATTTTTTTTTC
ATTGACACTTAGATTATTTCAATATCTTGGCTCTTGTGAATAGCGCTGCAGTAAACATAGGAGTGCAGATATCTCCACAAGGT
GGTGATTTTTTCTATCTTGGGTATATTCCCAGAAGGGAGGTTGCTGGTCATACAGTAGTTCTAGTTCTAATTGATTTAAGATC
ATCTTACTGCTTTCCATAGTGGTGGAGATTCAGATTAGTGTAGCTATTATGAAAAACAGTTTCAATGTTGGGGAGTGACTGAA
AAACAAATAATGCTTGATTATGGTTCTCCATGAGAGTCTCTAATAAACCTAATGGAAGTTCAGAAAGTTTCCTCACCTTGTTA
AGAAAACATTTGTTTTGCTCATAATTCTCTTTCAGCCCAGAGTTGGCAGTATGTAGAATGGAGGCTGTTGGCTCGTTTAAGGA
TTCTGAAGCAAAGAACAGTAATGAGAGATGACAATAGAGAAAAAGAGAGAGAAGGAGATGCTGAATCATCATGGACTCATTCC
ACCTGCAAGCCTTTCACTGTAAAGCTCTATTGCTAAGGATCCTGAGGATTCTATACTCCCATGAATGCATAATCAGGATCCCT
CAATTCAAATTTTATTGGCAGAGACACACTGGGACCCCTCTAGGATATGTGCCCTACATTACTGGCTCAACATGCCGCACTGA
GAATCCTGCATTAACTGGCTTTATTTGTAGTGGTGAGTAAAGTTCACAGTTTTCAGTCATCCATGAAGGGGAGATTTTTTTTT
TGGTTCATATAATTTTTGCAGAAATTCAGGTATTAGTGAAAACCAATAAGATTGAGGATTTCTGGATATTTTAGCAACACTAG
GGATGATGGCCATTTTGTAGAAAAATTTACATTTTTCAAACTGACCTACATGTTAGGCTGACATAAAAAAATCCAACTACACA
GCAATATTATGGCAACACTTCAATACACTTGGTGGTGAAATACCTCAGAAATGAAATGTTACACAGATTAATTGAGTTAATGA
AACTGTTCTGAACTATGATAAACATTTGTTTGCACCCAGATTTGCTTGAATTCAATTTGATTATTATATTCAGCTGCTGCCCT
AACTTATTTGAATGAGTAAGTTACTATTTAAATGACCCTGTCTGTTTGATTTGTTATATATACATCTGAATTAAAGAACTTAA
AGGACAGGTTTGTGCTATTATTAGAAAGAGATATTCTGGGGGGCCCTTGTTTGCTCCAGGAACCTCCACATTTTTAACTTAGA
ATTAATATAAATTCCTTGTGAATTGGGTCAGTCTTCAAGAGACCTAATCTCTAAAACATATACCCAGAACCTTCTCCAGACAG
ACCATCCAGAGGAAGAATCTTTCCAGTAATTTATCTCCATGGTGGAAGGTCCTTCATTGTCATGCAGAACCCTCTGCCCAGGC
TTCCTTTATTATGCAAATAATTAATATTAGCCAGTAGGGTAAGATTAAACAAAAATAGACCGGAGATGCTGCAGACAGGGAAG
GAAGTAATAGACCAAAATCAGCTTTATTAATGGAGACTGCTTTTAAAGGTCACAGCCAAGAAATGGAAGAGGATAAAATCAAT
GAGATGAAATTGTAAGAAACTTTGTCCAGTTCAATCAAGCCATCAGCAACCAGATAGCTTCAGTGGACATTATGTGTATTACA
ACATGGCTAAAGATTCTAGATTACACAAGGATTTTCTCTATAGTTTGCATATTGACAAAGTGGAAGATGGCATGGGAGATCTG
GTGGCAAACACTTAAGGTGCAATAATAGCTATTTTTCCTATATCATGACAATACATGGCATGCCTCTATATTCATTTCATTCC
AAAGAAGTCCTTCAGAAGGTCAAGTAAATGGAGAATCTTACATGCATGGCCCAATGCAGTCTCCAAGAAGTGATTTTGAATGT
ACAGCTACACCAGTTACTGCAATGCTGTGTCTGACCTTCCCAGCATCTAAGATATTCATGAGTATCAAGGGGGAGATGGGTCT
AGGTGAAAGAAAAGGAAGTAGTCATTCTTGAGAAGAATGGTATGGCCAAGATAAGCCTGAACTCTCTATCTTCTTCCATTTGC
TGCAGGTTCTTATTGCCCGATTGAGGTCACTCGCCCATGGTGGTAATGACATCAGCAATGCAGTACATTCTCTGGTGGCTTTG
TATCTGGTTTATAATGTGGGAGATGTTTCCTCAAGAGTGGTGACGCCAGTATGGCTTCTGCTCTCTGGTGGTGATGGCATCTG
CATTAGCCTAGGGGTTTGGAGAAAGAGAGTTATTCAGACCATGGGGAAGAATCTGACACTGTCACACCGCCTGGTGCCTTCAG
TACTGGACTGGCTCCTGCCCTCATTGGTGATTGCATCAAATATTGGCCTCCTCATCAGTACAACACATTGTAACAGTCTTCTT
TGTACCTGGCTTTAATCCAAGAAAGTTGTTGACTTATGGCTCTTTCATTATATTGTATGGCCTGGTTTGTCACAATCTTTATT
TCTGGAATTATCAGTGCTGCCATCTTGGCTGACTTCAAGTATGTCATCCTCACAGTTTGAAGCTGCTTGACATTAACATTTTT
GTCAATGTTTGGGACTACCTTACATATTCCGGCTCTCTGAAAGAATGATTAGCGTTAGGGAAGGCTGACACTAAATTTGGGAG
CCAGAGAAGGAAAGTGTTACTGTGCTACAGTTGTTTTGTGATAAATATGGTTAGGTTAAAAATGAGCTATGTAATGTAGCCAG
GTTTCCACTGAGTTCCACTTTGCTTCTTGGCTGTCTATTCCTGTGCAAGTTTCTATATATTTTGTATCAGGCTTCAATTCCAT
TATGTTTTAAATGTTGTCTCTAAAGATAAACAAAGATTTTTTAAAACTACCAAACATGCAGCCATTTGACAGAGTGTGCGCTG
CATTTTTAGTCTCACCATCTTCTGCCCTAACAAGCACCGAATCTAACAACACAAATATCATGGAAGCTTTCCTTGGAGTAGCT

FIG. 6 (Cont. 16)

CCTGTAATTAGAATCATTGGTATTCTGCCCTCCTGTCAGTGGTGGAACGTTCTATTGGCACATGTGGAAACCTCTTAGAGGGA
TGAGTTTCTTTGAACACAATAAAATTTTAAGTTAGGAATAACTTATTTGAAAGCAATTCATTGAAGGTTATTGCTAAGAAGAA
GTTAGAAGCAGTCTTTTGGCAGTCATTTCTTCAAGATGTATGGCAGCGTAGGATGGATATATGAAGTGGAATAGGAACTTGGG
CTAGTTAAATGGAATAGCCTCCAATGTTAATCTGTTTACCTTTTAACTGAATGAAAAAGCCTATAGTTGTAAGAAAAGAAAAA
ACAATACAGTGCTCCCCTGTCCCACACATTACCTTCTCATCAGTATAATTAATCTACATTGAAGATGAGTGTGGTAATGCAGA
GACTCTATTTAGGGAGGAGAACATAGGGAAATGCAAAGACAATGGGAGAAAAAAGTCAAGGACAGTAGAGCAATTCGAAGCCT
CTGATACCAATAGCTTGAGGACCAAGGTCATGACTCAACTTTGGTGGACACAGAGTCACTTCTCTTAGGGAAACTGCAGTAT
TCTAAGGTGACAATATGCAAACATGATGAATGTACACTTGCTACATCTCCAATTGTGTACTGTTTTCCTTACTTCTGTTTGAA
GAAGGGAGTCGTATACTCAGGTCTAGTATCAGTGTAGGGGGTGCTCCCTATTTGCAAGATACTAGAAAAAAATGGTAAGTTAG
AGGCCCATTGTTATAAAAATCTACTAGCTCCGTGTCAGTGTGTGTGTGTGTGTCTGTGTGAATGTGTGTGTTATTGAAACAGA
AGACATGGAGTGGGCATTGATCCACAAGCATAGATACCTACAGGCACTCTTAGATGTAATATTTAACTGCAGGAGTCTAAATA
AAATAAAGGATTCGCCAAAAGTCTTGAAAATTTTGGTGCTGACTATGTGTCCACTGATTCAATGCATCCTGAGTTCCAGGGAA
GGGAATCCCCAATTCTTTCATAGAGTTGACTGGGTCTCCTAAGGTCAATGTTTTCAAACGATGGTGTCAGTAACATATGGTGT
CACTGAAAGAGCATTTTAAACTAGGGCATGGCCACTTCCTATAGCCCTAGAGACACTGAGAGGTAAATGCCCTGTGAGCCCAG
ATGGAAACCTCCATGCAGGGCAGAGGCAGTGCTGCAGGGGGCGCCCAGGACCCACCCAGAACAGGCTCCAGCCCCAGAGCTGG
TGCACAGGAGGCTGCAGAGGGAGTCTCTCACAAGGACTGAGTGTTACTTTACTGAAAACCAAAAAATTATAACATGCTAAATA
AGAATTTTATGAGGACTATTTATGTATATTTAAATACCCTAATGTATTTAGAAATAAATAAATCAATAATTCAGTGAGAACCA
CATTTAAAAGGCAAAATTATTACTGCTTTGAGATATTTTACTAGTAAAAAGATAAAGAACAAGAATGGTTTTATTAAATAAAA
ATGTACACATTTCAGAGACACACTGGTCCCGAGAGTAAGACTGCGGAGAGCAAATCCTGGAAAGGGCGGAGGCTGTCCATGTG
CCATGGGAACTTGGGCTCACGCTGAGAACCATGTCCGGTGTGAGTCAGCTTCTTAGCGGAGAAATTCTCCCTTCACAAATTTC
CGGGCATATAAAGGGAAACATGTCATTAAATAAGAATGAAGATTTGTACCTCAGCATCCCACAGTTGTGTGGTCCATGTGAGA
TCTATTTTCTCTTTCTCGTGCTGGATCAGGTGTAATGCTATGAAGTAGTAGTCCTCATGAATACGCAAATCACCTGAGGTGAA
CACTACAGATAACTCTGTGCCCTGAGAGCATCACCCAATAACCACATCCCTCCTCTAGAGAAGCCCCTGAGAGCACAGCTCCT
CACCATGGAGTGGACTTGGAGGATCCTAATTTTGGTGGTCGTAGCTGCAGGTAGGATAATTCTCAGTCCCCAGGACTAAGGTG
ACTGGGTCCAGTCAAAGGGGGTTTTATCCACTCCCGTGTCCTCTCCACAGGTGCCCAGTCCCAGGTGCAGCTGGTGCAGTCTG
GGGATGAGATGAAGAAGGCTGGGGCATCAGTGAAAGTCTCCTGCAAGACTTGTGGATACACCTACCTTCACCAGTTACTCTAT
GCACTAGGTGCGCCAGGCCCATGCACAAGGGCTTGAGTGGATGGGAAGGATGTGCCCTAGTGATGGCAGCATAAGCTACGCAG
AGAAGTTCCAGGGCAGAGTCACCATGACCAGGGACACATCCACGAGCACAGCCTACATGGAGCTGAGCAGCCTGAGATCTGAA
GACACGGCCATGTATTACTGTGGGAGAGACACAGTGTGAAAACTCATATCCTGAGAGTGTCAGTAACCCTGAGGGAGGAAGCA
GCTGTCCCAGTTTTCAGGATATGACAGGATTTATGGGGTTTAATGTTGTTTAGAAAATAGGTTATATAATTGAGGAAAAGAAG
AAATAGAAAGATATATGCATTCTAATTATATAAGAAATATTCTTTTCAAATCTCACCCTATAAGCAAAATTAACAGAGTGGGA
AAAGCAGCAATCAATCAAGCTGAAACAAACATTCCCATGGAGGATTTGTGGGGGCAGACGTTTTAAAATTGAATGGGTAAATC
ATTTAGGGCAAGATTGCTTGATCCAATACTAAGACTAAATGTAATTTCTGAGAAACTGCCTATCTTTTTATATTAAATTTATT
ATAAAGCAGTTTTAGGGTTACAGCAGATGTAAAAAGTAGAAACAGAGAGCTCCCATGTACCCCTGCCCAACACATACACAGCC
CTCCCCATGATCAGCTCCCTGAAACAGAGTCCTAACTGCGTTATGTGGGATGAACCTACATGGACACACTAGTTCTTTCCTTT
CCTGGTGGTCCCCCGGTATAACAAACATAAATTATTTTGAAGCGCCACGGGTTCTTCAAGTGGGTTACTGGGAATGATGCCAG
TTAGAGGGAAAGTGGGTGGGGCCATTCCTTTTTGCACTCTTTCTTCAGGAATCCATAAAATGCACATTGACTTAGAGCTCATC
TGACTCCTGGTTTTCTATGCCCCTTCCCAGAGGGTAAGTTCTCCAAGCGTGGGAGGAAGGTCCATTTCACTAAAAGGCCAGAA
GCTTCTGGTGAATTCCATAATGCACAACCTTTTTTGAGAAGTGGAGACTTTGGACATGAGGGATTTCATGTATGATGCCCTGG
AGTTGGATTAAATACAGCATAAGCTCTTGGGGGTATTTCTGGAGGAGGCCCTTTCTGCAGGAAATTAGAATACATGCAGGGGA
TCCAGGCAGGAAGAATCACTTCCTTTGACATCGTTTGGCACCTGAAGGAAGCCCTCTCAGCATTGGGCACTGGTCCCACTTGC
TGGCTGCACTTTAGCCAGAGGCCTGCGCCTGATCATTCTTGCAGTGGGAGAGCCTTACTGGGGTCACAGGTTATAAAAATGCC
TGTCACTCTCCAGCTGAGCAAGTCCATATGCGTGCTTGTCAGTGTCAACCCCATGATGAGTGCACTCTGGAAGGTGACAATCT
GCACACAAACCTCCTCCCACTAGTTACCCACTACTATACACTACTTTAAAAATTAATACTTATAATTATATAATATAATATAT
ATTATATAACTATATAAAAATGATTATGATGATGACATTTGGCTGTTGCAATTTCTTTAGGATCTCTGCATCTCTCTTCACTA
GACATGTAAGTCTTCAATTTCTTGTCCCTGTGACACGTTGCCCAGTGTTTGAAGTCAAAGTTGTGCCGAGTACCTGAGTATGT
CCTCAGAGAAGATCTCAGCAATGGTTGATTGTTCTACAGGGACTTTTCCAGGAGACCTGTCCCAGGGAGTCATGAGGTTCCTC
TGGAAATACTAGCCCCTGCAGGAGATGAGACGGAAGCAGGAGAATCAAGAGCAGGTGACAACATTGTCAGCAGGAGGCTCCAG
ATGCTTTCCAGACACAGTGAACCTTCACCCACTTGCCACACTGCACAGGGAGTTTGCAGGGGCACAATGAGGTGCCTGTCTGT
GGGATGTTGGGGGACAAAGTGAAAACCTGAGCTCAGCATCCAGGAAAGTATGAACTCCAGCCCTGATAATATGTAGCCTGTGT
TTTCTTTCCTTCTACGTGAACACTTTGCCTTATTGTTAAGAACAGAGGATTCTAGCTCTAAGTGCACGGATTGCAGACAGCTA
TGACTTTCCTCCGGGCCAGGCTCCTCTTAATGTACTTCTTGGACTTATTTGTTGATGAAGGTTGGTTCCATTAAATACCAAAA
CAGGGTTCATATTAAAGAAAAATGAAAGAGTGACAGGTAGATTAAACCCGAGCATCCAGTTCCAGTGATTCTTTGACCCTGCC
TTCCCAAAAATCTCCGATATGAACAATGACAATGCCCTCCATGGTTAGATTATATTATAAACTAGATTGAGCTAGAGTGTTTG
GTGTATTAACTCACTATTTTTTTTAGCTTCCCTGTTAGTTTTTTGTTTGTGTGTTAGCATTTACTTTAAAATTCTATTAATCA
GTTCTCTAGTAGGTAGAAATTCATCTGAGAGTTTCTTCTCTTGTTGTCCACTTTGATAAGATTTCCAGAAGACATAAGAACCC
TTTTTGTTTGCAAAAATATTCCAAAGTTTTACACTAACTAGGAACATATATACTTAATTCTAATTTTTAATTTGTTTAAAAGC
TCTAATAAGTGCACTGTTTTCTGCCTTTTGAGTTAATTTCACAACACATAGGAGAATATATCCTAAATGAAAGTTTGTGCTAA
TAATACAAATTATTGGTAAATAACCTCTGTTTTAATTATTGAGGTATTATCCATTAATATATAATCTTAAATTGATGTTCTCA
ATGGGACTCTTACCTAAAGAATATACAAAATATTTTCCTGATCTTGACATAAAATAGATGTGAACACATTCTTAGTATTCAGC
CATGTCTCCTGTCTATCACATTATGAACCACATGCTAACTTTGATTTACTTGGGACTTGTTCTAATTTCAAACTAGTTATTTT
TTTATCTTCATGCAGCTGGATTATTATGTGTGGCTATTTTATCAGAGAATGATAAAGACAATTTTAACAATTTTCACTGCAGG
CACGTCTAGGCAAGCCCCCTGTGCACAATGACCTTCGTGGGTTGGACATTCTATGGGGACTCTCCCCTGTCTGCCTAGGAGAG
TTATCTGCCTCCTCCCTCTATCATTTTCCTCTTTGAATAAGCGCATCTAACTGCCGTTAGAATACAGACAAAGGCCAACCTTA
ACTGCTCCCAGCTGACAGGGGATGCTGTTTTGGGAAGATCTCCCTTGAGGTCTGTCTAAGGGACCTAGTAAAAGGGAGCCATT
ATCCCAGGCTTCACTTGGATGACCATTTGGAGTTGATGCCTGAAGGTGAGAAGAGACAAACCAGGTTATTAGAAGACATGTAT

FIG. 6 (Cont. 17)

CAAAACCAAACAAGGTGGTAAGGACAGTTTGAAAAAAAATTCCAAGGCTGCTGACACACCCAGATAACTGGCGGCTGTAGTTA
TGCCTGCTAAGATTTGGGTGCATGGGGCTTGGCTTTCGTTAGCTCCCTAGGACTTATTTTCCCAAACAAAGAAACCTCCGGGT
TAGGGGGACCCTATTTATTCCAGTCACCTGGCATGATTTGCAGGATAATTGCTCAGAATTAAAATATTCGTCCAGATGTTTAT
ATAGCCCATGCCTGTGTTTCTTCTGAGCTGCAGCCAGAGATCATTGGTTCGTTCACAGCGATAAGCAGAGTTAGTCTAAAATG
GAGGCAAATACTTAAAACAATTGGAAGAGACTGTAATTTAAAGACAAATGTATGATATGTTTTGAAACATAATTTTTCTCTCT
CCAGTTCTGATTTTTGTCAGAAACTAATCATTATAGGACTGAGTGATTTGCAAAATAAACTTTAGTCTTGTGGTTGGTCTGAT
CATTTGCATAAAGTGGAGCAATAATAATTAATAATAATTCTGTAGGAAAAGCCTGCAAGCACCAGGAGCTTCACAGTCTAACA
GTATGAGCACATGCATCCTCCAGCAACTCACTGAATATTTTCAAGTCAGCTGGTTCTTAGCTTAAATAACATCCAGTTGGTAT
CTGTCCCAGGAACACTAATATATGGTTCTCTCTGCAGGCCCCTCTCGCCACAGATTTAAGGTTTATTTTTTTCCTCTGTGATA
TCAACTCAGATATGTTGAAGGTTTTTCCCACATTTGTGGTTTTTCAGGTTTGTTGTTAATAAGGTCAGAATAAGATCATAGTT
TACTCATTTTTTTACATTCCCATGCTGAGTAGCTACTTTTCTCTATAAAATCCATTAGCTGAGAGAAAAAATAACATTTTCCT
AACGGTGAACAATTAAATAGTTTGACATATATTTGTGTACCAGTATATAATGCAGCTTCGAATCAAGGTGTGCCTCAATCATA
AAAAACATGGCTAAATTCTCAAAGAATTGTGCTGAGTGAAAGAAGCTAAGGAATTAAGAGTAAATTTTATATAATTCATTGTA
GAAATATTAGAAGATGCCACTACCATAAATTAAAATGAAGAAGACTTAAATTTTTCTGAGAAAATGGTGTTGGGAATGATGCG
GATGTGATTTAAGTTTCAGAGGAATAAGGAAAAAGATTTAGGGATTAATTTAATTATTCAAAAGTTGATTGAAGTGCCGAGTG
AATGGGTGCAAACATAGCTCTACATTTTTCAAATCATTCCCTATAAATCTGAATTAATTATTTATTTATTATACTTGAATAAA
GCAATAACGAAGAAATAAATGAATATTTTTGCTAAAATGGAGCAATAAAAAGACTGATATTGACAGAAGAAATATGACTGACT
TCTGAAAACACACATGAACCATGGTTCTCTCTGCATATTTAGGTGAATTACAGAAAGTTGTCATAACAGATGGGGAATCCTGC
AGACTTCACTAGGCATGGTCCACGCTGCCCTGGAGTTGTCTCAGGGGAGCTGCCTCCTCCGGTGATTAGAGCACAGGCCCAGA
TAATAGGATTACATTTTTTTAGATGTGTAAACTTAGACGCACTGCACAGCTGCTGTATTCTCTATGTAAATTATCTTCTGTAA
AATACAACATTAAAGGCTGCATTAAATATATTGTGTAAATATGTAAAAATAAAATCAGATTATGAGAGCTAAATGTTAATCAA
GGCACAATCACATAATATAAAATTATATTTTCCTGAATGATGGAATTACTACCAATCTCCCCCAGGAGACTTCATCTGCACTG
GGCCCGGCCTCTCCTCAGATGTCCCATCACAGAGCTTGCTATATAATGGGGGACATGCAAATAGGGCCCTCCCTCTGCTGATG
AAAACCAGCCCAGCCCTGACCCTGCAGCTCTGGGAGAGGAGCCCAGCACTGGGATTCCGAGGTGTTTCCATTCAGTGATCTGC
ACTGAACACAGAGGACTCGCCATGGAGTTTGGGCTGAGCTGGGTTTTCCTTGTTGCTATTTTAAAAGGTGATTCATGGAGAAC
TAGAGATATTGAGTGTGAGTGAACACGAGTGAGAGAAACAGTGGATATGTGTGGCAGTTTCTAACCAATGTCTCTGTGTTTGC
AGGTGTCCAGTGTGAGGTGCAGCTGGTGGAGTCTGGAGGAGGCTTGATCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG
CCTCTGGGTTCACCGTCAGTAGCAACTACATGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCAGTTATT
TATAGCTGTGGTAGCACATACTACGCAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTA
TCTTCAAATGAACAGCCTGAGAGCTGAGGACACGGCTGTGTATTACTGTGCGAGAGACACAGTGAGGGGAGGCCATTGTGCGC
CCAGACACAAACCTCCCTGCAGGAACGTTGGGGGAATCAGCGGCAGGGGGCGCTCAGGAGCCACTGATCAGAGTCAGCCCCGG
AGGCAGGTGCAGGTGGAGGCTGTTTCCTGTCAGGATGTGGGACTTCATCTTCTTCCAACAGTTTCTCTAATGAACCTCTCTAA
TTTTAGAATTCTGTGGTTCCTAATGTCATCTCTACATATTTTCAAAAGATCATTTTAACATGAGGACATAACCTCTCATGCAC
CAAATGCACATTGATGCTTACAAAGATGAAAAGTTCTCAACCATTGTGACCAGGATCGCAGTCCTGAGGAAGCTCACGGGTGT
CTGATGAGTCTCCTCCATTCAGGCCCAGGACAGAAACCTCAGAGGGATTCCTGGACCAGAACGGCAGGGATTCTGATCACAGC
CAATAGAGAGGCTGGGCCAGGGTCAGTGTCCTGTAGAAGCTCACAGGGTTCAAGTCTGACCCTTCTCCTGACCCTAAAGCCAA
TGAGCATCAGCACTGATCTGGTGCTGCTTTTGCTCCCAATACATGTTCTTTCTTTGGAGTGTTTGTTCTCCCTTTTTTATTTG
CTTTTCTTTCTTCCTGAAAAAGAAACACATGGTCTCTGTGATCTACACTCCAGGGCTCAAGGCATTTTCTTAGAACTCAGGCA
AGGCTCAGGCTTGGCTACTCCAGCCACGTGGGAGAGGCTGACGGGATTTCCTTCTCTCTCCATATTCTCAGGGCCCTCCTCTG
TGTTGTGTGTAGACTCATCTGGGAATGCAATTGGCTGTTAGTAGTGAAGGGGATGAACTCATTTGATCAAAATGGGATGTGGA
TGTGGAATTAACCCTGTTCTATGCACACTGTCAGAGTCATCTTCTTCAGAAGTAGTGTTAGAAAGAGCTTGTGAAATTTATCG
GCAACAAAATGGATCCCCTTGTGTTAAAACCCTAATGAATGAAGCTGGGGAAGGCCATGAAGGAGGGTTCTAACACATATTCC
TGATAAGATGAACTGTCATAAATAGACTCTGCACAGCCACAACCTTTTACACGGAGACCACCACAGCCTTAAAAGCTTTATTT
CTCCAAGTAAATCTGCCCTGCAACTGCCTGTTCAACCTTACACCGCTGTCTCAAAATAGCTGCTGTCACCCTCCTCATTTTTC
CTTAATTCTCTTTTTTATTATTTTTTAAATTATACTTTAAGTTCTAGGGTACATGTGCTCAAAGTGCAGGTTTGTTACATATG
TATACATGTGCCATGTTGGTTTGCTGCCCCCATTAACTCATCATTTACATTAGGTATTTCTCCTAATGCTATCCCTCCCCCTT
CCCGCCACCCCATGACAGGCCCCGGTGTGTGATGTTTCCCACCCTGTGTCCACATGTTCTCCTTAATTTTTTATCTTCCTTTT
CCTACCTGAATGTACCCATACATATTTTAATTGAAATGCACATCCTGGAAAAAATATTATTATACTTTAGAGTCTCTTTCTGT
CTGTTATTCAGGTTGACAAGCTGCAGACGGACATGCCACATTTCTGTGAGACATAGAGGATGACAGTTTTTGGAGATGTCTAG
GAATCTCCAATGTCCATAAGATCAGCCATCAATAAATGCAGACTGGAGGTCCCAGAGAGAAGTGAAGCTGCTGAATCGCCGTG
GAATTTCATTTTCTCCAGTTCTGCTCTGATGGAATCAGGCCCACCAATTTTATCAATGACAATCTACCTAACTTAGAGTCAAT
TGATAACAGTATTAATATCATCTATTAAGTAAATTCATAACTATATATAGTAAGAGAGGGAGAGAGAGACAGAGTCTCG
CTCTGTTACCCAGGGTGGAGTGCAATGTCATGATCTTGGCTCACTGCAACCTCTGTCTCCGGAGTTCAAGCAGTTCTCCTGTC
TCAGCCTCCTCCCAGTATCTGGAAATACAGGCACACACCACCATATCCGGCTAATTTTTGTATTTTTAGTAGAGACAGTGTTT
CACCACATTGGTCAGGCTGGTCTCAAACTACTGACCTCAGGTGATCCACCCGCCTCAGCCTCCCAAAGTGCTGGGATTACAGG
TGCAGGCCACCAAGTCCGGCTAATTTTTGTATTTTTAGTAGAGATGGGGTTTCACAATATTGGTCTGGCTGGTCTCAAACTCA
TGATCTCAGCCTCCCAAAGTGCTGGGATTACAGATGTGAGCTACTGTGCCCGGCCAACATCACCTATATTAATGTTGGATTGA
ATAACTACAAAGTCTACCCTAACCAAGTGTACCATCAAACTTACCATTACCCAGAGGGAAGAATCTTTAACATGAGATCGATT
TCTTAAGTGTTTTAAGGTGCAAAACTGACCACTGTACAATCACCCAATTATGATTTTGCTAATGAGTTGTAGAAGTTGCATGT
ACATTTTGGATATTAACACTTTTTCAGATGCACAGCTTATAATTATATTCTCTCTTTCTGTGGGTTGGAAATTTTTTCCATGC
TTTGCAGCATCTTTTTGCTGTGATGTAGTTCTGCTTGTTCAATTCTGCTTTTATTGTCTGTGCCTTTAATTTGAAATATAGGA
AATCATTCTTAATATTATTTTCTGGGTGGGGGAAATTTTACAATTGCAAGCCATACGTTTAAGTATTTCGCCCATTTAGAGTA
AATTTTGGTATTTAATCTAAACTAAAATTCTTAATTCTTTGCATGTGTAGATTCAGTTTTTCTAACACCCTCTTAGGGAGAGA
CTTTGATTCATCCATTGTATATTGTTAGTTCTCATGCTGAAAATCAGTTTGCTGTAGATATATTAGTTTATTTCTGAGCTCTC
TCTATATATTAATGCCAATACCATCCTGTTATTATTTATGGATCAAAATGTGCATATTTGTGAATTTCAAAATGTTGTTCAGA
ACTTGTGCATGCCAACAACTGTGTTTCTCCTGCACTCTTGGGCTAGTGAAGCTCTCACAGACCCTCTCTCTCACCTGTGCTGT

FIG. 6 (Cont. 18)

CTCTGCATTCTCCATCACAACCAGTGCTTCCTGCTGGAGCTGCATCCATCACCCCCCGCAAGGAAGGGACTGGAGCGAATCAG
GTGCACAGGTCATGAGGGAGTGCACATTCCAACCCACTCCTCAAGAGTCCAGTCACTATCTCCAGATCCACATCCAAAAAACA
GTGTTTCCTGTAGCTGAGCTACCTGAGCAACAAGTACACAACCATGAATTTTAATACAAAAGACACAACGAGGGGAAGTCATT
GTGAGCCCAGATACAAACCTCCCTGCAGGGGAGCTCAGAAAGAGCAGGAGGCACTCAGGACACCAGGGAACACTCTGGACACA
TCAAGGCAGGTGCAATGGGGGGACAAGGGGCTGGAGATGGGGTTTGGCATCACCATCGTATTTCACCACTGGACACCCACCAC
CGTGTTTATTCTCATGTACCTGATTCTGTGTATTATTAGAAAATGGCATTTATATAAATATATAGCCATATGTAGGTGCATCA
AGTTGTCCTCTCCATCGTATGTGGACCTTTCCACTAAGACTCTGAGTCCCTGTATTTATATGAGCACCTCATAAATTATGGTC
AATTTTGTGGGATCTCTATCTTTTCTTTCTCCCTTCTTCCCTCCTTCTCTCTCACTCACAAACTCACACACACGCAAAATTCT
ACAACTTCAGTTACGTGATGTGTTGAAGACAGTTTATAATGTGCAGCTTTTCCAGTTTAGCTGATGTTCATATTGCTGTGAGA
ATAGGAACATTGTGTTTCTCAGCTGTGTATTTCTCTAAGGTAGCAGCAACTTTTTTTTTTAATTTGACATTTTTTAAAAATTT
TATTATTATTATACTTTAAGTTTTAGGGTACATGTGCACAAAGTGCAGGTTTGTTACATATATATACATGTGCCATGTTGGTG
TGCTGCACCCATTAACTCGTCATTTAGCATTAGGTATATCTCCTAATGCATTTTTTTAAATACCCAGATACTGAAAGCAATCC
AAATATCAATCAGCAGCTTAATCATAAACAAATTGTGGTAAATTCATTCCCTGGAAAATCACCCACTGTTACATTCTGGTACC
GCTGGATACGTTCAACAGCAAAGGTAAAGTCACAAGTACATATGATGAGTCAAATAAGACAAATAAATACAAGTACACACATA
CAATTCCTCTTTTATAAATTCTATAAAATTAATACCAATCTAAAGTTACATAAAGAAAACCAGTAGTTGACTCTGGGTGTGGT
GTGAGAAGGAAAGGTGTAGGAACAAGAAATTACAGGAAAACAAGAGGAAATTTTGAGGGCACTTGAGTTTTTTCTGTGTTGAG
AAAGGTAATGGTTATGTCACTATTTGTCAAATTGTGCACATTATGGGATGGCTATTATTTGCTAATTTCACCTCATTAAAATA
TGCCAAATTTAAACACATATAATTTGGTAGAAAATAAGTTAGACAGAGATGAATAAAATATATGAGAAATAAAAAAAGAAAAT
CACAGAACGTTGGCATAAGGACTTCACTCATCAAACTGAAGAAATTTTAAATTTCTCAACACAGAATTAAAGATTTAATTAAA
GATATATGAGAAATCAAAGACTCCTGGATATATACATGAATAAACCCTAAGCCTACCTATATTTTTAGGGAAACACTAGAATA
CAACAAAATAATGTCATGAATTCATTACATAATGGGCGTTAATCAAACCCCACCAGGCATGTCCAGCTGTGTCCTGGGGTTGA
TTCAGGGAACAGGTGTGTCCTGTGGTTAGGAGAAGTGGCAACAAGCTCACAGCATCTGTTCTAGTTGACACCATAAAAAGGCC
AAGAGATCACAACCAAAATGTAGTGTGGATGTCACATCTGTGAGTGCCGCACACTCCCCCATGTGAATACGAAAAGGTTGATT
ACCTCTTGAGGTGTCTGCTGAGAGTAGAGCTGGTCTCTCAGGAATGTCCAAAATGGCTCGATAGAGCAAGAAAGGAGACTGGC
TCAGGTTGCTATACCAGTTTGGTGGTGGAGGCAGAGTGAGGGTTCTCACTCACAGAAATGGGTTTGTGGGGTTTGAACCTCCA
AATGGCATCAAATGAGGGAGTTCTTGTGATTCCTAACTAGATCCACCTCGTGTCGGAAAGAAAGGAGATGATGGAGGAATGAG
CCTTAAGTTATCAGCAGTCAGACATCAAAACAAGTCTGATGACTTATTCTATGTAGCAACTATAAATAAATGAATAAAAATAG
ATCATAATGAATTATTCATAATAAATGAATAAAAATATGAATAAAAATAGATCAGTGTCCAATATGGGTGGACAAAAACCAGT
CTACACAAAACAAGAAGACTGCTTATAAGAATAAGCAAATCATAATGAAAAGGAGGAAAATGAGGTGAAAGGCACGGGGCAGG
GGATTACACAAGGGTCCTGTTCCAATGTCTTGTGTGGAGACTTTTCATTACCTAAAATCATCCGCTTGTTCTGAATGTCTTAG
GTGAGCTGTCTGCTCCAAAACATCAGAAGCGCCAGAGGATTCATGAGGATATTCAGTTTAATATCTTCTATTTAAGGTGCCTT
ACAATAGTGTAAAATTCTTAATTATTATTATTATAATAAGAGATAGGGTCTCACTGTGTCACACAGGTTGGAGTGCAGTGGCA
CAACCATAGCTCACTGTAACCTTGAACCTCTGGCTCACACAATCCTTCTTTATAAGCCTCCTGAGTAGTGAGGACATGAGACC
AAGCTGATTTTTTTTTAATTCTTTCATAGAAGTGGGGTCTCTCTATGTTATCCAGGCTGGTCTTGACTACTAGTCTTATGTGA
TTCCCCTGGTTTTGCTTCTCAAAGTGGTAGAATTATAGACATGAGCCACGATATTCGGTCTGAACTGATTCTTTAGTTGCAAA
ATATCAACCCAAGAATTGACTCCCTTAATTTTTTTCTGCAGTGTTTTGGTTAATATTGCCTGATAAAATTTATTCTAATTTGT
TTCAACAGCAGAATTCTTCCTGACGTTTTTTCCAATATATGTATTTTCATGGTTGAAGATCACAAAATACTGTTAAAACATGA
CATAAAAAGGCAACCTTAAACTTTTGGTGATTGGAGTTAGTATAATACAAAAATTACGTCCAATATTGTGTAACACACACATG
CAAAAAGACGAAGGTGAGCAATGAGGGTAAACTTTCTAAATGTATGAATCTTCCAGCTCCCAAGTCATAGGATAGTAACTGAT
GTGGCCTGAGGGAGGTACCAGAGTGACACAGTGCTAGTGGCATAACTCTTGGCCAAGAGACTTTCAATATTTTATTAAAGTTT
TTATATTTTTTTAATTTAATGATGCCATTTTTTTCAACATATTCAGAATATTGTGAGTGGGATTGATTCTGGATGATATGAAC
AATGGGAATGCCTTCTATGTTTAGATAATATTAAGGACCAGGTTGAGATTGAAAGTTTGTAGAAATGATGCACCATAACATTA
TTCTAGTTTCCATACTAGGTTTTTTCTCTTTGCTTGCATTTCATTTCAAATTTATATGTCAGATATCTAGAATGTAATAATTT
ATTTAAAAATTTCTTTTCTTGTAGTCCATTTTGATGGGGCTTCCAGAAGATTTGAAAACCTCTTCTGCCTGCAGGACATTTTA
AAATTCTGCACTACAGTAAAACATCTGTATTTAATCATGGTCTTCGGTTTATTGACAAGCTCTAGTAAGTGCAATAACTTCTG
CCTTCTCGGCTGATTTTACATCAGATAGAGGAATTTATCTTAAATGAAAGTTTGTACTAGCAATATAAATTATGAGTTAATAA
CCACCACCTTTATTATTTAGGTGTTATTCATCAAGAAATAATGTTAAATCAAGGCTCTCAACGGGAATATTATCTAAGGGATG
CACAAAATGTTTTGCTAATCTAGATAAAATAGATGTGAACACACTCTTAGTATCCAGTCATGTCTCCTGTCTGTCACATTATT
AACCACACGGTAACTTTGACTTCACTTCGGACTCGTTCTAATTTTCAAATTCGTTACATATTAAGCTTAATGTCTCTAGACTA
TTCTAGCAGAGTGAAGAAAGACAAGCTAGACTGACAAACAACCTAGGATGACAAACTTCTTGTCACTCTCTATAAGAACTTGC
TTCTCCCTGAACTTCAGACTTGTCGCGTGTTTTGAAACATTAATTATCAAAAGTATTAAAGAAAATTTGCAAAGCTACATCTT
CTATGTTTATGTTATTGTTGATGCAATTGTAAAAAATAAGGAAAATGTATTCCTTTTCTATGTGCGTTTCCAAACTTAATAGC
AGATTTTTAGTAAGACCCAGAATAATAAAAAATTCAAATATTGTTCAGCTGCTTAACAGAAAAACAAATTATGGTAAATTTGT
TTGCTAGAATGCTATCCAGTATTTAGAATAAATAAATGTCTGCTATACCCAACTATAAGGTAAAATATCGAATTACATATGTT
AAGTAAAATAAGCCAAACAAATAAGAATATATACTGCATTGATTTGTATAAATTTTAATAAACTAAATGACTCAGCCGCAATG
TATAGCTCAGGAGTTGCCAGAGAAATGGTAGAAGAATGAAAGGGAAAAGGAGGAAGAATGTAGAAGAACAAAAGGAAATGTTG
AGAATTCTCTTGTCCACCTTGATAACAATGATGGTTACATTATATTTATCAATTGTACAATTTAAATATGTGAAAGTTTATTA
TCTGTAAACTAAAACTCTCAAAATTTATTACAAGCAAACAAATGGAAACTTAGACAAAGAAGGAGTGATAGAAAGATAGAAAA
AATGTATATTAAATTTCAGAAATACCTAAGAACTTATCTGCCTGAACCCTAGTTCTCACCATATTTTTAGGTGAATGCTAGAA
TGCAGCAAAATCACACGTGTTCTCACTACAGAAAGTGGGTTCCACAACCACACTAGGCACGCCCAGCTCTGTCCTGGAGTTGG
CTCAGGGAGTAATTGGGGCCAGTGATGAGGAGCACAGGCTCAGGTACTGGGGCTTACTCATCCAGACGTGAGCTCTTAGACAC
ATACTTAGCCCTTTCTCCATGCGTGGTTGACTTCCACATCTGTACATGGAGAAACAATTGACTCCGACAAAACATAATTTGCA
CAAATATGTAAAAATAAAATAGGATGATGAATTCAAAAAGTTTATCACAGCATAATTTTATAATAAGACAGCATATTTTCTGA
GTACCATCGTTGTCACCAAATTCTTGCAGGGCACAGTCATTTTATCTGGGTACTGCCTTCTCGTCAGGCTTCCCACCCCAGAG
CTTGCTATATAGTAGGAGACATGCAAATAGGGCCATCTCTCTGCTGAAGAAAACCAGCCCAGCCCTGACTCTGCAGCTCTGGG
AGAGGGGCCCCAGCCCTGGGATGCCCAGGTGTTTCCACTTGGTGATCAGCACTGAACACCGACTACCAACCATATGAAGTCTG

FIG. 6 (Cont. 19)

GGCTGAGCCGGTTTTTCCTTGTTGCTATTTTAAAAGATAATTAATGGTGAACTAGAGATACTTAGTGTGAGGGGACATGAGTG
AGAGAAACAGTGGATAGTGTGGCAGTTTCTGATCACGATGTCTCTGGAGGTGTCCAGTGTGAGGTGCAGCTGGTGGAGTCTGG
GGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCCGTTAACTACTGCATGCAG
TGGATCTGCCGGGCTCCAGGAAAGGGGCTGGAGTGGGTAGGTTTCACTAAAAACAAAACTAATCGTGGAACAACAGAATACGC
CGCGTCTGTGAAAGGCAGATTCACCATCTCAAGCGATGATTCCAAAAGCATCGCCTATCTGCAAATGAACAGCCTGAAAACCG
AGGACACGGCCGTGTATTACTATACCAGAGACACAGTGAGGGGAGGTCAGTGTGAGCCCAGACACAAACCTCCCTGCAGGGGC
GCGCGGGGCCACCGGGGGCGGTCAAAACCCACTGAGGACAGGACAGGTCCCAGGAGCAGATGCTGGGGTAGTTTCCTTTCTC
ATCAGCTGGAGAAGTCAGGTTTGTATTTGCAGGACTCTGCAGCATTCTAGGCTGTGACATTTTATCACTTGTATTTATTATGA
CTTTATTATCGTTAGTATTTAAATTTTAGTAATTATTAAAATTATATATAAGTACATTTTAAATATGTACTTTGAAGATATAA
ATATTCCTAATTATTTGCACTGATTCTTCCAGAGTTTTATTAACATTTGTTGACATCAGCAACTACATAGCTATAGGGACATA
AATTTATAAACATAGAAATATGTATCGGCAAGACATGGTGGTCTGTGCCTGTAACCCCAGCTTGGGAAGCTGAGGCAGAAGTA
CTGCTTGAACCCAGAAGGCGGAGGTTGCAATGAGCCGTGATCGCACCACTGCACTCCAGCCGGGCAACTGAGACTCCATCTCA
AAAAACTAAATAAATAAAAAGAAAGAAAGAAAAAAAGATGTACAAATACACAGACCTATGCATATATGTGTAGGCATTCATAT
TAAACATTAAGATAAAATAATTCTAAAAACATGTCCTGAAGAATCAAAATTAATGATGAACTAAATATAAATTATTAGAGTAA
TTCATAATTGATTTTGGTTATTTTTAATTGTTTACATGTTGTGATTTTACACAAAATATTAGTCATTTATCCTGATAAAACAG
GTCAAAATGTTATATCAAGAGTTTATTTACTTTGTATTACTAATAATATAAAATGTTCCACATATTTTTAGCCATGTTTTACT
TATCTGTGAAATGTGTTTATTAATTTTTCATTTTAATATGTCACCTTTATCTTTCTAATTTCCTGGATTTAATTCCACTACAG
CTGAATGCATTTTAATAATTATTGTAATCACATTTACATTTTTTATTTGAATTTTCATATATATTTTATTAGGATTTTAATAT
CAATATAAATATTTTCCTACCATTGTCTATTTTCTATTTTTATGATATAAAATTAACATAAAAATGCTTAGATTTTCAATGTA
CAGCTTGAGGGCTTCTGACAAATGTGCGCACAAATAAGAATTATTTGCTTACTTTTTAGTGTATACTGAGGAGTGGGATTGCT
GGGTAAAATGATATCTCTGTTTTAAGTTCTTTAAGAAATCTCCAGTCTGCTTTCCAAAGGGCAAGATTAACTTATATTCTTC
TCATCAGGGTATAAGTGTTCTCTTTTCTCCAGAGTCCCACCAGCATTCATTGTTTTTTGACTTTTTCGTGATAGCCATTCTGA
GTGGTGTGTTGCTGCACACCTACAATCATCTCATATTTGATAAGGCTGATGAAAACAAGCAATAAGGAAGGGACTCCCTGTTC
AATAAATGGTGCTGGGACAACTGGCTAGCCATGTGATGAAGATTGAAGCTGGACGTCTACTTTCAACATACATAAAATTAACT
CAAAATTGATGAAAGACTTAAATGTAAGACCTCAAACCATAAAAATCCTTGAAGACAACCTAGGAAATACTCTTCTCGACCCC
AACTTTGACGAATAATTTTTGGCTGAGTATCCAAAAGCAAATTCAACCAAAACACAAATAGATGAGTGGGACCTAATTAACTA
AGGAGTTTCTGCACAGCAAACCCGCCAGGAGATAGATGCTCAGGACACCAGAGAGAACTCAGTTAAACCAGGGGGCGCTCAGA
ACAGCAGAGTGTGCTCAGGACACCAGGGGGCGCTCAGAACCACCAGCAGGAGCTCAGAACAGCAGAGTGTGCTCAGGACACCA
GGGGGCGCTCAGAACCACCAGCAGGAGCTCAGAACAGCAGAGTGTGCTCAGGACACCAGGGGGCGCTCAGAACCACCAGCGGG
CGCTCAGAACAGCAGAGTGTGCTCAGGACACCAGGGGGCGCTCAGAACCACCAGTGGGCGCTCAGAACAGCAGAGTGTGCTCA
GGACACCAGGGGGCGCTCAGAACCACCAGCGGGCGCTCAGAACAGCAGAGTGTGCTCAGGACACCAGGGGGCGCTCAGAACCA
CCAGCGGGCGCTCAGAACCACCAGGGGGCGCTCAGGACGGCAGGGGTCGCTCAGACACCACGGTTCCCTTAGGAGGCAGCTCC
ACATTAGGTCCCTGGGCAGGGTGGGGTTTCCTTTTTGAACTTGCTATTTTTTGACCTTGTAAAGCAAAGGTCTTCCCCAGGAT
CTCTTAGTATTTCTTCCTTGTAACTCATGTCTTGTCTTGTTTTGTTTTTGTTTTTGTTTTTGTTTTTGGTCATCTACAAAAA
CTTAAACTTAGAACAGTTGATTCAGAAAGGCAGGAAAGCAGGCATTCCTCTAAGTCTCCCCTGAGACAAATACATATATGATT
TCTTCCTCCCCACTATAATTTATGTAAAAATGAAGATTCACTGAGTCAGACTAAATTGTGTATTCAGTGGAAGGATAATAAAT
GACACAAAAGAATGCAACCTATTGTCTCTTATCTTCTTCTAACCTGCAAGCCCCCATTTTCATTTGTCCTGGCTTACAGGAAA
AAAAAATGTACATTTCACATGTATTGACTGATGTCTCATGTCTCTGTAAAATGTATAAAAGCAAGCTGTACTTCAATCACCTT
GTGCACATGTCTCAGGACTTCCTGAGGCTGGTTATGGTTGGGTTCTTAACTTTGGCAAAACAAATGTATTAGTCTGTTCTCCT
GCTGCTGATAAAAACATAATCAAGACTGGGTAACGTATAAAGGAAAGAGTTTTAATTGACTCACATTTCCACGTGGCTGGGGA
CACTTCGCAATCATGTCAGAAAAGGAAGGGACATCTTACATGGTGGAAGACTAGAGAGAGCTTGTGCAGATGAATTCCCCTTT
AGAAAACCATCAGATCTAATGAAACTTATTCACTATCATGAGTTCATCATGGGAAAGACCTGCCCCTATGATTCAATTACTTC
TCACTGGGTTCTTCCAATGACACATGGGAAATGTGGGACTACAATTCAAAATGAGTTTTGGATGGGGACACAGACAAACCATA
TTAATAAACTTCCTAAATTGACTGAGACCTGTCTCAGATATTTGTTGTTTATCCTACTCATGTACAGCCTTCAGAGTTCCAAA
GCCTATATCAGTTTTCCAGGATTGTTTCCCCTTTTTGTTGGTTATTTCCTCCTTTATTTTCTATGTTTAGTTCCCTTTTCTC
CCACTATTTTTTCATCATTGGGATGTGAGACTTCACAACATTTGAAAGGTAGGTAACAATGAGCTATCTTAACAACATGGGAC
CTGTTTATCTAAGAGTAATCCATTCTATCAATGAAAGATAAAACAAAACAGGAGACCAGAAACTCATTTGGTTGTAAAATGCT
TCCTCTGAATGATTTTGAAAAGGAACAGGTGGGGAAAATATAAAAGGAAAATAAAAACTTGTGCTGTCAATTCATTATGTCAT
GAGGGGGGAAAATCCTAAAGGATGATCCATGCAAGAAACTGATTTTCCTTCATTCCTAAGAGAATAGCTACAAATAAAAAGT
TAAATATCTTCACAGATAGCTACTCTTTGTTCATTTTACTTTATATAAAGTGCTAACTTAGTTCAGGAGAACTACATAATTTT
TCTGTTTCCCTATGTGCTTCTCTCTCATTACAACATGTAAATTTTCATACTGTCCCTCTTTCCCCTCTATCCAGCTTTCCCCC
CTTTTTTGTATTGAAAGCCCTGAAAATCATCTTTGGGGAACGGCACTGACCACAAATTTTTCTGTGATTACTTGTATTTTCAT
TCCAGGCATGCCCTAACTTTGGCAAAATTAATTTTAATTTGATTGAGATCTGTCTCGGAAACCTTTGGTTTACACTAGGAAAG
ATCCCAAATTACGAGTCAATTACTATAAAGCTCAGCCTTCCCACTGTGTATGTGTGTGTGCATGTGTGTGTGTGTGTGTAC
ACGTGTGTTTTAATTTTTGTGGGCTTTGAGCCATGTAGTTCTCTCTGTGGACATACTATTTGGCGTGATCTTTGAATAGAGAA
TTCTGAAAGAAATAAGAGGCTCCTATGAGTTCTCTGAAAGTTTCTGGACTCACCATGGATCTTGACTGTGTCATTGCATCTGA
CAGTCCCAGGGAACAGACTCTCTGGTGGTTTCAAAGAATCTGTGCTTGGGCTCCCCCTGCAGTTTACTGGGTACAGTAATGTT
AAATCACTGTTTCGAGAGACAATTTCGAAAGCATTAGATGCTGCTGAGAGAGGATTGTGAACCAGGGGACAGCCCCTTCATTC
TGGGGGAGCGACATTGGGAGAATATGCTCTGTGAGCCCAAACAGCATCCTCCCCTGCCGGGTGAGGGCAGAGCTGCAGGACAG
GCCCAGAAACCACTCAACACAGATGTCAGCCCTGGAGCAGCTGCAGAGGAGTCTGAGGAGAAAATTTTACCAGCATCTGAATT
ACACTTATTTCAAAACAAAAATGCAATTAAAAAGTTAAAATAAGTAATTAATGTCCAGGCACAGTGGCTTACACCTATAATCC
CAGAAATTTGGGAGGCTGAGGTGGGAAGATTTCCAGGAGTTTGAGATCAGTCTGTGAAACATAGTGAGGCTTCATCTTTACTT
TTGAAAATAAAATAAAATAAAACATAAATAATTTAGCAAAAACTACCGATGTGTCTTCCATATCCCATCGTACTTAGAGCATT
GATGTAACCCAATGAGTCAATGAGAACCAAATTTGAAAGGAGAAAATTTTAGAGTTTTCAGATATCTTAAGAGTTGGAAGATG
TAGAACAAAACTAATTTTATCAATTCAATGTGTGCAAACATGGAGAGACACACTCATGCCAGTAGTTCAACTTGCAAAGGGCA
AAAACCAAAAAAGTTTGAAGTTGCTAGTGATCCATTTGTAGGTGAGATCATTTTGAGGATCATGTCCTGTGAGAGGCTGTTTC

FIG. 6 (Cont. 20)

TCTATTAGAGGAGTTCTGTGCTCATGAAGTGCTGGACATGCTAGGGGACAAATATCAGTAAACAAACATCAGAACTTGAATGT
CAGCTTCCCCCTGCTGCATTCTCCGTGTGTCATCTCTCTGTTATTTCTCATGCTAGATCAGGTCTTTAGCTATGAAATATTCC
ACCTAATTTACATGTCAATAGCTTGAAGTCTACTGAGTTTAATTCATATTTTTTCTATATGTTACAGTTACAGTTTGTCCACA
AGGACAAGGTTTGTCCACAAGTTTGTCCACAAGGTTACAGTTTGTCCACAAGGACTCAATCATAGAAGTGCAGAGTCCTTTTC
GGGCCACATTTAATTCACTTTATCAGTGCCCTTCAGTATGTGGTTCCTGAGAATTTCACATGACAACACATTTACCACACTGG
AATTTAAGCAATCCAACACATGTTTGTAGCTTTATCTTGTAATAGGCTGTATTTCATATGGCAGCCTCTGCTTCAGTTTAGCT
AACACTATGGCTTTGTTTCTCTCTACAAGAACTTGTTTCTCCCAAGATTTCCATGTTTGTGAAAGGAAAAGAAATCTCTGGGA
CCCCCAAATCACTAAGCCAAAGGGAAAAGTCAAGCTGAAAACTGCTTGGGGCAAACCCACCTCCATTCTTTCCCTAAAATGAT
AGCTACTAACTGTCAGGCCTCTGAGCCCAAGATAAGCCATCATATCCCCTGTGACCTGCACATACACATCCAGATGGCCGGTT
CCTGCCTTAATGGATGACATTCCACCACAAAAGAAGTGAAAATGGCCTATTCCTGCCTTAACTGATGATACTATCTTGTGAAA
TTCCTTCTCCTGGCTCATCCTGGCTCAAAAGCTCCCCTACTGAGCACCTTGTGACCCCCTCTCCTGCCCGCCAGAGAACAACC
CCCCTTTTTCCTTTACCTACCCAAATCCTATAAAACGGCCCCACCCCTATCTCCCTTCGCTGACTCTCTTTTCAGACTCAGCC
CGCCTGCCCCCAGGTGAAATAAACAGCTTTATTGCTCACACAAAGCCTGTTTGGTGGTCTCTTCACATGGACACGAGTGAAAC
TAAGGTTTTAAAAAACTACATACCTCCTTCAAAATTTGACCACAAGGAAAAACCTTGTGGACCAACAACAGACAGAGTCATTT
CTCTGCTCACATAAGTCAAATGCCTATCTGATTGCCACCATTTCTCTATTGTTTTGCTAAGCCAGACTAAGGCCTACGTGACT
ATTCCTGTAAATTGTGCATTCAGTTAAAGGCTAATCAGAAACTCAAGAGAATGCAAGCATTTGTCTCAAACCTACCTGTGATC
TGGACGCTCTCTCCCCACTTCAGAAAGTCCTGCCTTTCTGAACCAAACCAATGTACATCTTACATATATTGATTACTGTCCCA
TGTCTCCCTAAATTGCATAAAATCAAGCTGTGTCCCACCACCTTGGGCATATATCGTCAGGACTCCCTGAGGCGGTGTCACTG
CCATGTCCTTAATCTTGGAATACGAACTTCCTAAATCTATTGAGATTAGTCTCAGGTACTCTTTGGATTACAGGTTTGTTTTT
TATTTCATAACTTCAATTATCTGAAATACTAAACAAAATTTGCCAAAGTGTACATTCTCTTGTTGCTGTTGTTGCAAAAAATA
TATTTATGTAACTTATATATAATTTATCATCTATGTGTGTTACCAAGCTGAGTAGCAGATTTATTAGTAAGACTTAGAGAGAG
TAATGAAAAATTCAAATGCCAGTTAGTAACTTAATAGAAAAACAAATTATGCTACATTTGTTTGCTGAAATGCTACCCATTAT
TTGTAAGAAATAAACACATGCAACATAAAAGATTTAATTCTCAGTATTTCTATTGAGAGAAATAATCCACATACATAAGAGCA
TATACTATATTTTTTCATTCTTATAAATTCTAGAATATAAAAGCTAGTCAAAAGACATGTGAAAACATCAGTAGATTTATAAA
GAAATGGTAGAAGAAGGGAAGGAGAAAAACCAAAAAAATATAAAAGAGCAAGAGGAATGCTGAGGGGAGTTGACTTGTCACCT
TCTTAAAAATAGAGATTTTATTTTTCAAAGTTTACTATTGTACAGAATAAATATGTGAATTTTCTTATCTGTCAATTAAACCT
CATAAAATTTATTACAAAAAAACTGAAATTTTAGACAAAAAGAGGGTGATAGGAAGGAACAAATAAATATGTTAAATGTCAAA
TATACCTAAAAATTTATTTGTCTGACCCCTAGTTTTCTCCGTATTTTTAGGTAAATGCAGCAAAATCACACAAGTTGTCGTGG
CAGGAAGTGGATTCTGCAAACCACACTAGGCCCGTTTATCTCTGTCCTAGAGTTGGTTAAAAGAGCAACTGAGGCCAGCTGTG
AGGAGCATAGGCCCGGGTACTAGGACTCACTCATGCCAGATATAAGCCCTTAGACACATACATAGCCCCTCCATGTGTGGGTT
CACTTTTACATCTGTACATGAAGAAACCACTGATTCCTAAATAACATAATTTATACACATAGGTAAAAATAATTAAAAATGTG
ATAGTTATTAAGTGTTTATCACACAACAATTTCACAATAAAACAGCATTTTCCCAAATGTAATCATTGTCATCGAAATCCCCA
AGGACACTCTCATCTGCCCTGGGCCCTGCCCTCTCCTCAGGCATCTCACCCCAGAGCTTGCTATATAGTAGGAGACATGCAAA
TAGGTCCCTCCCTCTCCTGATGAAAACCAGCCCAGCCCTGACTCCGCAGCTCTGGGAGAGGAGCCCCCGCCCTGGGATTCCCA
GGTGTTTTCATTTGGTGATCAGCACTGAACACAGAAGAGTCATGATGGAGTTTGGGCTGAGCTGGGTTTTCCTTGTTGCTATT
TTTAAAGGTGATTCATGAGGAAATAGAGATATTGAGTGTGAGTGGACATGAGTGAGAGAAACAGTGGATTTGTGTGGCAGTTT
CTGACCTTGGTGTCTCTGTGTTTGCAGGTGTCCAGTGTGAGGTGCAGCTGGTGGAGTCTGGGGAAGGCTTGGTCCAGCCTGGG
GGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATGCTATGCACTGGGTCCGCCAGGCTCCAGGGAA
GGGACTGGAATATGTTTCAGCTATTAGTAGTAATGGGGGTAGCACATATTATGCAGACTCTGTGAAGGGCAGATTCACCATCT
CCAGAGACAATTCCAAGAACACGCTGTATCTTCAAATGGGCAGCCTGAGAGCTGAGGACATGGCTGTGTATTACTGTGCGAGA
GACACAGTGAGGAGAAGTTAATGTGGGACCATGCAGAAACCTCCCTGCGGGAACGCTGGGGAAAGTCATCTGCAGGGGCGCT
CAGGAGCCACTGATCAGAGTCAGCCCCAGCGGCAGGTGCAGATGAAGGCTGATTTCCTGTCACGATGTGGGACTTCATCTTCT
TAAAGTTTCTCTACTGAACCTAAGTTCGGAATTCTGTGATTACTAGGGTCATTTCTACATATTTTTAAAATGATTGTTTTAAT
ATGAAAACCTATTCTCCTATGCAGAAAATGCAGATTGATCCTCACAGAGGAGATGAAAAGTTCTCAACCATGGTCACCACTGT
CAGAGTCCTGAGGAAGCTCAGGGCTTCCTGGTGAGTCTTCTCCAGTCAGACTGAGGACAGGAACTCCAGAAAGAATCCTGACT
AGAACTGAGGTATTGCTCCTCACAAGAGAACTCAAGCTGCGGGGGGGTCTGTTCCTGCAGACCCCTGACCCGGTGGCGGATGAA
TAAAACGTACACTGACACACAGATATTCTGTTTTGCCAGTTCAGCTGAGGGTCCGAGGCAACTTACAGACTCCAAGAAGAATC
CTGTAAAGAACGGCAGCAGTGGCCCTGAGCAGCTCGCACTCCAGGCGTGTATTGAGTATAGAATTAACAACAGAAGCTCTGAC
AACACACTTGTGGATAATTAACATGGTTAAGAGAGTAGTTCTACGAATGATTAAAGCTCAGGGACTGCGGTCTAAAGTAAATA
CCATTAGGGGGCAATACCCTGGTTAGTTAATGGAGGTAGGGTAACCAGACTTAACTGGGGAGCCCTCTATTGTCCCTAGTATT
TACCCTATGCCTAACGCTCTAAGGTAAGAGCTGCCCACCTTCAGCCTGTTCAATTATTACAAGCTATGTAACCTTTCGGCCTT
CTAGAGAGGTATATGACTATTCCCTATAACTTTCCTTAATATTCCCCTTTAATATTTCCGCCACCATCCTGAGTGAATCCCAG
CAAGGACAGTCTTTGGGGATTCTGATTACAGAAAAAAGAGAGCCTGGGCCAGGGTCAGTGTCATGTAGAACCTCACAGGTTTC
TCGTAGGACCCTTCTCCTGACACTGAAGAATGCAAATCAGAATCAATACTGATCTGGAGCTTCTTTTCCTAATTCATTTACTG
TCTTTTTTAGATGTTGTTCTCATTTTTCCATTTGCTTTTCCTGCTTTCCGAAAAAGGAAGATGTTTTTGCTGTGGTCAAAATT
CCAGACCTCAAGCCCTTTTCTTGGCGCTCAGGTGGGTCTCAGGCTGTGGCTGCTGCAGTCACGCAGGAGAGTCTGGTGGGACT
TTCTTCACTCTTCGTCACTCAGGACCCTCCACTGTGTTGCATGGAGACTCATCTGGAAATGCAAGTTGCCAGTGGGAACTGAA
GGGACAAGCTTGTCTGGTTAATGTGGGATGTGGATGTGTTTCTAATCCTGTTCTGAAAAACCGTCACACAGTAACGTTCTTCA
CTAGTGGAGAAGGAAGTGGGTGTGAACGTTGTCAGAATAAAAATGGAGCCACGTGTGTTATAATCTTTACAGGCGAAGCTGGA
AGAGGTCATGAATAGAGGGTTCTCATGCACACATCCCTGATAACAAGAATTACCCTAAAAATACTCTGCACAACCACAATCTT
GAACAAAGGCTACCACAACAATAAGAGAATTAATACTGAGGGGATATCTGCCCTGCAACTCCCTGTTCAGCCTTAAACTGATT
CTACCCTTGTTATTGATTCTTCTACCCCAGGATAATTGTCTCAAAATAGCTCAGGTAATCTTCTCATTTATCCTTCAGACACT
TGTCTTTCTTTACCAACCTAAATGTGACCATGGATAATCCCATTGCAATGCTCATTTTCAAATAAATACGATTTGATTTTGGA
GAATCTCTTTCTCTCTGATGTTTAGGTTTGACAAGCTGCAGAGGGACACACCACTTTCCTGTGAGATGTAGGGGATGACAGTT
TTGGGGGATGGCTGGAAACGTGCAGTATCCTTAGGGTCAGCCATCAGTAAATGCAGGCTGGAAATCTTAGAAAGATCTCAAGC
TGCTTAATCACCACGGAGTTTTACCTTCTCCAGATCTGTTCTGATGGAATCAGGGCCAAGTTTGTTATTGATGATAATCTACC

FIG. 6 (Cont. 21)

TAATATTGAGTCAACTGATCACAGTTTTAATAACATCTATTTAAAAATTCACACCTGGATTAGTGTTTGATCAAATAACTACA
AAGTATTGCCCAACCAAGCATACCATCAGGCAGACTGTTACCCACAGAGAAAAACATTGAACATGAGTTTGAGGTTCTCACAT
TGTTAAAGGTGTAAAACCGATTATGTTTAAATTATGCTATTTTTATTATTGTTATTGAGTTGTAGATGTTTCATTTACATTTT
GGATATTAACGCTTTTTCAGATTCATGGCATATTATCCAATTCTGTGAGTTGGAATTATTTTGTTACTTTGCGGAATCTTTTT
TTAAATCTAGTCCCACTTGTCCAATTCTGTGTTTTTTTATTTGTTTGAATGTAAAATCCAGAAAAAGATTGCTAATTTTTTGA
GGGTTGAGAGTTTTACAATTGCACGTGTTTCATTTAAGTATTTAATGCATTTAGAATTAATTTTTTTGTTTATTCTAACCTAA
AATTCTTAATTCTTTGCATGTAAATATCCAATTTTCATAACACGCTCTTTGGAAGACACTATAATTTAGCAATTATATATTGA
TGGTTCTCACGCTGAAAGTCAGCTGGCCATCAATATGTGGGTTTATATCTAAGCTCTCTGTATGAATTTATGCGAATGCCATT
CTGATTTATTACTGTATGTTTCTAATAAATGTTGAGGCCTGGAAGTGTAATACCTCAAGCTTTATTCTTGCCTTGTTACAGAT
ATTAGACCAAAATATTCTAAAATTTTACTATTGAGTATAATAATAGCTGTGGCTTTTGTTAATTGGTTTCATTATGTACAAGT
AGTTTTCTTGTCTTCCTACTTTGTTCAGAGTTTTTATAATGAAATCCTGAATTTTTTTCAAGTGTTTTCTGTGTCTGATGAAA
TGTTACTGAGATATTTTTTCTTTAGTTTTTTAATTAATCAACTGAATTGATTGATTTGAGAATGTCAAATCATCTGTGCATCT
CAGAATAAATTTGAGTTGATCATGGTGTATGGTCTTCTATAAAATCTTTAGAATTTATTTTACTATTGTTGGGGGGTTAATTT
ATGTCTACTAATGATATTGGTCTATGATTTTCTTTTATTGTGGTGCCTTTGTCTATTACTGGTAGTACTCTAACGGTAGCCTC
ATAGAAAGAGTTTGGAAGGTGTGTTGCAGACTACCTTTAAAATAGATTTTATCAGTGGAGAAACGGTGATAGTTTTTTTCTTC
AGTTTTCTGTTGGGAAGAGTTTTGTTGTTTGTTTGTTTTTTTGTTTTTTTGTTTTGTTTGTTTTTTTGAGACAGAATCT
CGCTCTGTTGCCCAGGCTGGAGTGCAGTGGCAGAATCTCGGCTCACTGCAAGCTCCGCCTCCTGGGTTCATGCCATTCTCCTG
CCTCAGCCCCCAAGTAGCTGGGACTACAGGCGCCTGCCACCACGCCTGGCTAACTTTTTGTATTTTTAGTAGAGATGGGGTTT
CACCGTGTTAGCCAGAATGGTCTCGATCTCCTGACCTCGTGATCCGCCCGCCTCGGCCTCCCAAGGGAAGAGTTTTATGTTGT
TTAAAAGATATTCTGAATAACTTAACCTGCTTAATGGGCTTACATAATATTCCTTTCTTCCATTCTTTTTAAAGAACTGCTTA
CCTTTCCTAATTATTTTTAGGGTGATTTTTCACATAAAGATTGTGCAATACATTTTGAGGTGAGACTTAGTGGATTTTCTCTA
ATGAATTAGAAATAATAAATCACTTAATTGACTATTGTATTAAGGTTGATTTGTTGAATATTTGCTAAAGGCCAGTTCTTTAA
GCTGTGCCATGTACTAAATCCCTAACCGACTATTTTATTCAGGTTGGTTTGTTGAATATTTGTTAGAGACCAGTTCTTTACAC
TATGGCATGTAATAAATTCCAAATGGCAGTACGTCATTGTTTACTTAGCTTTTGTGCTTATATTTTTCAGAGGAAAAAAAATA
CTGTAAATTGTAAATACCCAATACCTAACAGTATTGTATGCAAATCTGTGACTGTTGGCAGTGTCATCTCTGAGAAACAGATA
AAGTTTATTTACTATATATAAAAAAAGAGTTTGGAAGGTGGACTCCTCACCAATTTTTGAAAGAGTTAGAGAAGCATTAGCAT
TAATTCTTTAAATGTTAAGACTAATTTTATGATGTAACATATAACCTATCATGGAGAATGTTCAATGGGTGCTTGAGAAGGAT
GTGTATTACATGGCTCTTGGTTGGAAGGTTCTGTAAATGTCTTTCAGGTAAATTTGTTCAATACTGTTGTTCAAGTTCAGAGG
CTTATTAAGAATTTTCTTTCTGGATTTGCAATACATTATTGCTAAGTGAGGTATTAAGGTTTTCCCTTATTTTTATATAGTTT
TCTATTTCTCTCTATATATATATCTTAAAGTTTGCTTAATGCATTTATATTTGTATTTGTACTGTGTAAAAAGTAAAATAAAA
TAATAATTGCTTAGTGAGTTTCATGGCACAATCACGTTATGAATAATCATATTTTCCCAAATGCTGTCATTGCCACTAACTCC
TCCAGATACATGGTATATTATCCAATTCTGTGAGTTGGAATTATTTCGTTGCTTTGCAGAATCTTTTTTTGTTAATCTAGTTC
CACTTGTTCAATTATGCTCCTCCGGGAGTCTCACATCTGCTCTGGGCACTGCCTTCTTCTCAGGCATCCCACACTGGAGCTTG
CTATAGAGGAGGAGGCATGAAAACAGGGCCCTCCCTCTACTGGTGAAAACAAGCCCAGACCTGGCCCTGCAGCTCTGGGAGAA
GAGCCACAGCCCTGGGATTCCCAGGGGTTTCCATGTGGTAATCAGGGCTGAACACAGAGCTCACTATGGGGTTTGAGCTAACC
AGAATTTTTCTTGTTGCTATTTTAAAAGGTGACTCATAGAGAAATAGAGTGAGTGAGAGTGAGTGGATATAAGTGAGAAAAAC
AGTAGATGTGTTTGGCAGTTTCTGACCAGGACGTTTGTGTATTTTCAGGTGTTCAGTGTGAGGTGGAGCTGATAGAGTCCATA
GAGGGCCTGAGACAACTTGGGAAGTTCCTGAGACTCTCCTGTGTAGCCTCTGGATTCACCTTCAGTAGCTACTGAATGAGCTG
GGTCAATGAGACTCTAGGGAAGGGGCTGGAGGGAGTAATAGATGTAAAATATGATGGAAGTCAGATATACCATGCAGACTCTG
TGAAGGCAGATTCACCATCTCCAAAGACAATGCTAAGAACTCACCGTATCTCCAAACGAACAGTCTGAGAGCTGAGGACATG
ACCATGCATGGCTGTACATAAGGTTCCAAGTGAGGAAACATCGGTGTGAGTCCAGACACAAAATTTCCTGCAGAAAGAAGAAA
GGATTCTGGGCCGAAGGGGACACTCAGCACTCACAAAACAGGTGGAGCCCCAGGGCAGGTACAGAAAAGCAGTCAAGGGCTGC
TGTCCTTCAGGATCTGTGCTTTCCTCTGCATGTAGCAGTTCCCCTCGAATCCTCTGCACTTTTATGTTTCTGTGCCCACCATG
AGGTCCCTGGATTACAAAACTTTAATTTAAAAGAGGAAACATTCTTATATGTCCCAAAAACAAAAGTAAGTATTAGAGGCACA
AAAGTGCACAGGCGGCCAGGTGAGGCTGTAGACACTGCCACCCCGCAATGCCAGTCTCACAACTAGCACTGGAGAGTAGTGGG
CATTCAGTGGAGCTTCCTACCTATCCTGTGGTCCGAGCTAAGTCCAGCAAGGCCATTGGTGCCTTCCAGAGCACAGTAGTCCA
TCAGGAATCTCCCATGTGTCCCAGCAGCAGCCTTGCCTCAGTATCTCCACTGTGCACAGCCATTGTCTGGGAGGGAGCTCCCA
GGATGAGTGTCTTTGGCACACACCAGGTGGCGGGTGTTAGAGTGCAGTACAGCAGCTGGCTGCCTGGTCTATTGGGCTCCCTG
ATGTTGGAGGGATTTGAGGTGCATTCTCAGGCCCAGCACCCTCTTTGTGAATTTTTATATAAAAACCCTGATTTTACTTCATT
TTCTCAGATGACATAGATAACTAAAAACAGAATCTGCAAAGAAATTGTAATTTTCAACTTTACCCCAAATTCATTGTTTCTTA
ATTCTGTGCAAGATCCAAACATATTTTTGGCTTCCACATGAGAAATTGTTCTGTTTAAACTGAAATCATTTCTTCTCATATTC
TTTCTTTTGGGCCAAGTACAGAGATCTTGTTGAAAATAAGTTGGGTTCTTTCCACACACTAACCCTCACCTCCCCTAGAGAAA
GAGCAGAGATTGTCCTCACTCTGAGTCTAGGGGAGGAGCTGTTCCTGTACAATTCAGAGCCTGCAGAGACCCCCCCCCCCCGC
CAGGTGCAGCTTCAGTGAGTCAGACATTTCTCCATGTGGGCGACCTCCAGTGCCTGTGACTGCTTCTCAGGCCTAATTGTGGG
TTAAGAATTAGGACACTCTTTAAGTTATCACATCTGAATCCTATTCTGAAAATCACCATAAAGAGAGATAGTTCAATGGCTAT
TCTCCTGACATAAGTTTCTCTTTATTACTTGGTTCCAAGTATGGAGAAACATGTGACCCAATATTTGTCTGAATCCAACATCA
GAATCCCCTGCATTTCTCTGGGAAACTCCCGGATCGAACACAGGTGAGCTCTTTATTCTCACAGAAATGTATGTAGTTGGGAA
TTTCAACAAATTGTCCAGAACCTGTGCCTGCCAACAACTGTGTTTCTCGGTGCACTCTTGGCCTGGTGAAGCCCCCAAAGACC
CTCTCCCTCATGTGTGTCATCTCTGCATTCTCCATCACAACCAGTGCTTCCTCCTGGATCTGCATCCATCACCCCCTCTCTGG
GAGGGAATGGAGTGGATTGGGTCCATAGATGATGAAGGGAGCACACATTACTCCCCTTTCCTCAAGAGTCCAGTCACCATCCC
CAGATCCATGTCCAAAAACAGTTCTTCCTACAGCTGAGCTACATGAGCAACAATCACATAGCCATATATTTTTCAGCAATAGA
CACAGTGAGGGAATACACAGTGTGAACTCACACCAAAACCTCCCTGTGGGGATGCATAGGACAGAAGGGGTTGCTCAGGTCCC
CAGGGGGCTCTCAGGACACCAAGGGTCACTCAAGACCATTGTAGAGGCACGCAGGTAGCCGGGGGCTCTCAGGAACCATGGGG
GAAAATCAGGACACCAAAGGGTGCTTGGTACAGCAGGGGGCTCAGGACAATTGTGGGGATTCAGAAAGAACAGCTTCAAGGCT
CAGCTTCAGGGCAGGTGCAGCTGGTGTGAAAAGGGGCTGGATGAGGCGTTTTGTGTCACCATCATGAAACACCACCAGACACC
CTCCACTACATCTGTTCTAATGCATGTGTTTGTATGATTAGGAAATGATATTGATATAAATATATAACCATAGCTAGGTGTGT

FIG. 6 (Cont. 22)

CTTTTTCTGCCTTCCGTCCTCCCTTCTTCTCTCTCTCTCACACAGAAATTTACATACACCCACCCCACAACACACATAAATCT
ATAACTTTTATTACCTGATGTATTCAATAAACCTGATTAATGTGTTTTGCAGCTTCATTGTTTATGGTGTTGTAGCAATAAAA
ACCATCTGTTTCCCAGCTGTGTACTTCTCTAAGCTGAGTAGCATCTTTGTTCATAATACCCAGAATGAAAAACAACCCAAATG
TCAATCATCAGCTTAACTGGTAAACACATTGTGGAAAAGTCATTCATTGACATACTACCCACTACTACCATCAGCTAATGTTG
GCTATGCTCCAAAGCATGGTTAAATTCACAAGTACTTCAGATGAGTAAAATGAGCCAAAGTGATAAAAGTGCATACATAGGAT
ACAACTTTCATAGGTTCTATAGAACCAAAAGTAATCTAAAGTTGCCAAAAAAAAAATCAGTAGTTCACTGTGAATATTGTAGGA
GAAGGGATGGTCTAGGAAGGAGGAATTATGGAACAAGATAAAATGTTGAGGGAATTGACTTGTTATCTATGTTGATAGTGATA
ATGTCTATGACAATATTTGCCCAATTGTACACTTCATGTGGAGATTATTGTTTTTAGTTTAGCCCCATTAAAGATAGTATTAA
TTAGAACAGGTATAAATTGGTATCACAGGAATTAAAGATAAATAAAATACATGTAAAGTCAGAGAATCCTGAATATACACATG
AATGAGCACTGGACATCTCTGTATTTTTAGAGAAGCACTAGAATACAGCAAAATAATGGCACAATTTTACATCACTAAGAAAG
TTTATCAAACCCACCAGGCATGTTGTATTAGTTCATTTTCACACTGGTATAAAAAACTACTTGAGACTGGGTAGTTTACAAGG
AAAAGAGGTATAGTTGGCTCACAGTTCTGCATGGCTGGGGAGGCCACAGGAAACTTACAATCATGGTGGAAGGTGAAGAGGAA
GCAAGGCACGTCTCACAGCCCAGCAGGAGAGAGATAGAGGAGGGGAAGTGACACATACTTTTAAATCATCAGCGGTTGTTAGA
ACTCACTCACTATCATGAGAACAACATGGGGAAACTGCCCCCATGATCCAATCACCTCTCACCTGGTCCCTCCCTTGACATGT
GGGGATTAGAATTTGAGATGATATTTAGGTGGGGCAGAAAACCAATCTATATCACATGTCCAGTTCTGTCCTGGAGTTGTTTC
AGGGATCCAGTGTGTCCTGTTGATAGAAACAGTGACACCAAGTTCATATTATCAGTTGTAGTTGACACCATGCAAAGCCAAGA
GATCTCAAGTGAGATTTAGTGTGTATGTTGTGTCTAATGAAGTCACACACTCAGAGCAAGTGAATAGGGAAAAGTTCATTATC
TACACTGTAGAGGTGTCTGCTGAGTGCAGGGCAGGTCTCCCAGGAAAATCTAAAATGGCTTGAAAGAAAACCAAAGGAGACTG
GCTCAGGGTTTTTATAATGGTTTAGTGGTGGGGGCAAAGTGAAGCTTCCCACTCACAGATGGGGGTTTATAGGGTTTGAAACT
CCCACTGGCATCAAATGAAGAAGCTCCTGTGAGTCTGAACTAGATTCATCTTGTGTGGCAAAAAAGGAGACGATGGAGGAGTG
AGCCTTAAGTAATCAGCAGTCATGCACCAAAAGATAGAGTGACAACTTATTCCATGCAGCAGGAATAAAAATAATGAATAAGA
AAGAAGACAAGGGTTCAGTATGGGTGGACAACACCCAGATCTGCAGAAATGAGATGACTTTAGAAATGTAAGCAAAGAATAAT
GAGAAAAAGAAGAAGTGGATGGAAAATTAAACAGGGGCCTGGTCTAATGTCTTGGGTAGAAGCTTTTCACAATCAAGGACTAT
CAGCTTATTCTGCAGGTCTTAGGTCAGCCATCTGCTTAAAAACATCAGAAACGCCAGAGGGTCTATGAGGATGCTCAGTTTAA
CATCTCCTATTTGAGTAGCTTTACAGTTGTGTGGAATTCTTAATTGATTCTTTTTTGTTTGTTTTTAGGGACAGGCTCTCACA
CTGTTCCACAGCTTAAAGTACAGTTGTGTGATCATAGCTCACCTTAAATTTGAGCTCCTGACTCACACAACCTTTCCATCTTA
GCTTTCTGAGTATCTACAACTAGATGGGCACACCACCCCTACCCTCCTTATTTTTAAACATTTTTTCATAGAAATAGCATCT
CTTTATGTTGCTCAGGTTGGCTTCGATTGCCTGGTCTCATAGGATTTCCCTCACTTTGCTTCTGGAAGTGGTGTGATTATAGG
GAAGATCCACTGCATCTGACCTGAATTTATTCTTTAGTTGTAAAATATGAAGCCAATAATTAACTGCCTGAATGTTTTCTGCA
GTGAGTTAGTTAAAAGCATCTGATAAGGTTCCTTCCTATGTGATTCACGAGCAGTATTTTCCGCTGATGTTCCTTCCAGTTTC
CTTGCTGAAGATCACAGGGAATTGTGGAAAATATGTAGCAAAAAGGCAGCCTTAAACTCTTCATTGTTAGAGTGGATATCACA
CAGGAATCACTTTCAGTATTTTGTAACACATGCATGCAATAGAGCAAACATGATCTCTGGGGGTAAAGTCTATAAACGTATGG
GCCTTTTAGCTACCAAGTCATAGGGTAATAACTGATGTACCCTGAGGACTGGACCATGATTCCATAGTGCTAGTGGAAGAACC
CTTGACCAAGGGAGTTTTACATTTTATTAAAATATGTAGAGATGCCACTTTTTAAACATTCCCAGAAGGTTGTGAGTGGGATT
GACTCTGTCTCGTATGAACAAAGACAATGCCCTCCATGATTAGATAATATTATAAACTAGATTGAGCTACAGTGTTTGCTGTA
TTGAATCACTGTATATTTTATTTTTTAGCTCCATGTTAGTTTTGTGTCTGCGTGTTAGCGTTGGCTTTAAAATGATATTAATC
AGCTCTGTAGTAAGTAGAAATTCATCTGAGAGTTTCTTTCCTTGTTTTCCAGTTTGATAGGATTTCCAGAATACATAAGAACC
CTCTCTGTTTGTAAAAATATTCCAGGCCAGGCCAGTGGCTCATGCCTGTAAACCCAGCACTTTGGGAGGCCGAGGTGGGGGGG
ATCATTTCAGGTCAGGAGTTTGAGACCAGCCTGGCCAACATGGTGAAACCTCCTTTCTACTAAAAATACAAAAATTAGCCGGG
CATGGTGGTGCTTGAGGATTGCTTGAACCCTGGAGGCTGATGTTGCAGTGAGCCGAAATTGTGCCACTGCACTCCAGCCTGAG
AGACACAGCGAGAGTCCATCTCAAAATAAAAGAAAACAAAACATTCCAAAGTTATGCACAATCTAGAAACATATGTACTTAAT
TCTCATTTTTAATTTATTAAAAAGCTCTAATAAGTTCAATGTTTTCTGCCTTCTCAGTTGATTTCACAACACATATAATAATA
TATCCTAAATAAAAGTTTGTTCTCTTAATACAAATTACTAGTTAATAACCCTTACTTTATTATTGAGGTATTATCCATCAGTG
TTCATCAATGCTCTCAATGGGACTCTTACATAGAGAATATACAAAATATTTTCCTGATCATGACATAAAACAGATGTGAACAC
ATTCTTAGTATTCAGCCATGTCTCCTATCATGTTATAAACCACATGCTAACTTTGACTTTATTGGAACTTGTTCTAATTTCAA
ACTAGTTATTTTTTATCTTCATGCAGCTGGATTATTATGTGTGGTTATTTATTCCGAGAGTGATAAAGACAACATTAACAATT
TTCACTGCAGGCATGTCTAGGCAACCCCCTGTGCACAATGACCTTGGTGCATTGGAGATTCTATGGGGACTCTTCCCTACCTG
CCTAGGAGAGTTCTCTGCCTTCTACCTCTATCATTTTCCTCTTTGAAGAAATACATCTAACTGTCGTTAGAATAGAGACAAAG
ACAAATCTTAACTGCTTCCAGCTGACGGGGGATGCTGTTTGGGGAAGATCTCTCTTGGAGGCCTGTCTAAGGGACCCCAGGAA
AAGGGAGCCATTATCCCAGGCTTCAGTTGCATGAGCATTTGGAGTTTGATGGTCTGAAAACGAGAAAAGGCAAATCAGATTAT
TAGAAGACATGTATCCAAACCTAACAAGGTGGTCAAGGTGGTAAGGACAGTTTGAAAGAAAATTCCAAGGCTGCTGACATGCC
CAGATAACTGCGGCTGTAGTTATGCCTGCTAAGGTTTGGGCGCATGAGGCTTGGCTTTTGTCAGCTCCCTGGGATTTATTTC
CCAAACAAAGAAACCTCCAGGTTAGGGGCACCCTATTCATTCCCATCACCTGGCATGATTTAAAGGATAATTGCTTAGAATTA
AAATATTGATACAGATTTTTTTATATTCCCCATCGCTTTTTGTTTCTTCTGGGCTGTAGCCAGAGATCATTGATTGGCGCTCA
GGAATAAGCAGTCAGTCTAAAATGCAGGCAAATACTTAAACAACTGAAGAGATTAGAATTTAAAGATGATCGTATGATATGTT
TTGAAATACAATTTTTCTCTTTCCAGTTCTGGTTTTTGTCAGAATCAAGTAATTGTAAGACTGAGTTGTTTGCAAAATAAACT
TTAGTCTTAAACTTGGCCTGATTATTTGCATAAAGTGCAGCAAGAATATTAATAATAATTCTGTAGGAAAAGCCTGCAAGCAC
CAGGAGTTTCACAGTCTAACACTATGAGCACGTGCATCCTCACGCAACTCGCTGAATATTTCCAAGCCAGCCTGTTCCTATCT
TAAATGCCATCCAGTTGTATCTGCCCCAGGTACACTAATATATGGGTCCTGCTTCTCTGCAGCCTCCTCTCTCCTCAGATTTC
AGGTTTTGTTTATTGTTTGTTTTCTCTCTGATATAAACTCAAATATGTTGAAGGTTTTTTTTGTGTGTGGTTGTTCAGGTTTGT
TGTTAATGAGATCAGAATAAGATAATACTTTACTCTTTTTATTTATTTATTTATTTATTTTTTGAGTCGGAGTCTCGCTCTGT
CACCCAGACTGGAGTGCAGTGGCCCTATCTCAGCTCACTGCAAGCTCCGCCTCCCGGGTTCACGCCATTCTCCTGCCTCAGCC
TCCAGAGTAGCTGGGACTACAGGCGCCCGCCACCATGCCCGGCTAATTTTTTGTAGTTTTAGTAGAGACGGGGTTTCACCGTG
TTAGCCAGGATGGTCTCGATCTCCTGACCTTGTGATCCGCCCGCCTCGGCCTCCCAAAGTGCTGGGATTACAGGCGTGAGCCT
CCGCGCCCGGCCCATACTTTGCTCCGTTTTATATTCCCATGCTTTAGTAGCTGCTTTTCTCTATCAAATCCATTAACTGAGAG
AACAAATCACATTTAGTTACAGGTGAACAATTAAATAGTTTGGCATATATTTATGTACTGGAACATAACGCAGCTTGAAATCA

FIG. 6 (Cont. 23)

AGGCATGCCTCACTCATATAAACAACATGGCTAAATTCTCAAGTAATTCTGTTTAGTGAAAGAAACTAAGGAGTTAAGAGTAA
ATTTTATATGATACATTTGTAGGAATTTTAGAAGATGCCATTATTGTAAATTAACACGGAGAAGATTTGAGTTTGTCTGACAA
TACGCTGTTGGGAGTAATGTGGATGTGAGTTGAATTTCAGAGAAATAAAAGAAAGATTTAGGGATTAATTTAATTATTCAAAA
CTTGATTGAAGTGCTGAGCAAATGGCTGCAAACATAGGTCAACATTTTTCAAATCCTTCACTATAAATTTGAATTAATTACTT
ATTAATTACACTTGAATAAAGCAATAACGAAGAAACCAATAAAATAACATTTGACTAAAATGGAGCAATAAACAGATCGATGT
TAACACAAGGAATATGACTGACTTATGAAAACATGCACATGAACCATGGTTCACTCTACGTATTTTGGTAAATTACAGAAAGT
TGTCATAACAGATGGGGAATCCTGCAGACTTCACTAGGCATGGTCCACGCTGCCCTGGAGTTGTCTCAGGGGAGCTGCCTCCT
CCAGTGGTTAGAGCACAGGCCCAGGTAATAGGACTAATTTTTTTAGATGTGTAATTTTAGACACACTGCACAACTGCTGTGTT
CTCTGTGTAAATTATCTCCTGTAAAATGTAACATTGAAACCTGCATTAAACATATTGTATAAATATGTAAGAATAAAATAAGA
TTATGAGAGCTAAATATTAATCAAGGCACAAGCACATAATATAAAATTATATTTTCCTGAATGATACAATTATTCCAATCTGT
CCCAGGACACTTCATCTGCCCTGAGCCCAGCCTCTCCTCAGATGTCCCACCACAGAGCTTGCTATATAGTGGGGGACATGCGA
ATAGGGCCCTCCCTCTGCTGATGAAAACCAGCCCAGCTGACCCTGCAGCTCTGGGAGAGGAGCCCAGCACTGGAAGTCGGCGG
TGTTTCCATTCCGTGATCAGCACTGAACACAGAGGACTCACCATGGAGTTTGGGCTGAGCTGGGTTTTCCTTGTTGCTATTTT
AAGAGGTGATTCATAGATAAATAGAGATGTTGAGTGGGAGTGGACATGAGTGAGAGAAACAGTGGATGTGTGTGGCAGTTTCT
GACCTTGGTGTCTTTGTGTTTGCAGGTGTCCAGTGTGAGGTGCAGCTGGTGGAGTCTGGGGAAGGCTTGGTCCAGCCTGGGGG
GTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTCTGCTATGCACTGGGTCCGCCAGGCTCCAAGAAAGG
GTTTGTAGTGGGTCTCAGTTATTAGTACAAGTGGTGATACCGTACTCTACACAGACTCTGTGAAGGGCCGATTCACCATCTCC
AGAGACAATGCCCAGAATTCACTGTCTCTGCAAATGAACAGCCTGAGAGCCGAGGGCACAGTTGTGTACTACTGTGTGAAAGA
CGCAGTGAGAAGTCAGTGTGAGCCCAGACACAAACCTCCTGCAGGGTACCTGGGACAATCAGGGAAAGCCTGGGACACTGTAT
ACTGGGCTGTCCCCAGGGGCAAGTCCAGGTGATATAAGCCTGGGTTTCCTGTCATGATCTAGGGTTGCATTGTTAGCAAATTA
CCCCAGGGACCATCTCTAGATTTCCAATTCTGTAATAACATTTGATGTCGTCTCTGACTGCACAATGTCCCCTCAACTTTGTA
TCTTTTTTTTTTTTTGTAACAGGAGGACACATCCTCACCCTGCAGAAGCCTGAGTGTCACTTTGGGGGCAGAAATGACCTGCCT
TGATCACATTGATCACTGTCCTGAGGAAAATACCCCACAGGGGACCCCGATGACTCCAGCAAAGGCTCTGCCTCAAAACCATT
GAAGAGTCCTTCCTTTCATTAGAATTGACCACAGCACCTGGGCTTCAGCACAAGCCATACCACAGACGTCACAAAGCAGCAGC
TTGACACCTGATCCAGGTGCATTTTCTCACCTTTAGAAGCTGAGAGAGGGGTGTATTCTCAAGGTCAACACACTCTTTGTGGG
TTTTTACACAGAAAACCTGCTTTTACTTATTTCATTTGAAGATAAATGAACAAATGTGCATCTATAAATGATTGTAATTTTC
ACATTTATTCCAAATCCAATATTTCTGAATTCTGCATGATGTCCTGGCACAGGGTTGTGTTTTCTACAGGTATTTTTCATCAA
ACCAAGAAAATGCATTTTCCACTTTCCGTGGTTTTTCTCCATGTGCAGAGGCCTTGAGTAGAGCACGTCTGACTGTGTTTGTT
TTCACGCTGCTGATAAAGAGACCTTGAGTAGATCACGTCTGACTGTGTTTGTCTGTTTTCACGTGGCTGATAAAGACATACCA
GAGACTGGGAAACTTACAACAGAAAGAGTTTTATTGGACTTACAGTTCCACGTGGCTGGAAAGGCCTCACAATCATGGTGGAA
GGTGAAAGGCACATCTGACATGGCGGCAGACAAGAGAAGAGAGCTTGTGCTGGGTCTCCCCTTTTTAAAACCATCAGATCTCA
TGAGACTCATTCACTATTAAGAGAACAGTGCAGGAGAGACACAACCCCCATAACTCAGTCACCTCCCACTGGTCCCTCCCACA
ACATTGAGAATTATGGGAGCTACACATCAAAATGAGATTTGAGTGAGGACACATCCGACCCATATCATTCCACCCCAGGTTCC
CTCCCAAATCTCATGTCCTCACATTTCAAAACCAATCATGCCTTCCCAACAGCTCCCCAAAGGCTAAACTCATTTCATCATTA
ACTCAGAAGTCCACAGTACAACATTTCATCTGAGGCAAGGCAAGTCCCTTCCCCTTATGAGCCTGTAAATTCAGAAGCAAGTT
ACAAGCATTGGGTAAACACACCCATTACAAATGACAGAAATTGCCCATAACAAAAAGGCCCCATGCAAGTCCAAAATCCAGCA
GGGCAGTCAAATCATAGAGCTCCACAATGATCACCTGTAACTCCCCTTCTCACATCCGGGACATGTTGATGCAATAGGTGAGT
TCCGATGGTCTTGGGCAGCTCCACCCCTGTGGCTTTGCAGGGTACAGCCTCCCTCCTGGCTGCTTTCACAGGCTGGTGTTCAG
TGTCTGTGGATTTTCCAGGCACAAAGTGCAAACTGTCAGTGGATCTACCATTCCAGGGTCTGGAGGATAGCAGCCCTCTTCTC
ACAGCTCCACTAGGCAGTGCCCCAGTAAGGACTCTGTGTGGGAGCTCTGGCCCTATATTTCCTTTCCTCCTTGCCCTAGCAGA
GGTTCTCCATGAATGATCCACCACTGCAGCCAACTTATGACTGGACATCCAGGTGTTTTCATACATCTCCTGAAATCTAGGCA
GAGGTTCTCAAACACCAATTCTTAGCACTCTGTCGATAATGGTTCATTTTGGTGGCCTGTTCATTACTGGTATTTTCCAAAGG
AATCTCACTTGAATCTTTACTCTTTTGCATTTTGTCTCCATGACAATGTTGGGAAGTTTTACCTCCACCATCATAACATGATC
TAGTGATCTCACACATTTGTGGCAAACAATACCTACAAATTCAGAAGCTCTTTGCTTTTCTTTCCATGAAATATAATTCTTTC
TGTTCTGTGTATAAGCATATCTTAGCAACTCTGTGCACACCCACATAGATGTCCACAAGCCTATGAATTATTCTCTGTAAATA
AAAATTTATATCAATTTCCCTCAATGTTCATAATTCTCCTGAGGGTGAGGAAGCTCCTTCTCGATCTGTTCAAACAAAATGCC
CAGAAACCATCTGGTAGGTAAGGAGTTCACCTGGCTCTGGTGTGGGGTCTGTCTCTTTCCCTCTGTTGTCACACAGGTCAGCC
CAGTTGTTCAGGTCCTAAGAAGAAAGCCCAGGTTTGTCCTGATTTTAAAACACATCAAACTTCTGATGACTCTCCTGTTACCC
ACATCCATGGAGGATAGATTATTTATTATATAATTCACCAAACTAATGTCAAATGCCCAAGTTGCAATACCACACATCCTAGG
GTATGTTCATGCAATTCACTGGAGGAGAAAGTCTTTCAGAGACAGATGGATCTGAAATGATAAATATGTGGGTAAGGACTCTG
GGCTTGAGTATCATTGTCCAGCCATGTTTCACAAGTGTGTCCTGTCAGGGGAAGGACAAGAGTTCCTTGTGTTCTCAGAGGGA
AGGGGTCACAGAGTTCCTCTCTGGTCCCAGGAAAGATAATCGCACTAATCTTCATGATCTTCATGAGACTATCCTCCAGTGC
TGACCTGTTATAGAGTTTTTGTCTGAAGTTCTCACTGCAATCCCCAATCTACATATTTTCAATCAGAAGTGTTTAGAGGGCAG
GACATATCTTCACGGACACACATTGAGAAGGATGTAGATATGTCCCACTACCTTCTCCTGAGATCTCAGACAGAATCCCAGAT
TTCAAAAGGACACAGAAGGACAGCTCTCAGGTGCTTTTAAAAAATGACCCACTTCCAGGGACAGGGAGCTTCCCTATAACCAT
GGTGGATGTTCTGAACTACAATAAACATTGGATGGATCCAGGATTGTTTGAAGTCACTGTCATTATTACATTCAGCTGCTGTT
TCAATGTGTCTGAAGTAGTAAATGACAATTTAGATGACAATTTATATGAATCTTCAAGGGTAGAACAATATTGACCATATTCC
AAAATCTGTCCTTGATCCATGATCACACTCATCTCCCAGACCAGGTCCTTCAGCACGTCTCTTTACCTGAAAGAAGAGGACTC
TGGGCTTGGAGAGGGGAGACCCCAAGAAGACAACTGAGTTCTCAAAGGGCACAGGCAGCATCCTACTCCCAGGGCGAGCCCAA
AAGACTGGGGGCTCCCTCCTCCTTTTTCACCTCTCCGTACAAAGGCACCACCCACATGCAAATCCTTACTTAAGCACCCACAG
GAAACCACCACACATTTCCTTAAATTCAGGTTCCAGCTCACATGGGAAATACTTTCTGAGAGTCCTGGACCTCCTGTGCAAGA
ACATGAAACACCTGTGGTTCTTCCTCCTCCTGGTGGCAGCTCCCAGATGTGAGTGTCTCAGGGATCCAGACATGGGGGTATGG
GAGGTGCCTCTGATCCCAGGGCTCACTGTGGGTCTCTCTGTTCACAGGGGTCCTGTCCCAGGTGCAGCTGCAGGAGTCGGGCC
CAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCACCTGCACTGTCTCTGGTGGCTCCGTCAGCAGTGGTGGTTACTACTGG
AGCTGGATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTATATCTATTACAGTGGGAGCACCAACTACAACCCCTC
CCTCAAGAGTCGAGTCACCATATCAGTAGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGACA

FIG. 6 (Cont. 24)

CGGCCGTGTATTACTGTGCGAGAGACACAGTGAGGGGAGGTGAGTGTGAGCCCAGACACAAACCTCCCTGCATGGACGCGGAG
GGGACCGGCGCAGGTGCTGCTCAGGACCAGCAGGTGGCGCGCGGGGCCCCCAGAGCATGAGGCCGGGTCAGGAGCAGGTGCAG
GGAGGGCGGGGCTTCCTCATCTGCTCAGTGGTCTCCGTCCTCGCCAGCACCTCGCTGTCACCAGGGCTCCTCTTTCTTTATTA
TCTGTGGTTCTGCTTCCTCACATTCTTGTGCCAGGAAAGAAACGAGGAAGACAAATTTTCGTCTATAGTTGAAGCTTCACCAA
TTACTAGGAACTTGCCTACAAGTTCCTGCATGACCCATTATAACTTATCGATTAAAAAATATATATTCTAATGCTTCTCACCA
TCTCTTGATTTGTATCATCAACTGAATTGTACCCTCTTTGAAATTCATATGATGAAACCTTAAATTCAATGGATCTATATTGG
AATTTTAATGAAATAATTAAGGTTAAATGTGGTCATAATTGTAAGACCCTAATGCAATAGACGTGTTGTCTTTATAAGAAGAG
GAAGAGACACCAGAGACCTCTCACTTTTCACGTGCAGGCAGAGAAGAGGCCATGTGGAGACATAGTGCACTAGAAGGTGGCCC
AGTGCAAGCCAGGAAGAAGCCGCGCCAAGAACCAGCCCTGCCAGCACACTAATCTTCAACATTCAGACTGCAGAATTTTAAGA
AAATCAGTATTTGTTGTTTAAGCCACCCACTCCTGTTGTCTTCTTATGAAGATCCAGACAGACTAATACCACATAACTCTGTT
AGTGCTGTCCCCTGGATGGAGAATTAGCCTCCTGAGGCTGGGCACATCTCTCAGATTTCCACATAAAACAGGTAAAAAATAGT
AGTTCTGATATAAAAACTTGTCATGTCCCTGTTGGCCAATTTCTGGGCAAGGTCTTTTAAATAAGCCAAGTTTGCGGGGAAAT
GGAGACCATATGTTTGTGGGACTCTAACCGTGGAATCTACTGCATTGCTCTAGCAGAATCAAAAATTGAACACCAGTGAGCTC
TTTATTCTCATTAAAATGTGTGTCTTTGGAAATGTTAACATTCTGTCCAGAATCTGTGCTCACAAACAACTGTGTTTCTTAGT
GCACTCTTGGCCTGGTGGAGCCCTCGCAGACCCTCTCCCTCACCTGTGCTGTCTCTGGATTTTCCATCACAACCAGTGTTTCC
TGCTGGAGCTGGATCCACGAGTCCACATGGGAAGGACTGGAGTGGACCAGGCGCACACGTCATGAAGGGAGCAAAAATTCCCA
CCCACTCCTTATGAATCCAGTCACCATCTCCAAATTCGGGTCCAAAAAACACTTGTTTTTACAGTGGAGCTATGTGAGCAACA
AGCTCACAGCCATGTTTTAAAGAAGAGACAGAGTGAGGGGACCACGGTGCGAGCTCACACCCAAACCTTCCTGGAGGGGTGCA
CAGGACAGCAGGAGTCCCGATGATGGAAGGGGGTGGTCTGGATTCCAGGTCACTCTCAAGATCATTGTAGAGGCACTCAGCTC
ACCCGGGGGCTCTCAGGAGCCATCGAGGTAAATCAGGACACCAGAAGAGACTCGGTACAGCAGGGGGCTCTGGACCATTGTGG
GGATTCAGAAACAGCAGGTTCTAGGCTCAGCCTTAGGGCAGGTTGAGATGGGGTGAAAAGGGGCTGGATGAGGGTGTTTGTGT
CACCATAATATTTCACCACTAGACACCCGCCACTACATGTGTTCTACTGCATATGAGTGTATGATTAGAAAATCATACTTCTA
TAAATATATAACCATACGAAGGTGTGTCAAGTTTTCCTCTTCAACTTCTATCGGCCTTGTTCGTAAGGACTAATTCCCTGTAA
TTACTTGAGGACCTCATAAATTGTGGTCAGGTTTGTAGGTTTCCTCTCTTTCCTTGTCTCCCTTTCCCCTTATTCTCTCTCAC
ACAAATGGACATAATCCCCACTCCACACGCAAAGAAATCTATAACTTTCATTACCTGATGTATTGAATAAAATTGATTAATGT
GCAGCTTTCCCATCTTTGTTGTTGTTCATGCTGCTGTAAGTATAAGAACCATGAGATTCTCAGCTGTGTACTTCTCCAAGCTG
AGTGGCAGCTTTGCTTATCATACTGAGATGGCCAACAATCCAAATGTCAATCATCAGCTTAACTGGTAAACAAATTGTGGAAA
AGTCATTCATTGGCATACTACTGACTGTGACCACAATATACTAATGTTGGATACGCTCAACAGTATGGTTAAATTCTCATATG
GTGAGTAAAATGAGCCAAACAAATAAAAGTACACACATATGATACCACTTTTATACATTCTCCCATCCAAGTACTAACCAGGC
CCGACCCTGCTTAGCTTCCGAGATCAGACGAGATCGGGCGCGTTCAGGGTGGTATGGCCGTAGACACACTTTTATACATTCTA
TAGAATAAAAACTAAAGTTACATAAAGAATCAGTAGTTCACTGTGAATATTATAGAAGGGAAAGTGTAGACAGGAGGAATTAC
AGAAAAGAGAAAATTTTAAGCATAATTGACTTGTTATCTATATTGATAATAATGATGTCTATGATAATATTTGTACAATTGAA
CACTTCATGTGAAGATCTTTTTTTTTTAGTTTAACATCATTAAAGATAGTACTAACTGTAACGTGTGTAATTTGGTAGAAACGG
AGTCAGACAGAGATAAAATACATAAAAAGTCAGAGACACCTGAATATTCACATGAGTGAGCCTGCACTTCTCTATGTTTTTAT
GAAAACACTACAATACAGCAAAATAATGACATCATTTTATGACGTGAAGGGGGTTTATTAAACCACTCCAGGCACGTTGTATT
AGTTTGTTTTCCCACTGCTACAAAGAACTACCTGAGTTTGGGTAACTTATAAAGAAAATAGGTTATTGACTCATAGTTCTACA
TGGCTGGAAAGGCCTCAGGAAACTTGCAATCAAGGCAGAGTGTGAAGGGGAAGCAAGAGACATCTCACATGGCAGCAGGAGAG
GTGGGGAGAACCACCACACACTTTAAATTATCAGATCTCCTGAGACCTCAATCTGAGACCTCAATCATGAAAACAGCATGGAG
GAACCACCCCATGAGCCCATCCCCTCTCACCAGGTCCCTCCCTGGACGTGTGGCAATTCCAATTCGAGATCAGATTTGGGTGG
GGACACAGAACCAAACCATATCACATGTCCAGTTCTGTCCCAGAGTTGGTTCAGGAATCAGATGTGTCCTGTTAACAGGAGCT
GTGACACCAAGCTCCCAGCACCACTTGTAGTTGACGTCATGCAAAGGCCAAGATATCTCAACTAAGATTTAGTGTGGATGTGA
TGTTGGATGGTGACACACCCTCAGACCAAGTGGATATGGAAGGGATAATTATCTCTATTCTAGACGTGTCTGCTGAGAGCAGG
GCAGTTCTCTCAGCAAAGTGCAAAATGGCTTGATAGAACAGGGAAAGAGAGGGCCTCAGGGTTTGGTGGTGGGGGCAGATTGA
GTCTTTCCACTCACAGAAAGGGGTTTATAGGGTGGGAAACTCCCACTGGCTTCAAATAAGGAAGCTCCTGTGATTCTGGACCG
ATATTCACCTTGTGTGTAAAAAAGGAGGTAATGGAGGAATGAGCCTTAAGCTATCAGCAGTCACACACCAAAATACAGTGTGA
CAAGTTATTCTATGTAGCAACTATAAAAATAATGAATAAAAAACGAGATAAGGGTTCAATATGATGGGCAACACTCAGGTCTA
CAGAAAATGAGATGAGTGTTTATAAGTCAAAGCAAATAATAATGAGAAGCAGGAGGAGGGTGTGCAGAATTAGACAGGGGTCC
AGGTCCAGTGACTTGGGTGGAAACCTTTTGCTATTAAGGATTATCAGCTTAGTCTGAAGGTCTTAGGTCAGCTATCTGTTTAA
AGACATCAGAAACACCAGAGAATCTTTGAGGATGCTCAGATTAACATCTCCTATTTTAGTAGCCTTGCAGTTGTGTGAAAACC
TTTTTTATCTTATTTCATTTTATTATTTATTTATTTATCTGTTGAGATGGAATTTCGCTCTTGTTGCCCAGGCTGGAGCGAAA
TGGCACGATCTTGACTCACCGCCTCTTCCACCTCCCAGATTCAAGCGATTCTCCTGCCTCAGCCTCCCAGTAGCTGATATTAC
AGGCATGCACCACCACGGCCCAGCTAATTTTGTATTTTTAGTAGAGATGGGGTTTCTCCACATTGGTCAGGCTGGTCTCAAACT
CTCAACCTCCGGTGACCCGCCCACCTTGGCCTCCCGAAGTGCTGGGATTACAGGTGTGAGCCACTGCTCCGGGCCGAAAATCT
TATTCATTCTTTTTTGTTTGTTTTTTAGAGACAGAGTCTCTCTCTGTTGCACGTTGAAAGTGGAGTGGTGTGATAACAGCTCAC
TGTAAATTTGAACTCTTGGCTCACAGAGTATGTTCCTATGTATCGTGCAGGTGTGTCTGTGTGTGTTTACCCGGCTTGGGGTC
CTCTAATTTTTGGATCTGTAGTTAGGTGTTTCACATTCTTAAGATATTTTTCTTAAGAAATATATCTTAAGATATAAGTATAT
CTTAAGATATCATTAATTCTTAAGATATTTTCTCTGTTTCTAATTTCTATTTTTGAAATTTGAAATATATCTACACTATACTT
TTTGATGTTAGTTCTTAAATTTCTTCACTCTTTTTCCCTTTGAAATTCACTTTGTGTAATTTCCAGTAACGGAGTTGAAGTCC
CTGGTTTCATTTAAGAGCTGAGCGAATTCTACTGCTGAGCGTGCCCAAGGTATATTCAACTTTATACTGCATCACTTTTGATA
ATTTTATGAATTTCCATTTGATTCTTTCTTAGTATTTCTCTCTGTCAGTCACCTATCTAGTCTTGCACTGTGTCCACATTTTC
TTTCAGATACTTTTAACAAATTCAATTACTTTAAATATCCTACTTAATAAGATAGTTCTAGTATTGTGTCATTTACAAATATC
AATTCTGAGGATTTTTCCATTATGACTTTGGTGTTTTTTATAACTTATATGACTTTGATGAATGTTATAATTTTTGTTGATAA
CCAGCCATATTTGGACCCTTGATATTGACGTATTATTTTATTTTGTGCATTTCTGCCTGTATTTGACCACACCCTATCTGTGC
TGGGCCTTGATTGTGGAGATGTCTGTGCATCTCTTCAGAGCTACATTTGACATTTACTTTTGCAACGGCTGTAGCAGTTGAAG
TGTGTTCTTCTATGTCCACTGGAGACTTCAGATACTCTAGTGATACCTTGTTTTCATGCCTGCTTGGCTTTGTCTATTCACCT
CATTCCATTCTACAGAGAATCTCCTTCACATTCCTAGGGTGGATTAAAGTGTTATATTTAACTGCCAATTGTGAAATTGGCGG

FIG. 6 (Cont. 25)

AAGGCATTAGACTAAAGGAAGAAACTGACCTCTCGTTGGGCCATAATTCTAGAAAGCCGTTGTGATCCTGAGTCTGAGTGTGA
CCTTCCAAGTTTTCCCGACCCTCCTGCAAGTGAGATACTGGTCTGTGTGTTCTTGCCTCTTCCCCTGGGGTAGAGTCCTCCTG
TTTTCCCCAGTTGTTCCCTCCCACAGCTCTCACAATCTCTGTTGGTGTCCCCATCTTCCAGATCTGCTGCCATGACCTGCAGA
TTAAGGCTCTGATTCCATAAGAAACTGAGGGGAGCTGCTTCTCAATAGATCTTTGATGGGGACCTCTGTTCCCATATCAGTTC
ATGAGGGGCTGCTCCAGTGCCCTAGGATGCTGATTTTCATGGCTTGCTCCTGCAGGGTAATATCTGAGTTTCATAGTGGGAAT
CAGAGAGTTGGGTCTGGATGCATTTCAGAAGTGTGGGCTCTCATTCTCTCCCAGACAGTCACTTTGGGAAGGATAGATTCTTG
TGACTGTAAAGGTTCTTCAAGAGAATAGCACAACTCTTCAGTATGTTGTCCCTTAGAATTTCTCACTACAACACGCTTAACAC
ACTCGACTTCAAGCAATGCAATGTGTATTTGTGCTCCATCTTGTAATGGCCTACGTTGAATACGACAGACTGTGCCTCAGGTA
ATTTCATATCTTGACTTTATTACTCTGTACAAGAACTTGCCTCTCCCTAGATTTCAATTTTTTTTGTTTTAAACCTTCAGTTA
TCTGAAGCATTTAATAAAATTTGCGAACTTCCATCTTTTCTGTTTATCTGTTATTGCTGATGTTATTGTTTTAAAAATAAATA
TATATTTCTCATTCATGTACATTTTTAAGCTGAGCAGCATATTTTTAAGTAAAACCTGGAATAATAAAAGAATCCAAACATTT
TTCAGCTGCCCCAAAAAAACCAAATTATGGTAAATGTGTTCACTGGAACACTACTCATCACTTATAATAAATATATTTCTGGT
ACACAGAGCAACAAAGAAAAATATCTAAGTGTTTATGCTGAGTAAAATACGCCAGACAAATAAGAATATGTACCATATTACTC
CATTTATGCAATTTCTTTTAAGTGAAAAAGAATCTAAAGCAATATCCAGAAGATCAGTAGTTACCTGGAAAAAGGGTAGACCA
AAGGAAGGGGAAAGGAGGAAACTTACAGAAGAACAAGAGAAAATGTTGAGGGGAGTTCACTTGTCCAGCTTGGAAATGATGGG
TTACATCATGTTGATCAATTGCACACTTTAAATATGTGAAGTCTATTATCTGCCAATTAACACTCGCAAAATTTATTGCAAGC
AGACAAATGAAAAATTAGACAGAGAGAGGATGGTATAAAGATAGAAAATATATATTAAATGTCAGAAATGTCTGAGAATTTAA
CTCCTGACCCTAGTTCCGTCCTTATTTTAGGTGAATGGTAGCGTGCACCAAAATCACACACATTCTCAGTACAGGAAGTGGG
TTCCACAAAGCACACGAGGTATGTCCAATTCTTACCAAGATTTGGTTCAGGGAGTAACAGTGATGAGGAATCACAGGCCCAGA
TACCGGGGCTCACTCATCTCAGACATGACCTCGTGGACACACACTTAGCCCCTCCTCCATGTGTAGGTTGACTTCCACATATG
TAAATGGAGAAACCATTGACTCCTACAGAACATAATTTACAGAAATATACAAAAGATAAAATAGTGCAAATACTTATCACAAC
AAAATTTCCTAATAAGACAGTGTATTTTCCAAATACCGTAATTGTCACCCAACTCCTGTGGGGCCGTGTCATTTTATCTGGGG
TCTGCCGTCTCCTCAGGATTCCCACCCCAGAGCTCTCTATGTAGTAGGAGACAAGCAAATAGGGCCCTCCCTCTGCTGCTGAA
AATCAGCCAAATCCTGACCCTGCAGCTCTGGGAGAGGAGCCCCCGCCCCGGGATTCCCAGCTGTCTCCACTTGGTCATGAACA
CTGAACACAGAAGACACACCATGGAGTCTGGGCTGAGCTGGATTTTCCTTGTTGCAGTTTTAAAAGGTGATTTATGGAGAATG
AGACACACTGAGTGTGACTGGACATAAGTGAGAGAAACAGTGGATTTGTGTGGCAGTTTCTGACCAGGGTGTCTCCGTGTTTG
CAGGTGTCCAGTGTGAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTAGTAAAGACTGGAGGGGTCTCTGAGACTCTCCTGTGC
AGCCTCTGGATTCACCTTCAGTAGCTCTGCTATGCACTGGGTCCACCAGGCTCCAGGAAAGGGTTTGGAGTGGGTCTCAGTTA
TTAGTACAAGTGGTGATACCGTACTCTACACAGACTCTGTGAAGGGCTGATTCACCATCTCTAGAGACAATGCCCAGAATTCA
CTGTATCTGCAAATGAACAGCCTGAGAGCCGACGACATGGCTGTGTATTACTGTGTGAAAGACGCAGTGAGAAGTCAGTGTGA
GCCCAGACACAAACCTCCTGCAGGGTACCTGGGACAACCAGGGAAAGCCTGGGACACTGTATACTGGGCTGTCCCCAGGGGCA
AGTCCAGGTGGTATAAGGCTGGGTTTCCTGTCATGGTCTAGGGTTGCCTTGTTAGCAAATTACCCCAGGGACCATCTCTAGAT
TTCCAATTCTGTAATAACATTTGATGTCGTCTCTGACTGCACAATGTCCCCTCAACTTTGTATCTTTTTTTTTTTTGTAACAG
GAGGACACATCCTCACCCTGCAGAAGCCTGAGTGTCACTTTGGGGGCAGAAATGACCTGCCTTGATCACATTGATCACTGTCC
TGAGGAAAATACCCCACAGGGGACCCCGATGACTCCAGCAAAGGCTCTGCCTCAAAACCATTGAAGAGTCCTTCCTTTCATTA
GAATTGACCACAGCACCTGGGCTTCAGCACAAGCCATACCACAGACGTCACAAAGCAGCAGCTTGACACCTGATCCAGGTGCA
TTTTCTCACCTTTAGAAGCTGAGAGAGGGGTGTACTCTCAAGGTCAACACACTCTTTGTGGGTTTTTACACAGAAAACCTGGT
TTTACTTTATTTCATTTGAAGATAAATGAACAAATGTGCATCTATAAATGATTGTAATTTTCACATTTATTCCAATTCCAATA
TTTCTGAATTCTGCATAATGTCCTGGCACAAGGTTGTGTTTTCTATAGGTATTTTTCAACAGACCAAGAAAATGCATTTTCCA
ATTTCCCTGTTTTTCCTCCATGTGCAGAGACCTTGAGTAGAGCACGTCTGACTGTGTTTGTCTGTTTTCACGCTGCTGATGAA
GACATACCAGAGACGAGGAAACTTACAACAGAAAGAGTTTTATTGGACTTACAGTTCCACGTGGCTGGAAAGGCCTCACAATC
ATGGTGGAAGGTGAAAGGCACATCTGACATGGCGGCAGACAAGAGAAGAGAGCTTGTGCTGGGTCTCCCCTTTTTAAAACCAT
CAGATCTCATGAGACTCATTCACTATTAAGAGAACAGTGCAGGAGAGACACAACACCCATAACTCAGTCACCTCCCACTGGTC
CCTCCCACAACATTGAGAATTATGGGAGTTACACATAAAAATGAGATTTGAGTGAGGACACATCCGACCCATATCATTCCACC
GCAGGTTCCCTCCCAAATCTCACGTCCTCACATTTCAAAACCAATCATGCCTTCCCAACAGCTCCCCAAAGGCTAAACTCATT
TCATCATTAACACAGAAGTCCACAGTACAACATTTCACCTGAGACAAGGCAAGTCCTTTCCACTTATAAGCCTGTAAATTCAA
AAGCAAGTTACAAGCATTGGGTAAACACACCCATTGGAAATGACAGAAATTGCCCATAACAAAAAGACCCCATGCAAGTCCAA
AATCCAGCAGGGCAGTCAAATCATAAAGCTCCACAATGATCACCTGTAACTCCCCTTCTCACATCCGGGACATGTTGATGCAA
CAGGTGAGTTCCCATGGTCTTGGGCAGCTCCACCCCTGTGGCTTTGCAGGGTACAGCCTCCCTCCTGGCTGCTTTCACAGGCT
GGTGTTCAGTGTCTGTGGATTTTCCAGGCACAAAGTGCAAACTGTCAGTGGATCTACCATTCCAGGGTCTGGAGGATAGCAGC
CCTCTTCTCACAGCTCCACTAGGCAGTGCCCCAGTAGGGACTCTGTGTGGGAGCTCGGGCCCTATATTTCCTTTCCTCACTGC
CGTAGCAGAGGTTCCCCATGAATGAGCCACCACTGCAGCCAACTTGTGACTGGACATCCAGGTGTTTCATACACCTTCTGAA
ATCTAGGCAGAGGTTCTCAAACCCCAATTCTTAGCACTCTTTCCATAATGGTTCATTTTTTTGGCCTGTTCATTACTGGTATT
TTTCAAAGGAATCTCACTTGAATCTTTACTCTTTTGCAATTTGTCTCCATGACAATGTTGGGAAGTTTTATCTCCACCATCAT
AACATGATCTAGTGATCTCACACATTTGTGGCAAACAATACCTACAAATTCAGAAGCTCTTTGCTTTTCTTTCCATGAAATAT
AATTCTTTCTGTTCTGTGTATAAGCATATCTTAGCAACCCTGCACACACCCACATAGATGTCCACAAGCCTATGAATTATTCT
CTGTAAATAAAAACTTATATCAATTCCCTCAATGTTCATAATTCTCCTGAGTGTGAGGAAGCTCCTTCTCGATCTGTTCAAA
CAAAATGCCCAGAGACCATCCGGTAGGTAAGGAGTTCACCTGGCTCTGGTGTGGGGTCTGTCTCTTTCCCTCTGTTGTCCCAC
AGGTCAGCCCAGTTGTTCAGGTCCTAAGAAGAAAGCCCAGGTTTGTCCTGATTTTAAAACACTTCAAACTTCTGATGACTCTC
CTGTTACCCACATCCATGGAGATAGATTATTTATTATATAATTCACCAAACTAATGTCAAATGTCCAAGTTGCAATACCGCAC
ATCCTAGGGTATGTTCATGCAATTCAATGGAGGAGAAAGTCTTTCAGAGACAGATGGATCTGAAATGATAAATATGTGGGTAA
GGACTCTGGACTTGAGTGTCATTGTCCAGCCATGTTGCACAAGTGTGTCCTGTCAGGGAAGGATCAGAGTTCCTTGTGCTCTC
AGAGGGAAGGGGTCACAGAGTTCCTCTCTGGTTCCCAGGAAAGGTAATCGCACTAATCTTCATGATCTTCATGAGACTATCCT
CCAGTGCTGACCTGTTATAGAGTTTTTGTCTGAAGTTCTCACTGCAATCCCCAATCTACATATTTTCAATCAGAAGTGTTTAG
AGGCCAGGACACATCTTCAAGGTCACACATTGAGAAGGATGTAGATATGTCCCACTACCTTCTCCTGAGATCTCAGACAGAAT
CCCAGATTTCAAAAGGACACAGAAGGACAGCTCTCAGGTGCTTTTAAAAAATGACCCACTTCCAGGGACAGGGAGCTTCCCTA

FIG. 6 (Cont. 26)

TAACCATGGTGGATGTTCTGAACTACAATAAACATTGGATGGATCCAGGATTGTTTGAAGTCACTGTCATTATTACATTCAGC
TGCTGTTTCAATGTGTCTGAAGTAGTAAATGACAATTTAGATGACAATTTATATGAATCTTCAAGGGTAGAACAATATTGACC
ATATTCCAAAATCTGTCCTTGATCCATGATCACACTCATCTCCCAGACCAGGTCCTTCAGCACGTCTCTTTACCTGAAAGAAG
AGGACTCTGGGCTTGGAGAGGGGAGACCCCAAGAAGACAACTGAGTTCTCAAAGGGCACAGCCAGCATCCTACTCCCAGGGCG
AGCCCAAAAGACTGGGGCCTCCCTCCTCCTTTTTCACCTCTCCATACAAAGGCACCACCCACATGCAAATCCTCACTTAAGCA
CCCACAGGAAACCACCACACATTTCCTTAAATTCAGGTTCCAGCTCACATGGGAAATACTTTCTGAGAGTCCTGGACCTCCTG
TGCAAGAACATGAAACATCTGTGGTTCTTCCTTCTCCTGGTGGCAGCTCCCAGATGTGAGTATCTCAGGGATCCAGACATGGG
GATATGGGAGGTGCCTCTGATCCCAGGGCTCACTGTGGGTCTCTCTGTTCACAGGGGTCCTGTCCCAGGTGCAGCTGCAGGAG
TCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGTAGTTACTACTG
GAGCTGGATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTATATCTATTACAGTGGGAGCACCAACTACAACCCCT
CCCTCAAGAGTCGAGTCACCATATCAGTAGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGAC
ACGGCCGTGTATTACTGTGCGAGAGACACAGTGAGGGGAGGTGAGTGTGAGCCCAGACAAAAACCTCCGTGCAGGGAGGCGGA
GGGGACCGGCGCAGGTGCTGCTCAGCGCCAGCAGGGGGCGCGCGGGGCCCACAGAGCAGGAGGCCCGGTCAGGAGCAGGTGCA
GGGAGGGCGGGGCTTCCTCATCTGCTCAGTGGTCTCCCTCCTCGCCAGCACCTCAGCTGTCCCCAGGGGTCCTCTTTCTTTAT
TATCTGTGGTTCTGCTTCCTCACATTCTTGTGCCAAGAAAGAAATGAGGAAGACAAATTTTCGTCTGTAGTTGAAGTTTCACC
AATTACTAGGAACTTTCCTAGAAGTTCCTGCATGGCCCATTATAGCTTACAGATTAAATATATCAAGCTTCTCATCTCTTG
ATTTGTGTCATCAACTGAATTGTGCCCTCTTTGAAATTCATATGCAGAAACCTTAAATTCAATTGATGTATATTGGAATTTTA
ATGAAATAATTAAGGTTAAATGTGGTCATAAGTGTAAGACTCTAATTCAACAGACGTGTCGTCTTTATAAGAAGAGGAAGAGA
CACCAGAGACCTCTCACTTTTCACGTGCAGGCAGAGAAGAGGCCATGTGGAGACGTAATGCACTAGAAGGTGGCCCAGTGCAA
GCCAGGAAGAAGCCTCACCAAGAACCAACCCTGCCAGAACATTGATCTTCAACATTCAGACTGCAGAATTTTAAGAAAATCAA
TATTTGTTGTTTAAGCCACCCACTCCTGTTGTCTTCTTATGAAGATCCAGACAGACTAATACCACATAACTCTGTTAGCGCTG
TCCCCTGGATGCAGAATCAGCCCGCTGGGGCTGGGCACATCTCTCAGATTTCCACATAAAGTAGGCAAAAAATAGTAGTTCTG
ATATAAAAATTTGTCATGTCCCTGTTGGCCAATTTCTGGGCAAGGTCTTTTAAAGAAGCCCTGGGGGCTTTGTCACAAAAGTT
GCCTTTTATCATTTATTAGGACATAACTGATGAACAATGAGTACCAGTTGGATGGAGACTGACCACTGACCATCTTCTGCTGT
CTCCTAAGTATGCCACAGAAAACCACACCAACATTACTCTATGTCTTCAACTTTCTAAATTTGCACTGATTGGTATTTAAGGC
AGGCCCAGCGTTGAATAACTCCTTTAGTTTTTGCTTCTCTGGGAAAGGTCTTATCTATCCTGGCCTTGGTCTTCAAGTTTCAG
CAATTCTGGGAAGCCAAGGACGCCTCTATCTCCTCCTCCATGCTCTGCAACTCACCTGAGAACAGCTTTCTCATTGGAATGTC
TTCTGTTTAAGGAATAAGAGTCCCTGTTTCAGGCTTGGGTGCCTGAGTACACCTACTGGATCCAGCCCAGGATTGGAGAAACT
TTCCAGAACACATCACCTGAGAAATGACCAGTCACACTGTTACACTTTCACAATTTCCGCTTCCTCATGAGAAAATTAAAATT
GCAGAGACTTTTTCATAAGCGTTGTGCCATGTCCTTTCTTGTTTTCTTGCCTGTTCATTTATGTCAGACCAGGTGCCACATCT
ATGTAATCAGGTTAGAATCCTGCCTCCAGTAACACATGAAAAGGACCTATGGTTGTACTTTTGGTCTTTGCTCCAAAGTGTAA
AGATTACAAAAGTCATCACCCTCATTCTTATGCCAAGAGTCATCTGCACAATCTGATCTTCAATACATTTTAGAATCCATCAA
ATGAATGAAATTCCATTTTTTAAATTACCACCCCAAAAACTAGAGAGATGGGCATGTCCAGAATAGCAGTTGATGGTTGCTTA
ACTGGAAGAGAAGTTTCAGAAGCCACAAGCTGTTGAAGGCACTTACGTGGTTAGCACTATAGACGTCTGCAAGACAGATGTGG
ACTAGGGTGAAATGACAGTTCCAGAGGGCCGCACTCTCCTCAGTCTTCTGGAATTTCCCTCTAGAAATCTCCAGAATCTAAAA
AATACAATCCAAATATGTTTCCTATGGGTCATAACTGGGGAAGTTTAATTACTGAAAAATATACCAGGAGCCTTCTCCAAAAG
ATCCTACAGGGAAGAACTTTTCCAGAACCTCATACTATGTGAAGGGAAGAAAAATCTGCCCATTCCAGATCCCTCCCCACTTC
CTCCATTATTATACAAATGAGTAAGGTTAGCCAATAGGGTAAGATGTAAGCAAATAGTCCAGGGAAACTGAAGCCACAAAAAG
GAGTAAAGATGAAAATTCAGCTTTTCCCCTGGAGATGCCTGGTCAAGGTCACAGCCCAGAAAAGGAATCTGATTGAGTCTCTA
GGTTTCCATGGTCAGAACAAGCAGTGCTGACCCGCACTGCACAATCCTTTCTAACCAGGATGATGGCTCTGGATTAAATATGA
GAGTGTGCCAATGCACAGTCTCTGAGGAGAACATAGGGACACTAAAAAAGCAATGGCAGGGAGTTAGACAAGGACAGTAGAGC
AATATGAAGCCTCTGACGTGAACATTTTAAAAACAAGATCTTGGAAACTCCCTCATTCACCTCAGCTTCTTTTATCATGAAG
ACTTTCCAAGATTCTTAACTGAGACAAAGAAAATAACAACCTGCATGCACTTCCGAAGTCTCCGCTTGTATCCTGTTTGCTTT
AGATCTCTAGGAGAAAAATGTCAGACACCTGGGCCTAGTGTCAATGTGGGAGGCACTTTCTACAGATGAGGCGCAAGAAGGAA
GGGAAAACGTGTGTTATTGGAATAGTGGATATGAAGTGTGCTCTCATCTGAAAGCATCTGCACCTGCTGGAAATCTCAGATGC
AACATTCAACTGCAAGAACCAAGGCACACCCAAATCTCCTGTAAGATTTTGGATTCATTATCCACTGATTCAGTGCAACTGGA
GCTTCAGAGAAGGGGCTCCCTCCTGTGTCATAGCATCCTTGCTTTGAGTTCATTAGATTTAGTAAGGCTAATCAATTGTTTGA
AGAGATGGTGTCAGCAGCGTATGCTGTCACTGAAGGAGTATTCTAAACCAGGACAAAGCCATTTCATGTTAGGCGAGGGAAGC
TGGCGGAAAATGCTTTATGAGCCCCACAGGAACTTCCTTGCAAGGCAAGGGCTGGGCTGGAGGGGGCGCGCAGGAACCGCCCA
GCACAGGTTCCATCCCCGGAGGGGTGCACAGGAGGCTGGGGACGAGGTTCCCTCTCAGCGCCTGTGTCTTCCTTTGGCAACAA
AAAAAATCCTAAGTGTTCAAGAAGTTGCTGATGTGTCTTTAAGTATCCTGTTCCGTCAGAGCCTTTCCTATAACTGAAGGCAA
CCAGAACTGTGTTTTAAAGTCGGTTCCGAGGACTGCAAGTATCTTAATAGTGAGGATATAAAGGATAGGAATGGTTTTACTAA
TTGAAAGGATACAGAATTGTGGGGTTCCGAGGACTGCAAGTATCTTAATAGTGAGGATATAAAGGATAGGAATGGTTTCACTA
ATTGAAAGGATACAGAATTGTGGGAGTCACTATGTTCCTATGAATAAAAAATTCAGATTTCAGTGTTAAGTAATGTTGCCTAC
ATTGTGTGACTGACAGGGCAGTGGTGGATCTGAGAGTGTGGCAGGTGCACAGACCTAGTGAGTCAGAAATCAATATGGAAAGA
TGAGGATCTATGGATATGAACTGAAAGTAAGTAAACAGTTCATGAAATTCTATTAAATGGAGTAGGAAATAAAACCCAAACTT
ATCCAAAACACAAATTCCTTGGCGATTATTTTGGGAGCAGTGAGTTCATCAGGAACCCCAAACTTCTCTTACGTCTTCTGATT
CCTGTTGTCCATGAGATGAGAAATTCAGCTCTAATTGTGCATCACAGGGCAAATCTGTAAACCAGGAGTGTTTCTATTGAGGA
TCATGGTGGATCAGGATTCCAGGCAGGTGCTGGAGACACTGTCTCAGGAGCGCCAGATGATCTCAGGGGACCTGCTGGACA
CTCACGTGGAACATCAGCAGTCACTTTCTCAGAGTAACCAGTGAGCTGTGCTGGTGCCTGATGGGACTAGGATGGGGTCAAGG
CACCTTCTCAGTGTCATGGAGAGTGATTGTTCCAGAAATCATCCAGGTGGTCTCTACGCTAATCAAATATGGGTTCACAGGGA
GGAACATGTGCTCTGGGTGCTTGGTCTTCAGTGAAAGGACGTCTGGCCACCAAAAGTTTGTAAATGGAGCAGGGCATGCATTT
CCTCAAGGAGGATTAGGGCTTGGAGCATCAGCATCCCACTCTTGTAAGGCTGATGTGTCATTTACCTTCCCTTTCTTATCCCA
AATCAGGGTCTTCAGCTATGAAATGCTCTGACTCATGAATATGCAAATAACCTGAGATGCACTGAGGTAAATATGGATATTTG
TCAGCCCTGAGAGCATCATCCAGAAACCACATCCCTCCGCTAGAGAAGCCCCTGACGGCACAGTTCCTCACTATGGACTGGAT
TTGGAGGGTCCTCTTCTTGGTGGGAGCAGCGACAGGCAAGGAGATGCCAAGTCCCAGTGATGAGGAGGGGATTGAGTCCAGTC

FIG. 6 (Cont. 27)

AAGGTGGCTTTCATCCACTCCTGTGTTCTCTCCACAGGTGCCCACTCCCAAATGCAGCTGGTGCAGTCTGGGCCTGAGGTGAA
GAAGCCTGGGACCTCAGTGAAGGTCTCCTGCAAGGCTTCTGGATTCACCTTTACTAGCTCTGCTATGCAGTGGGTGCGACAGG
CTCGTGGACAACGCCTTGAGTGGATAGGATGGATCGTCGTTGGCAGTGGTAACACAAACTACGCACAGAAGTTCCAGGAAAGA
GTCACCATTACCAGGGACATGTCCACAAGCACAGCCTACATGGAGCTGAGCAGCCTGAGATCCGAGGACACGGCCGTGTATTA
CTGTGCGGCAGACACAGTGTGAAAACCCACATCCTGAGAGTGTCAGAAACGCCAGGAAGGAGGCAGCTGTACTGGCATGGAGG
GGATGACAAAGGTTATTAGATTGAAGATTTTCTTAGAAAACGACTTCAAGTCATTAAAGAAGAGGAACAACATAAATGTGTAT
TTGTGAAATTTTAATTGAGAGATTTTTCATACAACATTTATTCTGTAAGCTATTTCAGGGATTGGAATATGAATCAAATTAAT
AAAGCTGATATAGACATCCTCTGAAGGCATCTTCGTAAACATCAATTTCTGAATCAGTGTTGTAAATATTTTGGAACACAGAC
ACAAGATCACATTTTTACTCTACTTTTATCTCTATTTTTAAAAAATGCCAAAAAGAATCTTATTTTGTGCATGCCCCATTTTG
AATTCCCACCGTCAATGCATGATAGTTCTTGGTTTTCCTCATTCAAGTTGTCATTTGTCATTAAGAGTGTTGTGTGTTTTAAC
CATTCTAATAGGTGAGTAACGGTATCTAATTTTTATTTAAATGCACATGTCCCTAAAAAATTCATATTTAACAATTTTTATAT
AATTTTTGGTGAGATGCCTCTCGTGATATTTGGTTCATTTTTTAAATGCATTTTTTATCAGTTGTAAGTATGCTTGCATATTG
ATTATAAAAGTCATTTAACAAATTAAAATAATTCATTTAACAAATATGCATCTTGGAATTTTTTTCTCCAAGTCTGCAGTTGT
CTTTTACTCCCTTATCCCTGTGTATTGCAGAAAAATGTTTGTGTGTGTGTGTGCCTGTGTATGTACAAATTTAGATTTTAAAA
ATGTACATTTTTATTCATTTAAAGATCATGTCTTTGGCAGTATATCTGAAATCTCATTGTAAAAGACACAATAGTCATTATTT
TTTCCATGTCTCTAATCTTAGGACACAATCAACTCATGAGTGTTTAACCTTCCCTACCTGATTGGAGGACTATCCACCTGAGA
CATTTGGAATACTTCTGTAAGGAGATGTGTCCTTCCCATTATTTCTTTATTTAGTCATCTATTGATGTTCCTATTGGTTTATG
GATGTCTATTTCATACTCCGAAGAAGATCCTTGTTACATTACTTGTTTTATTGTTCAAAACACCACAGCTTTATTAGGTGCTG
GGAGCTCATTTAGTTTGGATCCTGCATCCTTACAGCACACCTCATCTTTTTGTTTTTAGACATTTCCCTGTTTCCAAGTATTA
CAATAAATTCTAAGCTTGTTCTCTACGTTACCTTTTTTGTACATAGAATCAGCCATTTTTCTAAAGACTGCTCGTTTTTCATG
TTAAAGAACAGTATTGAAATTTAAAAATGTGATCCTGGGTATGTGTGTTGTTAATGTGGTATCAGTACTTCTTCTAGGATATC
TCCACCAATTGGCCTAGTAAATGGGCATGTTTATAGGAACCCAAGTTTATGGACACATCGAAACTATTTATGTATCTAATCCT
CTGTAATGTGATTACATTAAAAATGAGAACACACTGGTGTCTCCATCCAACTATGCTACCATATGGATGTTTCCAGCCTTCCT
TCCCTCACTGTCCATAACCACCCACTGCAAAGTGAGGAACCCCATCCCACCATATGCCATTTTATTACTTAGCTGCACAATTT
CAGGACACATGCATAGCAGTATCAGAAATGTAAAGCTCGTTGGAAACATGTTTATCTACTAGAACAGACTGCTTATGTGCAGT
TTCTTTACACTGTAAACTTATAGAATTCTTCATTTTCAAAGTTGCTTAGGTCAGCAACTTCATTTTCCACTCTCCTCAGTGA
AGTCATTTCAATGACAATGTATAATGTCATTTATTTGAAATTCTTTCAAAGCCAAAACTATAGTCCGGTAAACATATAGAGGA
TATTCAAGGAATTTAGAGAGTGGGTATAAAATAAGTAAAAATGGCACTGTTTAAGAAGAGTAAAATTGTTTTTAGTGATATAC
AATGGTTGAGACACAACACAATTAATTTGGCTAAGCTCATACTTTTGTGACAGAAAATATAAACCTAAATATATACAATTTTT
GTAAAAAAACTTTAGCAGTTCATTAACCCCAGGGTTAAACAAGACTGTGTAAAATTATCTAATAACTTATTTGATGAGGGTGG
GGATATCATGAGACATATGCAACAAAGAATGAAGGCATTTTCCTCATTTGCATGTAAGATGTTACCATTCACTAAAGACCTTT
AATAAAAAAAAATTTCTACGTGATCCAGTATTTTTTCCTTCTGTCAAGCAAATAACTCATAGGATTCTTTTCTTTCCTTGGT
TGAGAAAGATTTTCCTACAAGCTTCAGCACACGTCAGGCATACACTGTCCCTGAATGGGCATTTACCCTCAGATGGGTACACA
CACCTGTCAACATGGGGGCTCTTCTGTCAGACAAACACACCTTTACTCATGTGGATTCTTCCCTCAGACAAACACACATGTCC
CCACGTGGACTCTTTCCTCAGATTACAACATTTGTCCTTACATTTACTATTTCCTCAGAAAACAGACATTGCATCATGTGGTC
TCTTGTCTCAGACAAGCAAACATGTCTTCAGTCAGATAAGTCTGTGGATTTCCACATTGACTGTTTCCTTACACAAGCACCTA
TATCCAATATTTAACTGTTTTGTGAGAAATTTATCCCTTTTCTCTGGAAATGTATTTTTATGTTCTTACTGGACATATTTTTT
AATAATGTTTGGTACTATGAAGATACCCGAACACTGTCCATACGAGAGAATAAGAAAGAGTAATAAGCAGATTAACCCTGTGC
ATCCAGACCCAGGAGTCCTTTGATCCTGCCCTTCCGAAATGGAGACACAGAGGAAGGATGAGCAATGCTGAGCAGTGCACCCA
TGACCACAAAAGGAAAGACATGGCAATGTGTCCCCTCCCCTCCTCATGAAAGGCAGCTCATCCCCTGTTCCTTCAGGCCCTGG
TGAGGAGCCACCCCATGTATATTCCCTTGATCAGTGTCCACACCATGGGGTCTGCACTGATCTGGGCTTCCCTTCTCATCACC
CTCAATATTAGTGTCCCTTGTGAATCAGGTCCAGCTGCGGCTGTTCCACATGGGGCCGTTCTTCCATTTCCTCAGTGTTTGCA
GAAGTCCTGTGTGAAGTTTATTGATGGAGTCAGAGGCAGAAAATTGTACAGCCCAGTGGTTCACTGAGACTCTCCTGCAAAGC
CTCTGATTTCACCTTTACTGGCTACAGCATGAGCTTGGTCCAGCAGGCTTCATGACAGGGATTGGTGTGGGTGGAAACAGTGA
GTGATCAAGTGGGAGTTCTCAGAGTTACTCTCCATGAGTACAAATAAATTAACAGTCCCAAGCGACACCTTTTCATGTGCAGT
CTACCTTACAATGACCAACCTGAAAGCCAAGGACAAGGCTGTGTATTACTGTGAGGGACACAGGAGAGGGAATATCTGTGTGA
GCCCAGACACAAAAATCTCTGCAGAGAGACAGGAGGGAACTGCATGGTAGATGCTCCTCATAACCACAAAGGGGCAGTCAGGA
CCATCAGGAGGAGCTCAGGACACCTGGGGGTGCTCAGAACCATGAGGGGTGCTCAGGACATCGGGGGCTCTCAGAACCATGAG
GGGTGCTCAGGACATCAGGGGGCTCTCAGAACCACCAGGGGGCGCTCAGGACACCTGGGGGCGCTCAGAAGCATCAGGGGTGC
TCAGGATATCAGAGTGCCCTCAGTACCACGAGGGGGCGCTCATGACACCAGGGGCACTCAGAACCACCAGGGGGGGCTCAGTA
CACGGGGGTTCTCTTAGGAAGCAGCTCCACATCAGGAGCCTGAGAGGCTGTGATTGCGTTTAAACCTGGGTGATTCCCGACC
TGGTCAAGAAAAAGTCTCCCCCAGGATCTCTCACCATTTCTTCTTGGTAATTCCATGATTTTTTTTACCTACAAAACATTAA
GTTAGAACAGGGATTTAATTCAACTTTTAATTCTGCAGATTTTCCGAGTAATAGTAGCAATGTTCCCTCAGGACAATTTTTAA
AATTGGCTATTTATATATTTTATTTATGTAAAATGATACTATCTTGAAAATAGTAAAATTTTTAAAATCATACCTCTAATCCC
AGCACTTTAGGAGGTTCGGGCAGGCAGATCAGTTGCGCTCAGGAGTTTTAGAACAGCCTGGCAACACATTTAGATCTTTTCCA
TACAAAAAGAAAAAGAAAAAGAAAATAGCTAGGTGTGGTGCTACCTCTGGTACCAGCTATTTGAAAGTCTGAGGTGGGAGGAT
CCCTTAAGCCTGGGAGGTTGATGCTGCAGTGAGCTGTGATTGTGCCACTACACTCCGGCCTGGTTGACAGAGTGAGACCCTTT
CTTAAAAATACAAACTGTTTCAATAAGTAGAGCTTTGTGTCTTTGTGCTGTAATAATCAGTTGTATATATTTTCTAACTGTAA
CTCAGCATATGCATGGTGTTCTGTTTCTTTTTCTTTCATTTGCTGTTGGTGGAAATTAAACACCTCTTTAAACGCTCTTGTTC
TCCCCTTTGGTTCGCTTCGGGTGTCCTGTTTAACAGACTATTTCTTCATCTTCCCTTTTTCTTTGAAAGTCTTTTTCTTTCTC
AGTTTCCATGCAGGATAAAGAAAGTCCCTTTACTTTCTGTCCTCCAAGTCTGGTGAACAGCTCCCTTCTCTTCATAACCACTG
AAGCCAACCAAGTTTAGGAGGATAACAGCTCTCCTTAGAATATGCTCGTCTACCTGGAGACTCTCTGCCCTCCTCACCCTTTT
CTAGGGTCCTGCACACATCACACTCATCCCATCCCCTCCCTTCCCTAAGTACCACAGAGTGGGCTCTGCAGTTCCTGCTTCCC
TGTGTGTGCTCAGCCCTGGGGCTCACTAGTGCTTTGATGATGACGTTCAAATCCCCATGTGCTTAGACTCTCTAAGACCACCC
TCTAGGAAGATGCCATTGTGAGTGAGTCCTGGAAATCATGGGCTGTGTTCAGTTTCATATTGCTGGATCTTCTCTATTTTAAA
GGAATACTGGCAATTAAGATTAGAGTTTGTATTGAATATTCATGCCAAAAAAGTTTTCTTTCAAAACTTTTCAAATAAAACAA

FIG. 6 (Cont. 28)

TTTTTCCTGCCTAGTTTGAAAACTACAATGTAAATTCAACAAATAATATAATACAATTTTAAAGGTGACGTTTGTCTTATTGG
TTATTCAATTTATTAAAAACAGAAGATATTTAAAATAAATTCCATTGCACATTTAAGTGATGTATTTGACAAGAATGGCATTT
ACATACATTTTTACCAAAACACGTATTTAAATATATTTGTCTTTTTAATATTGGTAGAGGCAGACATACACGTAGAAAAGCAT
CATTTTGTACTACAATCTCAAACTGTAAACACAATTTAAATTCAGTTAAATAATTAGAATAATATGAAACAGGCCGGGCGTGG
TGGCTCATGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGCGGATCACGAGGTCAGGAGATCAAGACCATTCTGGCTAA
AACGGTGAAACCCCGTCTCTACTAAAAATACAAAAAATTAGCCGGGCGCAGTGGCGGGCGCCTGTAGTCCCAGCTACTTGGGA
GGCTGAGGCAGGAGAATGGCGTGAACCCGGGAGGCGGAGCTTGCAGTGAGCCGAGATCCCGCCACTGCACTCCAGCCTGGGCG
ACAGAGCGAGACTCCGTCTCAAAAAAAAAAAAAAAAAAAAAAAATGAAACAAATAGGTGCGTTGTTTTGGTGTTTAGATATACA
TTCACTTTTGCATGGGCACATGTATGTGTCTTTGCTGGGCTGTTGTGTATGTATGTGTGCTTGTATGACCATCAAGTTTTCAA
ATACATCATTAAATTTCATAGTTACATTCGTCTTGGCCAGGCACGGAGGCTCAGGCCTGTAATCCCAGCATTTTGGGAGGCTT
AGGCAAGCAGATGACTTGGAGTTAAGAGTTCAAGACCAGCCTTGTCAACATGCCAAAACCCCATCTCTACGAAAAATACAAAA
ATTAGCCAGGTGTTGTGGCACGTGCCTTTAGTCCCAGTGCGACAGGGAAATGCTGGGTCAGAAATCCCACACAAAGTCTCTAC
TTGGTTACCACCTAATGGAACTGTAGGAAGAAAGCCACCATCCTTCAGAACCCAGAATGGTAGATCCACTGACAGCTTGCACA
GTGTGCCTGGAAGAGCCAGAAACACTCAGTGACAGCCCATGAGTGTAGCCAGAAGGGAGATTGTGCCCTGCAAAGCCACAAGG
GCAGAACTGTCCAAGACCATGGGAACCCACCAGTTGCATCCGGTAACCTGGATTTGAGACATGGAGTCAAAGAAGACTATTTT
GGAACGTTAAGATTTGACTGCCCAGCTGGATTTCAGACTTGCACGTGGCCTGCAGTTTGGACCAATTTCTCCCATTTGCAATG
GCTGTATTTACACAATGCCTGAACCCCCATTGTACCTAGGAAGTAACTTGCTTGTTTTTTATTTTACAGGCTCATAGATGGAA
GGGAGTTGCCTTGTCTCAGAAAAGACCATGGGCTGTGGACTTTTGAGTTGGGGCTCAAATGAGTTAAGACTTCAGGGGCCTGT
TGGAAAGTCATGAATGGTTTTGAAACGTAAGGACATTAGATTTAAGAGGCGCCAGTGTTGGAATCATATGGTTTGGCTGTGTC
CCTGCACAAATCTCATCTTGAATTGTATCTCCCACAATTCCCACGTGTCGTGGGAGAAACCCAGTGGGAGGTGATTAAATCAT
GGAGGGAGTTCTTCTTTGTGCGTTATTGTGATAGTGGATGACTCTCATGAGATCTGATGGTTTTAAAAAACGGGAGTTCCCTG
CCCTCTCTTTGTCTGCTGCCATCTCCATGTAAGATAAAACTTGCTCCTCCTTGCCTTCCACCATGATGTGGAGGCCTCCCAAG
CCATGTGTAACTGTAAGTCCATTAAACTTTTTCCTCTATAAATTACTCAGTCTCATGTATGTCTTTATTAGCAGTGTGAAAAC
AGACTAATACAGCAAATATCAATCTCTTAAAATATTTTGTTGTTCTGCATGTAATATAGCACAGTCTAATATGGGAGGTAAAA
TAAATCATCCATGGACCTTCAGATATAAGTCATAGGGTAATTATGCCTGTGTCCCTGAAGGAGTGAACTAGAGGTTATACACA
CTAGTGGCACTACCTTTGGCAAAGGGTGTTCAGGGGTTTCTGAAAGTTCTGATAATTTTAAATTTGAATTTACTATG
TATTTCTTCATCAACCTTTCCAGAAGATTTTTGGCAGTAAGAACAGCCTAGTATTGGAGTAATACTGATGAATTAGAGAGTTA
TTTTGTAATTATTCTCCTGAGATTTGCATGAATCAATTGATATAGAAGTTCGTATGTCCCAAGTTGAAACATCAGAATCAAGA
AGGCTTCATCACCCTTAATGGCTGTGGTTTTTGGCAAGGCAGTACTTCAATTCAGCCAGAAAGAGAGACAACAATAAAACTTT
CAAATGCAGGGGAGTCTGACCTCAGTCTCTCTCTCTTATAAAGGCAAAGGCAAAGCTGTGCCACATCAAGATTTTTCTTCAAG
CCTTCAGAGTCAACATTGGGAATGGAAAAGCCAATCACTTTGTCCTTAGAGAAGGCGAAGATCTGAGAGGAATGCAGAGTTGT
GTTCATGAAGGTGATGACATTGTTATTTCTTCTCCTTTGCCCAGTGACTGCTTTCAAGTTGAGTGTTTCAGATGTCAGACCTG
ACTTATAGGGATGGTTGTGACTGCACGTGTCTGACAGGGGCTGAGACTCTATATCTCTAAGTGTCCTGTCCTAGGAGCAGCTA
CAGGAGTCAGCCCTAGACTGGAAGTGCCCTCACTGACCCTCTGCCTCACCTGTGCAGCCTCTGGCCAGTTGAAGAAAGTTTTA
TCCCTGGAACATCTTTTGTCAAAACCACTCCAACTAGTATTCATGACCTATGGTCCACACCCTCAAGTACACAGACATGATCA
TGCTATGACTTGGTGTCTAGAAGATCCCTGCACTTTTAATTTTACCTCTAATATTAGACTCCACTTTATCACATGCGGACACA
GCAGAATATTTTAAGACTTTCATATGTTATGCTGAAAAATTCAATAGTTCATAAAAGTCTACTTCCCATCACTGCCAGTGTTT
ACTACTGAGTAAGGATCTGCCATCCCCTAGGGAGGAACTATAATGGATGGTGTGCCCTGTTAGTGGTTATGGGAATGAATCCA
TCTTGTGGCAAATGGCAGCATCTTCTTGTTTTGCAAGATTAAATAGTTTTCTATGGTGTATAAAATACAACATTGTCTTTATCC
ATTTGTCTATCTACTGACACTCAGATTGTTTCCATATATTGGCTAAGATTAATAGTGTTTCAATAAACATAGGATTCAACTAT
CTTAACAAGGTGGTAATTTCATCTGCTTTGGGTATATTTCTAAAAGCAGAATTTCTGGTCATATAACATTTCCAGTTTTAATT
CATTTGGTGCCTTTATATTGCTTTCCATAATTGTGAAAATATAGAGTGGTATAGCCATTATGAAAAACAGTTTCAGTTTTGAG
GTATGATCCATAAACAAATAATGTTTGATTATGGCTCTCCATGAGAATTTCTAATAAATATGATAGAAGTCAAGAAAGCGTCT
CACATTAAAGCAAGGATTAATTTTATCCCTTACTCCCTCAAAAGCAAAAGATTGGAAGCATGCATGATGGAGGCTGTTAGCAG
GGTTCAGAATGATATCATAAAAGGAAACTCAGTTGGATAAAAATGTTGGGCTTTCAGTCATAGGTATGTCGATACTCAATATG
AAACCGCGAAGTCAAATGAGGATCTAGAATGTGTTCACTTGAACCAACAGCACATTCTCAGACGCACCTATTGCTGCATCACA
AGGGTGATGAACTTTTGAAACAAGTAAAGTGTGAGTGCACAGTAAGTGATAAAGTTATCACCTTTACATGAAGTTTGTTCAAT
ATGCCAAAGGCTTGTACAGATTAATCATACACAAATATACACAATGTATTTTTGCATACACAGATGTCTAGAGGATGATTCTT
TTAGGGAAAATTCTTCAGGTCACAGAAATCTGTGTAAGTTGGAGGTCCCATGAAAAAGTATCTCTTTATAAATACTGGTCTAT
TGCTCAATTAGGGAAAATGATCTCTGTTGGAGAAAGCTTCCAATTTGGGAGATTTCTTCATTGCTTCTTGAGTTGTAAGACAT
GAACCAAAAAATTGACTGGAGTTTTTTGGAGTTTCATGGCTGGAGTTTCATGGCTGTGTTGTTAAAAATTTCTTATACGGTTT
CTTTCAATTATTTGAGATCAGTTTTTCTGATTTTTTTCTCCAGTAGATAAATTTTCACAAGATCTCAGGAAACCATGTCTCTG
GTGCTTTAGTTTGAAAAACTAACTTCCTAGGTAAAGAAGCTTCTGTCTAACCATGATGAGCTCATTTCTTCTGCATACCATGA
AGTTTGAGACCCCATTGTCCAGAATCATGAAAATTTTACACTCCAGTTTACTGAAAATCTTGACTTTGAATTTAATATTGATT
GGCATTGACAAAAATGGTTCATTCTTGGATGTGTCCTAAGTTGCTCACCCAACATATCAGTGGACTGAGAATCTTCCATTAGC
TCCCTCTGTCCATAGCACTGAGTCTATTGACAATCTTTGCAGTCCTCTATGAAGGAGAGTCCTGAGGTTCATCAGATTCTTGT
AGACACTCAGATGAACCAAAGGAATTAACGGAATTGAGGACTGCCAGCCATTTCCACAACACTAGGAATAATTACCATCTAAG
TGTAAAGGTCTACATCATTCAGAATACCCTGCATGACAGGCTGATGCAAAAAAAAATCCAACCCTGCAGAGGCTTCACAGCAA
CCCTCACAGTTCCTTCAGGGAAGAAATAATCTCCAAGTTCAGTGAGTCAGTAAAGCTGTTCTGAGCTACAGTAAACATTGGAT
TGGGCCCAGTTTTGTCTGAGTTCAATGTGATTGTTATACTCAGCTGCTGATCCTATATGGACTGAGTATGGATAATTTAAATG
AGCCTGGCTGCGTGGTTTGTTATATGAAAACCTGAACTAAATATAAATAAAGGGCATGTCTGGACTAGCATGAGGGTGAGAGA
TTCTGGGAGCTCCACCCCCCTTACTCTTATTGCCCTTTCCTCCAGGAACCTCCAGGTCCTCAGGGTGAGAATCCACACAGATC
CCTTCATGGCTCTATTGCCAGGAGACCAAATCTCTGATAAAATCACTCAGACCTTCTTCAGACAGACAACCCAGGGAAAGGGC
ATTTTTACACCCTTATGTATGTGGGGAAAGGTAATCCATACCCATTAGAAGCCCCTGCCAGCAGCCTAACTTTATCATGAAAA
TGGGTAAAATTAGCCAATAGGGGTACATTTAAGAAAATTTTCCTGTGATGTTCCATCCAGAAAAGAGCAAAAATCAGCTTCAC
ACCTGGAGACTTCCTGTATCGGGCACAGCTCAGAGAAAGAAGATCACCACAGAATTAAAATGCAACTGTAAGAACATGTAATG

FIG. 6 (Cont. 29)

CTTCCGTGTTCCACACATTATGTCTCACCAGTTTAGTCAATATGGATTAAATATGAGAGCGTGGCAATGCACAAACTCTATCT
GAGGAGGAAAGTCAGAGAAAAAATGTTAAAGAAAATATGGCAATTTGAAGCCTCTGACACCAGCAACTTCAGCACCAAGGAAA
TGATTTCACCCTCATTGGCCTCAAATTTACTTTTCATGGAGCATTTTCAGGGTTCCAAAGTGAGACCAGGTGAATTCAATGTG
CATGCACTTCTCAGGTGTCCACGTGTATTTTGTTTATTTTATTTCTATTTGCAGAAAGTAAACACATATTCAGCCTTAGTGTC
AGTGTAGGGAGTGCTTTCCATGACATGAATACCAGAAAAAAAGGAAAAACATGGGGCCAATTAATGTAAAAATTAGCCACTGT
GTGTGTGTGTGTGTGTGTGTGTAGGTGTGATTTGAATACTAGAGTTGGAGTGGGCTTCTATCCACATGCACCTGCACCTGCAG
GTAGTCTCAGGTGCAATAATCAACTGCCTGACCCTAAAGGAAACAAGAATCTCCCCAAACCCCTGAAGAGTGTTTGGGTTTAC
CGTGTGTCCAGTGATTCAGTGCCTCTAGAGCTCCAGGAAGGGGCTCCCCCGGTGATGCCTGAGATCTTTTCTTCAGGTCTCCC
CTGCAGAGTTCCTCTGGGTTTCCTAAGGGCAATTCACTATTTCAAAAGATGGTGTGAGAAGCACATGCTGTCACTAAAGGAGA
ATTCTGAGCCACGGCACAGCCACTTTATACTGGGCTAGAGACACTGGTATGAATATACTCTGTAAGTTTAGACAGAAAGCCTC
GTGCATGGTAGGGGCTGGGCTGCAGGGGGTGCTCAGGATAAACGCAGCACAGTCTCCCGCCCCAGAGCAGGTGCACAGGAGGC
TGGGGAGGGGTTCCTCTCAGGGCCTGGGACTTCCTTTGAAAATATCTAAAATAAGTATTTCACAAGGGCTGCTGTTGTTTGTA
TAAATATCCTATTCAATTGTGAGCATTTATCAAACTGGATGTTGTAATGACAACCACTTTTACAATGGGGATTTCAAACTCCC
CTAGATATCTTAATAGTAAGCAGCTGGAGGTCAAGAAGAGATCCTTTCTTTTAAATAAGTGCAATTTTTGGAGAAACATACTC
ATTCCCAAAATAACGCATTCACATATTAAGGTCTAGAAATGGCTCAAGTTGTCCCTGGTGCATTCGAATGTGGGTTCAAAGTG
AGGTGCGTGTCCTGAGGGAGCTTGTTCTCCAGTGGAGGAAGCTCTGTCAACACAGAGTTCAGGGATGTGTAGGGGTCGTATCG
CCTCTAACAGGATTACGGCTTGAACCCTCAGCATGTACAATTGTGTCGTCCATCTGTCATGTATTTGCTCTATCTCATCCTGG
CTCAGGAATTGGGCTATTCAATAGCATCCTTCGTGAATATGCAAATCACTAAGGTTAATACAGATATCTCTGTGCCGTGAGAG
CATCACCCAACAACCACACCCCTCCTTGGGAGAATCCCCTAGATCACAGCTCCTCACCATGGACTGGACCTGGAGCATCCTCT
TCTTGGTGGCAGCAGCAACAGGTAAGGGACTCCCCAGTCCCAGGGCTGAGGGAGAAACCAGGCCAGTCATGTGAGACTTCACC
CACTGCTGTCTCCTCTCCACAGGTGCCCACTCCCGAGTGCAGCTGGTGCAGTCTGGGCCTGAGGTGAAGCAGCCTGGGGCCTC
GGCGAAGGTCTCCTGCAAGGTGTCTGGTTAAACTGTCATCACCTATGGTATGAATTGGATACGACAGACCCCAGGACAGGGGC
TTGAGTGGATGGGATGGATCATCCTACCCTGGTGAACCCAATGTATGCCCACAGATTCACACACGGTTTGTCTTCTCCATGGA
CACCTCTGTCAGCACGGCGGATCTGCAGACTAGCTGCCTAAAGACTGAGGATGCAGCCATTTATTACTGTGTGAGGTACACCG
TGTGGAAACCCACATCCCGAGAGTTTTAGAAACCCTGAGGAAGGAGGCAGCTGTGATGAGCTGAGGCAGTGGTGCAGCATGTC
TCTAAACTTCCATTTTATCTAAGTTTGCATTGAGTTCCGCTTTAATATTAGCCAGGAATGTGGGATAGACGGGTGCTCCTAAG
AGGTCCTTAATTTGCCCATTTTGATGGGTTTTCCAGAAGACGTGAGAAGCCACTTTGTTAACAAAGCATCCCAAAGCCATGCC
CTGCTCCAGAAACACGTGTACCCATTCCTGGTCTTTGGTTAACTGACAAGCTCTCATCAGCGCACCTGGGCTAATTTCTCAT
CAGGTAGAAAAATGTGTTGTAAAGCAAGGCTAACGTTGTGATAGCAATTCCTGCTCAATAACCTTCAGCATCGTTGTTGTGT
GTTCTATCAACTAATTACGTGACTTCAAGGTTCTCATTGGGAGTGTCTTATAAATTTAAGGGATATATAGAAGTTCCCCTAAT
TAAAATAAAACAATTGTGAGCACAACCTCAGTGTTCAACCATGTCTCCACCCTTCCCACCATTCACCCCAAAGAAATGTTCAC
CTCTCCTGGAAGTCGGGTTCATTTTCAAATTAGTTATTTTTTATTTTACTATATCAAGATTATTGTATGTGACTACTGTAGCA
GAAAGTGAATTATGGGAACTTGAAGTAACCAACGAAAGATAAATTCAGAACTAATTAAACAAGATGTCAGAACGTGATTGGCT
CTAGTCTTTTAAAATTCAGCAGGTTATGTAACCAGGCTTTAAATTTACACATCTTCCTGTTACCTTCACGGCACAGTCAACTC
CCATTATGTAAGAAATGGCAACTGCATTCCCAAGCGTCATCCAAAATTGTAAAAATAGACTGGGTGAGGTGAGGAGTTGATTG
TTTAAATTCCGCTCTGAAGAAGCAGCATCAACTCAACAAACCACCGCTTTTCCCTCAGTGACTAGAGCTATGTCGCAGGCCAC
ATGGACCTAAATATCCTTGATAGAGATAATAGGACTACATAAATTGGGCTGATCATTTTTATGCTGTAAAATTAATAGGTGAG
TCTGCACTCCAGCCTGGGCAACAAAACAAGTCTTGCCTGTAAATACAAAAGAAAGATAAATTAATAGGTACTGACTTTGACAT
TTCGGATAATAATATTTTCATAAACCGAATTTAATTATACCCACATTGTTACCTACACCTTCACTGAAAAGTTCCTAGTTATC
ATGAGTTCCATCAACACTCCACGTGTTCAAATCTGGACATCCAAGAGAGTCTGGAGAATAAAATGCAATGAGGGCAGTGAAAC
TTGCATATATTCAGCACCTCTTAACTCAGGAGGACTCAATACACCCTGGAACACTCTGCTTTTCTGAATGGCTCACAATGACT
CCAGCTCACTCTCCAACCTCCTCAAACATCTGGCTTCTGTTTGCCCTAAGTTCACGCTCTGCTCTTAGTCTGTGCTCTGAAGT
CTTTGCAAAGGTGAAAATGAGCTGTCAGATGGAACTTCCTTCTCACCTCAGCATGGAATTTACTGTTTCATTTAATGACCACT
CTTTCCATAATGGTTGATTTCTTTCAGCCTGTTCATTACTGGTGATTTTCAAGGGAATCTCTATTGAATTTTTACATTTTTGC
ATTTTTGTCTCGGTGACAATGTTGAGAAGTTTTTACCTCTAGCATCATAACATGATCTAGTGACCTGACACATTTGTGGCAAG
CAATACCTACAAATTCAGAAGTTCTTTGGTTACTTTCCACAAAATATAATTATTTCTGGTCTGTGTATGAGCATATCCTAGCA
ACCTTGTACTCCACACAGGTAGATGTCTACAAGCCTATGAATTAATCTCTGTAAATAAAAATTTATCTCAATTTCTTTCAATG
TTCATAATTCTTCTGAGGATGAGGAAGATCTTTCTGGATCTATTCAGACAATAGGCCCAGAGACCACCTGGTATGTAAGGAGC
TCACCTGGCTCACCTGGTTCCCCCTGTTGTCTCACATAAGGTCAAGCCCACTTGTTCAGGTCCTAAGAAGAGAGCTCAGTTTT
ATCTGATTTTACAACACTCCCAATTTCTGCTGACTCTCCTGTTACCCACATCCATGGAGATACATTATTTATTATACAATTAA
CCAAAGTAATGTCAAAGGCCCAATGTGCAATATTGCACATCCTAGGGTATGTTCATGCAATTGAATCGAGGAGAAAGTCTTTC
AGAGACAGATGGATCTGAACTGGTAAATATGTGTGTAAGGACTCTGGGCTTAAGTGTCATTGTCCAGCCATGTTTCACAGGTG
TGACCTGTCAGGGAAGAACCAGAGTTCCTTGTGTTCTCAGAGGGGAGGGGTCCCAGAAGTCCTCTCTGGTTCCCAGGAAAGGT
AATTGCATTAATCTTGGTGATGAGACTATCATCCAGTGATGATGTACTATAGAGTTTATGTTTGAAGTTGACACTCTATCGCA
ATCTACATCTTTTCACACAGAAGTGTTTAGAGGTCAGGCCACATCTTCAGGATCCCACATTGAGAAGGACAGAGATATATTCC
ACTACCTTCTCCTGAGATCTCAGGCAGAAACCCAAATTTCAAAAGGTCTCAGAAGGGCAGCTCTCAGGGGCTATTTAAAAATA
ACCCACTTCGTGGGACAGGGAGCATCCTTCTAACCATGATGGATGTTCTGAACTACAATAAACATTGCATGGAACCAGGGTCT
GAATTCACTGTGATTATTACACTCCACTGCTGTTTCAATGTGTCTGAAGGGGTAAATGACAATTTAGATGACCTGGGTGTGTG
GTTTGTTTTACATAAATCTTCAAGGATAGAACAGCATTGAACCTATTCCAAAATCTGTCCCTGATCCAAGATCACACTGATCT
CCCAGAGCAGCATCTTCAGCACATTTCCCTACCTGGAAGAAGAGGACTATGGGCTTGGTAAGGGGAGGCCACAGGAAGAGAAC
TGAGTTCTCAGAGGGCACAGCCAGCTTCCTACTCCCAGGGCAAGCCCAAAAGACTGGGGCCTCCCTCCTCCCTTTTCACCTGT
CCATACAAAGTCACCGCCCACATGCAAATCCTCACTTAGGCACCTACAGGAAACCAGCACACATTTCCTTAAATTTGGGATCC
AGCTCACATGGGAAATACTTTCTGAGACTCATGGGCCTCCTGCACAAGAACATGAAACACCTGTGGTTCTTCCTCCTGCTGGT
GGCAGCTCCCAGATGTGAGTGCCTCAGGGATCCAGACCTGAAGATATGAGATGCTGCCTCTCATCCCAGGGCTCACCGTGGTT
CTCTCTGTTCACAGGGGTCCTGTCCCAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCC
TCATCTGCGCTGTCTCTGGTGACTCCATCAGCAGTGGTAACTGGTGAATCTGGGTCCGCCAGCCCCCAGGGAAGGGGCTGGAG

FIG. 6 (Cont. 30)

TGGATTGGGGAAATCCATCATAGTGGGAGCACCTACTACAACCCGTCCCTCAAGAGTCGAATCACCATGTCCGTAGACACGTC
CAAGAACCAGTTCTACCTGAAGCTGAGCTCTGTGACCGCCGCGGACACGGCCGTGTATTACTGTGCGAGATACACAGTGAGGG
GAGGTGAGTGTGAGCCCAGACACAAACCTCCCTACAGATAGGCAGAGGGGGCGGGCACAGGTGCTGCTCAGGACCAACAGGGG
GCGCGCGAGGCCACAGAGCCCGAGGCCGGGTCAGGAGCAGGTGCAGGGAGGGCGGGGCTTCCTCATCAGCTCAGTGATCTCCC
TCCTCGCCAGCACTCAGATGTCCCCAGGGCTCCTGTTTCTTTATTGTCTGTGGTTCTGCTTCCTCACATCCTTGTGGCAGACA
AGAAAGGAGGAAGACAATTTTTCTGTTTACTGTTGAGGTTTCACCAATTACTAGGAACTTTCCTACAAGTTCCTGCGTGACTC
ATTTTACCGTATATGTGTGTGTGTATAAATATATACACATACACACACACCATATATATACACCATATATATTATATAGAT
ACACACCATATATATTATATATATACACACCATATATATTATATATATACACACCATATATATTATATATATACACACGATAT
ATATAATATATATATACACACCATATGTATATTATATATAAACACACCGTATATATATATGGTTTCTCACCATCTCTTGATTT
GTGTCATCAATGGAATTGTGCCCTATTTGAAATTCATTTACCCAAACCTTAAATCCAATGGATCTATACCGGAATTTTAATGA
TGCAATTAAGGTTAAATGTGGTCAAAGTGTGAGACCCTAATTCAATAAACCAGTTGTCTTTATAAGAAGAGGAAGAGACACCC
GAGACCTCTCACTTTTCGCGTGCACACAGAGAAGAAGCCGTGAGGAGACGTAGTGCACTAGAAGGTGGCCCTGTGCAAGCCAG
GAAGAAGCCGCGCTAAGAACCAATTTTTACAGCTCCTTGATCTTCCACATTCAGACTGCAGAATTGTAAGAAAATCAATATTT
GTTGTTTAACCCACCCACTCCTGTTGTCTTCTTATGAAGATCCAAACAGACTGATACCACGTAATTCTGTTAGCTCTGGTTCG
TGGAGGGAGGAGCAGCCCCCTGAGGCTGGACACTTCTCTCAGATTTCCACGTGAAGTAGGTAAAAATAGTAGCTCTCATATAA
AAATGTGTCATGACCCTGTTGGCCATTTTTGAGCAAGGTCTCTGAAACCAGCCCTTGTGTGTGTGTCACAAATGTTTTCTTTT
ATCTTTTATTTGGACATAACACATAGACAAGGCGTACCAGCTGGATGGAGACTGGTCACTGCCCATCTTCTGTTGTCTCCTTA
GGATGTCACAGAAAACCACACCAACATCACCAACGTCACTGTTTTTCTTCAACCACCTCAAACCGACTATAGAAATGATCCCT
GCAGTATAAGTCTATTTCTTCAAACTTTCTAAATTTGCACTGGAATCTCTTCCTAAATGGGGAGCTACATGGGGTCTGAGTTT
TGTTCCTTTCTTCCCAGTCTTCCCCAAGTGCCAAGGACAGAATAGACTTAAAATAAAATTTGGCCGTCAGTGGCCCCAACCCC
ACATCACTTTCTAAAACCCACATCCTGCATCCATCCTTCTCTGGACACCCCTCATCGGGCTACCTACGAATGGCCAGAAGCTG
CCATCACCTTCTGGGCTGAGGCCACGAGTTATACACACGTGTGATTTCAGTCACACACACTCTACTGCAGGACACACCTGTGT
TCTTGAGGCACTCAGGCACCCTGCTGATCTCAGTCATTCTCTAATAAATTACACATCTCTTATTAATAAAGGTCCAGATGGTC
CCATCAGCTGCAGAGCAGTGGAGTAAAGCTCATGGGTGGGTCCGTCAGGTAGAAGTCAGACAATGGATGGGATGGCTGGTCAC
TTCCCTTTTCACTGATGTCCCCAGTGAATATTAATGGAATAAAACCATATTAACTACAGAGGGACAGAAAAGAAGACTAGCTC
ATCAAGGTATTTAAGGACCAGGAACTTTATTTGGGGGGAAAGTGAAGACACTTTTAAATGGAAAGCCCTAAAGCACATACAAC
AGCTGACAGAGTGGCCACTGTGCACATGAAGGCTGAGGAGACGGATGGCAGCGTCCGTTCCTCCAAGATGTCCCTGGGTGTGT
GATGGTTGGACTCCTTATGCATATGAATATAAGAGCTGGACTCAGGGAGAAAAAAGGGCCATATCTCATAGGAAAGGAAGCCC
AAAAAAGCAGATGGGCATCCCTGGAGAGAGCTCATTAGATTTGGTGTGTTTAAGACAAAAATTTCTTCCAAAAATTGTAATGT
TCTAAGCTAAATATGAACCTCTTCAATAAACTGAGAATTAACAGGAGAATAGAGCTATGAGTTGAGAGAAGAAACAAATCATG
AGAGAGCAGAAAGCAAATCCACAAAAAACTGTCATATGACAGAAGTCAGAATGGAGCTGGGGCAGCTACTTCATTATTCTGAA
GACTTGTTGACCATGTGGAGAAGGGGCTTGAACAAATGGGGACGTTCTCCAACCTTCTGAATCAGCCTCCTTCTTATGCATGA
GTAAAAATCATAGTTCTGGGTGTGACCTTCCCAAATTTCCTGTCTGTACCTCTTCCCCCAGGGGTAGAGTGTCTTCCCACCAC
AATGGTTTCTCACCAGTGTCCTCAGCTTCTCCTCCATTGAACTTACCCTGCAGATTAAGAATTTCTTCTAGATGTAGTTCTTT
GGGAATTTTCTGTTTTCTTTAGTTTCTGTTGACTCCACCACACCCCATAGGTCACAGGTTTGATTGATTTCCCCTGGAGACAG
TGGAGGTGGATCCAGGCGTTCAACAGTCCTCGCTGTTCCTCCCTTCCTGTCAGCACCACAGGACAGCAGATAAGGGAGTTGAC
TGTAGATTTTTCGAATTCTTGGGAAAATCCTGCAAGGACTAGTAGATTCACACTCCAATACCATTAGCACATGCATCCAAAAA
AAATACTCACGAAATATTTCCAGGTTAGCCTGTTCCTCTCTCAATGCCATCCAGTGGCACCTGCCCTGGGTTCACCAACATGT
GGGCCCCACTCCTCTCTGCTGGCATCTCTCTCCTCACATTTCAGTCTTCTCGTTAGCTCTGTGAAAGCAACTCAGATATGTTA
AAAGGTTTTCTTCTTCATTTATTCAGTTTTTCAGGTTTGTTGTTAATGAGGTCAGAATAAGACCATAGTTTTCTCATTTTTCA
CATTCCCACACTGAGTAGCCACTTTCTATATAAAAGCCAGAAACTAAGGGAACAAATCAAATATCCATATCCACTACAGGTGA
ACGTTAAACAATTTGACATATGATTATGAACTAAAGTACAATGCAGAATTAGAATCAAGGCATCCTCATTCTCATAAAAGCAT
GTCTACATTCTCAAATAACTCTGCTGAGTGAAAGTAGCTGAAGAATTAAGAGTGCAATTCATAAACTTCTAATTGTATAAACT
GCAAAAGGTCCAACTATTCTAAAGTAACAGAGCAGATTTGAAATTTGTGAGAAACGGGTGTTGAAAGTAATTGGCTGGTGAGA
TGAAATTACAGAGAAGTGACAGAAAGATTTAGGGGTTAACTTAATTGTACACAACCTGATTAAAGTTTGCACACATACGTTAC
CATTTTCCAAATTGTGCAGTGTAGATTTGAATTAATTATTAATTGTACTTAAAAAAAGCAGTAACAAATAAACACATGAATAT
GTTTACTGAGGAGGAACAAAAAATAGATGGGTATGAACACTGGAAACATCTCAGACTCTTGAAAGTACACAGGCTTGAACACT
GGTTCTCTCCGTATACTTCCGGTAAACGGCTGAATACACTAAAAGAAAACAGAGATGTCCTGGCAGGGGTGGAATCCTGCAGA
CCTCACTAGGTGTGTCCCACACTGCCCTGGAGTTGTCTCAGGGGAGCAGTCTCCTCTAGTGGTCAGAGGCACAGGCTGAGATA
ATGGGGTTAACTCTGTCCAGCTGTGTGACTTTGAATGCATTGTATAAACACTCTGTTCTGTATGTAATTTATCTTCCTTAAAA
TGCAACATTGACACTTACATTAAATGTATTCTACAAATATGTCAAAAAGAAGATGATGACTGCTAAATGATTATCAAGGCACA
ATCACATAATATAATGATATTTTCCTGAGTGATAAGATGACTACCAATCTCGGGGGCACTTTGTCTGCTCTGAGCCCTGCCCC
TCCTCAGGATTCCCATCCCAGAGCTTGCTATACAGTAGGAGACATGCAAATAGGTTTCTCCCTCTGCTGATGACCAGTCCTGA
CCCCATAGCTCTGGGAGAGAAGCGCCAGCCCTGGGATTCCCAGGGGTTTCCATTTGGTGATCAGGACTAAAGACAGAGGACCC
ACCATGGAGCTTGGGCTGAGCTGGGTTTTCACTGTTGCTGTTTTAAAAGGTGAACTAGAGAGATTGAGTGTGAATGGATACAC
TTGAGAGAAACAGTGGATATGTCTGGAACTTTCTGACCAGGACACCTACAAGTTTGCAGGTGTCCAGTGTGAGGTACAGCTGG
TGGAGTCTGAAGAAAACCAAAGACAACTTGGGGGATCCCTGAGACTCTCCTGTGCAGACTCTGGATTAACCTTCAGTAGCTAC
TGAATGAGCTCAGATTCCCAGGCTCCAGGGAAGGGGCTGGAGTGAGTAGTAGATATATAGTAGGATAGAAGTCAGCTATGTTA
TGCACAATCTGTGAAGAGCAGATTCACCATCTCCAAAGAAAATGCCAAGAACTCACTCTGTTTGCAAATGAACAGTCTGAGAG
CAGAGGGCACGGCCGTGTATTACTGTATGTGAGTCACCAGGTAAGAAGACATCAGTGTGAACACAGACACAGAATTTCCTGAA
ATAAGGGAGGAGTCTGGGCTAAAAGGGCACTCAGGACCCACAGAAAACAGGGGAAGCTCTAGGGCAGGTGCAGATGGTCATCA
TGGGCTGCTTTCCTTGAGGGTCTGAGGCTTCCTCTGCATCTAACAGTTTCCCTGGGAGCCTCTGGACATTTATGCTTCTGTGG
CCACCCCTGAGGTCTCTGGACATTCTCATTTGTTGCAAAGGCAGATGTAAGTATTGGAGGCATAAAAATGCACAGGAGGCCAG
GGAGTCTGTAGACATTGTTACCCCAGAAGGTCAATCTCACCACTAGTGCTGGAGGAGGGTGGGAGTTTGATGAAGCTGCCCTA
AGTATCCTGTGGTCTAAGCTAAGTCCAACGAGGCCATTTGTGCCTCCCTGAGCACAGTTATCCATCAGAGATGTCCCATGTGT
CCCAGCAGCAGCCATGTCTCAGTGTCTTCACTGTGCACAGCCAGTGTCTGGGAGGAGCTCCCAGGATGGGTGTCTTTGGCACA

FIG. 6 (Cont. 31)

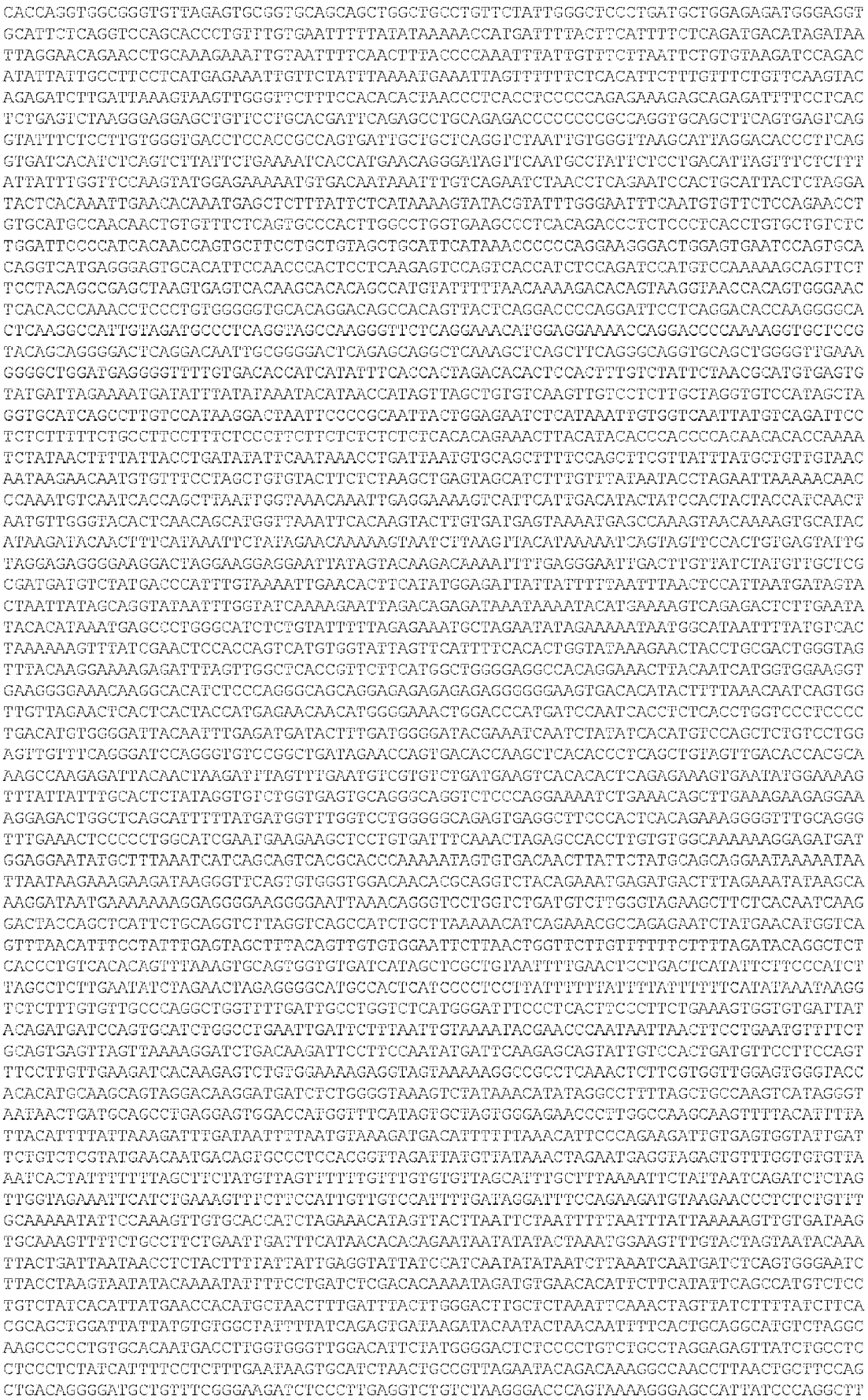


FIG. 6 (Cont. 32)

CACTTGGATGACCATTTGGAGTTGATGCCTGAAGGTGAGAAGAGACAAACCGGGTTATTAGAAGACATGTATCAAAACCAAAC
AAGGTGGTAAGGACAGTTTGAAAAAAAATTCCAAGGCTGCTGACACACCCAGATATCTGGTGGCTGTAGTTATGCCTGCTAAG
ATTTGGGTGCATGGGGCTTGGCTTTCGTTAGCTCCCTTGGACTTATTTTCCCAAACAAAGAAACCTCCGGGTTAGGGGGACCC
TATTTATTCCAGTCACCTGGCATGATTTGCCGGATAATTGCTCAGAATTAAAATATTCGTCCAGATGTTTATATAGCCCATGC
CTGTGTTTCTTCTGAGCTGCAGCCAGAGATCATTGGTTGGTTCACAGCGATAAGCAGAGTTAGTCTAAAATGGAGGCAAATAC
TTAAAACTTATTTCTTCTCTCAGTTAATGGATTCTATAGAGAAAAGTAGCTACTCAGCATGGGAATGTAAAAAAATGAGTAAA
CTATGATCTTATTCTGAACTCATTAACAACAAACCTGAAAAACCAATTGAAGAGACTGTAATTTAAAGACAAGTGTATGATAT
GTTTTGAAACATAATTTTTCTCTCTCCAGTTCTGATTTTTGTCAGAAACTAATCATTATAGGACTGAGTTGTTTGCAAAATAA
ACTTTAGTCTTATGGTTGGTCTGATCATTTGCATAAAGTGAAGCCATAATAATTAATAATAATTCTGTAGGAAAAGCCTGCAA
GCATGAGGAGCTTCACAGTCTAACACTATGAGCACATGCATCCTCCAGCAACTCACTGAATATTTTCAAGTCAGCCGGTTCTT
AGCTTAAATAACATCCAGTTGGTATCTGTCCCAGGAACACTAATATATGGTTCTCTCTGCAGGCCCCTTTCTCCACAGATTAA
GGGTTTTTTTTTTTTTCTCTGTAATATCAACTCAGATATGTTGAATGCTTTTTCCTTATTAGTGGTTTTTCAGGTTTGTTGTTA
ATGATTTCAGAATAAGATCATTGTTTACTCATTTTTTTTAAATTCCCGTGCCGAGTAGCTACTTTTCTCTATAGAATCCATTA
ACTGGGAGAAAAAATAACATTTTCTTATGGGTGAACAATTAAATAGTTTGACATATATTTATGTACTGGTATATAATGCAGCT
TGAAATCAAGGCATGCCTCAATCATAAAAATCATGGCTAAATTCTCAAAGAATTGTGCTGAGTGAAAGAAGCTAAGGAATTAA
GAGTAAATTTTATATAATTCATTGTAGAAATATTAGAAGATGCCACTACCATAAATTAAAATGAAGAAGACTTAAATTTTTCT
GAGAAAATGGTGTTGGGAATGATGCGGATGTGATTTAAGTTTCAGAGGAATAAGAAAAAAGATTTAGGGATTAATTTAATTAT
TCAAAACTTGATTGAAGTGCCGAGTGAATGGCTCCAAACATAGTCTACATTTTTCAAATCATTCCCTATAAATTTGAATTAAT
TATTTATTTTTATACTTGAATAAAGCAATAACAAAGAAATAAATGAATATTTTTGCTAAAATGGAGCAATAAAAAGACTGATA
TTGACAGAAGAAATATGACTGACTTCTGAAAATACACACACATGAGCCGTGGTTCTCTCTACATATTTAGATAAATTACAGAA
AGTTGTCATAACTGATGGGGAATCCTGCAGACTTCACTAGGCATAGTCCACACTGCCCTGGAGTTGTCTCAGGGGAGCTGCCT
CCTCCAGTGGTTAGAGCACAGGCCCAGGTAATAGGACTCATTTTTTTAGATGTGTAATTTTAGACACACTGCACAACTGCTGT
GTTCTCTGTGCAAATTATCTCCTGTAAAATGTAACATTGAAACCTGCCTAAATATATTGTGTAAATATGTAAAAATAAAATC
AGATTGTGAGAGCTAAATGCTAATCAAGGCGCAATCACGTAATATACAATTATATTTTCCTGAATGATGGAATTAATACCAAT
CTCCCCCAGGACACTTCATCTGCACGGAGCCCGGCCTCTCCTCAGATGTCCCACCCCAGAGCTTGCTATATAGTCGGGGACAT
CCAAATAGGGCCCTCCCTCTGCTGATGAAAACCAGCCCAGCTGACCCTGCAGCTCTGGGAGAGGAGCCCAGCACTGGGATTCC
GAGGTGTTTCCATTCGGTGATCAGCACTGAACACAGAGGACTCACCATGGAGTTTTGGCTGAGCTGGGTTTTCCTTGTTGCTA
TTTTAAAAGGTGATTCATGGAGAACTAGAGATATTGAGTGTGAGTGAACACGAGTGAGAGAAACAGTGGATATGTGTGGCAGT
TTCTAACCAATGTCTCTGTGTTTGCAGGTGTCCAGTGTGAGGTGCAGCTGGTGGAGTCTGGAGGAGGCTTGATCCAGCCTGGG
GGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGGTTCACCGTCAGTAGCAACTACATGAGCTGGGTCCGCCAGGCTCCAGGGAA
GGGGCTGGAGTGGGTCTCAGTTATTTATAGCGGTGGTAGCACATACTACGCAGACTCCGTGAAGGGCCGATTCACCATCTCCA
GAGACAATTCCAAGAACACGCTGTATCTTCAAATGAACAGCCTGAGAGCCGAGGACACGGCCGTGTATTACTGTGCGAGAGAC
ACAGTGAGGGGAAGTCATTGTGCGCCCAGACACAAACCTCCCTGCAGGAACGCTGGGGGGAAATCAGCGGCAGGGGGCGCTCA
GGAGCCACTGATCAGAGTCAGCCCCGGAGGCAGGTGCAGATGGAGGCTGATTTCCTGTCAGGATGTGGGACTTTGTCTTCTTC
TGACGGTTCCCCAGGGAACCTCTCTAAGTTTAGCATTCTGTGCCTATGAACGTCTTCTCTAAGTATTTGAAAGAGATTATTTT
AATATGAAGAGCAGTTCTCACTCGCCCAAAATGTGGATTGATGCTTACTGGGATGAAAAGTCCCCAAACATGGTCACCCCGAT
AAGAGTCTGAGTGAGCTCAGGGCTTCCTGCTGAGTCTCCTCCTATCAGACCAAGGACAGGGACCTCAGTGAGGTTCCCCCGTC
AAGAACAGTCTTTATGGATACTGATTGTGGGCGGCAACCCACCCAGGTGCCGACGCAAGAGACCGAGGACACGAGCTGTTCCA
GTACAATAAAATATAAAACAAGAATAGTTATACCAGATATAGATCTTAGATATGATTATATATGAATATCATTAATCATTAGT
TGGTAGCAATTACTCTTTATTCCAATATTATAATAATCCTCACTCTACAATCATAACCTAGGAAAAGCCAGGCCATACAGAGA
TAGGAGCTGAGGGGACATAGTGAGAAGTGACCAGAAGACAAGAGTGCGAGCCTTCTGTTATGCCTGGACAGGGCGACCAGAGG
GCTCCTTGGTCTAGCAGTAATGCCAGCATCTGGGAAGACGCCTGTTGCCAAGCGGACCATGGTCTAGTGGTAGACTCAGTGTC
AAGGAAAAACACCTGCTACTTAGCAGACCAGGAAAGGGAGTCTCCCTTTCCCCGGGGAGTTTAGAGAAGACTCTGCTCCTCCA
CCTCCTGTGGAGGGCCTGATATCAGTCAGACCCGCCCGCACTTATCCGGAGGCCTAACAGTCTCCCTGTGATGCTGTGCTTCA
GTGGCCACACTCCTAGTCCGCCTTCG[redacted]CTTCTAGATAGCAGTAGCAAATCAGTGAAA
GTACTAACAGTCTCTGATAAGCAGAAATAATATTGTAAGCTGTTTCTCTCCTTCTCCTCTCTCTCTGCCTCAGCTGCCAGG
CAGGAAAGGGCCCCCTGTCCAGTGGACACGTGACCCATGTGACCTTACCTATCATTGGAGATGGCTCACACTCCTTACCCTGT
CCCTTTGTCTTATATCCAATTAATATCAGCGCAGCCTGGCATTCAGGGCCACTACTAGTCTCCGCATCTTGGTGGTAGTGGTC
CCCCGGGCCCAGCTGTCTTTTCTTTTATCTCTTTGTCTTGTGTCTTTATTTCTATGCTCTCTCGTCTCCGCACACGGGGAGAA
ACCCACTGACCCTGTGGGGCTGGTCCCTACACTGATCACAGACAATAGAGGGTAGGCCAGGATCAGTGTCATGTAGGACATCA
CAGGTTTCACCTCTGAACCTTTTCCTGACACTAAATATGCAAATCAGCATCAGCACTGATCTGGTGATTCTTTTGTTCCTAAT
CCATTTACTTCCTTTTTCAGTCGTTGTTTTCATTTTTCCATTTGCTTTTCCTGCTTTCTGCAAAAGGAAGATTTTTCCCTGTG
GTCAAAATTCCGGACCTCAAGCCCTTTCCTGGCGCTCAGGTGGGTCTCAGGCTGTGGCTGCTGCAGTCACGCGGGAGAGGCTG
GTGGGACTTTCTTCACTCCTCGTCACTCAGGGCCCTCCACTGTGTTGCATGGAGACTTATCTGGAAATGCAAGTTGCGACTGA
GAACTGAAGGGGAC[AAGCTT]

GAGTATTCTATAGTGTCACCTAAATAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGT
TATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAG
TGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGTTTCCAGTCGGGAAACCTGTCGTGCCAGCT
GCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGCTCTTCCGCTTCCTCGCT
GCTTATCATCGCAATTTCTGCCATTCATCCGCTTATTATCACTTATTCAGGCGTAGCAACCAGGCGTTTAA
GGGCACCAATAACTGCCTTAAAAAAATTACGCCCCGCCCTGCCACTCATCGCAGTACTGTTGTAATTCAT
TAAGCATTCTGCCGACATGGAAGCCATCACAAACGGCATGATGAACCTGAATCGCCAGCGGCATCAGCAC
CTTGTCGCCTTGCGTATAATATTTGCCCATGGTCAAAACGGGCGGCGAAGAAGTTGTCCATATTGGCCACG
TTTAAATCAAAACTGGTGAAACTCACCCAGGGATTGGCTGAGACGAAAAACATATTCTCAATAAACCCTT
TAGGGAAATAGGCCAGGTTTTCACCGTAACACGCCACATCTTGCGAATATATGTGTAGAAACTGCCGGAA
ATCGTCGTGGTATTCACTCCAGAGCGATGAAAACGTTTCAGTTTGCTCATGGAAAACGGTGTAACAAGGG

FIG. 6 (Cont. 33)

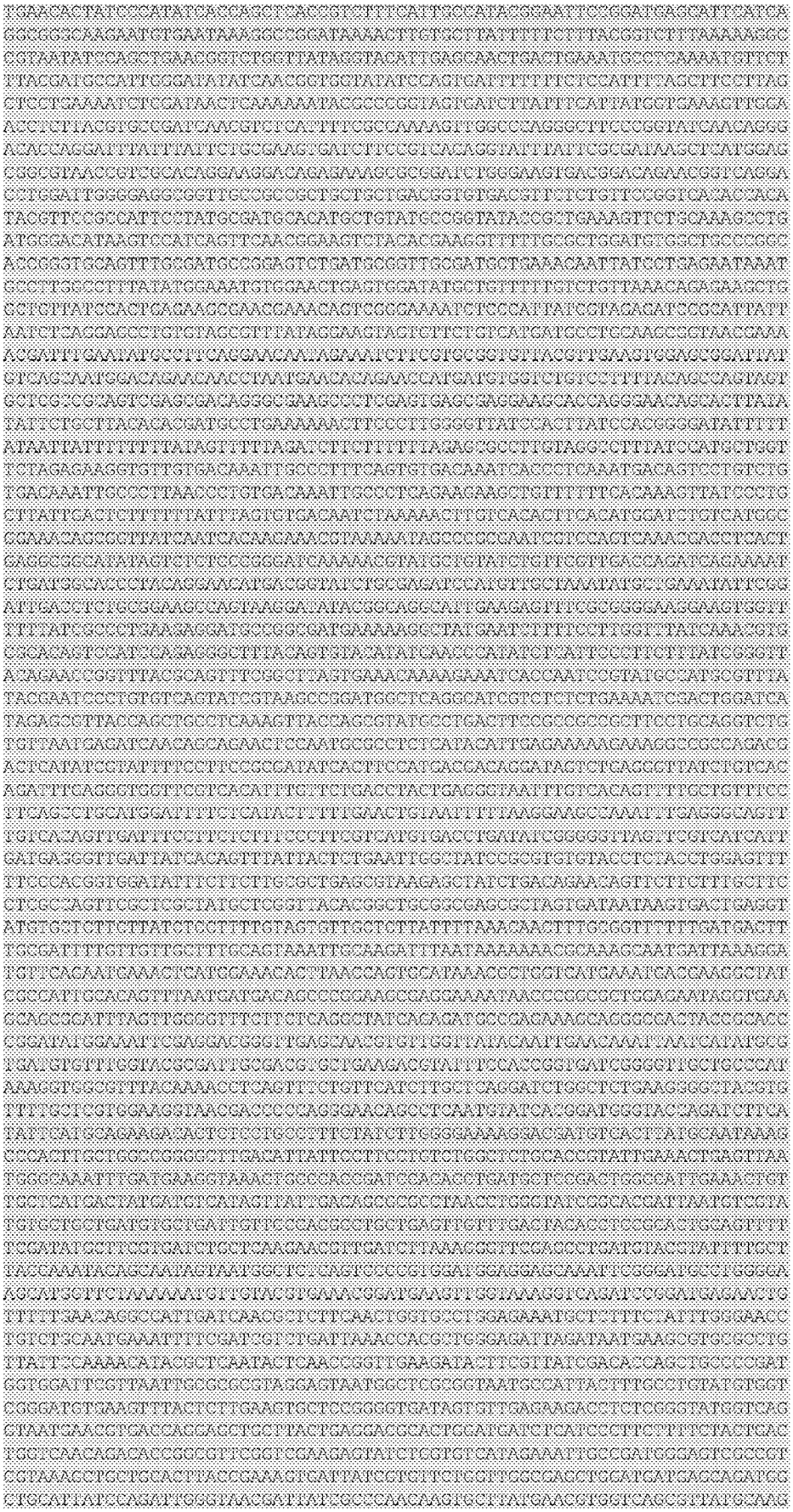


FIG. 6 (Cont. 34)

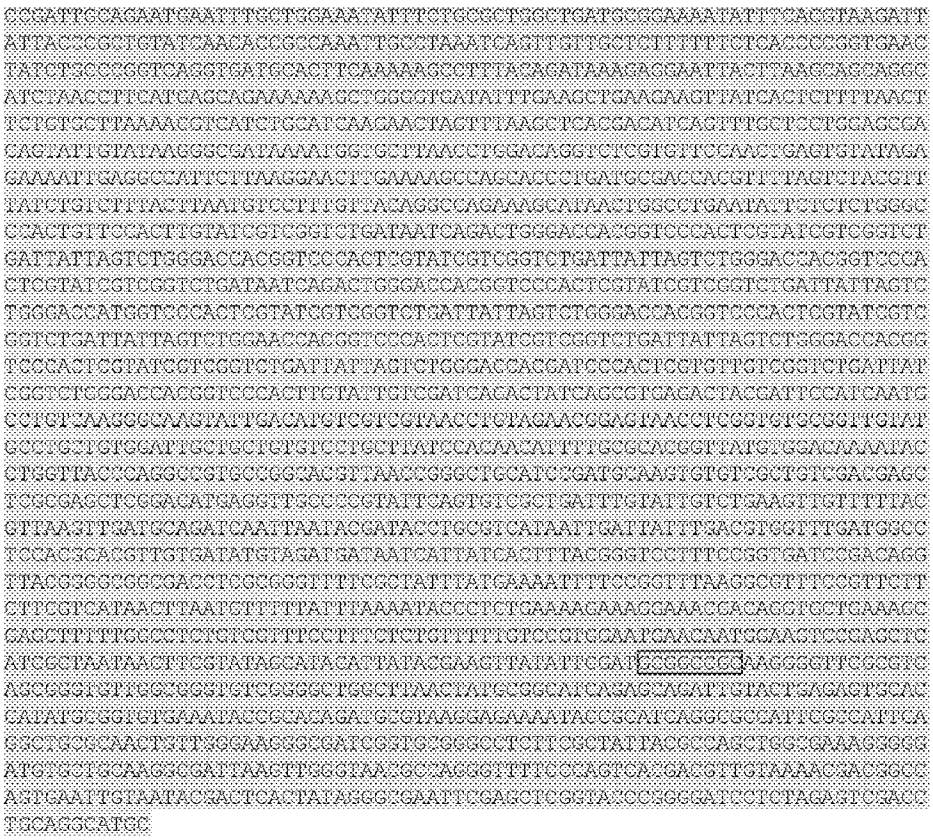


FIG. 6 (Cont. 35)

BAC (14+5)

- The human sequence can be cut out as a single 210 kb BsiWI-fragment. The BsiWI sites are boxed and in red font.
- Overlap with the 3' of BAC9 is highlighted in yellow.
- Overlap with the 5' of Annabel is highlighted in blue.
- Human VH3-43 is highlighted in green.
- All other human VHs are highlighted in grey in the order of VH5-51, VH3-49, VH3-48, VH1-46, VH1-45, VH3-21, VH3-20, VH1-18, VH3-15 and VH3-13.

CGTACGaatacagacaaaggccaaccttaactgcttccagctgacaggggatgctgtttcgggaagatctccttgaggtctg
tctaagggacccagtaaaagggagccattatcccaggcttcacttggatgaccatttggagttgatgcctgaagglgagaaga
gacaaaccgggttattagaagacatgtatcaaaaccaaacaaggtggtaaggacagtttgaaaaaaaattccaaggctgctga
cacacccagatatctggtggctgtagttatgcctgctaagatttgggtgcatggggcttggctttcgttagctcccttggact
tatttttcccaaacaaagaaacctccggttaggggggaccctatttattccagtcacctggcatgatttgccggataactgctc
agaattaaaatattcgtccagatgtttatatagcccatgcctgtgtttcttctgagctgcagccagagatcattggttggttc
acagcgataagcagagttagtctaaaatggaggcaaatacttaaaacttatttcttctctcagttaatggattctatagagaa
aagtagctactcagcatgggaatgtaaaaaaatgagtaaactatgatcttattctgaactcattaacaacaaacctgaaaaac
caattgaagagactgtaatttaaagacaagtgtatgatatgttttgaaacataatttttctctcccagttctgatttttgtc
agaaactaatcattataggactgagttgtttgcaaaataaacttagtcttatggttggtctgatcatttgcataaagtgaag
ccataataattaataataattctgtaggaaaaagcctgcaagcatgaggagcttcacagtctaacactatgagcacatgcatcc
tccagcaactcactgaatatttcaagtcagccggttcttagcttaaataaca.ccagttggtatctgtcccaggaacactaa
tatatggttctctctgcaggccccttttctccacagattaagggttttttttttctctctgtaatatcaactcagatatgttga
atgcttttttccttattagtggttttcaggtttgttgttaatgatttcagaataagatcattgtttactcatttttttttaaat
tcccgtgccgagtagctactttttctctatagaatccattaactgggagaaaaaatagcatttttcttatgggtgaacaatttaaa
tagtttgacatatatttatgtactggtatataatgcagcttgaaatcaaggcatgcctcaatcataaaaatcatggctaaatt
ctcaaagaatttgtgctgagtgaaagaagctaaggaattaagagtaaatttttatataattcattgtagaaatattagaagatgc
cactaccataaattaaaatgaagaagacttaaatttttctgagaaaatggtgttgggaatgatgcggatgtgatttaagtttc
agaggaataagaaaaaagatttaggcattaatttaattattcaaaaacttgattgaagtgccgagtgaatggctccaaacatag
tctacatttttcaaatcattcctataaatttgaattaattatttatttttatacttgaataaagcaataacaaagaaataaa
tgaatatttttgctaaaatggagcaataaaaagactgatattgacagaagaaatatgactgacttctgaaaatacacacacat
gagccgtggttctctctacatatttagataaattacagaaagttgtcataacigatggggaatcctgcagacttcactaggca
tagtccacactgccctggagttgtctcaggggagctgcctcctccagtggttagagcacaggcccaggtaataggactcattt
ttttagatgtgtaatttagacacactgcacaactgctgtgttctctgtgcaaattatctcctgtaaaatgtaacattgaaac
ctgccttaaatatattgtgtaaatatgtaaaaataaaatcagattgtgagagccaaatgctaatcaaggcgcaatcacgtaat
atacaattatattttcctgaatgatcgaattactaccaatctccccccaggacacttcatctgcacggagcccggcctctcctc
agatgtcccaccccagagcttgctatatagtcggggacatccaaatagggcccctcctctgctgatgaaaaccagcccagctg
accctgcagctctgggagaggagcccagcactgggattccgaggtgttccatcggtgatcagcactgaacacagaggactc
accatggagttttggctgagctgggtttccttgttgctatttaaaaggtgattcatggagaactagagatattgagtgtga
gtgaacacgagtgagagaaacagtggatatgtggcagtttctaaccaatgtctctgtgtttgcaggtgtccagtgtgaggt
gcagctggtggagtctggaggaggcttgatccagcctgggggggtccctgagactctcctgtgcagcctctgggttcaccgtca
gtagcaactacatgagctgggtccgccaggctccagggaaggggctggagtgggtctcagttatttatagcggtggtagcaca
tactacgcagactccgtgaagggccgattcaccatctccagagacaattccaagaacacgctgtatcttcaaatgaacagcct
gagaggcgaggacacggccgtgtattactgtgcgagagacacagtgaggggaagtcattgtgcgcccagacacaaacctccct
gcaggaacgctgggggaaatcagccgcaggggcgctcaggagccactgatcagagtcagccccggaggcaggtgcagatgg
aggctgatttcctgtcaggatgtggcactttgtcttcttctgacggttccccagggaacctctctaagtttagcattctgtgc
ctatgaacgtcttctctaagtatttgaaagagattatttaatatgaagagcagttctcactcgcccaaaatgtggattgatg
cttactgggatgaaaagtccccaaacatggtcaccccgataagagtctgagtgagctcagggcttcctgctgagtctcctcct
atcagaccaaggacagggacctcagtgaggttccccctgtcaagaacagtctttatggatactgattgtgggcggcaacccacc
cagglgccgacgcaagagaccgaggacacgagctgttccagtacaataaaatataaaacaagaatagttataccagatataga
tcttagatatgattatatatgaatatcattaatcattagttggtagcaattactctttattccaatattataataatcctcac
tctacaatcataacctaggaaaagccaggccatacagagataggagctgaggggacatagtgagaagtgaccagaagacaaga
gtgcgagccttctgttatgcctggacagggcgaccagagggctcttggtctagcagtaatgccagcatctgggaagacgcct
gttgccaagcggaccatggtctagtggtagactcagtgtccaaggaaaaacacctgctacttagcagaccaggaaagggagtct
ccctttcccccgggagtttagagaagactctgctcctccacctcctgtggagggcctgatatcagtcagaccgccgcgcactt
atccggaggcctaacagtctccctgtgatgctgtgcttcagtggccacactcctagtccgccttcgtgttccatcctgtacac
ctggctctgccttctagatagcagtagcaaatcagtgaaagtactaacagtctctgataagcagaaataatattgtaagctgt
ttctctccttctcctctctctctctgcctcagctgccaggcaggaaagggccccctgtccagtggacacgtgaccca.tgac
cttacctatcattggagatggctcacactccttaccctgtccctttgtcttatatccaattaatatcagcgcagcctggcatt
cagggccactactagtctccgcatcttggtggtagtggtcccccgggcccagc.gtctttctctttatctctttgtc.tgtgt
ctttatttctatgctctctcgtctccgcacacggggagaaacccactgaccctgtggggctggtccctacactgatcacagac
aatagagggtaggccaggatcagtgtcatgtaggacatcacaggtttcacctctgaaccttttcctgacactaaatatgcaaa
tcagcatcagcactgatctggtgattcttttgttcctaatccatttacttcctttttcagtcgttgttttcatttttccattt
gcttttcctgcttctgcaaaaggaagatttttccctgtggtcaaaattccggacctcaagccctttcctggcgctcaggtgg
gtctcaggctgtggctgctgcagtcacgcgggagaggctggtgggactttcttcactcctcgtcactcagggccctccactgt
gttgcatggagacttatctggaaatgcaagttgcgactgagaactgaaggggacaagcttgtttggttaacatgggatgtgga

FIG. 7

tgtgtttctaattttgttctgataaactttcacagagtaactttctgcactagtcatgtgaggaagaggatgtgaacgtagtc
agaataaaaatagaacaacttgtgttataatctttacaggtgaagctggagaaggtcatgaatagagggttctcatgcacaca
tccctgataacaagaactaccataaaattactctgcacaaccacaactttcaacaaaggctaccacaacaataagagaattaa
tattgtgaggatatctgccctgcaactcccagtacaatcttaaactgattccacccttgttattaattcttctacccccagga
taattgcctcagaacagctcatgtaagtcctctcatttatcccttaaaacaaccttttaccaaccttactaacctgacttcct
ttacctacctaaatatgcccagggataatcccactggaatgctcattttcaaatacatattatttgattttggagaatttctt
tctgtctgatattcaggtgtgacaagctgtagagggtcacaccactttcctgtgagatgtaggggatgacaatttgggggat
ggctggaaacatccaatatcctcagggtcggccatcagtaagcgcaggctggaagtctcagaacgagttgaagttgcttaacc
acggaattttaccttctccagatcagctttgatggaatcagggccaaactggttatcaatgataatctacctaacattgagtc
aactgatcacagttttaataacctctattaaaaattcacaccaacacttggattagtgtctgatcaaataactacaaagtatt
ttccagccaagtataccataaaacagaccattacccatggagaaaaacatttaacatgagttctaggtccttacattgttaaa
ggtgtaaaactgattatttttaaattatgcttttattttgctattgagttgtagaagtttcatttacattttggatattaa
cgctttttttcagatacatgatatattatccaattctgtgagttggaattatttcattgctttgcagaatatttttttaatcta
gtccaacttgttcaattctgctttttttttaaatgtgctttgaatgtaaaatccagaaaaagattgctaatttttgaggattgg
gagttttacagttgcaggaatttcattgaaatatttaatgcatttaaagttaatttttgtgtttattctaacctaaaattctt
aattcttcacatgtgaaaatccagttttcataacatgctctttggaagacaccataatttagccattgtatgttgatggttct
catgctgaaaatcagttcgccatcaaaatgtgggtttatatctaagctctctatatgcatttatgctgaaaccattcggattt
attactctgtgtttgtaacaaatgttgaggactggaagtgaaatgcctcaagctttattcttgccttattacagatattagac
ccaaatattctaaccttctactagtgagtataataatagctgtcgctttttttttttttttttgattcagagtttcactcttg
ttgtgtaggctggagtgcagtggtgtgatctcagctcaccgcaacctctgcctcccgggttcaagcgattctcctgcctcggc
ctcccgagtagctgggattacaggcatgcaccaccacacccggctaattttgtatttttcagtaaagatggggtttctccatgt
tggtcaggctggtcgcgaactccagacctcaggtgatcctcccgcctcagcctcccaaagtgctgggattacaagcatgagcc
actgcacccagcctcttcatttttttttttattcatatgttcattcagcagccactatgtcttcccattgatttctttggtttc
ctctttactatctttttctttttagtaaagctgttactcctaagggaagatgggaggtgggcctggacagggatttggtgcat
tcctctcttcactcacagttcttattgatctctccagtgtctctagaacactggtttttcctggcattaccgctgcagataatt
tctcttgcaatgtagtgctgatgaggaggtgtgtctggatgcatttcagctatagttgctgttttgctttccctgacacaacc
gtcccaaggggtagaggctggagcattttgtgatgtgtccccagtactgaagaaaaagccttcaatagcaggaggaattcctc
aactgtatacactctgagaatttaaacaataacttctctatcacactcaaatttaaaccatccaatgaatatgtctactttaa
tcgtgtgttaacttaaatgatatttggcagcctctgtcccagaaaagattatcatctgctcctgtttatttccctgcaagtct
ttatctctcttcagatttcagatatcttgtttgtcttataacatcaaaaatctgatgaatttaagaaaatgtgctaatttgca
gatcagtaagctttagtagttgtgagaataataacaaatttttatgggatgcctgcatctccaagctgagtagcatctttatt
tctaacactcagaaactagaaacaatgcaaatatcaagaagatatatagataaagagtaatggcatgctaatttacggtaatc
atagccatcactagaatcaatacactgttgatgctcaatgtggttgaatcacaagtagttataatgagtgagaagccacacac
ataaaacacatactatataattcctgtataataaattcttgaaactcaaaaccaaagtattcaatatgaaggattgactcaga
atatggcaagggaaaaaaatgaattgggaaggaggaattgtagagtaacacaaggaaacttttaagtgtaatttatttgtttgt
tatctggatggtttttggggatgcacaggtgagcacgagtggaattacattttgttgtgtttgttttttctgaagagatgtg
gtcctactctgtgacccaggcaggactgcagtggtgggatcatagttcaatgtagcttccaacttctggtcaccaacaatcct
cctgcatctgccatctaagtagctgaaactacagttgtgtgccaccaggctcagcttgagtacttattaaatcaaacacttta
tgcaatatttaatgtatggcaataatgtctcattgagagtattacaaataaatgaatggataatttgttcagtacagattgat
ggaaaatagacactaacatgaggaatgtctgacatttatgaacatacaactgcataaaatgtgttctcttacattcattaggt
aaacacaatagtgcatacacatcaaaccatgctttcattacaggaaggaagttctgaaaatgtcactgggggtgacccacgct
gtgctgggcttggttcgggggcagtcaggccggtggtgagaagcacaggcccagatacccaggcttactctgcaaatgtgag
ctctggggacattgtaccacccatctgtgcttctgctggtaattttccatctgtaacgtggaaataacattgatactacatac
cgtgatttctccacatatgtaaaaataaaataagatgattgctgctaagtttaaataagggcagttttcataggtccattgta
cctcaataaaattactttaaaataaaaattacaaatacagttgtaggtttaaagagtttatcacagaacaaacttataataag
aaactatattttcaaaaattgtatcaatatctctaaactcccccaggacacactcacctgctctgggctctccactctcctca
ggattcccaccccagagcttgctatatagtaggagacatgcaaacagagccaaacctctgctgatgaaaagcagcccagccct
gaccctgcagctctgggagaggagccccagctccaggattcccaggtctttccatttagtcttcagggctgagcacagaggac
tcaccatggagtctgggctgagctgggttttccttgttgctattttgaaaggtgattcatggggaatgagttgaatgtaagtg
aatatgagtgagagaaacagtggatgtgtgcggcagtttctgaccagggtgtctctgtgtttgcaggtgtccagtgtgaggtg
cagctggtggagtctgggtgaggcttggtacagcctggagggtccctgagactctcctgtgcagcctctggattcaccttcag
tagctcctggatgcactgggtctgccaggctccggagaagggggctggagtgggtggccgacataaagtgtgacggaagtgaga
aatactatgtagactctgtgaagggccgattgaccatctccagagacaatgccaagaactccctctatctgcaagtgaacagc
ctgagagctgaggacatgaccgtgtattactgtgtgagaggcacagtgaggggaggtcagtgtgagcccagacacaaacctcc
tgcagggcatctggagccacaaggggcgctcaggatacacagaggacaggggcagccccagggcaggtgcaggtggaggtc
aagggctgctctccttcagggtctgtggcttcctctcatctaacagttccgcagggagcctcttgtatttacagtgatgtgct
actgaggtttctaagtttgtaaagtttattactacaggaggaaccactatcaaacgcccttaaggcaggtgtcactaatggag
aaaggaaagtgcacaggaggctgggtgaggctgtggacactgtctgcctatgattcaagtttcacaagcagtgacggagaaat
gggagtttgatggagctccctaactaccatgtggtctaaactaagtccaactaagtccctgagctctgggtgcccatcaggga
tccgccatgtgcccggcagccgcgtgccttttgtctcctctgcgcccaatcactgtctgtgatgagcttccaggatgtgtgt
gtttggcacaaaccaggtgatggacgtcagacagcagcagctggtgcccggatcatgggctccctaatgctggaggaatgaga
ggtgcattctcagggacaagacattgttgatggatttttatgtagaaaccacgattttacttgcttctctcaggagacataga
agaagcaaccatgcagtcagcaaataattataatttccacaattaccccaaatggttaatccttaattctgcgcagggtccca
ccgtagagtcacctttctcatgaggaatggttgaatctagaatgagtccacatgattttcatatttttggcttctgtccatgt
tcagagagttagagtagagtaagtttggacctttccacacactaagcctcacctcccccacagaaagagcagagacttcaact
attcctgagtgtggggtaggggctggtcctgcacacctcagagcctgcagagactgccacgtgcagtgttatagacttgggtg

FIG. 7 (Cont. 1)

ttttctcattcaggaggggtgacctccacggcctccgatttctgctaagatataactgtgagtgcagaattaggacactatta
ggctatcatgcctcacttctattctgaaaatcaccctctttatagtaaaagaaaacaattcaatgtccatgcccctgaaagtc
atttctttttaatttggttgcgagtttaccacatagtgcctgaatttattctcagaatctactgaattgtttataaatctcac
aaattgaacaaaagtgaattcttcattcttactaaaatgtgtgtatgtaggaatttcagtgtgttttccagaagccatgcaca
ccaaccactgtgtttcatggtcatttattggcctggtgaggccctcacagacccctccctcacctgtgctgtctctggattc
tccatcacaactagtgcttcctgctggagctggatccgccagtcctcagtcaagggagtggatcagggcataggtcacgaggg
agcacaaattctaacccactcctcatgagctcagtcaccatctccagatccacgtccaagaaccaaatttttcttttagctgag
ttctgtgaccaacaatgccacaaccttgtattactgtgagaggaacagaagagatgtcagtgtgatcccagacacaaacttcc
ctggagaggggcccaggaccaccaaagagcactcaggcccatgaaaacagggcccaagctggagaacgggtttcctgtcaccc
tcacctttcaccattagatactctacactatgcctatgctgaggtgtgtgtttaatataattagaaaatggtatttatatacg
tgtataatcatatctagtgtaagaatttgtagtttccaccttatgtgaccattaaagacaacatctctcacgttattcaagga
ccttataaagtataatacttttacataagatttatctccttttgtgtgtttctccttctgtctatattctctctctctcttcc
tccctctttctctctctctccatctctctctctctgtctctctctcacacacaaatacacacacatgcaatcggtgacagt
atataggctaattaagaatatattcccatatgatttaaaaataacagttttacaaatatttgcctttaatttttcaaagaaaa
ttaaatccaaatgccagtgatttttttatgtgacttttaaaatttaaattgttaatttgtgttttcatcaatgcttgtatgtgt
gcttgtgtattctcacagattatgtggtgccttcacagaattaaacatgtgaaactctccacttgaatttctgtgactcagga
ctggtgagcaaaaagttagaagtcactctcctgatccttccctacagctgcagattcctgaaggtaatgacctcacagtagac
caaggccctcaaaggtgaccttgagttccagcacatcttgggaggccaagcggatgtttgtgaaagaaatagtggctatgtga
cagtttctaaccagaatatctctgtgttttcaggtatccagggtgaggcccagcttacagagtctgggggagacttggtacac
tgagaggggcccctgaggctctcctgtgcagcctcttggttcaccttcagtatctatgagattcactgggtttgccaggcctc
agggaaggggctggaatgggttgcagttatatggcgtagtgaaagtcatcaatacaatgcagactatgttaggggcagactca
ccacttccagagacaacaccaagtacatgctgtacatgcaaatgaacagcctgagaacccagaacatggcagcatttaactgt
gcaggaaacatcgtgatgggaagtccacgtgggctcagagacagactgccatgcaggacacaggggtggcttggctgaaggg
ggcactcagcacccacagaagacaggagcagcccagggcaggggcaggtggagttcaagggctgctttcctgtcaggttctgt
ggcttcttctgcatcaaatgcgttctcctgggagcctctctatatttatggttctctgcctaccactgaggcctctggattgg
aaaagattactactagaaaaaaaaaattctcatataccccctgaagaatacatcattaattgaggcagaagatgtcacaggaggc
cagggaggctgtggaaactgtgcgacgtggatgcacatctgacaacaaagacatgaaaaatcagggaacactgataaaacctc
ctaattatgccatggccctctctaagcctagtaaagccattgatgccttcctgggccaaacccaccccatcaggggatcactcc
tgtgtcccagcagcagacatgccttagaatctccactgtatgtaatcactgtctgggaggagctcccagggcatgtgtctttg
cattaaccaggtgatgggtgtcagacaacagcagctggatgcctggtctatgggttccctgatgttgaagaaatgggaggtgc
agtctcagagccaatacactgtttatgcatttttatatagaaaccatgatttttcttgcttctctcagatgacatagaggatc
aagaaaacagtctgtaaacaattgtaatgtccccatttcttctgaataaatgcattatttcttaattctgagtgggggtttgt
cagaccatgcccttctcctaagcaattgttcaatccaggctgaaaccacatggggatcacatactttggtttggttcaggtgc
agaggtcttcagtagagcaaatttggtccttcccacacagtaagcctcaccttcctcagagaaagagctgagattgatccaac
tttgtctgaggtgggagctgcttctccacaccttggagcttgcagagacccctaaatgcagctttattgagtcaggtgtgtct
ccatgtgggggacttctgctgctagtgatctctgctcagttctaaatgtgggttcagaattaggacacttaggttatcacgcc
tcaaaaattaccatcattgtagatagaaataatagtacaatgccaattgttgtcacttgtttcttattattattggagtataa
gtttgaagagacaaattgttaccatatatttgcataaatctaatgtcagaatctcttgaattgctcttgaacacttacaaact
ggttagaagcagattcttatttttttctatactagtgtattttgggatgtcaacattttgtccagaacatgtgagtaccaata
actgtgtgtttcagaaatgactgtgagattcagtcatttctatcgagtgggaaaaccagttaactttgtctttgatatatgga
tggaagcccaagatagaggcttgtcagtcattgtttctgtgccttctcccttgggaatgtctgtatttttttatgctctgtcc
tgggtctatacccaatggttcccctactccatggcacctgcctgtgcctgtgcatgcccctgcccacactctccgtgaaaca
tctgctttggctcaggaagaaccccctcctctgccttttttcctcctgcccctggtccacattcttctccatccacaggctctc
agcagcacctcccatccacactaaccctacatggggtcataccttgtccaccacttcctctctcttttcttctgagctttgcc
ttttattccaacagcctgtttccatctcacctggacttgtgtacaggaaaggatttaccgagcagtcttgggttgtgcaaacc
ctgaacattcctgaaaaagtgctttctcaagctaggcccatattcagctcctgggagatgatatctgccttttggcatactc
ctcctggtagtattattaaaccacttgattaagataaggtttacatctgtaaaactacacattatttaacatacttaactcat
tgagtttggagtaagtatacatctgcaaagttatcccatcatcaaggtcataaccatagaaatcacttccaaaacattcctc
ttatctctcttaatattgtgattattttattagttaaaatgtatttttgtttgtgtttgtctgtgtctctgtgtgtgtagcct
gggtgcacgctatactacctgttttcataatgacttatggtgaatgcctattagtgctcaagaggccggcgtctgagcactgg
aggtcaattgtgcaggtgtcacacacatctgtgatgggcccaataaacagccctgggcacaagcactcaggtgagcttccctg
gtggacaatgcttcacacatgttgtcatgcatcactgctgggagaactggggacaagagactcctcagggaaagaacacctgg
gagctcatgcctggattctcagggccttctccctggtgccttgctcattttaattcatattcattcgctataataaagctgc
acccatgagaataacagcttttcttgtgtccttttatttgtactgattaaggggcctgaggatggtcttgggacactcaacaca
attacatcagagttggagaatgctagaaagttcctgattgctgacgcatggctagaggatttttataacatcaaaggatgag
aaagtgcgggataaaagacattcaatgcccagatggctacagaatcatatggcatgagatggcatgtacactccaataaggag
caggaagtgaaagtaatccatggaatttagaaacaacagatacagcttcctaggagttgttccctgaaaaaggaaaagtaaaa
ataatgaggaacaacccgaatatgcaattcatatctgtgatagctaaaataatagtaaaaagatgcacatccagccctgcagt
gtgccctgtgagccgaggctgctagactcccattcaccaccaaagggtacagttgtccagaaacaacacacaacacataagag
tgacacagaaggtagcccagagtttgggctggggagaggaatccactagacaactataacaaggaggacagcatggaaagtgg
catcattttgtgatatgattgatatcattaatttatatcatcggattgtgaacaaagttagccaatggactatgagagtgact
gacgtagcagcttctctggcttcgtgtgctgcagatgagaggagaatgtttgggaggatgctggacccacagctcacaacaga
catatgacagacgtagctgatcccaacctcaagtaggatgttcttgatgagacagcttccctggtgcactggatatcagatcc
tgtatagtttcagaacttgtgtagtttgtgttgctttggctttttctctggatcttttaggtgctaatgaaatgagagtgctt
cacaaaaaaatggggcagacaaaggggatagttaagggcctcctccaagcaatgtggatatcataaaataaatgttaaaaaat
gaaagaactaaacaagaaggtgctggggttgacacaaaggacttaaaacagcactaccaggagttgggtgcagcaatgggcat

FIG. 7 (Cont. 2)

ccettcaggtccatcagcaagtcagagacctaaacaaatattcectattcatgttgaattggcagagtgtaaaaatctagaag
acaaaatggccaggaaaaatgtgcgattttgcatgggtgaaggtctggcaagttaatcatcttgaggactgttgaggtcctga
ggtggtcctgccttgcttgatgcccaggccgtagtccaactcacacgaaattgccagggaatagacagtagttttttagta
gttcttgttatcaggcataagtgcatttgaattttctcttcatggcctttcctggcactatttctcatttttttaacacaca
tagtttcaactagatttatcaccttcacagggtcacagagaagggtggaagaagggaggccctggtatgggtctcgaagaaac
atggaaaagagtggagagggacaatagcagggtgtaaggaattattgagaccttactctgcccctcccaggaggctcaggcca
gcctttttctgcatttgaggttctgggttataaacgctgtagactcctcccttcagggcagggtgacaactatgcaaatgcaa
gtgggggcctccccacttaaacccagggctcccctccacagtgagtctccctcactgcccagctgggatctcagggcttcatt
ttctgtcctccaccatcatggggtcaaccgccatcctcgcccctcctcctggctgttctccaaggtcagtcctgccgagggctt
gaggtcacagaggagaacgggtggaaaggagcccctgattcaaatttgtgtctcccccacaggagtctgtgccgaggtgcag
ctggtgcagtctggagcagaggtgaaaaagcccgggggagtctctgaagatctcctgtaagggttctggatacagctttaccag
ctactggatcggctgggtgcgccagatgcccgggaaaggcctggagtggatggggatcatctatcctggtgactctgatacca
gatacagccgtccttccaaggccaggtcaccatctcagccgacaagtccatcagcaccgcctacctgcagtggagcagcctg
aaggcctcggacaccgccatgtattactgtgcgagaca cacagtgagagaaaccagccccgagcccgtctaaaaccctccaca
ccgcaggtgcagaatgagctgctagagactcactcccagggggcctctctattcatctggggaggaaacactggctgtttgtg
tcctcaggagcaagaaccagagaacaatgtgggagggttcccagcccctaaggcaactgtatagggacctgaccatgggagg
tggattctctgacggggctcttgtgtgttctacaaggttgttcatggtgtatattagatggttaacatcaaaaggctgcctaa
caggcacctctccaatatgacagtattttaattagtgaaaatttacacagttcatcattgcttgcttgcctcctccctcct
gtccactctcactcactccttcttttattttctacttaattttacaaaatcatttaacccctttttgaactattaataggtta
tctttgtttggtgattgttttcctttcaataatatgtactgaataattcatctttgtgccaattcataagtattctggtgtaa
taaagacttctttcataaaaattggataaattaaaataaagataaatttttaaaaacatacgatctatcaaaactgaaccata
aagaaataaaaactctgggttgggtgtgtttgctcattcctgtaatcccagcactttgggaggccatggcggtggatcacct
gaggtcaggagttcgatatcggtctggcaaacgtggagaaacgctgtctccactaaaaatacaaaaattagctggacatggtg
gtgctcgcctgtagtcccagatacttgggagcctaaggccagagaagagattgaacccgggaggcagaggttgaaataagccg
aaatctagccactgcattccagactgggcaacagagtgagactccatcccgaaaaaaaaaaaactgaacagacctatgagtaaa
gagattgagtcagtgatttttcaaacatctcaaatcaaagaaaagtcaagaacttcatggcttcactactgaatttatcaaa
aatttaaaaaaaaaactagaatctctatacaaatttccaacaaaataaagaggaaaaaatacatgcaagcttatttggaaggt
cctatttccaaagcaaggaaaagacactccaaataaataaaattacaggctaatatccctgattatctagtttcaaaaactct
caagggtggtgagaaaccaaattcaacagcacattaacaacagaattcaccatgatcaggtgtggtttatctctaggaagcaa
tgaagtttcaacctgcagaaataaatgtgatatatcaaatgaaaatattgaaggactaaaaccatatgcaccatatgtccatg
tcaatagatgcagaaagagcctctgtcgaaatccactacactctaatttttaaaaatctgaacatattatgcataaaacatat
atacctcaacataataaagaccacatatcacaagcccacatctaacatcatacacagtgatgaaaatttattttcctctaag
actagaaactagacaagatgcttcactatcaccaatattattaaacacagcactgggtggtctagacaaaacaggccagaaga
aaaaaatagaagtcatccatatagtaatgaataaatataaaatatatttttacatattacatgctcttatttatacaaagcct
taaacactccaccaaaaaagattgaaactaatgaagaaattcaataaagttgcagaatccaaaatcaaacttacatttcaaga
tggcaggttagaggcattgctagtattcctcttccacttggaaggacaaactgatgtggagagatgaacatcgcggacttatt
ttcaagaagcaatgcaggaactgaacagaaacactgaaataatctacaaacttctgaaaaagcaggaagctgcagcctacac
tgtgagtcaggtgaagggctgggagtccccagcatttgagggagaacagccaaaaatttcagccagtggtcccaagttgaaag
tagctctcaacaggggtgtgtaatataacctagggttgggacgaactcccttggccagggcctgggtagggaagtgttaaaag
tggtctctgcaagtttaggagccatgggtgcaggagctggtgccctgctttgcagcagacaggaaggggcatggcatgaaacc
catggctgcagtctccatggggacagcctatgactcctggcatttggaggtattgatcacagattgactgaaactcatctcac
tgctgccagtggaacaccacgggagtggatcagcctcaccaagtatgtgggaactgtgtgggcctaccaccacctgccactc
cccacccccctgcccaaacttctgtggaggagaggcagccatggtcccatctggaacatcatcccagtggcctgagaaccacc
ctgtccccacacccacaggggctgctgcttgccctgcatacagagactcagaggggaaacccacctggcccaaccctcacct
tgctttgtgcagccacctgccctggcagcttaacacaaaagacagcatcttttgggagctacatagccacacccactgcctaa
gaatccatagtagccccctacctgggcaacacaaggcttgcaaaaatcccaccgctaataatgcagctggtgctctttgca
agcaccacctcttagctggaggccaaccaactatgcattacagcatctcctagtagactaacactgcatcctggaaggagaaa
atgactgtgcgatctcagttatcaccatggcctgcaccactttggatgaccaggagatcctgagtctctccatgtgaccagtt
cattgctactataccccatcattcaagaaagccagtacacaaaggctatcaatatccatggaatttcacagagtctccttcact
ctcctgcctgccactcccatcagaccccggttctgctgttcactgttgaaaaatatgaggacagttcacatcactggatcactt
agagacatttgcccacaccagcctgaagtgtgtcaacgtcactgggcagctagacctagagaagaaacataactcacagtacc
atggctccaggttctcctcctcttaggggaagggagtgcaccacattgagggaacacctcatgggacaagagaatctggatg
gcaggccttggacaccagatccctccactggtgggaaacttcttctagcagaagtacagttgcagcactgggctcagctggga
aagtcttcagctctttctcaacagacagccctgttgcttgtgaagaatcttgaagaagaggaagccttccccttgtacacc
actgtaggcacacttggggtctctcccacaagacctcagcatgggtgcaactatagacagccttttctggaacacatcattgtg
actgcatccccagaaacagcactttctggattcaggcttgcatgagacagagagtcacagttcctctctatttggcacatga
acatttgtacagatgaaaaaacatgcctgtcttatctgaatagccggaatactgggacagcagtatgtctgagaggtggataa
atttcctactgacttgacaagagagctgaggtggttccaacccttcccaccgataagacctcagtgggactcactaaaacctc
tttcagccaactctgtcaaggctgggacttaatttacccacctgctttagccacaactagtttctacccaaggaaaagtcctc
cactgatgtgaagcttgagccatcaagcaaataaataaatcactggggacaaataaaataaacatgtgcatgccacagaggaa
tgagataaggtttaagagacctctaccattctaaccccatagaagacagtgaacttgctcacagaccgagcagatttctactg
caatcaacacataggaaagccatcatacaaagattctccataaccccggaactcttacagagtcttcacccctctaaggacca
aaaaccaaatcaggttgtaattaattataagcattaaagtctcattcttaagggaaaaaaatccatttaaaaacaaacacaag
aaacagtcaaatcaaacataaattcaataataattagaaaatctaccaaaatgagaggaaatgagaaaaataactggggaaaa
atgagaaaacagggtgctgtgccagtgccaaaaggtcacaaggtcacactacctctccagcaataaaccataacaaaaatgga
gtctttgaaatatcagaaaagaaaatcagaatgttgattgataagctactcaagaagatatcagaaaaaggcaaaaatcataa

FIG. 7 (Cont. 3)

taaataaatttataaaactgttgagaatatgaatacaaatttttacagagagatagacatcctaaagagaaaccaatcagaac
tcctgaaaatttaaaaaaatgcagggaattggaaagggaattacaaaatgccatggaaagtttgaaaaatagactagaaaaaa
gtagcagaaataacaatagactagaaacagtacaaaataaaagtagaagtaaaatattcgaggaaaaagaaaaaggaaacagt
taaagaaaaaagtagaaagaccagactattattgaaataaccaaatcagagaaaaataaatttaaaaagagccaaaagaagtg
aaaaaagtctccaggaaatatgggattatgtaaaacaaacaaatttaagaataattggtgctcctgaagaagaaaaaataata
ataagtttgggaaaacttctctgaaggaataattgagaactacttctctggcctgactaaagacctagatatccaaatccaaa
aagttcaaggaactcctggggaattcattgcaaaaataccttcaccaagcatacagtcatcaggctacctaaagtctacatga
aggaaataattctaagagcagtaaaacgaagaaacccatcagaataatggcagacgtctcagcagaaacttgacaagcaagac
agattagggttctattttcaaactccttaaacagaaaaactttcaaccaagaattctttttttatcccgccaaactgttttata
aataaaaaagaaataaagtcattttcagaaaaacaaatgctgagggaattcatcactatcaaaccagcactacaagaaatgct
agaataagtttctaaaccttgaaacaaaaggccaatatgcacaaaaatggaacctcttaaaaattaaaaactcacgggcctat
aaaacaataacacaatatcaaagaataaacaaaattaggtaacgacatgacaaagagaatagcaactcatatctaaatattca
cattgaatgtaaatcataaaaggcatggaagaaggaatttcacaaaaatagaaaccaggagtgagcaggactagctatttttg
atctcagacaaaacaggacttcaaagcaaaaacaatttaaaaagacatagatgatcactatacaatgataaaaggatcaattc
aacaaaaaattacaattacatatttatatgcaccaaacactggaggaactagattcattaaacaagtactgctagacctaaaa
aactgagagagttagcaaaacaatcataatgggagattttagtacaatcatgacagtactaaacagatcttcgagacaaaaag
tcaacagataaacaatgcacttaaatgactcactggaacaaatggatgcagcagatatttacagaacattctatccaagatct
gcagaatatacattcttctaatcagcacatgcaacattctccaaggtagagcatatactaggccacaaaacaagtctcaataa
atttttaaaacaatgaaatcatatcaagtatcttctcagaccacagcagaataaaactaaaaatcatctcgctaaagaactgt
cgaaaatgaacaaatacatagaaattaagaaatttgcttctgaataatatctgggttaacagttacatcaagatgaaaatttta
aaaattatcttaattaaattataataatgagacaagttattgaaacctcaaaaataaaggaaaagcagtgataagaggaaagt
ttatagtgccagctgcctgcatcaaaaagtctgaaagagcacaaattcacaacctaatgtcacaccttgagaaattggagaaa
caagaacaaactaaacatagagccagaagaagaaaagaaataacaaagatcagagcagaactaaatgcaatccaaacaaaaaa
aagcaatgaaacaaacagttggttatttgaaaaaataaacaaattcatgggtcattagctagattaacaaagaaaagaatatc
aaagatccaaataagctcagaaatgaaacgagacattacaatctacaccactaatataaaaaataatttgagactactaagtt
caccttcatgtgcacaatgtagaagacttagaggaaatggaaaaatttctagaaacatacaacactcctagattaaataaaaa
agaaacagttactttgaatagacaaataacaaacagtgagattgaatcagtaattcaagaattgccaacaataacaacaatga
aatagggccaggtgaattcacagctgaattctatcaaaaaatttaaagaagaattgctgccaatttttgctgcaactatttttt
aaatttagataaaaaagaatcctccctaaattattctatgaagctagtataaccaagataccaaaaccaggaaaacacacaca
cacagacacacacacactctacagatgaatttccctgataaatatagatgcaaaaatagcaaaaaaaaaaatagctagttgag
ttcaacagcacatcaaaaagataattcctcatgatcaagcgtgtttcatctcagaattgcagggattatttgaacatactcaa
gtcaataaatgtaatacatcacataaacagaattacaaataaaaaccttacgattgtctcaatagatgcagaaaaagcattca
acaaaattcagcatttttaatgataaaaactgtaaataaatgaggcatagaagaaacctgcctcaaactaataaaagttaca
tatgaaaaatccacagctaatatcatgctgaatgtgaaaaagttaaaagcatttaccctgagaacacaaacaatacaaggatg
cccaagttcaccaattctattcaacatagttctggaagttctagccagagcaattagtcaggagaaaaaaaataagggtatcc
aaatttaaaaagagaacgtcagactatcactgtttacagatcaagggattatatatattaaaaccctagactcctccaaaata
ctaatagttttagtaaatgaattcagttaagtctcagattacaaaatacatgtacacaaattagtagcacggctatatatcaa
caacagcaatgctgagagttaaatcaagaactccatccctttacagaagctgcgaaaagatagtatatttaccaatatactt
aaccaaaagggtaaaagatctcaacaaggagaactacacaacactgctgaaagaaatcatagatgatacaaacaaatgcaaat
gcatcccctgatcatggattgcaagaatcgctattgtgaaaatgaccataatgcctaaagcaatctacagaatcaatgaaatt
cttattaaaatacccaacattatttttcttcagaattcaaaaataataacgctgaaatttatttgaaaccaaaaaaaagccaaaa
tacccaaagaaatcctaataagataaagaaaattggagccatcacattactgaacttcatattacaccacaaggctgcagtta
ccaaaacaacatggcactgacataatagtaggctcatagaccactggaacaaaatagagaacccagaaataaagccacatatg
taaatccaactgatgctttgcaaaatgtaccaaattttaaattgaaaaatagacaccacatttaacaaatggtacaagaaaaa
ctagcaagccacatgtaaaagaataaaactggatttctatctgtcaccatataaaagaccaactcaagatgaatcaggtactg
aaatataagacattaaactcaaaaattctagaaaacaatattggaaaaacacttttagacatcagggtaggcaaagaatttat
aactaagacccccaaaagcaaatgcagcaaaaacaaaactaaatttatggaacccatttaaactaaagtgtttcttcacagcac
aactaagagtcaatggagtaaaaagacaactcacagaacgggagaaaatatgtgcaaacttcacatctgacaaaaaattggta
tattcagaatctacaaaatactaaaacaagtcgccaagaaaaaacaaacgatcccatttgaaagtggacaagggacataaata
gatagttctcagaagaagatatacaaatggccaacaaacatatgaaaaactgtgtaacatcactaatcatcaggaaaatacaa
attaaaaccacaatctaataacacctaatcctgcaagaatggccactataaaaagtcaaaaaacaaaagggaatgcttataca
ctgttgatgaaaatgtaatttagtataaccactatggaaaacactattgagatttcttgaaaagcagaaaggtagatctacta
ttttttttttctttttgagatggagtctctctcagtcacccaggctggagtgcagtggtgcaatctcatctcattgcaacct
ccgcctcccgtgtcaagtgatgctcccacctcagcctccggagtatctgggattacaggcacccaccatcatgcctggctaat
tgtttttgaatttttgtagagaaggggtttccccatgttggccaggctggtctccaactcctgacctcagctgatcctcccc
gctcggcagcccaaattactgaaattacaggcgtgcagcatcacacctggccagatctactgtttgatccagcaatctcatta
ctggagagctacccaaaggaaataaagtcattatatgaaaaagacgtgtatatgtatgtttatagcagcagaattcaaaattg
aaaatatgtgaaaccaatttaaatgcccattggccaatgagttcagaaagaaaatgtgacatcgcctgtaatcccagcatttc
gggaggccgaagagggcggatcacgaggtcaggagatcgacaccatcctggccaacatggtgaaatccccgtctctactaaaaa
tacaaaaaatttgccggacctgttggcgtgcacctggagtcccagctactcgggaggctgaggcaggagaattgcttgaaccc
gggaggcagaggctgcagtgaaccgagattgcagcactgcactccagcctgggtgacagagcaagactctgcctcaaaaaaaa
aaaaaaaaaaagaaaagaaaagaaaaagaaaatttgacatatatacatcatggaatactaccaagccgttaaagggaatggca
taatgtcctttgcagcaacttggatgaagctggaggtaatgagtataagtgaagttacacaggagtagaaaagcaaaaactgt
gtttgcacacttacaagtgggagatgggctatgaacttgcaaaggcatacagagtgatataagggactttggagactcagaag
ggaaagaataggatggatactagagagaaaataactacactttaggtagagtgtacactattcaggtgatgaatgtactaaaa
tctcagaatttattgctatataattcctccatctaacaaaaaaatatttaccccaaagctattgaaattaaacaaaaatcaa

FIG. 7 (Cont. 4)

cctacaaaaataagcatcttctgtatacactaaaaaatgattattcaaaattaaaatcaagaaaataaatctaaatacaacag
cttaaaattcataaaataaatttttaccaaaataaatttaacaaggatacaaaatatctgcacattgaaaattataatatattg
attaaaatgtaagaaaacacaaataaatggaaggctatcttgtgttcttgtgttactggaacatacattgttaatatgtccat
cctaacctaagcatttacagattcaatgcaatcccattcaaaatttcaaagatatgcatttacataaattgaaaaaaaaaacc
tctctcatttgaatggctggggtgattgaccggactatcaatttgaaatcagactactactccacaatggaggtgagacaga
gtatgtctggaatacaggagatttcttaggacatctcttagtattactttgccatgggattaagatcaatgggaaaaaacaac
ctaattcaggcaggaatacaaatggcccagatacttcagaaataaaagtttgggtcttcacccagattaaaaatcctgaccag
ccaaggtacttgctgaaggcaaaacaaatacagaatgggtagtggaagaaggtagttgtcaataccaggaatgaccacacgac
cagaagtggggaccgtaattgtcgtgagtatctccttaagctgataagcaacttcagcaaagtctcaggatattttctccata
tcttgttaggaatatatttctgcatgtgtataactgtactaagaaaatatcttcattgtgccggacacggtggctcacacctg
taatcccagcaatttaggaagccaaggtgggtggattacctgaggtctagaggtcgagaccagcttgaccagtatggtgaaac
gccgtctctaccaaaaatacaaaaattagcctggcatggtggcaggtgcctgtaatcccaggcttctcagaaggctgagacag
gagaatagcttgaacccctgaacccgcgaggcagaggtggcagtgagccaagattgcaccactgcactccagcctgggcaacag
actgagactccatctaaaaaacaaacaaacaaacaaaaatatattaattgttttcattgaatttgttttcttttttatcatgtg
tcacaagatttattgacttcctatcagcatttaaatgttgttaactatatgtagtggtatgtatgtaggttaaggattagtgc
actttcagttgtatgaaggatagctgtattatgttaggcataattatgaccttattattgtctttatttggagttcaagcatg
attgcagctagatgtgtaggggtgctaagttgacaagaggtgggcttttgatgcttgatactaggtgtcaacttgattggatt
aaaggatgcctacgtggctgggaagtattgtttcttggtgtgtctctgggggtttgccagaggaggctgacatttgagtcaa
tggactggaaatttgagtttgtcatgttgcatgatccttttaaagtcttatagaacttagttgactattattttggtgtagtt
catttgtataaatatttctttgaagtttaattttcttcctttgcgtttgtctgtcactggcaacacggtaattgtagccttttt
agaaatagcttagaaggttggcgactcatcatttttttaaaaaagttagagaacagttggcatgacttttttaaattctgagag
ccatttttttatctaacatataggctatcatgaagaatatttatagtgtgcttgagaagcatgcgtattacactgcgcttggtt
ggaatgttctgtagatgtctattaggtcagtttgttcaatagtgttgtttaagtccatgggcttcctaagaatttttttatgg
gtgttctatacattattgagggtgaggtgttgaagtctcctcctttcttattgttttctatttctcacttcatatctcttaaa
ctcttgttaatgcggttatatttctatttttataactatgtaaaatagaaataaaataataattgcttagtaattttaatggg
aaaatcacatataataagaaattatatttttcccaaatgctgccatcaccactaaactcctccaggagtctcacatctgctctggg
ctctgctctctcctaaggggtcccacatcagagtttgctacagaggaggagacaagaaaatagggccctcctctcctgatga
aaaccagccctgccctgaccctgcaactctgggagaagatctctagtccagaattaccaggagtttggatttgatgatcagct
ctgtacaaacatggctcaccatagagttagggctgagctgggtttcccttgtcattatttaaaaggcgaataatggagaact
tgagatatggagtgtgagtggatatgagtgaaaaaacagtgattctgtgtggcaggttctgactcagatgtctctgtgcttgt
aggtgtctagtgtgggtgcagatggtggagtcttggggagagttggcacaagctgaatgtgcctgagactctgccgtgcatc
ctctgaatccaccttctgtagctactagatcagctgaatctgccaggctccaggaaaggggctgcagtgagtagtagatataa
tgtacgatggaagtcagacataatatgcagactctgtgaaggtcagattcaccatctccaaagacaatgccaagcacaggttg
tatctgcaaatgaacagtctgagagctgagaatatggctctgtattattgagtcaaaggtaccaaatgaagggacatcagtgt
gaacccagacacaaaatttcctgcagggaggagggaggaggctgggctgcagtgggcactcagcacacacaaaggcagggac
agttccaggggcaggtacaggtgcaggtgaaggcaaaggtctactttccttccagatctgtggattcctctgcatccaacagt
tcgcctgggcctctgtctttatggatctgcgcctaccactgatgtctctgggttagtaaagtttgctactataggaggaaaca
ttgtcatttgtcagaaaggcgaataatggagaacaaaagatattgagtgtgagtggatatgagtgaaaaaacagtgattatgt
gtggcaggttctgaccaaaatgtctctgtgtttgtaagtgtctagtgtgaggtgcaggtggtggagtgtaggggagaggcaag
aggcagaaaagcgcgcaggaggccgggtgaggctgtagacattgtcagctcactatgccaatctcacaacagtgctggagaag
gtgggagtctgatggagcttcccaacaaccctgtggtctaagctaagtccattaaggccgctggttcctcctggaacatagct
gtccatcaggaatcccccatgtgcccagcagcagccacgcgttagcatcttcactgtgcacagtcattgtttgggaggagctc
caggatgggtctctttgtcaaaaaccgggtgatggtgtcagagagctgtgccgggtgcctggtccaggggctccctgacgttg
gaggtataggaggtgcgttctcagggtgggaacacctttatggaaatgtacagaagaaaacatgattttccttggtcctctc
agatgacatggagaagaaagcgcgcagcttgcaaacaattgtaatgtccttgtaatttcctactttatcccaagttcattgat
tcttgtaaaccttggtttctgtccaagtacagagatattgattagagtgagtttggttctttccacacactaaccctcacctc
ccccagataaagagcacattgtccttactctgagtctgagggaggagctgttcctgtacaactaagggcctgcagagacccccc
atgtacagctttgcagagtcagatctttccacatgtgaggcgacctccacggcccatgattgctgctcaggtctaattgtgga
ttcaggattaggacatcctttaggctatcacaggtcaatcagattctgaaaaatcactgttatcatagacagaggtaataatt
caataccactcccctgacagcagattctctttcttatttggttgaaagtttgaagaaaataagtgaccatttattattctta
ttctaactttagtatccactatttgttctaggggattcacaaatttcaaaacactgagctcttcattctcatgaaaatgtgca
tatttgtgaatttcaacgtgttgttcagaacctgtgcatgccgacatctgtatttctcgtgcgttcttggcctggcgaagccc
tcacagaccctctccctcatctgtgctgtctctgcttctccatcacaaccagtgcttcctgctggagctggatccctcagctc
cccagggaagggactggagtgaatcaggtgcacaggtcatgagggagaacacaacgcaacccacgcctcaagagtccagtcac
catctccagatccacatccaaaacacagtttcttctacagctgagctacctgagcaacgagtacacaaccatgaatttttaca
caaaagatacagcaaggggaagtcattgtgagcccagaaacaaacctccctgcagggaagctcaggaactgcgggaggccctc
gggacaccaggggcgctcaggacacacatcaaggcaggtgcaagaggaaaaggtgctggagatggggtttggcatcatcatc
atatttcactgacacccgccactgtgtttattctcatgtacgtgattctttgtattattagaaaatggcgtttatgtaaataa
ataaccatatgtaggtgcatcaagtcgtcctctccctttttttttttttttttttggagtcctgctctgtcacccaggtt
ggagtgcagtggcgcgatctcggttcactccaacctccgcctcccgagttcaagcgattctcctgactcagcctcccgagtag
ctggaattacaggtgtgcaccaccgcgcccggctaagttttgtatttttagtagagacggatttcgccatattggccaggct
ggcctcaaactcatgatctcagttgatccgcccgccttggcctcccacagtgctgggattacaggtgtgagccaccgcgcccg
gcccgtcctctccatcttatgtggaacttttccattaagactctgagtccctggatttatttgagaacctcataaatcatggt
caattatgtctctttctcctctttctccctttcttcactcctctctagctcacaaactgaaacacacacagaattttctaactt
caattacctgatgtgttgaagacaattgattaaagcgcagcttttccagttcagccactgttcatattgttgtaagaataaga
acgttgtgtttctcagctgcgtgcttctctaagatgagtagcagctttttaaataatacccagaggctgaaagcaatctgaa

FIG. 7 (Cont. 5)

taccaatcatcagcttaatcagtaaacacaaggtggtaaatttcgctcactggaaaaacaccgattgttacaatcaggtaaggc
tggatactctcaacagcaagtgtaaatttcacaagtatatatgctgattaaaataagacaaacaaatacaagtacatacatact
gttccactttttacaaattctataaaatgaatgctaatctaaagttacataaagaaaaccagtagctgactctggacctggtgt
gaggagggaagggttaggaaccagaaattgtaggaaatgaagaagaaatgctgaaggtagtggagttttttctatgttgatga
aggtaatagttatgtcactattaatcaaatcgtacacattatgggatgcctattatttgtgaatttcaccctattaaaatatt
acaagttaaaacaagtataatttttgtagaaaattagttagacatagatgaataaaatgtatgataaataaaaaaagaaaatca
cagaacaatagcataaggacttcactcatcaaactgaagaaattttaaatttctcaacacagaattaaagatttaattagata
tacataagaaatcaaagactcctggatatacacacaaataaaccctaagtccacctgtatttttagggaaacgctagaataca
agaaaataatgtcatgatttcattacataacgggggttaatgaaaccacatcaggcatgtccagctgtgtcctgggggttggtt
cagggaacgggtgtgtcctgtggttaggagacgtggcaacaagctcacagcatcagttctagctgacaccataaaaaggccaa
gagatcacaattaaaatgtcatgcggatgtcacatctgtgggtgcggcacactccccatgtgaatacggaaaggttaactac
actcttcaggtgtctgctgagagtagagctgtctctcaggaatgtccaaaatggctcaatagagcaagaaaggagactggctc
agggttcctgtagtgccttggtggtgtgggcagagtgagggttctcactcaagaaaggagtttgtggcgtttgaacatctaca
tggcttcaaatagggtaactcctgtgattcctaactagattcacctcgtgtgggaaagaaaggagatgatgaaggaatgagcc
ttaagttatcagcagtcagacatcaaaacaatagtctgatgacttattctatgtagcacctataaaaatcgttccgggcgcgg
tggcccaaacctgtcatcccagccttttgggaggctgaggcgggtggatcatgaggtcaggagttcaagaccagcctgaccaa
tatggtgaaaccccgtctctactaaaaatatttaagaaaaaaaatagttgggttatggtggtgggcgcctgtaatcccagcta
ctcaggaggctgaggcaggagaatagcttgatcccaggggggcgtaggttgtagtgagctgagatcacaccactgcactgcagc
ctgggtgacagagcaagactccgtctcaaaaaaaaaaaaagagtaaaaaaatatcagcccaagatgggtggacaacaaccagg
cctacaaaaaaggagaagactccttataagaataagcaaatcataatgaaaattaggaggaaaacaaggagagtgaggtgaaa
ggcatggggcaggggattagacaagggtcctgttccaatgtcttgtgtggagacttttcactatctaaaatcatccacctatt
ctgaatgtcttaggtgaactgtctgctccaaaacatcagaaccaccagaggatttttgaggatactcagtttaatatcttata
tttgaggtgccttacaactgtgtaaaatgcttagttattatcagtgtaattagagatagggcctcactgtgtcacacaggttg
gggttcagtggcacaatcatagctcactgttaccttgaacttctggcccacataatccttctgtctcagcctcctgagtagca
tggactagagaggtgcaccaccacacacagctgatttaaaaaaaattgtttcatagaaatggggtctctctatgttgcccagg
ctggtcttgaactcctggtctcacgtgattcccccctggttttgtttctcaaagtggtggaattaaaggcatgagccaccgtat
ctgctcagaaatgattatttgttgcaaaatactaacccaagaattgactccctgaattttctctgcagcattttggttaata
gtgtctgataagatttatttcaatagtttcaacagcagagtgttctcctgatgtttcctccaatagtgataatttcatggttg
aagatcacaaactactattaaaagatgacataaaaaggcaaccttaaacttttggtgatggagtgagtataataaaaaattac
tttcaatattgtgtaacacacgcctgcagtaggaggaaggtgagcaatgagggtaaaatttctaaacgtatgaatcttccagc
tccccagtcatagggcagtaactgatgagtcctgagagagggaacgtaatgccgtagtgcttgtgggataactcttggccaag
agagtttccatattttattaaagtggttataatttttaaatttaaagatgccatttttttcaacatatccagaatattgtgagc
gggattgattctgtatgatacgagcaatggcgatgccttctgtttggataatattacaaaccaggttaagactgagtggtgta
acgatgcaccagaacattatctagcttccatactagattttgtttttctctttgtttgcattagtttcaaatttatatgtaa
ggtctctagaatgtaggagtttatttgaaagtgtcttttcttgttggccattttgatggggcttccaggagatttaaaaacct
cctctgcctgcagcacagtttaaaattctgcgttacagtagaacatctgtatttaatcctggtctttggttgattgacaagct
ctaatacatgcaataacttctgccttctgggctggttttacatcaggtagaggaatatatactaagtgaaaatttgcactagt
aatatatattattaataaccaccacttgtattatttaagtgttattaatcaagaattaatgttaaatcaagggtctcaatggc
aatattacctaagggatatacaagatattttgctaatctaggtaaaatagatgtgaacacactcttagtatccagccatgtct
cctgtctatcacattattaaccacacagtaaattcacttgggacttgttctaattatctaattagtcacttacttatctcaaa
gcctctggattattatgtgtgactattttagcagagagtgaagaaagacaacccaggctgaccaaacaatgaggaaaatcaca
acctgatgaaaccagaaacctggatgtgagtggctccaggattgaataatttgacagctcatgtgcccaggctgtttcttgtc
tcagttttccacactgatacatccagaaaggcagcttcacccccagaggactcccatcatgctgtgacatggtgacaacatt
cccaaagctcacacacatatgttaaatattggctggaaaaggggcagagacatttctggaattctcttctgaaggaccatgaa
tgcctcaaccaaccatctcccctgcctccatgactagaaatgcaccacgtgcccacacggatattcatcctcatggggataa
gactccattgatgaggctgactattttatcatataaaattactaaagactgatttaagggtttcaaaaactaattgaactctg
ttgttctatgtccaccagagattacaaatcttccaatgatgccttctttgttttttgtctgcttgactttgtctcttcaactt
gttctgtaccccagagaatctctttcagctccctcaggtgcattcaattgttttatttaactgacaatttctaaatcagttaa
agacattacgctaaagactccatattcctaggtccatattcctttttccatattcctaggaaggcattgtgacccagagtctg
ggcatgaccttgtgagtgttcctgacccctcctccatatgagatgctggtctgggtgttcttgccccttccctggggtagagt
cctcctgttttccccaggtgctccctcccacagctctagtgttctcaatcagtgtcatcaccttccagatcttctgccctgcc
ctgcagactaaggctctgattccataagcaagatagggagctgctcctcaatagatctttggtgaggatctctgttcccatc
tcaattcctgtagggtggaaccagtgttcctaggattctggtttcagtagcttgtccctgcagagtaaattcttagttctgta
gggggattaagggagttgggtctgaatacattttagatgtcgaggatcttgttctctcccagaaagacacttcgggaaagtaa
gactttggtaactgtccccttcttggggaaagggattcaagaggataggttgcttttgggcatgtggtcccttaaaatttca
cactaaaaagcgtttcccacactcaatttcaagcagcccaatatatatttgtatttttttcttggaacagacaatattttatat
tccagactctgccttaggtaatttcaaaccctggctttgttactctctacaagaaattgcttctccataagcttcagatttgt
tgtgtgttttgaaattttatcagaaatattaaagaaaattggcaaaattccatcctccatgtttatctgttattgttgatgca
gttgtaaaaaataagaaaaatatattccttttttctgtacatttccaagcttagtagcaaatttttagtaacacccagaataa
taaaaaattcaaatattgtttagctgcttaataggaaaacaaattatagtaaatttgtttgctagaatgctacccagcattta
taataagtaaacatttgatatacccaactacaaggtaaaatatccatttatgctaactaaaataagccaaacaaatgagaata
tatactgttatttcatttttataaattctgaaaaattaaaatgaatttgcagcaatgtaaagatcagtagttgccagggaaat
ggtagaagaaagaaaggaaaaggagaaagaatacagaagaacaaaaggaaatgttaagaattctcttgtccaacttgataagg
atgacggttacatcatttttatcaactgtaatctttaaatatgtgaaagtttattatctgtaaactaaacgttataaacttta
ttacaagcaaaaattgaaagttagacaagaaggagtgatagaaagagaaaatgtatattaaatttcagaaatatttaagaatg
tatctgcctgaaccctagttctcaccatatctttaggtgaatgctaaaatgcagcaaaatcacgcatgttctcactacagaaa

FIG. 7 (Cont. 6)

gtgggttctacaaaccacactcggcacatttagctttgtcctggagttggtgcagggagttattggggccagtgatgaggagc
acaggccaagataccagcgattacttatcccaaacatgagctctaacatacacacttagtccctttccgtgtgtggtttact
tccacatctgtacatggagagaccactgactgacaaaatataatttatacaaatatgtaaaattaaatagggtgatcagttca
aggtgtttatcacagcataatttttacaataagacagcatatttcccaaataccatcattgtcaccaaactccttcaaggcaca
gtcatcttatctgggccccgtcctctcctcaggtgtcccaccccagagcttggtatatagtaggagacatgcaaataaggccc
tccctctgctgatgaaaatgagcccagccctgaccctgcagctctgggagaggagccccagccgtgagattcccaggagtttc
cacttggtgatcagcactgaacacagaccaccaaccatggagtttgggcttagctgggttttccttgttgctattttaaaagg
taattcatggtgtactagagatactgagtgtgaggggacatgagtggtagaaacagtggatatgtgtggcagtttctgacctt
ggtgttttctgtgtttgcaggtgtccaatgtgaggtgcagctggtggagtctgggggaggcttggtacagccagggcggtccct
gagactctcctgtcagcttctggattcaccttggtgattatgctatgagctggttccgccaggctccagggaaggggctgg
agtgggtaggtttcattagaagcaaagcttatggtgggacaacagaatacgccgcgtctgtgaaaggcagattcaccatctca
agagatgattccaaaagcatcgcctatctgcaaatgaacagcctgaaaaccgaggacacagccgtgtattactgtactagaga
cacagtgaggggaggtcaatgtgagcccagacacaaacctccctgcaggggcgcacagagccaccaggggcgctagggaccg
cctgagtacgggacaggtcccaggagcaggtgcaggggaggtttccttttccttggctggaaaagtcacctttatcttccc
agggctcgagccttctaggctgtgatattttattacttgtatttactgttcatttattatcattagtttttaaattttggtaa
tttttacaactctatggatatatttttaagtgtatactttcaagaaataaacattcctaattatttgcactgattctcccaga
gttttattaacatttgttgacatcagcaactacatagctatagggacaaacacttttaacgatagacagttgtttaggcctga
aaccccgtttatactaaaaatttacaaaaattagcctggcgtggtgaagggcgcctgtaatcccagctactcgggaggctgag
caaggagaattgcttgaatccgggaagcggaagtcacagtgagtggagtggactgccactacactccagcctggcgacagagc
gagactttgtatgaaagaaagaaaagaaaaggaagaaaggaagaaaggaaggaaggaaggaaggaaggaaggaaggaaggaag
gaaggaaggaaggaaaagagagaaagagagaggaaggaaggaaggaaggaaggaaggaaggaaggaaggaaaagagaga
aagaaagagagaggaaggaaggaaggaagaaaggaaggaaggaaagaaaagaaggaaagaaagaaaaaagatatataaacacgc
agacctatgcatataaccatagggatttatattaaacattacaataaaataattctaaaaatgtgtcctaaggaatcaaacat
aatgatgaagtaaatataaatgttagagtaatttataattgatttgttatttttaatcgtttacatgaatttatttctatttg
ttcatttaaaagtagtatattggtcatttcaagagagctaacagtaaatttcagatgttgttgttacgatatatgataagaat
ttgaggtggtgaatgataattatcttatttctcaattatcttagttattccatattgtattcacaaatcataacattgcttct
taccttataaatataaacaaccataatttgtgaaattacaatattttctttatttaatttttaatttatcccagatcatt
atctttttcttcgcttccagatctcactggatcatctcgagggcccatcctcacccctgtctcccgaagacttctggagaggc
tgcaggacgggcagaaggaggagccccgtgtgagtccacacgacctggagcctccctctccttggattaggccatctcctcgg
gatcacagggctcttcattatccttaccccgctgttgtaccaaacaagcaacatcacacttcaattcatcagggtttgcttta
attttctaaatcatcgtgaaggtgataatttaacagtaacgtatcacaaccaaataggataagccctttccatggaacagg
gtttcttatcaggatatacatgtattatggattctcaatttatttgtagatgagatgctattatctccatattgtagatgatt
ctgctaagtcatctcttaaaattaatttttccaaagactcaaacaaataaatgatataattacaaatttcaggtgtaatagct
gagccaacattgagattatattaacatttagaacatgaacttgcaaatattgttattttcctgtcggctgtccccaattgtga
ttttatacagaatattagaaatttatcctgataaatcaggttaaaatattatatcactagtttattaacttttataactaata
atataaaatgttccacatatttttagccatgttttacttacccgtgatatgtgtatttattaatttttcatttttaagatgcc
acctttatctttcttatttctgggattttattctagtagatagagctgaatgcatttttaataattatcataataatcacattt
acattttgcattttaattttcatatacatttttattaatattttaatttcaatataaaatattttcctacaaatgtcaatttttt
gatttttatgagataaaattaacctatacaaaatacatatattttcaatgtacagtttgagggtttctggcaaatgtgcacac
atttgtctccagcatctaagttatgatgaggagcaggtccatctccacaacaagtgtcctcttcggtgcttccagtcagctct
cacataaggaatttttttttcaaatttaatatagatacagagggtaaatgtttggatttgtcacgggggattattgagtgatgc
tgaggtttggaatacagattcccaccgacctctccctcccactctccagcagtccacagtgtctatcattctcataattatgt
ccatgtgtgctcaatgctgaggtcttacttaggagaatatgtggtattcagttttctgctcctacattaatttgtttaggatt
aagggccccagcttctttcatttttactgcaaaggacatgatttcattctttttcatggctgtgtagtattatacattgtagat
gtaccgcattttgtatattcagtctaccaatgatgtgcatctggtttgatctatgtcgttgccactgtgaatagcacagcaat
gaacatagatgtggatgtgtctttttggtagaattatttgcttacttttcagtgtatacccccgtggtgggattgctgtgtaaa
atgatatctctgttttaagttctttgagaaatctccagtctgatttccaaagtggaaacaccaatttatattcccctcatcag
tgtatgtgttctctttttctccacagtcccagcagcatccattgtttttgacttttagtgataaccattctgagtggtgcgt
ggctgcacacctacagtcatctcatctttgataaggctgatgaaaacaagcaatgaggaagggactccctgttcaataaatgg
tgctgggacaactggctaggcatatgatgaagattgaagctggatatctactttcaacatgtataaaattaacacaaaattca
ttaaagttttaaatgtaagacctcaaaccataaaaatccttgaagacaacctaggaaatactcttcttgacatcaggtttgac
aaaaaaatgttggctgagtatccaaaaccaattgcaacaaaaagaaaaatagacaagtggggcctaattaactgaggagctcc
tgctcagcaaaacaaacaaagaagcaaacaaaactaacagcacagtactcagacaacctacagaatgtggaaagatattcaca
aacgttccatccaacaaagccgtaatatccagaatctatagggaaattaaacaaatcaagaagcaaaaaataataataataat
aaccccattaaaaatgggctgatatggtttgctgtgtcccaccaaatatcaacttgaattgtatctcccagaattcccatg
tgttgtgagacggacccagggggaggtaattgaaccatgggggcctgtctttcccgtgctattctcttggtagtgaataagtc
tcaccagatctaatgagacttatcagggtttatctgatgggtttatcagggtttccgcttttgcttcttcctcttttttctc
ttgccatcaccaggtaaggagtgccttttacctgccaccgtgttttggaggccttcacagccatgtggaactgtaattccaat
taaacctcttttttgttcccagttttgggtgtgtctttgttagcagtttgaaaatggactaatgcgtgggcaaatgacacagac
acttctcaaaggaatacatacaagtgaccagcaaatatatttttaaaatgtttaacatcactaatcatcagagaaatgtaaat
agaaaaatgttctgatttctgtcactataggtccatttttcttgttttgaatttcatatacatggaataaaatattatagctca
tttttgtaagaagcttttactatctgtgaggttcattcatgtgatagcatctatcaaggttttgtcaacatatgtataaatat
gtatgtactcatacacatatagatatttcatatctgaatcagtccattgcattaataaatgacagattattaaataaatcagt
tcattaagtgaataagtgacaatatgtatatctatttttcctgttgatggaatttaaatttgtttccaatataaatatcataaa
caaaactgtcatacatatctttgtacaagttcttctgtttatattcacatatttttattgataaaatatgttgaaatataagt
atgcattatacctttcagctttatggagctatcactgacaaataaaatttttctgtatttaaggtacaccaattgatgtattg

FIG. 7 (Cont. 7)

atattcttggggaaatgctcataatgatcaaggtaattggcatgcctatcatctcagagagttaacattttatgcctttaatt
tattgtgtatgtgtgatgaaatcacctaatatctacttgtctggcaaaagatatgtttataatgcaacattcattagtatagt
cacattgctgtaggtttgatctccagaactatttcaacctgtgtattagtccattctcaccctaatgtaaggaactacctgag
actgggaaatttatggagaaaagtggtttagttgactcacagttctgcaggcttaacagcaagtattactaggaggtatcagg
aaacttacagtcatcacagaaagtgaaggggaagcaaggaccgcttcacatgctggcaggagagagagaaagagcaaggggag
atgcaccaccctttaaaccttgagatcttgtgagaactctgtcacaagaacagcaaaagggaagaccgcccgcatgatccaa
tcactccccatcagacacctgctacaacacttggggattaaaatttgacatgagatgtgggtgaaaacacagagccaaaccat
atcattccacccatggtctatcagaaatctcatgtccttctcacattgcaaaatatcattatgccttctcaacagtcttccag
gcttaactcatttcagcattatcacaaaaatctatagtctaaagtcacctctgagacaaggtaaatttcttcccccctataaac
ctgtaaaattaaaaagaagttagttatttccaagacacaatggagatgcatgtactgggtaaatgctcccattccaaatgggt
gtcattggccacagaaaaggggctacaggccccatgcaagtccaaacaccagtagggcagccattaaatgttaaagctacagc
ataatttccttttacccccaagtctcacatccaggacacactgatacaagggttgggctcccaaggccttaggaagctccaccc
tgtggctcaacgtggtacagtccccatgactgctttgataagctggcattgagtttctatggctttacaggcacaccatgcaa
gctgttggtggatctaccattccggggtctggaggaaggtgcccctcttctcacagatccactaggcatctagtgcctagtgc
ccagtgggtactctgtgtgggagatccaacaccacattttccttccacactggcctagtagaggtactccattagggctcagc
cctgcataagacttctgcctgaatacccagacattttcatacgtcatctgaaatctaagaggaagctcccaaacctcaactct
tgccttatgtgcacccgcagactcaacaccacgtggaagcaaccaaagcttagggcttgcaccctctgaagcaatggcctgag
ctggaccttggccccttagccatggctggcaggagagggacagggatgtcccaaggctgcacagagcagtcgggtcctgggc
ccggaccatgaaaccatttttctctactgggcttctgggcctgtgacgggagggaccgcagcaaagatctctgaaatgctctc
aagatgtttttcccatcgggttcctcattacttatgcaaatttctgcagcccgcttgaatttcttcccaggaaatggattctt
cttgtctaccacatggtcaggctgcaatttttttcaaccttttatgatctgcttccctttaaacataagttcaaatttcaga
ccatctcttaatgaatgcatatgacttacattttcagaaacagccagggcaaacattgaatgctttgctacttagaaatttttt
tctgctagataccttaagtcatctctccctagttcaacattgcacagatctctagggcaggggcaaaatgccactagtccttt
tgctaaagcatagcaagtgtgagctttactccagttcacaagaagttcttcatcttagcatctgagaccacctcagcctggac
tttattgtccatatcactatctgcattttgttcaaaaccattcagtaagcctctagaaagtttcaaacttttccacagcttcc
tgtcttcttgtgagccctccaagctttaccagcctctgtccattacccagttacaaagtcacttccacagttttaggtatctt
aatagcagtgcccactcctagtgcaaattttctgtattagttgattctcacactgctgtaaagaactacctgagactgggtaa
tttatgaagaaaagagtttagtagactcacagttcttcaggctaaacaggaagcattactgggaggcatcaggacacacaatg
atggccgaaggtgaaggggattcaaaaatcttctttgcaagatggcaggagagagacagcaagggagacgggaggtgccacac
ttttaaaccatcagatctcttgagaacttttatcaggagaacagcaaagaggaaggccacccccattacccaatcacttttatatt
aggcccttccttcaacatgtagggattacaatttggcatgagatttgagtgggaacacagagccaaactgtatcaacctgcat
aactgaaagttataacctctgaccaacatcacccaatttttttcctcctcccagccccctgggaactactattctactttgcttc
caagaacatgaatattttagattctacatataaatgtgttcatgcaacatttgactctctgtgtctcactccacttagcaaag
tgtcctctatgtgttgtaaatgttagaatttcctcgtttttaaaggcagaataatattcacttttaggtaggaataagccaca
ttttatctgttgattcatagatggacattgacctatttttctatatctaggctattatgaataatctcacaataaacatatatt
tgtcacactcactttatttttctctagatgtatactcagaagtgggtatattctatgttcaattcattgagtaatcttcatgct
gtttttttcataatggctgtactaatttgcattttgttccaaaccatacatggataactttgtaccacatattcaggtctttgt
ttaagtcttaaatccatttttagctgatttatatgtattgtgtgagataaggtcaatttttttttcttccgcatatggatgccc
agttttcacagcacttgttgaagagactgtttcttctctattgtgtgttcttggcagttcatcaaagatcagtttattgggaa
gaaattggtggacttccagattgtctgtaatgttctgttggattctatgtctgtttaaatgtcagcattatactgttttgatt
tacatagatttgattttgaaattatagaatatgatatattcagttatattttacccaaaattattttggctatttaaagcttt
tgtatttttacataaattggagaacttttttaatatttttgtaaaaccatgccatggagattatatatttatttttataggcata
taatagatatacctaatttatgggaacatgtaatatattgatgcatttataaacgtgtaaagatcagatcaggattggtatat
ctatcacattaaacgtgtatattttctttatgctaggcacatttgaacgactctcttctggccattttaacgtatacattaga
ttatcgttaactatagtcaccttactcatctgtcaaacatttaggttgtatttctcctatataactgtatatctgtcttcagt
aatcatcttctctttatcctcttctctcttgtatccaaccaggcttctggtaaacaacaatctactctctgtcttcaggaaat
ccaatgttttagttgtgacataaaagtaagaagatgcaatatttgtctttctgtgtttggtttatttaacttaacattatggc
ttccacttccattcatattgttgcaaatgacaagatatcaacatttatggctgaataatattctattgcctacatcgattata
tttttatatccatttctccacctacagacactgaggttgctttcatatctgggctattgtgaatagagctgcaagaacttgga
gtgcacatgcctttatgaggcagtgattttatcttctttagaacatactcagaataggatttgctgagtcatcagttatttct
atttttctttttatttggagtcttcatacaacttgcacaatagtggaaatacaaacggaaaaaccattataaaaagcagttt
cagttttgaggtatgatccaaaaacacacaacatttcatcatgattctcattgggagtctctaatgaatctggtggaaaggca
ggaagttttctaaccttgttaagaaaattatgagtttgcaccttttttcttttgaggctggaaattggcatgattcaagatgc
gtaatgttagcaggtttcagaatgatacagcgaaaatcataatgagaaggcaagagagagaataagagaaagacaggaaaaca
aagaaacaaataaatttcacaagagaagaaactgctggatgtcagtgttgggttttgttcctagacatatctgtactgagtga
gaaaccatgaagccaagggaagagtctagaacttgttcaagtgaagcatcagcatatttctccaaggcacctattgtcacccc
atcacaagggtgatgagtttttgaataccattaaatatgagttcctagtaagtaatcatgtttccatgaaattcagttaaaat
gcaaagggtgtgtccagatcactcacgcacaaaaatacaaaatttgcctttgcatttatggctgcatagaggtaaagtccatt
gagacttcagcaggttacagagatctgttaagttttggattcccataggagagtgcctcttagtgaaggttggactattaatt
aagtatgtacaaattccctctatgggagtagtgttccatttgtgtggaatttttaattccttattgaattgcaaaacaaatcc
caaggactgactccatggagttttactgtagtgttcataaaaatatttaataagattccttccagtgtttcaaggaaagtttt
tctctaaaatttttttctaatacataaatttttcctgcctaaaattgaaacaggctgttgttaaaaagacatactggaatggcag
ctttaatctattggtgataggaatgagcataatacatgaatctctttgagtgttctgcctcatccaaatactgtatggcaaag
gctagtactggaggtaaaatctctaaatgtatttgttccagccatcaagtcatggggcaataacagatacatccttgaggcag
aggaccataatgccacagtgctagtaggagtacatgtcgccaagggagttcaagggttccttaaaattgtgataatttttaatg
taagaacaccttattagagacagggtttcagcatgttgaccaggcttggtctagaactcttgacctcttgatctgcccgcctt

FIG. 7 (Cont. 8)

ggcctcccaaactgctgatattacaggagtgagtcactgtgtctagccagtccatttatttttcttctgcacatggatacccat
aaacttatgtggaagattgtgggaggttataacagtgtcatactttagtatcagccatacctcacagaatcattttataatag
ttcctttcatgggtgtacttcactcagttcatgcaaaacctggcaggtgacaggctaaaaacacaaaataccgaagcgtttaa
ccaactgaaagggctgtagccttttgtcaatgaattatttcaagacacggagaacacatatagattataaataaaatactttc
acatccccttaaaggtggaaattgaggaaattttacctaaatgtgtccaaagggccctgtggcttggtttctgtctaggtccc
aatgatagggttctcccaggattttgtggctgtcttgttacacttcatcaagaattaacctctgctgtttcctcaaagtgttt
aattggataatgaatttgtctataaattgaagagttgaaatacatcaaatattaatttgtaataatctggcacaaattatcta
agcaaattcaataactagatgttttttcatttatttttatttaaaatcaggatctaagcactgatatgctttaataacatctg
tgacccttctcagcagttttctcttctgagtatatgatctgctgtggcagttttcttagcttcaatgttacctcttttggcaat
gactaccgtctttatatttgccaggaatctgggataaaggagtgcttctaagagttccctaacttgcccattttggtgggtgt
tccagaacatatgagatgctctgttgttaacaaagcatcccaaagccatgcactgccctaaaatgtgtttgtttcctagtttg
acaaattggaagttctaataaatacaatcacttctgccatctgggctgattttacatcagatagagggctgtattccaaagaa
aagcttacattagtaatagcaattctagtcagaaacctagagttttatcattgaggtgcaattcataacaaataatattaggt
cgaggttctcagtggcagtgtctaaatctcttaggtgtacagggtcttccctgttaacatgaagcatttataagcacagtcat
agtttccagctatgcttctccctgtctcattatcaccacaaactatggcctcacctggaacttgggttaatttccaaataagt
aatttttagtgtttatgcctctagattattatgtgagaaagttaacattcagtagaaagttaaaaagaacatttgaactgac
taaacaacacagacaatcaagaataaaattcaaagcctagatgtgagaggctccaggcctggataatgcaatagttcatgtat
gcaggcagtttctttgcccagttctacactgatacacccagaatgtcagcttcatgccagatttgactcctattatgtagaga
catggcaatacattctcaagggtcacatgaaataatatgaaaattggtgggaataggggaggagacaactctgcaattctcat
ctgaaggaccaggaaagcctggacagaccatctccccagcctccgtgactgcaccacgtgcccacatggacactcatccctga
tagggtaagaagactccattgatgggctgagcattttatgatagaaattactagagactgacgtggaggtttcaacaactaa
tatttataaccaaaatttaattacccccacattgttaccattttcttcagtgaaaaattgcttgccatgattaagttttaagt
agatttccaatgttcacaactgagcttccaagagagtcttgagaacaaaaacaatgagggcagagaaatctacctttttctgta
ttcaccactaaactcaagtggactcagcactgcctttgatcactgctacttctctgcagagttcaggtttctacttctcacaa
ttctgacacacattctacctctcctcaaatgtttggcctctgcttcttgtaaggtcaccctctgttcttaacttcttctctga
gtcattttgtgaggtggtcatgagccattaaatggatattttatattttcccaacatgaatcacatgagtggtcatgaattat
acttctgattatggcagttgatttttcttggcatgttcatgactagtaatatttgaagccatttcattcaaatcttcggggct
tcgttttgttgctatgacatttttttcttctattgagtctttccactagtattataacatgacctagtatccaggctcagttg
tcattaataataaccacatatgtcaaaaatcatgcattcttttcacagcagacataatttcctctttctgcagatgaagaca
cactgctgagctacccccacttacaagaatatatgcacaattatgatatcttcatttatttgactaataagctatatcattct
ccttcaaattctttacccccagaagtcctggacaaatttctgcatctgctcaaacgataaactcagaactacatggtgagt
aaaagtcacctggttctggatattgggtccatctcttcccctccaatgtcccagagcacctcagcacacctgtccaggttcta
tcaagaaagagtagctcctgcacactgaaggaaacaattgagttaagagaggacctgcagatgatagacaatattgaaaacta
ttaatatgacaaaggattactaccaagcatgtgaaataagctcaacgggtgcggtggttcatgtctgtagtaccagcaatttg
ggaggcaagttgcgcagatcacctgaggttaggagctcgacaccagcctgaccaacataaagaacaccctgtctctactaaaa
gtacaaaattagccgggcatggtggcatgcgcctgtaatcccagctactcgggaggctgaggcaggagcatcacttgaacctg
ggaagtggaggttgcggtgagctgagatggcaccattgcactccagcctgggcaacaagagggaaactccatctcaaaaaaaa
aattacaaaaaattagctgagcgtggtggtgggcgcctgtatacccagctgctagggagactgaggcaggagaatggcttgaa
cccaggaggtgaaggttgcagtgagctgagattgcgccattgcactccatcctgggcaacaagagtgaaactccatctcaaaa
aaaaaaaaagagacttgcaaagggcaaatagatcatagacagacagatagatagatagacctattagtatacatacatacata
tatatacactaatattcaggaaaatgcaaattcataatgagatgtcttttcaccttcatctctgctagaaagtttgttatct
gaaaaacaaatacatacatacatacttattaaaagctggccaggatgcctagaaagtaaaactcatagaccactggtggaaat
gtaaattagtgcagccatcaagggaaaaaaatagaactaccatatattccagcaatccaactgctaagtatatatctatttaa
atatttaaaagaaaaaactaatattgaagagatacctgtacacccatgtttattgcagcactaatcacaatttctaagatatg
aaatcaacatatgtgtccatcaacagatgaatggatacataaaatgtgatatatttacacaatggaatattattcagccttaa
caatgaaattctgccgtttgaagcaacatggatggaatgggacaccactatgttgagtgaaatgagtcagacacagaaaaata
aataccgcatttctcagcgttacttctagaagtaaatagtagagtagtggtgatgagatgccaggaatgagagaaggctgaga
taagaagaggtttgttaacaaacacacaattacaggtagacaggagggatgtgctctagtgttctacagcacagtagggtgac
tacagttaacaatatattgtacgttttctgtttacaagaagccagaagagagaatttttctatgctaccaacacaaataaatgt
tagtgtctgaactgacgaatttgctcattgttctgattttggtcataccaagtggcacacatgtattcaaatatcacactgta
tcccataaacataagcagttattatgtgccaaatttgaaaaatcctttaattaaaaagaattatattggcgtacattacaaat
gattcaacacagagacaggaataaataccatttttctttgaaatagttaattaactaacaatgtagttacattcatttgcacc
aaatcgtgtatttgataatggtatgcatagacagatttatgcataggataatatcttttaattttagactactacttaatact
ataaatataaataatttttaaaacaactaagtaaaaagaataaagctgagaaaatgtgtgtgtggtgtgtgatgtgtgagcttt
ttcttgtgcaccactgtgtccttggtggatgtgtggttcatgtgtttgttttttatttactctgtttggggttctctttgcttc
taggatctgtagttcagtttctttcacaaaattgggaacattcttcgctattatctttttcaaatagtttctgtgtatttata
atttctccttctcagatttaaaatatacacatactataattttgatattaatgtttagtttctttcttcactctcttttcgtt
tgcaatttacttttgtgaaatttctagtgacatactaatcacatggttttattgaaaagctgagccagctctactgaggtgtgt
gccaaaagattgctcgatgtttatacagcattgcttttgatttcttatgcatttccatttgatttattcttagtattttcata
tttcagttccctatctatgtccacgatttctttaagagattcttgcgtgtgaattatagttactttacatatcttgtttaatt
agatatttataatatctgtttcatctacaaatctcatgctgatcatttgtttattacaacttttggtacttctcattaatgtat
gtaataattgttgatagccacagatactgggatggacagtggatactggccttattatttcatttttatgcatttctgcctgta
tttgaccacactttacctttgccaggcctttactgtggaagtatctgtgaatcttctcagaactatatttgacattcacttttt
gcagtggacatcaaagttgaagtctgttcttctgtgtccaccagagacttcagttcctccagtgataccttgtttttctttcc
tgcttggctttgtctcttcacctgttcctcctccagagaatcatgttcagctccctcaggtggattaaaatgttatttaact
gacaattgtgaaattggtggaaagcaatagaataaagggagattttctgaccttttcttgggttcatattgtgaacatgagtct

FIG. 7 (Cont. 9)

gggtgtgaccttcccaatgtttctgaacttcctccagatgagatgttggtctgtgtgttcttgctcttttccctgctgtggag
tcctcttgttttccccagttgttccctcccgcagctccaatgttctctttttgtgttatcaccttacagatttgctgactaga
actgcagattaaggctctgattaaataagaaggaggggagatacttctcaatggaacttaggtgaagacctcttttcccatct
cagttcctaagggattgcccagtgccctaagatactggtttggtggcttgcccctccagaataattctttgttctccagtggg
gatatggaaggtgggtctgaacacttttcagaagggtgggcacttttttctctcctagacagacacaatgggacagaacaattt
tggtgactgtccccatttttggggaaaaaggattcaataggataggaaaactcttcagtctgtggtcccttagaaattcaccct
acaacacatttaccacacttgacttcaagaaatccaatatatatgtgtgttttcatcttgtaatagcctacattttacatgcc
atactctgcctcagttcagctcataccccagctttgttactctttacaagaacttgcctctccctagatttcacatttgctgt
ttatcttaaaacttcaagtatctaaagtattatttttaaaaaatggccagttgtggtggctcacacctgtaatcccaacgctt
tgggaggctgaggtatgtggatcacctgaggtcaggagtttgagaccaccctggccaacatggtaaaacctgtctctactaaa
aatacaaaaaaaaaaaaaatagcttggcatggtggcaggcacctgtaatcccagctactcgggaggctgatactggagaatagc
ttgaacccacgaggcagagtttgcaagtcgtaccattgcactccagcctgggcgacagagtgagactctgtctcaaaaaaaaa
aattccaaaattccagctcctctgtttatctatttttgttgatactgttgttgtaaaacataagtaaaatatattattcatct
atgtacatttccaagctgtgtagaagaatttttaataagacccagagtaaaaaaagaatgcaaatatgtaggggccagcccta
cagggtctgtggatctttctccccatgtgcagagatgagagatcatagaaataaaggcacaagacaaagagatagaagaaaaa
acagccgggcccaggggaccactaccaccaagacacagactagaagtggccccaaatgcctggctctgctgttatttattgga
tacaaggcaaaaggggaagggtaaggagtgtgagtcatctgcaatgattgataaggtcatgtgggtcacgtgtccaccagaca
gagggcacttccctgtttggcagccgaggcggagagagagagaggacagcttaggtcattatttcttccattctcttctcaga
aagatcaaagactttaatactttcactaattctgctactgctatctagagggcggagcaggtgtacagagtggaacatgaaag
tgaaacaggagtgtgaccgctgaagcacagcatcacagagagacgtttaggcctctggagggctgcgggcaggtttgactgat
gtcaggccttccacaagaggtggtggagcagagtcttctctaactcccccggggaaagggagactcccttttccaggtcttcta
agtaatgggtgccttcccaggcactggcgctaccactagactgaggagccctctagtggccctgtccgggcgtgacagaggct
cacactcctgtcttctggtcacttctcaccgtgtcccttcagctcctattgctgtatggcctggtttttcctaggttataatt
gtagagcaaggattattataatgttggaataaagagtaatgctacagactgatgattaatgatattcatatataaacatatct
ataacctattactagtacaactattcttatttttacatattctcttcattacactagaacagcttgtgccctcagtctcttgcc
tcagcacctgggtggcttgccgcccagacaaatattgttaagcttcttaatagaaaaacaaattatggtaaatgtgttcactg
gaatactacccgtcatttataataaattaatgcctgatacacagagcaacaaggtaaaatatctaagtatttatgttgagtaa
aataagctaaacaaataagaatatatactatgtaatttcatttttataaattctgataaataaaaatgcatctgaagtaaaat
aatgaagataagtagttgcctggggaaatggtagaagaagggaggggagaggaggaggaatacagcagaacaagggcaaat
gttgagaagaattcacttgtccactttcttgataatgatagcagttacatcatttttattagttgtacattttaaatatgtga
agtttatcatctttcaattaagcctcataaaatgtcttacaagcaaacaaatggaaacttagacaaggaaagagtaatagaaa
gatagaaaaaataagttcaatgtcagaagtacctgaaaattaatgtgcctggatcctagttctctccatattttcagaagagt
gctggagggcagcaaaaccacacatgctcttattacggaaagtgggttctgataaaaacactagacacatccagctttgtcct
ggagttggtttaggggatgtcagagacagtgatgaagagcacagggccagataccggggttcactcatcccagacatgagct
cctagatgcatacagagccccccatgtgtgggtttacttccacttctgtaaatggagaaaatattgtctcctacagaacata
gtttacatgaatatttaaaatgaaatagggtgattagtgcaaagtgtttatcacagcacaatttcataataagacagcatatt
ttccaaatgcaatcattgccagcaaacttctacagggcaccgtcgtcttatctgggtacagcctactcctcaagggtcccacc
ctagagcttgctatatagtaggagatatgcaaatagggccctccctctactgatgaaaaccaacccaaccctgaccctgcagc
tctcagagaggtgccttagccctggattccaaggcatttccacttggtgatcagcactgaacacagaggactcaccatggagt
tggggctgtgctgggttttccttgttgctattttagaaggtgattcatggaaaactagagagatttagtgtgtgtggatatga
gtgagagaaacagtggatatgtgtggcagtttctgaccttggtgtctctttgtttgcaggtgtccagtgtgaggtgcagctgg
tggagtctgggggaggcttggtacagcctgggggtccctgagactctcctgtgcagcctctggattcaccttcagtagctat
agcatgaactgggtccgccaggctccagggaaggggctggagtgggtttcatacattagtagtagtagtaccatactacta
cgcagactctgtgaagggccgattcaccatctccagagacaatgccaagaactcactgtatctgcaaatgaacagcctgagag
acgaggacacggctgtgtattactgtgcgagaga cacagtgaggggaggtcagtgtgagcccagacacaaacctccctgcagg
ggtccgcaggaccaccaggggcgcacaggacactgagcacagggctgtctccagggcaggtgcaggtgctgctgagggctggc
ttcctgtcatggcctggggcggcctcattgtcaaatttccccagggaacttctccagatttacaatcctgtactaatatttga
tgtctctaaatgcaacctttttttttcctttttgtgtctgtttttttttttttaaaaacaggaggacacatcctcacctccaca
gaagccacagtgtcactttgggggcagaaataatcctttcgtggtcaacagggtgagagttttgaggaatcccagggaaacct
ggggaatgttttccaattagactcagggcagagacctccatgggaatctctgattagaacaggctttgagttctgatgggagc
caaaagagaggctcacccagggtcagggttcttaaaacctgatggttttcacagcaatccccctcatcttgtgaaactgggc
acatctgactcagactgattcagttgacctctttctgctaatccatttttcctttcccagtagacttgattctcacagatcct
ttcttcttctctttcctgaaaacagaggatgtgttttctgtagtctaaattccaaggctcaggtctgcaggagctgggtaggc
tgaggggtcttcctcactcactattgcctggaaaatcctgctgtcttctgtgcatggaggcatttggaaaatgaagcaggcat
tagtcatgaagggaataatactagttttctccaatgggatgttgatgtagagctgatcttatgcttctcacactgtcacaaag
tttggactctcacctgtgactttgaggagagcttgtgatacttatcttgttttaatatgaatagactctcccttagctcagg
aagctggaacagactccatttggctccttcatttgtaagacatcaagggctcctcacccacccccttcctcaaggacttaact
tgtttaagctgactcccagcatctcaaagagtgcgattaactgataaggtactgtggcaagctgtgtccgtagttcccaggaa
tttggccaggtgatggtacccctaaagccccctgcatttctgtctggcagataacacccagagcccccacacctatcatcttgtg
atgaatttaaagcccctgcacctggaactgtttgcctgtaaccatttgtcctttcaacttttttgcctgttttacttctgtta
gaatgctacagttaggctcccctcccctctctaaaccaaagtataaaagaaaatctagcaccttcttcgggggctgagagaat
ttccagcgttagccatctctcagttgccagctaataaaggactcctgaattcatctcaaagtgcggcgtttctctctaactcg
ctcggttacaacaagctgaggatggacactccattgtgcagtgagctctgggtgacagtaatcgtagggtctccccgggcagc
ctaaggtcaatactgctggccgtcgggaaagacaggctggaattcctgggaagacctgcatctgccatctaccacggagtcct
atggtcttctgttacactctctttgaatcagcaccacctagattatctaaaacactctttgtgacttcatgactgggaaaaaa
taatggcagtctctactaacacctgtgttaagccatgggagcaacacctaggctagtgtgtgattgagtagttgagactgtgg

FIG. 7 (Cont. 10)

tctagtcaaggtgacacataaaattgattgttgccattatgatattttatttttatatttgacaatataatcatgctcatatta
taaatatttctgttacattatttgtgtcagaggctttggaaccagaacaacttcatcttgaataaggggtaggaaaaataaga
ctgagacctgctgggctacattcccagtaagctaaggcgttcttagtcacaggatgagataggaggtctgcacaagatccagg
tcataaagaccttgctaataaagtttacagtaaagaaactggctgaagcccaccaaaaccaagatggtgacaaaagtgacctc
tgtttgtcctcattgctcattatatgctaagtattatgctttaacattctaaaagacactccccacagagccatgacagttta
caaatgccatagcaacatcaggaagtttccctagaaactaaagagtggaggaaacctcagctttgggaattgcccggggaatt
catgaataatccttcttttgtttaacgtataatcaagaaataaccataaaaatggacaaccagcagcccataccacttctctg
cctatatagtagccattctttattctcttacttcctaataaacttgctttcctttattctgtagatttgccccaattggga
tccctttccagtaacatttgtgttattattggttttctaagcagaaaactctgagaggaggtgtcagccgggcttcctgggtt
gagtagaggctcagaaagcagtgaaactcactcatttcctgcatcaggacttactttggtcctggatgaataatattgaagat
atatgcttaaaatattcctaacatcacaatttgtgcatgtgttttcttccctaagaaagctataaacagtgaaaattttgctg
taagcttccctgtgtcttctctccctctctccattccccctccccctgaaactaaaaggaatgttttaacattatgggctttta
agtctgtatttctgtgaccagcagaccttatctatgctcccaattcaaattccttgtaaacacaatttgtaaaatcctgcgag
atcctgtctccttggccacgccactgcaaggtcataaagtagatcaaacttaagttacaattctgattttcctcaagatctga
gacatgttaattgtctttgtttcttgctcaggtaacatctctttttgctctttttttatctctttttgcacttaaatctaagtt
tacattagtcatgtatctagaatgtagaaatatgtcttaaagttacttaacttttaaaaaatttatggggtttccagaagat
gtgagaacctcctttatttataaaatagctgattgcacgttgctcaataatttcctctttaatttatctctctcctgtcacat
tatactatgataagcaaaaagaaatgaaggcataccatcaacagtttacttagatatctcctcagctaaatttctaaggtata
atttactaattctaattttatccaatttaacataattaagataaattatataacaaggtacacatatgttccagttctaacac
catgtttgtgacagaaataaaacagagcttctctctgtaatgtggtcatctgagccctgaggtgatgggtcacataggtattt
ttatgatatttaagggtttggtcaagaacagtgataacaagtctgaacaagactggtcatacttgaaaggttacaggtaaagt
tactgctgttatttttatattaacgccttattagaataaagctcagaggaagaggccacatcctaggtcacagtaggaggagga
atggagctgtgctctgctctccacactacttttcacatcccaggcacaagcccaggttccatgacgcacggcatctagagggc
agttctcaggggatgatctcagggcacctgcttcctcgggcagggcgcttccttctctcaattgcagacttgctccttctgca
aggtctgaagtcagcacttgtattcccatgatttttacaggttctcttccctaatatggcaaaaatcttttttattaaatttttc
aattttatttttctctgaagcacactgcattagcagaaacgaatatatcacattccttatccgcccacacagccaaagattcct
gaagacagagctgatgtgacgtactcataggtggatctctgcccctcagaggtggccttggtcttcaagtttcagcaatttct
aggaagccaaagacacctccatctactcctcccctgctcgacagctcaccgagaacagctttctcattggaatgtcttgtgtt
taagaaataaaagttgctgtttgaggttagggagcccaggtgcacctaccagatccagcccaggattggagatactttcaga
agacaacatcacctgagacacgaccagtcccactgtttcactttcacaatttcagcttcttcagaagaaaattaaaattgttg
agacttgttcataagcgttgtgccatgtcctttctctgttttcttgcctgttcattgatgtcatgccaggtgccacttctatg
taataggatcagaattctgcctctagtaacacatcagaggtgaggtttgattgtacttttggtttatgctccaaaacgtagat
tataaaattcatcaccctcatttttatgtcaaaagtaatctgcataatctggatgtcaatacttttggaatctatgaaataa
cagaaattgcaagaaatattacccactccaaacctggagagacaggcatgtgcagaatggcaattgacacctgcttaactgga
gcagaagctgcagaagccacaagctgttgagggcacttacatggtaagcactacagacgtctgaagacagatgtggactcagt
aaatgtaacagttccagagggtcttatacttctaagttttctggaatttctttccagaaacctcaagattctaaaatgtacat
tccaaagacatttcctatagatcaaaattgcagatattaattactgagaaacataccacgagccttcttcaaaagcttctaca
ggaaaggacttttccagaaccttatcctatgtgaaggaagacaaatctcccactgcagatttctctcccattcttccataatt
gtagaaatgagtaaagttagccaatagaggtaagatataagtaaataatccagggatgctgaaaacaaaaaagggagtaatcg
cccaaaatgagcttttccccctggagacgcctggtcaagatcataggccagaagaggaagctgactgtgtctctaggtttccac
tgtcagaacaggcagtgcttacctgcactgcacaatccattctaaccaggatgatggctctggattaaaggtgaaagtgtggc
aatgcacagactctatctgaggagaacacaggaaaactaaaggacaacggcagagggtgagacaagaacagtagagcaatctg
aagcctctgacatcatgatttttaagaccaatgtcttaaacactccttcattgacctcagcttctttcatcatgaagcctttg
cagtgactctatctgagaaaaagaaaataacctcctgcatgcacttctcaagtctctgcttgtatcctgtttgctttaggtct
ctaggggaaaaagtcagatacctggacctagtgtcagtgtaggaggcacatcctaaaagctacaaactaggaagaagggaaga
tgggtgttattggaatagtggatatggagtgggctttcttctgaaagtatatgcacctgctggtattctcagatgcaacattc
aactgcaagagcccattgaagaaacaaggcactcccaaatctcctgtaagattctgtattcatttcagataagcccacatgtc
cccgcattaacttttcttcagacaagcacatacatctgaaactgaacagctatgtggcaaaataagctcaggatagaagtaa
ttgtggactccagctctgacaatttgtagatctgcatttttaaaattctaactgaagactttgctttattgtagaggacagtg
gtttacagctcgaattgcacagcctacaggcagatgtccatttcctctgggcaaggtttatttttatttgtttactgtactta
tttgttgacaaacattgatactataaagatacctaacagcgtccacatgaaagaaaaagaaagagcaatggacacatcaacc
ctgaacatccagtcccaggaatcctttgaccctgccctccttgcaacccagagatatagattggatgagccctgctgagcaga
acacacatgtccccaggagaaagacatggaaatgaggccctccctgctaatgaaaagcagctcttccccctcttctcctgcag
gtcctggtgaggagccacccaatatctgtgcccttcctcagtgtccacaccatcgggtctatgatgatctgggcttcacttgt
catcactctcaatattgaggttccccgttaaacagactgagtgaactgtggctgctccacgtgggggctgttctcagtctgtt
gcttctgtgcttgcagaggtcccctgtgaagttaattactggagtctctcagagaaatactacagaccaagaatttctcagact
tttctggaaaccctgtggattcactttcactgaaaacagcataagcttggtccagcaggcttcatgacaggggtgggtgtagg
tgataacatcagtaattcaagtggaagttctcagtgggactctccttgagtacaaagaagattaacagtcctcagagacacgc
ttttcagatgattctctcttaagatgattaacctgagagctcaggaaaattccgtttattactgtgagggacacggtgagggg
acatctgtgtgagctcagacacaaacctgcctgcagggagacacaaacctcccctgcatggtagatgcttctcagaaccaccag
ggggtgcacaggaaaccagaaggtgctcaggacaccaggggtgctcagaaccaccatgactcactcaagacgccaggggcgc
tcagaaccaccgtggggcactcaggacaccaggggacattcagagccaccaggggtggctcaggaaacctaggggggtgctca
ggacaccaggggactcaggaaactaggggtactcagaaccaccaggtggtgctcaggacaccagggagctctcagaaccat
ctggggcactgaggaaaccaggggactcaaacactagggtgtgctctgaagcaccagcggaccctcaggactgcaggggcg
ctcaggacactagggaacactcagaaccaccaggaagcgctcagaaccaccaggggcctcaggacatcagagcgtgctgag
gacctccgggggcgctcaggaccttcagagagtgatcagaacaccagagggcgctcagaacaccaggaggtgctcaggacagc

FIG. 7 (Cont. 11)

aaggggctctcaggacactagggtgtgctcagtaaaccaggggtccctcacaaccaccaggggcactcaggacaccagggga
tgctcaggacaccaggggccactgaggacaccaccgctcccttagcaggcagctccacatcaggcccctgggttggggcagga
agggtgttttccttttggatcttgccactaaactcttgggagtttttctccttcctttgtggtttcaagaaacattggtagat
tcttctcaggtataaagctctgctttcttgtattatgtaatgtttttggtttcggatgttaccagaattacactgcactgtga
gaggattcattcctcgtgtgtgcaatagtgaatgaaagctgcaatgttaggggtggctttgaaagctacgttaggggtggcta
agggcagttagcaggaaatgatcatcactatagaaggctactcatttctttgcacatttccataaataattgtagtttatgcc
ctaaaaactgcatgctttcttggccctttttcttaaatgcctccaatccaagaccagtcatctaattaagctgtatgtcaaag
accaccaatcaagttaagtctgtttaatgaaacactttgtaaacaaaaaagtacatctgtgtttgtatagtcagctttaaatt
ttacattgctttacaaatattaattttgtaaatttagtctcataattatcgtcagtatttaaaatcttaaagtcatgctatgt
taaattaagtaatcttagctttctcactatgaattagagttactaagaattagaatagtaagagcatgtaataagcttttggt
gaagtttataaagaaagatgaagatacgtttttgctttaaaatattttgttttccagtttacaggacctttctactggtttt
aagataacaatcactgtttacatctaacccttttttaaacacctgctgtttaagattataaaattataaaattaaaaacccta
gttaaaaccagattgatctttgtaatttaacaagatgttcagtattgttgttttaataaaaaaaaaataggtaaatacttagct
actagaaaaataatcatctacttaatcataaggttttacttaggtaaacacctaaatttcatgggttataaacatggttaata
ggtgaaaaactttaatggacaagtattacagttttcataaatattctaggtaagctatttaaaaaataaattaggtaaatgaa
ataaaataaaccatttaaataaacttgttctacaatttaaaaatctaaagtttaattaaataatatatattatataaatgttt
atgcattactaattgtttaaaatatatatactataaggaaaacttttaaaaatacatattataagaaaatatttttgaaaa
catttgtttttagaaaaataatttatttaattcaaaggttaattataaaatgtcgtaaacatacccagttagtaagagaggtt
taaagaaagttctagacatagagaagtacttttggtaagaaaggttaaaataaaaaaaaattatatgagaaggaattttgtag
gataacttttatatataaaagtgactatttatgaaagaataatgtttagaataaaacaagatgttcaagtatgccataaatg
gttcgtgtaagtcaaaataaggtttatagaaagctaacttattaaaaaaacttcatgttatcgagttgactataattgaaagg
gaagaatttattatagtctttatagggatctggctttcatatgaaaatatactaacacactgaagattggttagaatgacaaa
attgtcttaaagtattgatttattcaataaaattataaggtattataatttttaacccaaaattttaacttttgttgcatct
tgccatttttatttttttccatttgagaaggcttgagaggatctcaacttttcatcagctcctttaacattgtttcttactt
acagcagttagcctctgagttaacttctaactgttgttagtttctgactgctattatttcctgatgttaaaatcctctatctt
aaagttctaaataaaatgttttcttttcaatataatattcagtgtccttggctttctttaactgtctaaatttttctatgaaa
ccaaaatcttcacttgtaaagacacattcttcctaggtctgattaattcaaatacttttttcattagagttgacttgcaggtt
atgtacatggagttccccataggaaaaacagtcacagtgcagaaggctttatttttgctatttggtaactgggcatgagaca
aattttaaatttcattgaaataattcctatgtaagtgttattaagtttttcaactacttagtaatactgagagtttaagacaa
tagaaattaatgttatgacattcatgtaactatctgtataacttttaaagtccttgtgctgctactttactgagctttgaatc
ctaggtctaaaaaggacacacaacactttgggaggctaaggtgggcaaatcacctgaggtcagaagttagagaccagcctggc
caccatgacaaaaccccgtctttactaaaaaatacaaaaattagctgggcatggtggcaggtgcctgtaatcccagctacttg
ggagcctgaggcagagagaattgcttgaactcagggaggtggacgttgcagtgagcagatattgcactactgcactccagcct
gggtgacagagtgagactccatctcagaaaaaataaataaataaaataaaaaataaaaaggacaccaagtccagctaaatctt
aaacaccgacagcaattaaagccccatctacagacctggaagaaaatgacaagaaaaattgatcacactctcaagacacaagc
ccagaaattgaaactacttaaccaccccagccccagggactattacagaagaagtggctttgtaagattgtaaaagctaattt
tgagagatgaaatcagttcagagtttctttataaattaaacattaatgcaaggctagcatctgggcccctgtgccagattgac
cagggtttcttgaagaattaatccacatttaaatttaaaaaacagataaaactgtataaaagatctatgcaaattatttttat
ggtaaaagtaattataatttaatagatttatttttcagaattgatagttttaacttttctcatgctgttcttctaaggggtta
tattttagaaaatcaattctactctttcaaaaatatttttttttctttttttttagaaatcactgagttttcatgtggctaaata
aataacttattttacaataatctgtaatcctattttgtaatatcaagtgttgtaaacttttgatatttgacaaagttcacaaa
ataaaattctaaattcagtcatttgaacaccctgaaaagaaacacatttagcttatttggtacagttaaattatacaggaagt
aatgtcaaatttgcaatggttattaactttggactatatttatataaatgtggactatataatttgaatatacttatgtaaag
agtatatgttccaaaattctattagattcaagtgatttttatatgtcttagtatcagtagtacttatgattataatttaaaat
ttttgtttatcacagaaataaccaaatttttctcctcaattctgtctttaaccaggggtattctaaaaggtcggtcattcacaa
ttgttgttttactttgattctttatcaggtggcttataataatctatagaactttgagtagtactcttaaatatacaatatac
aattttgacaattttataaattgtgccattggtatagagagaaaaacttccatgagtctcatgagacctgaagcatttatgat
gattgttaatctaatatcaagcaggacaggatgtaattgcatgaactgaatgaaaaggagactgaaataatttttataactta
ttctttaaagcatttgctatttacttatgttttattgttcagaatcaagaaaactttgtctttttaagctattcacagttttta
acaattttaactatactctattgagaaaaattgaaaatataatttcttcttctctacataatttctccaaaatttggaaactg
taggtattcttatatcaaaatagttatttgcataggttcgataaaaatctgctttcttccataacagagcacaattagagaca
atggtcacttaccaaggctttaacttgaatgacatattttctgatttacttataaaatgaagagctgtacagctgatataa
gccccttggaaaactggcatttacctttttttttttttttaacagggccctgagctgtagtaagtaaatattttgctttc
tgacaggcccaggaaacccaagttttcttggatacttgaaaaaataaaaagtaaaccaatccatatagctatctgatggcaca
gataaaatattggctgggcttgaggcttttaaagatcttacccttagattccttataaaaaatagcaaaagcaatgtatgaat
aaaacagcctatgtacaacaaacaacaacaaaaacaaaaacaataaaaagagagctaatatgttaagtgattatttttgctgc
atcttatacaaaaaaatcaggccaagtataataagcctaaaatttatttacaaataaattagtcctattatgattttgtctc
caataaaattggggaattatagggagaaatattctttcaaaataaactatagtgcatctgttattaggttctaaccttgtcca
cttgtttttcaatttacaatattttccacaatttggactcaattttaaaatatttctttccacaagtctccaaaataacattt
tcagtgatttttcttttaaatatttttttcctatttgaaatctccagaaggtaaactgtgctttcttacagctagtcaactta
aactctaaaataaaataaaatcaatgatatggtttgtctctgtgttcccaccaaaatctcagtttgtatagtaataatttcca
catgtcaagggtggaaggaggtgaagataattgaatcacgggacgtgttttctccatgcttttatcctattagtgagtgagtt
ctcacaagacctgatggttatataaagggcctccctcttcacatgacacttctctctcctgcagccatgtgaagaggtacgtg
tttgctgccctttccatcatgactgtaagtttcttggggcctccccagccatgtagatctgtgagacaattaaaccttttttt
aaataaattatccagcatcaggtatgtccttatagcagcatgaaaattgtctaataccagcaacttaattatatacaaaaatt
ccttttataccctcctactgtgaagggaaaataaatcttgagaccccaaaattactaagctaaagagaagagtcaatgtggtg

FIG. 7 (Cont. 12)

ttacaggagatagaaagaaattatttaggtagatagttgggatgagagagtctctggcaaaataacttttcttctaacaaaaa
tcagctcagaaataacttcttctctaattacacacagttcaaagaaatcacttctaacaaaaagcagactaaataatcaggct
gtgaaatatagataagcaactctgccacagagagggtgtttctgggtgtaatcaccaaacctcacatatataggatgggtccc
agtaaaaacagtgagccttaataagcacattccttttctttttctgggagtacactaagatagaaaagctggaagcttgcacgg
ggtttgcgacgccggcacctgtgaggaagtacctgggaccaggcaagaaaacccttctggcctttcttagcacatgcacggtg
gaagaagataagcagtgtggaggagatcaagcaaagtgcccgcctgcccaatgaaagcatgaggtggggttgccagagacttt
gctctatgcagatggcacacattgtcctaactgtttttgcaccctatgctgataagacaccgtctccccacgagcacatttat
aaaaatccttacattttactgcagcacgataacccatttgggacccctctctgtgacagacagcttttttttttattttaccta
ttaaacttgtgctctaacctcaccttagcatgtctgcgaccttgatattcacggccgtgagacaaagaagttcgggtggtat
tccagacaacgaggctgccatactggaaagtgctttgggcaaatctgcctccccttctgtttaaagtgattcctctgaggcta
acctgagaccaatacacagctgattgcttcctcttcactatcatttatgtaaaaacgaagatccactgagtcagactaaattg
tgcattcagtggtaggctaataaagtactcaaaagaacgcaacctattgtctcttatctacttctaaactgcagtccgtgctt
ttgattcgtcctgccttacaggaaaaatccaaagtacattttacatatattgattgatgtctcatgtctctctaaaatgtata
aaagcaagctgtacttcaatcgccttgggcacatgtctcaggacttcctgaggatggtcatgggtgagttcctaactttggca
agataaacgtattagtctgttctcctgctgctaataaaacataacaaagaccgggtaattgataaaggaaagaggtttaattg
actcacagtttcacatggctggggacacttcacaatcttgtcagaaaagcaagcgacatcttacacggtggcagactagagag
agcttgctcagggcaactcctctttacagaaccatcagatctaatgagaagtatttactatcatgagaacagcatgggaaaga
cctgcccctgtgattcaattatctctcattgggtccttcccatgacacatgggaactgcaggactagaattcaaggttagatt
tggatggcgacacagacaaaccacattagtaaacttcctaaattgactgagacctgtctcagatatttgtcgtttacctaatt
catgttcagccttcagagttccaaggcctatatcagttttccaggattgtttccccttttgttgtttgttatttcctccttt
atttatatgttttacttctctttttttctcccactattttcttattaatggatgtgaaacttcacaacatttgaaatataggta
acaatgaactataataacaacttgggacctatttatctagaaataatccgtcctacccatgaaagaaaaaaacaaaaacaaaa
acagaagcccagaaacttattttgtggtaaaatgcttcctctgaaatattttggaaaggaaaaagttgggaagatatgaaatg
aaaataaaaacttctgatgtcaattcattatgtcatgaggggaaaaaaactaaacgatgatccacgcaagaaactgattttc
ctttcattcctgagaaaatagccacagacagataaaatgttagatatcttcacagatagctacaatttgttcatctttgaaat
acttagtgcaggagaaccacttgatattctatttccctatgtgcttcttttttcattactacatgtaagttttcatgcaattcc
tccttcccctctagccagcttttccccctttatatattgaaagccctaaaaaatgtcttttgggaatggcactaaccacgcatt
gtttctgtgattactttcttccaagcatgccataactttgaaaaattaatttaatttgattgagagctctctcagaaaacct
ttggttacactaggcaaaatccaaaatcaggagccaattattgtaaaaatcagccatagtacactgtgcgtctgtgtgtgtgt
gtgtgtgtgtgtgtgtgtgtgtgtgtacatgtgtgttttaatttttgtgagctttgagccatgtagttctctctgtggaga
tactatttggcgtgactttgaatagagaattctaaaagaaataagaagctcctatgagttctctgaaagtttctggactcacc
atggatcttgactgtgtcattgcatcagacagtcccagggaacagactctctggtggtttcatagaatctatgcttgggctct
ccctgcagtttactgggtatagtaatgacaaatcactgtttcaagagacaatttcaaaagcattagatgctgctgagagagga
ttgtgaaccaggggactgccccttttcttcttggagagcgacattgggagaatatgctctgtgagcccaaacagcatcctcccc
tgcagggtgagggcagagttgcagggcaggcccagaacccactccacacagatgtcagccctggagctgctgcagaggagtct
gaggagaaaatttttccagcacctgaattacacttatttcaaaacaaaaatgcaattaaaaagttaaaacaagtaattaatgt
ccaggcacagtggcttacacctataatcccagaaatttgagaagctgaggtgggaagatttattgaacccaggagtttgagat
cagtctgtgaaaaatagtgaggcttcatctttatttttgaaaataaaaataaaataaaacataaaaaatttagcaaaaactac
gatgcgtctttacataccccatcatacttgaagcatttacctaacccaatgaggtgatgaggacccaatttgaaaggagaaaa
ttttagacttttcatatatcttaatagttggaagatgtagaagaaatatatttatatcaattaaatgtgtgcaaatattgaca
gacacaccataccaggagttcaacttgcaaagggtaaaaccaaaaaagtttgagattgttaatgtgccatttgaaggtgagat
cgttttgaggaccatgtcctgtgagagtttgtttctctattagaggagttctgtactcataaagttctggacatgccaggaga
caagtatcagtaaacaaatatcagaacttgaacttcagcttcccactcttgcattctccatgtgtcatctctctactatttct
cattctagatcaggtctttagctatgaaatattccacctaattaacatgtaaatagattgaagtccacagagttaaatatgta
tattttctcctgtttttcccaattgttccctcccacagctccaatattctccactgttaccatcaccttctagatctgctgcc
atgccctgcagattaaggatttgattccatgacagagaggaggtgcatttcaatggaactttggtgagaacctcggtttttat
cccatttcctctggggctccaccagtgcatctggaataatgggttcagtggctggcccctgcagggtgattccttagttctgt
agtgaagatgagggaggtgggtctgaatgcatttcagaagtatgggctctcctctctcagacagacactttgggaaaataaga
tttttctgactgcacccattctagaacaaaggaattcaattggataagaatgctgataaaaaaaaacctcaaaccaaattaaat
ttaaaggagtttaattgagcaatggatgattcatgaattgggcagccccggaatcacagcagattgaaagagacttcagtgc
agccatgtggttgaagaagatttatacatttttttaaattatgtacagaaatcagaagtgaggtacagaaacagctggattgg
ttacaggctgatgtttgtcttatttaaacacagtttgcacactcaagagtgtatgagtggttgaggtatggctgctgaaattg
gccaacgctcagctgttggtgaggtgctcaggtacatactcctgagttaggttttcaatctcgtccacctattcaggtaggtt
accgtttgtccacaaggactcaaacatagaagtacggagtcctcctcaggccatatttaattcactttatcagtgcccttcag
catatggttcctgagaatttcacacggcaacatgtttaccaccctagaatttaagcaatccaatacatgtaataggctgtatt
tcacatggcaacttctgcctcagtttagctaacactatggctttgtttctctctacaagaactcatttctcccaagatttcca
ttttcctgaaaggaaaataaatctttgggacccccatatcactaagccaaagggaaaagccaagctgaaaactgtttggggca
aacccaccttccattctttccctaaaatgatagctgttaaggtgtttacaagctacatatctccttcaaaatttgaccgcaca
gaaaatccttgtagaccaaggacattgtagaccaagcagagagtcacttctctgctcacgtaagtcaaatgcatatctgattg
ctccctttgctctattgtttcactaagccagactaaggcctatgtgactattcctgtaaactgtgcattcagttaaaggctaa
tcggaaactcaaataatgcaaccatttctctcatacctacctatgatctggtagctctcccccccaacttcaatttgtcctgcc
tttttgaactaaataaatatacctttacatatattaattaatgtctcatgtctccctaaattgtataaaaccaagctgtgtccc
accacactgggcacgtatcatcaggactccctgaggctgtgtcacaggcatgtccttagtcctggaaaaatgaacttcctaaa
tctattgagattagtctcagatactctttggtttataagtatgttttctatctcataacttcaattatctgaaatactaaagg
aaatctgccaaataacacattatcttgtttatctgttattgttgttgcaaaaataaatatatttatataatttatgtataatt
gatcatctttgtacattaccaaactgagtagcagatttgttagtaagacccaatgtaataaaaaattcaaatatcaattaaca

FIG. 7 (Cont. 13)

acttaatagaaaaacaaattacgctacatttgtttgccgaaatgctaccaatttttataaaaaaataaacacatataacataa
atggtttaattctcagtatttctattgagaaaaataagccaaatacataagcgaatatactatattatttcattcttataaat
tctaccaaataaatactagtctaaagaaatatgaaaacatcagtagtttataaagaaatggtagaaaaagggaagggaaaaa
acaaataatataaaagatcaagaggaatgctgaggggagttgacttgttacctcattgaaaatagagattatttttttcaaagt
ttactattgcacatgttaaatatgtgaatttttatcatctgtcagttaaaactcataaaatttattacaagtaaacagccgaca
ttttatacaaaaaagggatgataggaagaaacaaataaatacattaaatgtcagatacgccaaaaacttatctgcctgacccc
tagttgtctccgtaatttttggatgaaaaccagcccacccctgaccctgctgctctgggagaggagccccagccttgggattc
ccaagtgtttgcattcagtgatcaggactgaacacacaggactcaccagggagtttgtgctaagctgggttttccttgttgct
atattaaaatgtgattcatggagaactagagagattgagtgtgagttacatgagtgagagaaacagtggatatgtttggcaat
ttctgacttttgtgtctctgtgtttgcaggtgtccagtgtgaggatcagctggtggagtctgggggaggcttggtacagcctg
gggggtccctgagaccctcctgtgcagcctctggattcgccttcagtagctatgttctgcactgggttcgccgggctccaggg
aagggtccggagtgggtatcagctattggtactggtggtgatacatactatgcagactccgtgatgggccgattcaccatctc
cagagacaacgccaagaagtccttgtatcttcaaatgaacagcctgatagctgaggacatggctgtgtattattgtgcaagag
acacagtgaggggaagtcaatgtgagcccagatacaaacttccctgcaggaacgctggaggaaatcagctgcaggggcgctc
aggagccactgatcagagtcagcccaagaggcaggtgcacacagaggctgatttcctgtcagggtgtgggacttcgtcttttt
accatttctctagggaacctctctaagttcagaattctgtgcttaccaatgtcatctctacatgtttttaatgattattttg
agaacctattcttacatgcacaaaatgcagatggatgcttacagagatgaaaagtcctcaaccatggtcaccaggatcagcct
tgaggaaactcaggggtgcctggtgaatcttctccagtcagactcaggacagaaacctctgtgagattccctgactagatcag
tcttcaggaattttgataccagccaatagagaggctgggccagggtcagtgtcatgtagaacctcacaggtttcacgtctgac
ccttctccttctcctgacactaaagtatgcaaatcagtatcagcactgatctgggtccccttttgctcttaaaccattctatt
tctttttatttgttgttgttcttgcttttcctcgtacttctcttgctccctgtaaaatggggaggtgtttcttgctgcaaaag
ccccaagcctcaagcccattccctgcagctcaggcggggctcaggctgtggctcctgcagccacatgggagtggctgttgggg
ctttctcttctcccattgctcagcaccctccagtgtgttgtgtggagactatctgggaacgaatgtggacaacaggagtgaag
gggatgagcttgcgtggacagaatgggatgtggatgtgaaatttatcctgtgctgtacaaacaaccacagattcaacttcctc
accagtagtattagaaagagggtgtgaaagttgtcagaataaaaatggaaacacttgtgttaacaccctgacaaatggaacta
ggaatgaccatgaagaagtttctcatgcatatactccagaaaacaagaactaccgtaaatggattctgcttaaccacagcctt
ggatagaagaaaccacaaccttacaaaaatcacttctacaaggatatcttcccagcaactccctgtttaaccctacagtgatg
ccaccttagtcctacaaaaatcacttctacaagaatatcttcccagcaactccctgtttaaccctacagtgatgccaccctt
agtcctgattctaggagcacaggataatcctctcaaaacgacttatgtaacccacctcattttcactgtgtaaacctatggat
tcacatcctggagtcactgctgcatttgttcttaatggtcattagccccttcacaatatttgaggctgttttctctgatgt
ctcttctaaaataaagaatttccaagtggacagcagtaaagaagctatttaggaagatgtaatgggaaggcatctttaacatt
ctgttgaatgtttccacatggcacttcaatccccctaaaatactttgctgtatcagcatgtgatgaatcggagtataatattga
aggtaaaatgggaaatacatgggcttttgatgaatcaagtcataggatgagaatgtctgtgtccttgaggaaggagaccatgg
gttgtaagttctagtggaggtacctttggcaaagggagttcatgagtttctgaaccttatgctacttttaatttaaggacgca
atttatgatgtatgtttacttaaatctttccagagacatttgtcagtaaggacagggtagcatttgtgtaatagtgatgactt
agagagttatttttgtaattgctcctgtaaggtatgcacattgctcacttgatacagaagttcaaatgtcacaggtggaaaaac
aggaataaaggtgggcagatcacaaggtaaggagatggagaccatcctggctaacacggtgaaaccccatcgctactaaaaaa
tacaaaaaattagccaggcatggtggcgggcacctgtagtcccagctactcaggaggctgaggcgggagaatagcgtgaaccc
gggaggcagagcttgcagtgagccgagatcgcaccactgaacttcagcctgggcaacagagggagactccatctcaaaaaaaa
aaaaaaaaagaaaacaggaataaagcaaatttttatgaactgtcatgactgtagtttttggcaaggacattatcatgtcaacct
gtaaataaacagacaacaataaaacatatcaaatccatggggagtctgacctatgtcccctctgtcttataagcacaaggcttt
gccacatccaaaatattattcaggctccagggtataaaatgcttttggactgtggaaggtaacagctctcccctcaggcaggg
gtaaggtatctggggaatgcagagttgtgttcataaggaagatgtcattatcgtgtcttctcctgtgcctggtagcaggtcct
gaaggtgaacgtctcagatgtcagacatgggtctatcgggttaggataggtacatgtgactgacagggactgattctccatgt
aatcacatgccctgtcccaggagcagctgcaggagtcagccctggacctgaatagcacacacttaccctctgcctcacctaca
ctgttactggccactccgtcacaaccagtccttactagtggacctggatctgccggctctcagggaggggctgcaatggataa
aatccattgctagtggtggtgggagtccatttgtcttgtggaaaatggcagcatttccttatttttataaggcataataatgct
atgttgtgtacacataccacattgtctttatccatttgcccattgacagacacttagtttccatatcttggctgttgtgaata
cagctgcaataatcacaggagcgcaggtatcttcacaaggcggtaatttcatctctttgggtatatttccataagctgcatca
ctggtcatatggtatttctgttttaattcatttaggagccaccacactgttttgcctaatggtaatgatgagaatacagaatg
tcatagccgctacgaagaacagttttagatttgaggtataatccaaaagcaaataatgtttgatcagggttctcatatgaggc
tctaataaataagtccagaaagttttcccatcttgggcaaggatgagtttgcccctaattgtctttgaggaagaagattggca
gaacgtgagatggagtctgttggcaggattcaggattcagtaataactagtaatggcacagaaaaatagagagatagagacat
acagagaaagagagagagaatatgaatctcataagaggaaaatttgctaaatatcagcattgggttttcagtcatagacacat
ttgtatgagccaggaaccatggagtcaagtgaggagtggagaatatgttcagtccaaaaatcagcatattctcagaggcaccc
attgccccatcacacaggtggagaatttggaaaccagtgaagtgcgagttcacattaggtgattaagctaccatgtttcgat
aaactttcattaacatgcaaagtacttccatagataactgatgcacaaatatacgagatgccttttgcgtttatggatgtct
agagaaaaataagtgagaaaattttccaggttgcagagatctgtttaagttgcagattccataggagagtgtctttgaatga
atactgttctattaattaaataggtcaaaattccctctgttggagcagccttccaattatatagatttctttatagcttcttg
agttgtgaaacataaacccaaggattgacttactggaatatgactgctgtgttgattaaatttctgataaggtttcttccaat
gatttgagaatagctttcctgttttttttactcaaggaaatgaattttcacaaggtctcaggacatcacgtttcaggtgcttta
gttaaagagactcttcttgggggcagtcagctttcttccaaccatgagctcatttcttcagcaaaccattcgctttgtgcctc
tattaagaattatgaagcttttgtacttcaatgcactgaaaatcatgcccttgaattaaatgttgattggcactgacatgaa
ttggccactcttgtatatgtgtcctatgttatgggctcaacataacagtggactgagaatcgtccattagctgcctctgattg
tggcactgaccagattgagaatcctcagagtcatccatgaaaaagagagtccttaggttcatgaggttcttggagacattcag
gtaagtggaggagagaaacaggattgggggctgccagccatttcaacaagactgggaacaattatcatctatgtttaaaggtc

FIG. 7 (Cont. 14)

tacatcattccaaacaccctccaggtttctctgagttcattgtgatgattacattcagctgcttctccagtgagtttaaatga
gcatgtggcaattcagatgagcctggctgtgggtttattatatgtaaatctgaactacataaacaaagagggcatgtctgac
cgtatgagggtgcaaaatcctggagacccccacacccacactcttgtgctttcttttctccagcaacctccaggttttttgt
atgagaattgtaatagattatctcatggctaagtcatcaagagacgtaaactctgagaaatacaagcagaaaatttctccagat
agaagatccaggggaagaacatttctagcaccttatctatgtaggggaaggcagtccatctccattacagacccctcacagca
gccttcctttataaggaaaatgggtcaaattagccaatagggtaagaatcctataatgttccagccagaaaagggaaagcatc
aatttgacttctggagactctgtatataggtcacattccatagaaagaagagcactaaattattaagattcaattgtaactac
atatgatacttccgggatgcacaaattaaagatgaaagtgtgacaatgcacaggctctgtcagagaaggagaacgtagggaaa
ctgaaagagaatggcagagagtaagacaaggacagaagagcaatatgaagcctctgacatcaactctgtaaggacaaggtctt
ggcaactcccgcattgaccacagattctgttaccatgggccatttgcagggttcctagctaaggaaaaagaaaaaaaaactg
catgcacttcccaagtctccacttgtatcctgtttttcttagatctctaggacaaaaaaaatggcataaacctagacctagtg
tcagtgtaggaggtactttctttataggcaagacactaggaagaagggaaaatgtgtgttattggactaggagatacagagat
ggctttaatctgaatagatctacacccgcaggtattctcgaatgcaacattcaactacaagagcctaatgaagaaacacgacc
ctccccaaaccccctgcaagctcttgtattcactgtgtctccactgatttagtgcacctggagcttcagagcactggctccctc
ctgtgtcctagaatcttttctttgggtctttctgcagaattcaataggattagttaggctaatcaattgtttcaagagatggt
gttggcagcatatattgtcgctggaagagtattctaagccaggacacaggcactttatgccggactaaagactctggagaaaa
tgttttgtgagccctgacagaaacctccttgaaaggtaagggctgggcaggaggggcactgaggagccacgcagcacacggt
ccagccctagaacaggaggctggggaggaggtttcctctcagggcctcggtttcccttcgtcagaaaaaaaaaaatctaaaat
aaccgttcaacaagttgctgatatgccttcaaatatcctgctacaatggaacaattcatataacttcaggcaatgagaactat
tttttaaattgggcttctaggattataagtatcttaatagtgaaaatgtgaagaataggtatgattttactatttcaatggat
acagaatttgtgggagtcactatattcctatgaacaaaaaattcagatttcagtgttaagtaatgttgcctacattgtgtgagt
gacggggcagtggtggatccgagagtgtggtgggtgcacggacataatgattcagaaagcaatatggaaagatgagtatctat
ggatacgaactgaaagtatgtaaatacttcacaaaatactaataaacggagttgaatataaaacccataattatccaaaacac
aaatttcttggaagttattttgggaacatgatttcttaaagaactccaaactcttgtttcaacttctgactcctcgtttctgt
gatataagaaaaccatttccaattatgcatctcagggcaattctgtaaacccagagcgtttctgctgaagatcctggggaatc
aagacaccgggcaggtgatggagacactgtctcaggtgcgcccaacgaatctcagaggaacctgctggagagtcacgtggaac
atctacagtcagtttctcagagtcaacagtgagctgtgttggtgcctgaggggaccatgatggggccaaggcacgtgcccagt
gtcgtggacagtgatggtccagaaatgatctagatggtcttgacgctaatgaaatatgggttcagagtgaggagcataatctg
tggggacttgttcttcagtgaaaggatcctgtccgcaaacagaaatggagcaggacatgcatttcttcaagcaggattagggc
ttggaccatcagcatcccactcctgtgtggcagatgggacatctatcttctttctcaacctcgatcaggctttgaggtatgaa
ataatctgtctcatgaatatgcaaataaccttagatctactgaggtaaatatggatacatctgggccctgaaagcatcatcca
acaaccacatcccttctctacagaagcctctgagaggaaagttcttcaccatggactggacctggagggtcttctgcttgctg
gctgtagctccaggtaaagggccaactggttccagggctgaggaagggatttttccagtttagaggactgtcattctctact
gtgtcctctccgcaggtgctcactccCAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAG
GTTTCCTGCAAGGCATCTGGATACACCTTCACCAGCTACTATATGCACTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTG
GATGGGAATAATCAACCCTAGTGGTCGTAGCACAAGCTACGCACAGAAGTTCCAGGGCAGAGTCACCATGACCAGGGACACGT
CCACGAGCACAGTCTACATGGAGCTGAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCGAGAGACACAGTGTGA
gaaaccacatcctcagagtgtcagaaaccctgagggaggagtcagctgtgctgagctgagaaaatgacagggttattcagtt
taagactgtttagaaaacgggttatatatttgagaacaaagaacaatagaaacacaatctaattgtaagagaaatattccatt
caagagccaccacataagccaaactgacagagtgggaaaggccacactcagtaaagttgatacaaacataccataaaggtgct
actatgaacaagtttttgaattagatgaataaatcatttggagcaaggttatttggtcatatgttaagagtaagcatgattct
tacaaagtgggaaaattgtctttcaaatgtttctgtcacttcttaccataaagttcattttagaggttttaggattacagtga
aattgcacagaaggtgtgagaattcccatgaatccctgccccgcacggacaccgcctcctccactacagccatcctgccccac
agtcacaaataagtcacaatggatgaatctacaagaactcttggttctttctttttctggtgatcccctaatataacaagcct
aaattatcttggaacacccaggtattttcaatggctttctagaagtgatattagtcagagggaaagtgagtgaggctattact
atttgagcactttcttccaaaatccacaaaatatatgttaatttggagtttttctaacttctggtttacaatgtcccttccca
gagagtaagatttttaagcttttagtgaggctggaaaaaaaaattttttaaaaaagagaaataagctttcctgtattaggctga
cttatcccagcggcagcaacaagcacagcccagacccaggaaaagtcttaataatattatctaatgtgctctggagactcttt
cagcactccctcaacatagggagaagaaaaacaaattttccttttgtcttatgatatgagtttatagagtcttgttctctgtaa
ctagtaacttcaagtattctgttttatctaagaagcacaacgaaggtcatgagaagcctagcaggccagaactacagctgtct
aggtaccggagtgagtgttatgagatcaaccagtgcaaggctctttagaacaaaacctagataacagacatctgggttgcata
gcaatggtcatgtgtaatcctgagttatgaacctgttacaatttgattaactgtctctgtcctgccatcccctgctttt
gtgcactctaagcttgcttcaagctagcccacccccattttgggaagtgtgtataaaagtcaagcgctctctttgttctgtgcc
cagtctttggtcattgagtctgctgggtctgggtgtactcagtaataaaaatatcctcctgtatacaccccaagatctctctc
tggtcctccggattctgcaacatttcaggcagattcacatctctaaaaggccagcaagttctggtcaatcccataatgaaaat
cctttaatgagacttggcacacgtgacaataagagactccttgtataatgccctagagttggattagacacactgtgagctct
tgggtggtggttctgaataaggcagtttgtgcagcaaatgcaaacacatgcatgggatccaggcaggaacaaaagcttcccct
tacaaagtgggtgggcatctggagggagccctcagaggtgggcagtggtcgtccttgctgactgcacattagccagaggcgtg
accataattggtcttgcagggaaagagcaccactgaggtcataggttatgaaaatgtttgtcatcctccagtgagcaagtcca
tcctgcttgcttgtgggtgtcaactccatggtggatacactctgggagatgacaagatgcacacaaacctcctctcactaatt
atccactaccacacactcaagaccaacctttgctccagaaaggaatacgtgtctgtggaaatagacagagcttaagtattttg
taacctggtgaacatactgtgcaaaaccaaacgtttcaggaagattagctcagaaatgtttatcaagtgactgaagggcagtg
gcgggtgaggtgatgggacagcctcagggctgcacatgaggagggctcctcccccatgcaggcttttcctccaggagctgca
ccaggaactcaaggaagatcagggagaattctgagaacaccctgctgtggagctgcctagagaagaagaataaatgatgaaaa
atacaactctgagtaatgcatgggtttttgttcatgaaaactctctctctgaaagcttgtgaaggtcttgaaatacccctgat
tagctgaagacaaacatttaaaccctccttccacagggagttcaagcaggctggatgtgtccttctatggatgatcttcctca

FIG. 7 (Cont. 15)

gcccctcctcttcccagctcatccctggctctctgtgtaaaaagttctcatcagcggaatgtggttgatgaagtgacgtctt
caatttcctcatcttctatgtggtcatgttatttttcctcatctgaagtttaaaaactcacctgcatgcagcacatgacaggct
aaaatctcttgtggacaaaacagtaacaaaggcacccaccatggttgagcacccgtgttgctgacaacgaccaccaggggtca
acgtcctcttcacaatcctgtgtcagagcagcacttgagtgatttcaataacaacttcccaggagaatcagctgaaaactact
tgtcccatttttccatacagatataacccctctatttttcctgaagaaatagaaagagctgaatgctgaatacactgaatgtctg
ctggttttgcaagtttgtgactatatcactttctaatttctgacctgtgcagaccactgtacagacttttctcactggtggga
ccaggcttccagatgtcaaatataaatgagcttcttcatataaaagtcaacacaagctcctcatggtttcagtgctcactgaa
tggagttggaaataaaacccacaattatccataacacaaattccttggaagttatttgggataatgagttcataacctgtag
accaagagtccaagagtgtttctattgaagagcctgggggatcaagacaccaggcaggtgatgcagacactgtctaaagagtg
cccagcggctctcagagggacctactggatactcacgtgggacatcagcaatcactttctcagagtcaccagtgagctgtgct
ggttcctgaagggtccaggatagggccaaggcacctgctctgtgtcggggagagtgattgttccagaaatcatagaggtggtc
tctatgcttataaaatctatgttcacagtgagaagtctgttctgagagggcttattcttcagtgaaaggacctctgcccacaa
atgttcataaatggagcagggcattcatttcctcaagcaggatcagggcttgagtcatcagcatctcactcttgcaaggctga
tgtgtcgtttgtcttccctttcttatcatcgaccaggctttgagctatgaaatgccctgtctcatcaatatgcaaataacctg
agatcgactgaggtaaatatggatatgtctgtgcccctgagagcatcacccaacaaccacatccctcctctagagaatcccctg
aaagcacagctcctcaccatggactggacctggagaatcctcttcttggtggcagcagccacaggtaaggggctcccaagtcc
cagtgatgaggaggggattgagtccagtcaaggtggcttttatccactcctgtgtcccctccacagatgcctactcccagatg
caqctggtgcagtctggggctgaggtgaagaagactgggtcctcagtgaaggtctcctgcaaggcttccggatacaccttcac
ctaccgctacctgcactgggtgcgacaggcccccggacaagcgcttgagtggatggcatggatcacacctttcaatggtaaca
ccaactacgcacagaaattccaggacagagtcaccattaccagggacaggtctatgagcacagcctacatggagctgagcagc
ctgagatctgaggacacagccatgtattactgtgcaagatacacagtgtgaaaacccacatcctgagaccgtcagaaacccca
aggaggaggcagcttcactgaatgaggaggttacagggcttacgatgtttaaagttgttcagaaaataggctaagcaattgag
gaatatgagtaatagaaatatgtacgcactctatacaggaaatatttctaataactgtcaccctatatgcaaaattcgcagag
aggtaaaagcagaaatcagtcaagctgatgcaaagttccccacgtaggctttgtgcagatgtaagttctaaaatcagatagat
aaataatttggagcaagattgcttgataacatggctaatgctgaatatgattcctaaaaactggccaaaatatattccaatttt
gtctctgccacctctcttacataaaatgtattaaaaagtagttttaagaccacagcaaaattgaacagaaggtgcagagattt
cctatgtgcccctgcttcacacatgcacagccttccccactgtcaccatcctgccccagagtcatcaataagttacaatggat
gaacttacatggatggattggttctttcctctccggcggtcccttggcataccaagtctaaactatcttgaagcacaacagg
ttcttcgagtgggttcctgggaatgaagccagttagaggaaaagtgggtggggctattcctattaggagtctttttagaaga
ctcataaaatgtatatgttcctatagattctgtgactcctgacttagtatccctcccagacggtaagcttcctaaatgtttа
gaggcagatccatatctatggaaagaaagcaagttctagtgaatcccataaggaatgtcctttaatgagaagtggagaccttg
gtcatgaggcacatcatgtatgattttctataattcctttagattcactgtaagcttttgagggtgtttctggatgaggccct
ttgtacagaaaatgaaaactcaggcatgagttccaggcacaaccaaccaacttccttccaaagtgggagggaatagaagaaac
cctctcctgtgtgggcgctggtcccctccattgctggctgcacattagccagaggcatgagcccaattagtcttggagggtg
acagccccactgggqttgctggctatagaaatgcctgtcctcttccagctgagtgagtcaacctgctcgcttgttggagtcaa
ctgcatggcaggtgcactctggaagatgacaagatgcacacaaaccttctgtaaagtatcaattactacacactcaaaaccaa
actgtattccagagacaggtgtctgcagggataaacagaatttaagcatttttgaatagggaagacactgccaaatgccata
tgtttcaggaagtttaactcagaaatgttgatgacataactcagaaacgtgaggtgacatgacagcttcaggggctgcacatg
aggagggctcacttccccatgcaggcttttcttccaggaactctaccaggaactcacagaagatgagggagattctgaaaaca
tcattctgtggtgctgcccagggaggaaaaataagatatgggaaaaaaaaactatataaattattagatttgttaatacaaact
atttctgaagccttgtggaggtcctgacataagccatcattagctgtgaacaaatatctacaccctcctttcctggggagttc
agttaggttgcgtctcttcttttatggacagtatcccccaaccccttttatttcctgcacacctgctgctctccatgggacgag
ttctcatcagtgaaatgtggttgatgtagtgaggtcttcacttttctcattgtattagtcaggattatctagagggagaacta
acaggatagaggtctgtatttgacgggagtttttaaggaggactgactcacacgatcacaagatgaagtctcatgataggcc
gtctgcaagctgaggagcaaggaagccagtccaagtcccaaaacctcgaaagtcaggtggaaaagtcgtttattgggatagta
cccactactacaatcagtaaatgttggatacgatcaacagcatggttcaattcacaagtacatatgatgagtatagtgagcca
aagcacatacatatgattccgttttataaactgtacaaagtgaatactcattggaaattacataacaaagatcactaactgac
ttctccatagtaagagaagcgaaggtataggagggagaaattgtgagagacaaagagaaaattgagaggcgaattgatttgtt
ttctctgtgaatggtcattaggtcaatgtttgtcaaatggtgaacatattgtgtgaagattatatgtctgtattacttcatta
aagctattataaataaaagtctaatgtggtagaaaaagatgaagagagaaataaaaatаatacaagaaaagtcatgaactcct
gaatgaattaacccttagtttttctctattacttataaaaacaccaagatacagccaaataatatcacgatatcattataaga
agagtgttttgtaaacctcactgggaatttatagctctttcctagagttaattttgggaacagttggatccaattgtgagaaa
tgcaggctggacactgagactggctcttatgagatgtgagctcttgtctatgtcacatggtccttccatacttgggggtttac
attcacatctgtaaatgaaggaaacattgactctcaaagaacatatttcatgtgcatgtaaaagtatgaatgctagtgagaat
taattacttatgaagtataatcacccacatccactcttggacacagcccactctgaggcatctgttacagaactcattatata
gtaggagacatgcaaatagggtcctccctctgctgatgaaaaccagcccagccctgaccctgcagctctgggagaggagcccc
agccctgagattcccaggtgtttccattcggtgatcagcactgaacacagagaacgcacc
gtttcctgtcgcatttaaaaggtcattcatcgataaatcagagatgtcagtgtgagtgaacacgagtgagagcaacagtgg
acatgtgtgcaatgtctgaccagcgtcgtcctgtgttgcaggtgtccagtcgaaatgcagtcgtgaagtctgaggaact
cctggtcaagccacgcgggatcccctgagactctcctgtgcagcctctggattcacttgatgactatgccatgcactgggtcc
gtcaagctccggcgcaaggatctggagtgggtctcttattagttcggatggtggtagcacatactatgcagactctgtgaag
ggccgattcaccatctccagagacaacagccaaaactcctgtatctgcaaatgaacagtctgagagctgaggacacggccttt
gtattactgtgcaaaagata
cacagtgaggggaagtcagcgagagcccagacaaaaacctcgctgcaggaagacaggaggggc
ctgggctgcagaggccactcaagacacactgagcatagggttaactctgggacaagttgctcaggaaggttaagagctggttt
cctttcagagtcttcacaatttctccatctaacagtttccccaggaaccctgtcgcaatgtcctgcagcacctcagaccacct
gtcctggttctatcaaggaagtttacctccagcacagtaaagaaaacaattgaaggaggagagaacctgcagatgatagacaa

FIG. 7 (Cont. 16)

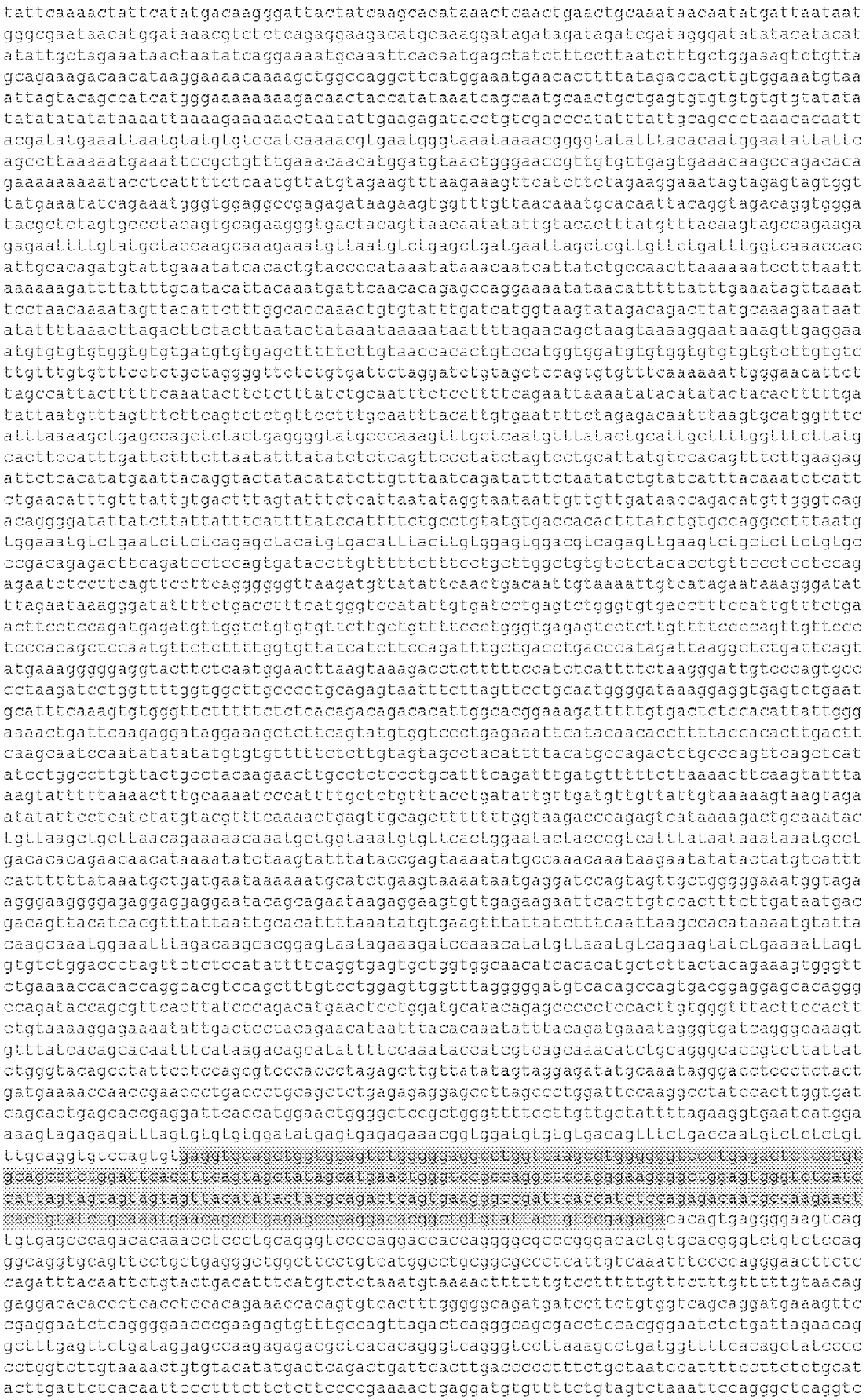


FIG. 7 (Cont. 17)

tgcaggacctgggtaggctacggggactttctcactcaccattgtctggactctcctgttgtcgtctgtgaacagagatgttt
ggaagatgaagtggacattagtcatgaagggaataatactagttttctccaatgggatactgatgtagagctggatcttgtgc
ttctcacactgtcacagagtttggactctcacccgtgactttgaggagagctgaggatggacactccattgtgctgtgagctc
tgggtaacaatagtagggccctggctaggcagcctaaggtcaatactgctggccttcaggaaagacaggctggaattcctggg
aagacctgcatctgccgtccaccatggagtcccatcgtcttctattatgccctgattgaatcagccccacctaggttatctag
aacactcttcgtgacttacgaaaaaataatgggaggctctactaacacctgtgttatgccatgggagcaacacctaagctagt
gtgtgattgagtagatgagactgtggtctagtcaaggtgacacataaaattaattgttgccattataatattttattatatat
ttggcaatatagtcgtgctcatattataaatacttttgctacgttgttgttatgtcagaagcttttgaataagaacagcttca
tcttgaataggggctaggaaaaataagactgagacctgctgggctacgttcccagtaagctaaggcgttcttagtcacaggat
gagataggaggtctgcacaggatccaggtcataaagaccttgctgatgaaggttacagtaaagaagctggccacagcccacca
aaaccaagacagtcacgaaagtgatctctattcatcctcactactcattatatgcttattgtattgccttaacatgctaaaag
acactccccctagtgcatgaccgtttacacatgtcatggtaacatcaggaagtttccctgcatggtctacaaaggaggggagg
aaacctcagcttcaggaattgcccaggggactcatgaataatccatccgttgtgagaaatacattcatccctttgagagaaaa
tgcacaggggtggaatgaggctgggaagctgatggcacatggtggaagcctgtccctgagtgaaggagaggggaagctgga
ttgggtggaaggtctctatatttgtgtgctgtgcaaggaagtgcaaaatataattgagttttgtgcaagtcagtgctgcctct
caggtgatccccatgactcccagaaatggctctgcttaggaatccctggggagtcagtcatttcattagagtagaccacagga
catgggcttcagcacacgccatgccacagatgtcagaaagcagctgctgggaacctgacccacctgcattttgctgcctgtag
gaaaaggcagggaggtgcatcctcagggacaacacactgttttggatttctataaagaacgctgcttttactgtgttttattg
gaaaatacatgaacaaatgtgagcctgcaaacaattgtaattttcagttatttaattgcattcatttgtaattctgcatgat
atgctgacacagagtcgcatttttcatagatattgttcaatgaatcaagaacatgcattttccactttcactggtttttctcc
gtgtgcagagaccttgagtagagcctgtctggcccttatccacactatctcttgtgtccccgggaaaaagcagagatttgcct
gactgcagaatctggggtaggagtctgctcagctcacagcctgcagagaagcccagtgaagttttatggagtcagagagcttt
cccatgtggggaacctctagcttacccatggccagagattactggtcagctgtaattgagagtttaacaattagagcactcag
aagcctatctcatcgcagcttcattatgtaacttaccaccattagactgcggtaataactcaatcttgatttttctgacccca
ttttctcatcttattcatttgtaaattgggttatagaaaatgttatgttttagactctgattcaaatctcagaagtttatgaa
ctcatcaggaataatacaaaatgtgtctagttttggggaaatgtaaatgaatgtccatgcagtgtgtgtgtttgttgtgtggg
gatatgtcagtcacaccccaatgaacatgatttctgaattacatcatcaaactacaattagatttgctgaaaattgcctgcag
taatgtctgtgatgatgaacctgtcaccttgttgtgaggatgctcagtgcacaggcgaggttgcacaggagacatccaaggag
cagcccccaggcttggcagaattcctggccaggagccagacataggactgggtgtctcaaaagcagattccccaaccccatcc
ctttatttggactgcatgggcatcatgaggaccagcaggagatgctcagaactcactcaaggcagagcaccatttaggagcag
gtgcagcgaggaaacagccagagaacctctgactagaagcttgggttgttttcttttgcttaagagcatccaagcctaagtat
atcaaccactatatgtatatatataagtagactatccactatatatagagagagatagatataatctgtatatatatacagat
tatatctatctatatacattatatatacagattatatatatatataatctgtatatataagaaagttatgagttacagattat
atatatacatttatatatatacatttatatatatttatatacatttatatatatacattttatatatattatatatatacaga
gcaaaacgaggttaatatgactctgccattaactccttgaacctgggtcatttttttctgagaatgccgtcatctacagcatga
tggttctcatgtcaaaatcaacacgcatagttagtcaccatgaagactgttttatctcatggtagaaatgtttatttaattaa
aaaattacatttcatacgaaagggtctgtattatttctttctcacactgctgtaaagacatcacctgagaccgggtaattcgt
aaaggaaagaggtttaatggactcacagttctgcatggctggggagcctcaggaaacttacaattatggtggaaggtgaaggg
gaagcaagtcccttcttcacaaggcagcaggatggagagagagagagagagagagaaggagaagcaggataaagagccggaaa
cttatcagacaaaccaatctcctgagaactctatcaggagaacagcgtggaggaaaccactcccacaatctaatcacctctca
ccagacccctcgcctgacacttggggtttacaattcagtattagctttgggtgaaaacacagagccaaaccatgtcagaattt
ctaggtgagaattggtcaattcataagttattagtgaagtatcagaaaaataaatagcaccagtgttgttgttatccagttaa
tttataaaccatgtcaatatccattttatgagaggtgtaggaaaagtgtgagatggatagatagatagatagatagatagata
gatagatctaccaaatacaatatatataactatattatatatattactatgtatataatatgtagtaagtgatatatggtata
tatatatgacattaattctaccaaatacttcacatatgtatgtgcatatatatataatattaggtatgatatatatatgaaat
atcaggacatatatatatatatatattttataatgtctcctgggatttagtgttgaatttttttaatatctacatgtattccag
gataaatgttggtggacttcataaaatatattctaatttttatgtgcaagatgatcactttcaaataaggtttagctacagaa
accagatgtatctttctaccagaaattactggaaagcacagtgaaatttcttaatcaggattttaagatgcttgacaccactc
aacaaagacagtgattactaagagagagaggaaataagcataaggagccctccggtgaatgcaggctcagatacttcctcaaa
ggtgttgccaggctacagtgctggagtggaaaccatgtggatttagcattaataaaatggagctggaaacccatgtaggccaa
gaagtgtggataccacaggatagcaagtggattgcagaaaactgtcagagagtgaaccccatagatggcaggaggaacaccca
gacttgacagagtgcagatcagtgtgtagaaagcagggaaggttgtacgtgagaacacaccctgctgcaggaagctctcccta
aaatccagagccatggtaaatatatgaatatacacttacaaactttaaaacatacggaaaggcaccataataaagtcaaataa
aggaaaggtgggttggctacattaaaatataaaaagagtatttctgagcaaataataatacttatgaggggaacaattttatt
ctaccatggcaaatgatttcagagaacaacattcgaaatgcttatggccataatgaggaagcttcaaacaagtatacgaatag
aattattaccagagtggtagtaccagagccctcagctttctgatgaaaactgattcttattatgaaagctaattattattata
agcttattattattaacactaattattattaattataatattatataattattataatattattatgaaagcttattattatt
atgaaactgatattactagagccctaagctaagtgttattaccagagtcctcagctttccgatgaaacaacaacgtctgataa
aaattgtaataacccaaacatataaaatcaattcaaattattctaaggatgcacagtaaataaaaatcattgattgataaagt
gtgctgctatagactgaatgtttatttccgccctcagacatttgttggaattctaaccccaatgtgatggtgttacgaggttg
ggccgttggtaagtgaatgggtcaccttggaagatgactaggccccatccaccctcatgaatggaatcagtgcccttgttag
agactccagaaagctccctctcctcttccaccaggtgaaggaaaagtagaaagatggtcaactatgaaggaggaagcaggttc
tcaccagataccagtttcaaagcatgttggccttgcacttgctgaccttcagaattgtgacaaatacatttatgcttgatctg
aaccacccagactattctcttacagcagctaaaacatcaagtctcagctagggcagtgagggcccacaatacttgagagacga
gcatcaccctctcctttccagttcaggatgacagaagcttgatctcgggctgaactgacaagcagagagtccttcctctcccc
cagatcgcagttgaggccgtggtgtcagatctctgtggttgagagtgaattccagtctgtgatttcatggatgcctttcttca

FIG. 7 (Cont. 18)

tctagttccacttatgagacagagattccatgctatgagttataggccaagaatagaggaaccccaattattcccacccagct
cacctgtagggcagaggatctggagagctttctgggtgaggcacaaagagactgtatgagtccacccctcccatgcagtttcc
tgtacttaaagcagaggtgtcccctctgacacagatgaaccctttcttccgcaccaaggcagaggcggttatatttttacagtg
gcagacagagggcataaaaacagaaatgcagagctctctctaatggatgtgactttatttgcagtaaaaggagaataatttca
accctaggtttttttctaaaatattataaatatttatggtaagttattaatagaaagctggtggcttcatgagagcaacacatt
aaacaggaatccactcatttcagcggacagaaggagaaaaaccataatttaggaataatgagctgggcactgtggcactgcct
gtggttccatccacttgggagtctgatgtgagaataacacttgagcccaggatttcaaggccaacctgaaaacgtagctagac
cccatttagtaaaataaataacattttggggtcaggacaaagttcaaaaactgcccctgaaatgaagcccaaatttaattgtg
taacactgtggattaatggatgacacaacagtgtcaccatgcctgctgtgagtgcagtgtaacacttggatgacatatgaaga
gatacagacacccaaacagagacatcagacagtgaagctgtcaaaggctgcactgccgagcgtcaggctttttatggaaaccg
tgtgtacatctggaactgcacctgggaatgacgacatcaacccttaatagtgtcggggaaagagacgtcactgaaatagaca
aactaagggactcaagaaataaatagagcgattggttttaccaatacaccagagcgttttgggtgatcactattcagagtttc
tgaattgtgttacctaactgtcattcagaaaataatttatgagatacacaaagaaaaaaataacgtcacgaatgtacaggaaaa
tttccagaaaacacaaactgtctttgagttggtacagattttggacttaacaaatggagacttcaaaacaattattataaaaa
tgcacaaatcacaaaggaatactatcctagaaaagttaaggaaggtatgatgacagtatctcaccaaaagttaatatcaataa
tgagagagggtttttgaaagaaagttatagacacgctaaaattaaaaacacagtaattcaaaactatatgtcagaggtgataa
gcagtatacttgaacctaaaaagaaaaaaaagcacacttagatatatattagtagatatgctatattcaaagaatagtgaaaa
ttgcaataaaatgaaataagcttaacataaaaggtggacccagctagacaaatcaacatatgtttagtgtgaacattagcatg
agaagagagaaagaaatatgtcacaaaaatatgtcataatataatgacagataattccatgatttttatgataaatactaata
tacacattgaagtatgaatagctcaacaaactcaaggtaaaataagttataagagatcctcaacaaaacacattataataaaa
tattttacagaaaaactactgagaaaatcttgaaggcagtgagagaaaaacaacttctcatatacaagataattctatcaaca
gctgatttctcatcaataacagctaatgctaaaaggcagcaggatgacatattttccctttgtatcccatttttatcctcaaag
gccacctgcatacaaagtagaccagtcttacaagaaaatcacagccctagtgttcttctctcaaggagcccggctatggacct
aatggtgccctccccaaagtcataagtataattcccaacctgcaatgttacagtatttggaaatgagacttttgaaagtgata
gagtttgaatatttgtcctctcccaaggtcatgttgaaatgtaatcaccaatgctggaggggggggcctggtgggaggtattgg
ataatagaggcagatccctcaagaatggcctatgcaatccatgtggtgatgagtgaatttttctgttagttcgcatgaaatctg
gttgtttagaaaagtctggagcctcctccatctcttctcttgccctttcttggccccatctcttctcttgccccttctcttgt
catgtaatgcacctgtgtgcctgctgcctctttgccttccacaatggttataaacttttctgaggccctcacaaagcagatgct
ggcaccacgcttattgtaaagcctagcaaatggaaagccaaaatgaaacctgttttatttataaattttccagcctcaggtac
tctttcctagcaatgcaaggacacagcaacacagaaaattggtatcaagaagtggagcattgctattaaaaatatgtgaaaat
atggacgcagctttggaacaggataaccgtcagggatttggaaggtttggagggctcagaaaaagtcaggaagataaagaaca
gttgggaaagttttagagactggttaaatggtttgaccaaaatgatgaaataaatatggacagtgaagtcaaggcagagaatg
cctcaaatgtaaatgagaaagttatagggaagtgaagtaaagatcgcctgtcaagcaaatcacttgactgcattatgttcatg
tcctggggatctgtgcaagtttgaacttacgagtgacgacttagggtatctgacagaaaaaaaattgtcagtagcaaagcatt
caagatggagtctgcctgcttctaacagtctaaaatcaggtgcagaagtgaataaatgacttaaagttggaacttctatttaa
aagagaagtggaacatggaagtttagaaaatgtacagcctggttctctggtaaagaaataatccagttacactgtgaagcaac
cgcttgctagaaagattagcttgactaaaaaggagctgactgtggtaatacgaaacaataggaaaatagtcttgaagtcaatt
cagaaatctttgaggccaattctctcattacaggcttaggtataggagcagagaatgttttgggggtgagaccagctagggc
tcaaaggtacagctcggttcaccacgtctgatggcgcaagctgtgatccttggtggcttccatgtggcataaagcctgggtct
gcacagtatgcaagagtcaacatggcttggtgactggcctctagatttcagaggatgtgtgagaaaggctaggtgccagaaat
gagcctacctcagggtcagagtacacacagagtaatttttccagggcaatgctgaggtgaaatgaagagttaaatccccccaaa
agagatccccaggagaacactgtgtagtggagctgtggagagaaggtcactggccctctagaacccagaatgggagatccaat
agcagcatgtgccccaagcctagaaacgctgaaggcactcagctctaaactgtgacagcagccgtgttggctgcactgagaaa
agtcacataagcggttttgctctcagacttgcgagcccataattgcaccggctgcaagatgtggagtcactggtcactttgga
ggcttaagatcgagcgcctgtcctgctaggttttaggcttgcatagagcctgttactcattcatttggcaagttcctctctttt
taaaatggagatgtttacccaatgtccgcaccaacattgtacctttgaagtaaataagttctttctaattttacaggctcaca
gatggaagaaatgtgggcatgaatcttagacaagactttggactttaatggtgaaacaagttcagatttaaggggcagatttc
gaggggtgggtattgggaagaaaatgatcccattttgcagttgagaaagatataagattttgggtgataagagttatgtggct
tccatatatgtccattcaaaaatctcatgtttgactgttatccccaatgttcgttgggggttttgcgttacgggggcggattcc
tcctgagtggcttagcgccatccacttggtgacgagtgagttctcacatagttagatcactcaggatctgattgtttaaggga
gacgtggatctccccctttccttctttccccctgctcaccatgtgacactcctgcttcccctgtgccttttaccagaaatataa
ggtttttgaagccctcaccagaagcagatagcagaaccacactcctgtacagccttcaaagcagtcagccaaattagaattt
atttttttataaatttctcatccccaggaatacttttatagcagttaaggaatttctataagaaagaaagtactgaatttaaag
gagacgatgagggtgaaacatcagaatgaaattactgacctcaggagtaaagacaccagacagtctctctctctctactttctc
tctctctatttctctctctctctctctctctctctcacacacacacacacacacacacacatgccctaaatgaaaagatcatatg
atcaagtaacaatatgatggctgctctgagccaaaagtagaagcctcaaactaaacctatcttgtcagcatcttgatcttgga
gttcacagcactgataaatggaataaaattaatgttgcacgagtcaccaagtatgacagtttgtaatggcagcttaaactgac
gaaagaaaatttggggttaagaagaggaaatctgatgttacaattatttgaacattgtgaaagtagcttggaattgggttatg
tgtaacaggatggatacctttgacatatatgaagaaatttgcatattgagggtcatgctgatagacagaaatgagtggttttg
gaaaatggagcaacagtcatccttatcataaagtttttttaaaaaaaacttggctgggcagtgatataatatttagtgaaagag
aagttgtgagtagtgagaaattgtgagtagctgagaatagttctaagtgttgaagatattttgcttgattcctcctgagtgct
taaaataagtgaggtagataaattaaaatcagaaaaaaataaaagaaaaagaatacaaaagctgagggcttagaaaattcaca
acctatccatattgcaaaaatcagaaactgtattctacaaagaacactgagtatatggctcaaatatcactcagtaagaagct
taagatactctatgaaaagaaatatttcaggttttaaagaatgagaattgacctgagacaaatttgatgaatactgttagatt
tttcagatttaatggcctggaataatagagctacttggctgcaaatgtacacaatttcttccagaagagagaaaaataagcttt
aaatttatttagaaaccatcagaccactgcctctatttcaacagaccagaaagcctgtttctaaaatcttgaggaagaaacca

FIG. 7 (Cont. 19)

cccaacagaggcttgggttgggagcacccagcaagccctgtgtgtagggctgcatgaggcccttgacatgggagctgggccta
gcagtgcctcaggagcggtgcctctgcctgcagctttggagctgattctgctgctcgaataagctgagaaggaaaaagaatgt
ttcagagaagattacagtggaggcttaaagcatatggaaatttgtttttcctatgcattgtatttgctggagacaaaccaccca
ttttaccccctatttttttctttggcaatgaagctttctattctatgcctaattcaacaggacacagcagcggctgtatccag
tttgacaagattcagcatgaaaggttcctattacctgtgccggatgcatcactgatatgcggccaccagtttcttaggttcat
atcactttaagggaccaaatacaaatgtcaatagcatatgtcattcttaaactgcagaaatggtgtcaaagaagaatgtggag
ataagagagcaggaggaattatgaaaatccagatagcatcttctcttctagagtggaaggtacactagtaatttcatgaaaca
ataaaatagatgaaatgtgtcatcatcatggagtgtctcacagtggcagtgcacaaataaatttctaaaaattccataaggta
ggtgtgatggatgaggcttatttccacacagggagcccataaatacccagataagtaaaaaatccaacacctggaacgaaaaa
tgcctcatcttgacatcacaaacccatctcagtaagtccgaggagtaatgtggaaatgaaacggaaaattcacaaacacattt
attgtgaaatttttagcacatgtttgaacattaaaacagaattgtccacaattttaggaaaaccactccatgacaatgagtca
ctacactcatagaaacaccactgagtcaacagagttctaactgtcagcaggtcagtactgaggcctcaggagaatcaaggctc
tagggtacattttacagaacccagaattgagccacacaatctatagccaaatgatctttgacaaacttaacaaaaattaacaa
aaatatacaccagaaaaaggacaccccattcaataaatggtgctggggaaatggaaatgaacatgcagaagaacaaaactaga
cccctaccctcaacacatacatactcaacacaaaatgaatttaaagacttagatataagacctcaaactataaatgtactcaaa
taaaataccaggacaactcttctgggcattggctgaggtaaagaatttatgactaacaccccaaaagcacacccaagagaaaa
atagacaaatgagacttaattaacctaaagagatatttcgcagcaacagagtgaacaggcaagttgcaaaatgacagaaaatt
ttcgcacaccttgcctttgacaaggaactaacatgaagaaattacaaggaattaaactatacaacgacaacaacaggaagaag
aaccaaataaccctattaaaatgagcaaaggacatgagtagacatttccaaagaacacatacaaatggataataaatacataa
acaatgctcaacatcactaaccattagggaaatgcaaattaaaactacaataagatattatcttacaaaagccacagtggcta
ttattaaaaactcaaaagtatcagatgttggtgaggatggaaggtaacaggaactcatctacactgtagatgaggatgtggac
gaggacaacctctatggaaaatagtatggagtctgcccaaaaaactggaaatagaactgccatttgatgcagcaatcccacca
ctgggtaactactcaaaggaaaataaatcattacttcaaaaagatatccatgcttctatgtttaccacaaaactattcttaat
aacacacatgtcaacctgagtgtccaccaacagatgattttataaaagaacatagcacgtatacacaattcaatactagtcaa
ccacaataataaatgaaactgtctttttgcagcaagatgcctagaactgggaacaacataattagtgaactaactcacaaacag
agagtcacatgtcacacattattatttataagtggaaggtaacaacgtgtccacaaggatatggagagagaaatgatggacac
cggagacttagaaggatgggaggtggaaggtgggagcatgaggagacattacctagtgggtacaatgtacattatttgggtga
gagtacactaaaagccaagaccactgtggaatatatccatgtgcaaaagttgcactcatagccttaaatttatataaataaa
tgtacaaacaaaaaaattaaaaatataaaataattaacagttgaccaatgatcttaaagttaaaatttagaccaggcgtggtg
gctcacgcttgtaatcccagcactttgggaggtcgaagcaggtggatcatgaggtcgggagtttcagaccagcctggccaaca
tggtgaaaccccatctactaaaaacacaaaaattgaccagatgcggtggcaggcacctgtaatcccagctactcgggaggctg
aggcaggagaattgcttgaacccaggaggcggaggttgcaatgagccgagatcatgccactgcactctagcctgggcgacaga
gcaagactccatctcaaataaaataaaataaaatgtaaaaaatgatcaataaatgaaattactatcagttgaaactcattaaa
tttaaagacattttctactcaagtaactataagaacatgaatgtcaagtttcagatgggaaactattttcaaatcagataacc
accaatttaattataataagaactctcaggactcaactgtgaaaaaaaaaaaaggaaggaaggaaggaaacaccccatggtta
aaatagaaaggttggtgcagacatttcatcaaataggatgtgcaggtgacataagcatttaaacaggctcttaacaggatt
tcccattaagggaatccaaatcaggcccacaatgagaaaccactatacacttttagaatggctgaaattaggaggaaataca
ggtaataccaatgctgatgagcataccaagttcctagtgtctacgacattgttaatgggactgcaaaatgaaacagctactct
ggaagataatttttagttttttctgcaatcaaacatgcccttaacacatgacctaaatatcccactcttgaattttgcttcag
agaaatataatcttatattcacacaaaacctctattcaaatattcaagatattgcgtgtgtgtgtgttagaaactaaaaataa
cataaatatctcaaaatctgaataggtgaaaaaactaggaagcaactataaattgaataccatcagcaataaaaaatatcaaa
tgatcgattcacaaaccattacaggtggaactccaggcattacgctaagtgagaggaagccagtctcgactatcaaagggaca
cagctgtaagcagcacggtcatcctcaggtgtcagtggtttgggctgggctttctttgtctctttcctgaccagacccagatg
ttgagctctgccacttggagatggaaaattctactattttcaaccatgcactgaggtgtgaattacttcacagactgaccaaa
caaacatgggctccactgaagagtgtctggcatttgtttcaaccacaagagaacttttcccagctcttccatgtccttggttc
tctcctgcaagccaggagccctggagtgtagcctgcatctcccatgtatccacccagctccttccaagggtcttccaccacac
cctccactgtttgtgagagcactgggaggctttcaatttttccacattctgttgttactgaagttaggatgtttaggacttat
taagatcatatttttatgactgaatttcattgccccctctctcctgggacagagctcctaaacaaggttctgcaggtgtagaca
aagttgagctgttttattcctcagcctaggagctgagcgctcagtggagggtcggagaggagcttcccaccttctcagcactt
cggttatggtgggggagaacctctgccataggacagagctaggaaccagagacccaatgttcccagtggcgctggacccaggg
gagagcctccatccatgagtggggctctatggaaggagtgagtctctggctctcagtagctcttgtccagcactgaacctcag
catcatgtgctgtgggcagggtcagagggccaacgtactgcccccctggggaagagtttcctctggtgggagttggtagaaggt
gccctgtcttcttggctgcatctgtccgcagtggagtttacatcatgctgagctgggatgtggaaggaaggaagagcaccttа
gatcaaatacgatgactggccttactgagttttctatattttcttaaataaatatttcttcacttgctttatgctgttagatc
ctttccaaaccctgtaatttttttcaaaataatattttcactggtctcatgagggcatggattcattgagcccctcatgctgttaa
agagaaatagaactgttttttttttttcacttttagcgaacatccatgggttataaaataattagttgacatttcttccaaca
ctttacagataccatcaactttcctcttgcttgtgaggttttaaccagaagaatgctatcatcatcttttctgttcttttgga
aggaatgccccctctactcacctccacttgcctgcatatatttctatttgtctttgcttttcagcagttttaataagatttac
ctaaatgtgtgtgggggaagcaggggtgttattctgttgttctgtgttctctgagatgcatggattcaccatttactctgcc
tccattttggggaacacagttagaaaaaatgtcagtgtgagcccagaaacaagcctccctgaaggggaacaggaccacccgg
gggcgctcaggacccactgagcacaagagccagcctcagggcaggtgcagacgggggttaaggtctggtttcccgtcagccct
gtggcttcctctccataaaacagtttcctctggggcacttctctggattccttatcctgttcttcctattcttcctgaagaag
aaacatttgtcgtaacaagagaaaaattttctcacatgcaccaaaggcagagtcacctacagtcacttattccggtttctcaa
tgtgaataaattatcaatgcttctgaatttaatcagctaaacctattaaaggtgcggtgtttaactcaacactgccgccagct
caacagaactccaagggtcagtgagcaggagggaggataaagggcatgctgggcactggggcagagggagttagcatccagtg
caagagaagaaaggccccgtggtggtcactgtcaggacttcaagcccatagttccaattgtaggtgaccacgttcaaaagaag

FIG. 7 (Cont. 20)

agagacctcatccatgattagtgtgatgtgtcaagtctgatagtgccacactcacacctcaggtgattatgaaaagatttacc
aactctactattgtctgctgagagcagcacaggcctctcaagaaattccaaactggaatttcctcaatggaacaggaaaggag
gctggcttagggctttataatgatttggtggtggggtcgggggtcatttattctcaggagaaggagcttgtgtgatttaaac
ctcacattggcatcagatgagggagcttctacgatttctgactagatttcccatatgtgggggacaagggagaagaagaataa
accttaattcatcagcagcaagcaccaaaataggacctgacactttattctccctagcagcttaagaaaatgagtgaaaaaga
gagatgagggtccactgtgtgtgaaaagcaaacagaaataaagaaaataaaaattttttattatggtaagcacataataaaaag
aaagagaagaaggaatgagacagacagtggtgctgaatcaatgtcctgggtggggccttttctattatccactgtcatcagtt
tattctgaaggtctcaggtcagcttcctgcttcaaactatcacaggcccttatagggtatataaaaatccttataggatatcc
acagtttgtcatactttactaaagtagtctaataattagatgaagttctgaatttaatattcagttataataaatattaaaaa
ataccacaatctacaaattaggaaaccgagactatatttttatcaagggttacagccatcccatatgctggaaagcatagttt
tggtaaagatgagagacagacactcccaagaagaaggagttgggcagaagatttatgctgaactgtttggctaaacagactta
gtcaacaggttacagagaggctactgatgttcatggaggtggtgctgacacatgcatactgaacacacatgcatttaacatgt
gagtcctgttcaattgccagtggtgacttagcatttaaattcattacagtcaggccctatgtgcaaacagcagaagcagagac
acaaaggcactcagggtgcagcctctgtaaacagccagagccaggccatggtcagcggtctctgatcaggagaaaggtcctga
tatcaaatgttcaatcaaagctgggggttatggcttgtggaacaggggggtcagttcagcagggatgggctgcaattgtcttcat
agtgcttgtctcagtgccagtgcttactgagccaccagagaaaacgaataacctattggcagttagaacatagtttatctttt
aagtgtagaagtgagtggcaaaatcctcgtctagcaaggccttaggtcttgtttataatttgacatcttactgccactgttct
gtcagtcttatgatttctattttaacataagtgttggccattgctgcgtctaaaccacaaagggaagaaggtataacgaggcg
tgtctgatctcttgtttagacatggttggaaacagtttttggatttttacgggggttccctaggccaagagatggactatttaa
tcagtcgtgggttttagggatttatttttaggttacagtttataaatatgaacccaactattgactttctgcaatttcactgc
tgtgttgtggttaaaagtacctgataaaattccttccaaagtggttcaagagcaatattctaccctgatgtttcttacaatag
atataattccctgctttaatgttattagaggctattgaaaagatgtagggaaatgatggtttaatctgttgatgaatagtgtg
ggtaaaatgcagtcatcactttcaacactttgtcatgcatgcatgtaataggacagaggtgagcattgtgggtaaatctctaa
atgtatgggccttccagctaccaaataataggctaataactgatgtctccctgaggggattaactataaggctctcttgctag
ggagagaatctttggccaaggaagttcaagattttcttaaggtttggacaattttagtttaaggatgacaatttttcttcaaca
ttttcagaagattgtggatgggatggatgctatgttgtatacataatgctaatgccttccatatttagataatattataaacc
cctgactgataagactgcttgcttggtgtgatgacccactacaatatgtatactttcagttggtatgctatgtcatttttcctt
caggtttttacttttccaagttacattagtcaggtctctaaaatgcaggactgcatctaaaatgtgttatttttgttgtgcattt
tcacatgttccagaaggtgggagaaatttctttgtgtgaagagcatcccaaagtcaggcactcctctagaacacgtgtttaat
ccttgtctttggcttattgatgagctctgttgactgcaataacttctgccatccgggctgacttgacatcacatagaggaaca
aattctgaatgaaagtttgctctactcaattgagtgcataacctcatttcattactgatgtataatgcatcagagataatatt
agatcaaggatttcaatgggaatctaatctaaaagatgtaaacaaattttcataatttagataaaattactgtgagcacactg
ctgctattcagccatgtctcctatcacactgaatccacactaactttgacctaaaagttagcatttgttctaatgttcagaat
tgttatttttatcataacgtctctagatgattacagagtgtggctatgttggccatcagtaaaggaaagctattttaactgaa
tgaaaatgagacaaagcacacaacctaatgtaatggaagtcaggacatgagtgtctccaggcttttgtgtttcaagagttcat
gcaccaggggatttcttttcttacttgtacacagagcaacacccaaaatgttcatttcctctcccatcgactcttatcatctg
tttctatgtcagttagctttgaatttttgaccccagctgcattcaagtagctgcaaataagcgtgatttcattctttttata
gctgcatagtattccactgtgtataagaaccacgttttctttatccagtctataacggatggacatttaggttgattccatgt
ctatggtactgtgaattgcacagtgatacacacgtgagtggatgtgtttttttgttacaataatttgttttctttgggcata
tacccagtaatgggattgctgaggggaattgtaggtctgttctaagttatttgagaaatctctagatcgatttccacagtgct
ttggccaagttacattttcaccaaaagtatgtaagtggcgcttttctctatagccttgcctgcatctgttaatttctgatctt
ttagtgatagcaattctgacatgtgttagatagtatgtgattgggttttgatttgcacttatctgatgatttgaggatgctga
gtatttttgtatgttagttggccacttctatgtctgtatttgaaaagtttctgtgcacgtcccttcccccatttttaatggggt
tatctgatttatgctgctgatttaagttccatatagattactgacttgcacacacggagaaagccagtattcccaactaaata
gaaaaacataatcacttgtaggtatagacatactgaatttggaatggtcatggcttgcatgttggtattgaaatgggacagca
actttggaaaatggtcttcactgaaaatctcatacacaagtgtacctggtgtcaccacttacagtagttgaatggagaatata
actcaagtgcccatcgactgccacagggatgaagacgccgcggtgtgtctgtgtgtctctaacccacagggatgaagacgccg
cggcgtgtctatgtgtctataacccacagggatgaagacgccacggtgtgtctgtgtgtctgtaacccacagagatgaagacg
ccgcggtgtgtctgtgtgtctgtaacccacagagatgaagacgccgcggtgtgtctgtgtgtctctaacccacagggatgaag
gcgccgcggtgtgtctgtgtgtctctaacccacagggatgaagatgccgcggtgtgtctgtgtgtctgtaatgcagctttaaa
gaggagtgaagcactgacataggctgcaacttggatgagccttgaaaacattgggtgactgaactgagggagacacggaagtc
tacatccctaattgtcccattgacacgaagcacgcagagcaggaaaatcccagatcacaggaggtcagggaaagggaaacaca
gagtgaccgcttaatggaggtgaggttcctttctgtgatgaaaatgttcccaaaccaaatagtggaaatggttgcacagca
ttgtgaatgtgtaaagtatcactgacccatacacttaccaagggctgaaatggtaagttttatgttatgtgtatctcaacaca
ataaaaatgagtgccacattttgtttagcatatcaatgacaataacagttcaggtgaatgctggattcctcatcacaaccagt
gcttcctgatggagctggattcaggggagggactggagtgggttgggtgcacaggtcatgaaggcagcaaaaattccaaccca
ctcctcaagagtccagtcgccacctccagatctatgtccgccggggcagctcttcctatggctgagctacatgagcaacaagc
aaataaccatgtttttgttgttgttgtttagttttgttttgctttgtttttagacagagtctcgctgtgtcacccaggctgg
agtgcagtggtgcgatctcagctcactgcaatctctgcctcctgagttcaagtgattctcctgcctcagcctgccctagtagc
tgagactacaggcactcactacgacgcccagctaatatttgtatttttagtagagacagggtttcactatgttggccaggctg
ttcttgaactcttgacttcgtgatccacccgcctcagcctcccaaagtgccgggattacaggcgtgagccaccgcgctcagcc
acaaccatgtatttttaagcaaaagacacagtgaggggacatcagtgtgagcccagacacaaacctccctatgcgggttcaca
ggacagcatggggtgctgaggacagaggtgggcactcaggaaccagcagggaaacccaggggcgcttggcacttcatggggg
ctcaggaccattgtgggctcagtggtcaggcaggctcaaggctcagcctcagggcaggtgcagcaggcggggaaaggccctgg
agactgggtttagtgtcaccttctcattgcgccactggacaccctccactacatctattctaatgtgtatgagtacttatgag
tttagaaaataacattgatattataaatctatagccatatgtgggtgcatcaagttaccctcttcaacctatgtggaccctgt

FIG. 7 (Cont. 21)

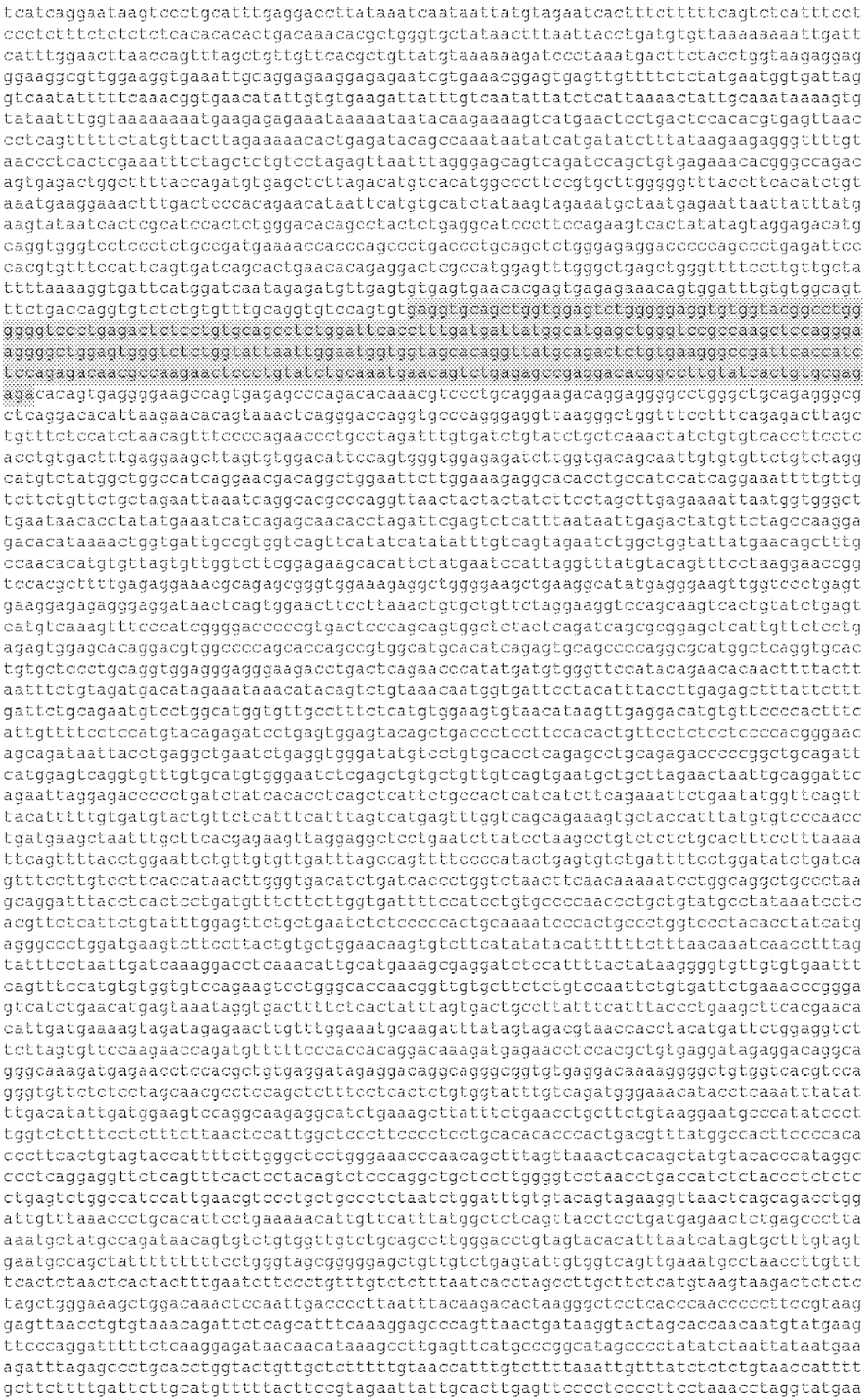


FIG. 7 (Cont. 22)

agttaatcaagccccttcctcggggcccagagaattttgagcattagccgtctctttggccgctggcttaataaaggactctt
aattcgtctcaaagtgtggcgttttctctaactcgcctgggtacaacatttttggaggccgcagcgagatattaacaccactg
ggcgagagccggtctcgctccgggctccccggaaggatggccagctcggaggagggacaccacctgaggaaagaattttcag
gtccgcaaagagtgaccgccttccagaggagagcggatcgaccactgtgtcagcgccctaaaagtcaacatctgagtcctcag
cttctgaccccggggtcaggtaggtcggatgtgacttcgtttccggtgagaggggagcggccctgacgagggcgctgagtcct
cagcttctgaccccggggtcaggtaggtcggatgtgacttcgtttccggtgagaggggagcggccctgacgagggcgctgagt
cctcagcttctgaccccggggtcaggtaggtcggatgtgacttcgtttccggtgagaggggagcggccctgacgagggcgctg
agtcctcagcttctgaccccggggtcaggtaggtcggatgtgacttcgtttccggtgagaggggagcggccctgacgagggcg
tccctcttttgactcagcccattactctaggatgctagtgggttgagccttcgttttccggtaggcgccttcgtatcttggtt
tgggtgggaagtggtcctgaccaggaccctcccttgacttagctcaagacccaggacgctggagagctaagccttggtttctg
gcagacctctctctctctcttctatcttccatccttcttttggaaatctccgggaaaggaaaaaaaaaaaaacctgttataaa
ctctgtgtaaatggtgtgtgaatgtgggaggacaaaggcttgcgtttgtcttccagtttgtagctccatggcgaaagctacgg
agtttgagtgggccctcacctgccgttctgtggtgacctcataaggcttaaggcagcatcgggcatagctcgatccgagctgg
gggtttatactggcctgccaatgctaagaggaacccaagtcccctcacggggagtggccaggcaggcatctaaatgatcccat
cacgggacccccttcccttgtctgtctaatagagaaggtaaaacaggaaaactgtcatcattgtttacatgccctagggtcaa
ttgtttgttttatgtttattgttttgttcggtgtctattgtcttgtttaatagttgtcaaggtgttacatgtcaggacatcga
tatagtccacgaggtctgggtaaaaatttcttcaaggtccttagtgctgatttttttgtcacaagaggttaaatttctaatcaa
tcatttagactggccaccacagtcttgtctttttctgtcataaacaagtaagctgttgttacggaaaagagtgtggagaacatt
cacctgattggaatttctggcaccatgaaggttgcgggtatttagattgtcataccccacgtcctagtgattggtcccccttct
aaactgaactggtggtgggttcaaaacagccaccctgcagaccttcttgctcacctcttctgtcattctgtaacttttcctgc
gcccttaaataggaccttgtgtaaagaaacctacgcccgtcatgctttacttcgtttagactcctattctgttccactgtggc
tactttctcatcttaaggacgatccgagtggtccttttccccctcgtccctgccccttaccccgcacatctcgttttccagtg
caacagcaagttcagcgtctccaagacttcgctctgctctcactccttgaacccttaaaggaaaaagctgaatttgaactgtt
tgcctttgaatcgtggagacataaaaaacacttaggatataggtctagaagaagaagaagagggagaacgcctagatcgaact
ggcccaggagacctcagactggccaccaatcccccctccctcaatcttaaagctacagcaatgtggcaagtggtattagctgtt
gtggtttttctgttctttctgatcatgttaattctgttttttccgacactccagccccccagggaaagagtttctctgccggtg
ttggatctgatatctctgctcaagactttgctaaattgtctttaaataataataataataataaacgggaaacacctcctcct
ggccccgtaagggttggagccctctccagtgtatgctggaaaatttttctcttggtttctcagaggactatggagtccgcctt
agaaaaggcaaggtctggacactctgtgaactagaatgaccaaagtttggagtcggatggccctgtgaagggtcattaaatcc
taccattgttcaagccgtgtgatgggttgttaccggaactcccggccaccctgatcagtttccctatatcgatcaatggctaa
gtttgattaggaatcctcctccatggctctgttcatgtgccattcgcaattccacctccaaagtcctcctgagccaggccgcg
ttttgcctcaaccctccgccagttcggctcccctgttttgcctccctctgaagaagaggagagtcttcctcacccagttcc
accgccttaccaccagcctgctcccttggcgccatcccgtgtctcttcgactgcgtcccctgtgggctgtgaccgcccattgc
cttccgctacgaccgcatgggaggaagcagccccctactcccactgagagaggcacgagtcccgcggctgatgagcgctcag
ccccctttcctggtttatgtccctttttctacttctgacttgtataattggaaaacccataatcctcccttctctgaaaagcct
caggctttgacctcactgatggagtccgtgctccggacccatcgacccacctgggatgactgccaacagctccttttaactct
gtttacctctgaggagagggagcatatccgaagagaggccagaaagcacttccttgcatcagccggtgggccggaggaggaag
actagagacctcctggaggaggaggaagctagagacctcctggaggaggaggaggtctttcccctcacctggcctaattgggg
cccagattcctcaggtggaaggaggctttggacgattttcaccagtatctcctcgcgggtattaaaggagccgcttggaagc
ccataaacttgtctgagacaactgaagttgtccgggggcctgatgagtcaccaggggtgtttttagaacctctccaggaggct
tatcgaattcacacaccttttgacctggcgactcccgagaatagccgtgctcttaatttggcatttgtggctcaggcagcccc
agatattaggagaaaactccaaaaactggaaggatttactgggatgaatatcagtcagcttttagaaatagcccagaaggttt
ttgaaaaccgagaatttgaaaaacaaaaacaagcgacacaggcagctgaaaaagctgccgataaagcatataaaagacaagca
aaaatcttggtaacagctatccaagagggcagaaaggaaaggcctgcattccagaaaaatggccaaggaacctcgggttccca
ccagaaaagtgaaagaggtgaacaggcccctctaggaaaacaccaatgtgcctattgcaaacagactgggcattggaaaaagg
agtgcccgttactgccaaaagaaaaatctgaaaacaaaaaggttctcaccctggccgcaacagaggagcctgatgattgatgg
ggacagggctcccttgctctcggcccccaggagcccatggtaactgctacagtgggggccagcctgtatgtttcctaggaga
caccgggggagagcactccgcactggagactcccctggggagtgtctcaaataaaaaaattgctgtacaaggggtaactggag
ctatacaagaatatcctgtcacacacacctgagaagtaatcttgggacagaaaagagtgacacactctttcctagtagttcca
gagtgtcctattcctctccttggacgggacctactccataagttacaggcctcaatctccttttcagctcagcaggctcatct
cacactaggaaatgcaacttcccccactgcccaactcttgctaactaccccctctgtcagaagaatacctttctggtttcaccgt
cgtaatcaccggaggagaatactaatactcttttgttagatctacagacactttttcccccgagtttcggccgagtcaaaccct
cccggactggctaaacaccatccgccagtagtcatagaactcttggccactgccataccggtccaggcaaagcaatacccccac
aagtcagcaggctagagaggggattaatccccacattcaacgactgttacaagctggcatacttaccccatgccagtcggcct
ggaacacgccatttttgccggtccagaaacctggaacaaatgattactggccagtacaagacttaagggacgttaataaatgg
actgttgctgtccacccaaccattcctaatccctatactctactcagcctgctcccaccagaacatacagtatacactgtcct
tgacctgaaagatgctttctttgctatccctctggcccccaaaatccagccgatttttgctttcaaatggacagatccaagat
caggagacactacccaactgacttggactcagttacctcagggttttaaaaattcccctaccctttttggagaggctcttcag
caagatcttataccttccgagccagtcaccttaactgtactcttctccaatatgtagatgacattttaataacaactgaaact
atggatggttgtctacaacacacaagagacctgctctacctccttcaggagctcgggtatggagtctcagccaaaaaggccca
gctttgtcttcccagagtgtcctacctggggtacaagataaacaaaggaaaaagggcactcactagtgcccggaaagaagcca
tcctgcgaatccccactcccgccaccaagagacaggtacatgaattcctaggagccctgggatattgtcgtctttggatatcg
gggttttgcagagattacaaagcctttgtatactgctacaaaaggtaatggcccactgatttggacagacaccgaggaacaggc
ttttcagaatctgaaaaaggctttaactgcagcccaggctttagccctcccaaatatctcaaagccttttcatctgtttgtcc
atgagagccagggagttgctaagagagtgcttactcagactttaggaacttggagaggcccagtggcttatttatctaagaag
gtggatcctgtggcctcaggatggccaagttgtttggcagccatagtggctacagcaagcctagtccaagaaactgataaatt

FIG. 7 (Cont. 23)

aactctaggccagaatttaacccttacagttcctcatgctgtagagacttgactacgaagtgcttcaggtaaatggatgtcaa
atgctcgtattttacaatatcagagtttactgttggatcagccttgtttgactttctctcccacaaggtgtttaaatcctgct
actttactcccagatccagattctaatactcctgtccatgactgtcaggagctgttagaagctaccgaaactggcaggccaga
tcttcaagatgtgctcctgagaaaggcggacgccaccgtgttcaccgacggcagcagttttctcgaacaggggatacgcaaag
ctggtgcagctgttaccacagagacagatgtgttgtgggttcaggctttaccggcaagcacctcagcacaaaaagctgaattg
attgcccttactcaagctctccgatgggttaaagataaacgtattaacatttatactgacagcaggtatgctttcgctactgt
gcatgtacatggagccatctactaagaacgcgggttgctcaggtcagaaggaaaaataattaagaacaaagaggaaattttag
ccctgcttgaagctgtgtggctccctcaacaagtggctgtaatccattgtaaaggacatcaaaaagaaaacacggctgttgcc
cgcggtaacccaaaagcggtttcagcagctcgggaagtggcgctgtcttcagctccgtccataaacctgctaccggcagtttc
ttttccacagccagatctgcctgacaaccccgcgtactcaacagaagaagaaaaactggctgcaaaccttagagcaaataaaa
atcaaaaaggttggtggattcttcctgactctagaatcttcgtacccccagctcttggagaaactttagtcagtcacctacat
tctaccacccatttggtgggacaaaattagctcagctcctccggagctgttttaagatccctcatctacaaagcctaacagat
caagcagttctctggtgcacagcctgcgcccaggtaaatgccaagcaaggtcctaaacccagcccaggtcaccgtctccgaag
aaactcgccaggagaaaagtgggaaattgactttacagaggtaaagccacaccgggctgtgtacaagtacctttttagtatcag
tagacaccttctccggatggactgaggcatttgctaccaagaacgagacagctaacacagtagttaagttcttactcaatgaa
atcatccccctggtacgggttgcctgctgccatagggtctgataatggacctgccttcacctcgtccatagctcaatcagtcag
taaggcattaaacattcagtggaagctccattgtgcctatcaaccccagagctctggacaggtggaatgcatgaaccataccc
taaaaaatactcttaccaaattaattctagacaccagtgaaaattgggtaaaactccttcctttagccctacttagagtaagg
tgcaccccttatcaggctgggttctcaccttttgaaattatatatgggcgggcaccacctatcttgcctaagctaaaagatgc
ccattttgcagaaatatcacaagctaatttattacagtacctgcagtctctccaacaggtacaagagatcattctgccacttg
tttgagaagcccatcccagtccagttcctgaccagatggggccctgccattcattccagctcagtgacctggtgtttgttaaa
aagttccagagagagggcctaactcctgcttggaagggacctcacaccgtcatcctcacgacgccaacagctctgaaggtgga
cggaattcctgcttggattcatcactcccacatcaaaaaggccaacaaagcccaaacagaaacatgggtccccaagcctggat
caggacccttaaaactacacctaagtcgggtgaaactgttaaattaactctttttatttgcttctttttgtttatccttgcctg
taatgtcttctgtgccttcctactccttcccccctcacctctctcacaacaggacgtgttttcgccaatactacttggaaggtg
gtactccagggcaagtcaccttgcagtcgacttgtgtatactgttcccggagccggctggtacccacgaagatcatcgcgac
ctgccagtcatgggagcaggaggtgtcgaccttgcagcaggatttggacactctgggagccaagccagatgtggaagctccaa
aggtgctgaaaaaggactccaaaaggttgacttttacctctgtcctgaaaatcaccctgatgctagctgttgagatacctacc
agttcgtccgcccggattgggcatgtgtaactttagccacttactctgggggatcaactagatctccaactctgtcaataagt
cgtgcttctcgtcccaaatcgtgttctaaaaataattgtaaccctcttaacatcattgtccatgaacctaattcagctcaatg
gtactatggtatgtcatggggattaagactttatgtcccagggttcgatgttggaactatgttcaccatccaaaagaaaattt
tggtcccctggagcccacccaagccaatcggacctttaactgatctaggtgaccctatgttccaaaatcaccctgacaaagtt
aatttaactgtgcccccaccattctcagttcctaagacccagctacaaagacatcaactccaacccagtctgatgtctatact
tggtggagtacatcatttcttaacctcagccagcctacactagcccaagattgttggctatgtttaaaagcaaaaccccccat
attatataggattaggagtagaagtcgcacttaaaggtagtcctttatcctgtcatgcacaacctcatgctttcacattagga
gatgtgtctggaagtgcttcttgtctaattagtactggatatgacttatctatttctccttttcaggctatctgtaatcagtc
tctgcttactcccatgagcatctcagtctcttaccaagcacctaacaatacctggttggcctgcacctcaggtctcactcgct
gccttaatggaactaaatcagaaccccctcttgtgtgttctagttcatgtccttccccaggtatacgagtacagtggatcagaa
ggacaactcctcattgctcccccggaattacatcccaggctacgcagagctgccccactactggtttctcttttagccggtct
tagcatagctgggtcagcagctattagtacagctgccctagttcgaggagaaactggactaatgtctttgtcccaacaggtag
atgctgatttaaataatatcttcagtctgccatagatatactacattcccaggtagagtctctagctgaagtagtacttcaaaac
tgccgaggcttagatctgctgttcctctctcaaggaggattatgcgcagctctaggagaaagctgttgcttttacgccaatca
atctggagtcataaaagatacactccaaaaagttcaaaaaaatctagataggagccaacaagaacgagaaaataacacagcct
ggtatcaaagcatgttcaattggaacccctggttaactactttaatcactggtttagctggacccatcatcatcatattattg
agtttaatttttggcccttgtatattaaattggttccttgattttgtaaaacaacgtattgcgtctgtcaaacttatgtatct
aagaactcaatataacccccttgttgtaactgaagaatcaacgacttgattcccctaaaacacaagtggggaaatgaaatgcc
taacggtgtttttacttaactcgttactttgaattttgtcctgcttgtctctttaatcacctaaccttgcttctcatgtaaa
taagactctctctagctaggaaagccagacaaactccaattgacccctagtttacaagacactaagggctcctcacccaacc
ccctttcgtgaggagttggcctgggtaaacagatcctcagcatttcaaaggagcccaattaactgataaggtacccacaccaa
caatgtatgaagttcccaggaatttctctccaagagataacaacatgaaaccttgagtttgtgtccggcatagaccctatatct
aattataataaaagatttagaaccttgcacctggtaccgttgctcttcttgtaaccatttgtctttaagttgtttatcactc
tgtaactattttgattattttgattcttgcatgttttttacttctgtaaaattattacatttgagtcccctcccctttcctaaa
cctaggtataaaatttactcgagccccttcctcgtggccgagagaatttgagcatgagctgtctctttggcagccggcttaa
taaaggactcttaattcgtctcaaagtgtggcgttttcttaactcacctgggtacaacagtgcagctggtggagtctgggggа
ggcttggtagagcctgggggtcccctgagactctcctgtgcagcctctggattcaccttcagtaacagtgacatgaactgggt
ccgccaggctccaggaaagggctggagtgggtatcgggtgttagttggaatggcagtaggacgcactatgcagactctgtga
agggccgattcatcatctccagagacaattccaggaacttcctgtatcagcaaatgaacagcctgaggcccgaggacatggct
gtgtattactgtgtgagaaacactgtgagaggacggaagtgtgagcccagacacaaacctcctgcaggaacgttgggggaaat
cagctgcaggggcgctcaagacccactcatcagagtcaaccccagagcaggtgcacatggaggctggggtttgtttcctgtc
aggatttgggacttcctctgcttctgacagtttctctagggaaactctttaatttagatttctgtgcccaccaatgtcatct
ctacatttttttaatcattgtaatatgataggaggacttattctcacatgcacaatatgtatattgccacctacgggaatgaa
aactcctcaaccatggtcaccagcatcagagtcgtgaggaagctcaggggtgcctggtgagtcttctccagtcagactcagga
cagtaacctcaaggggattcccttgtgagaactcacacactttcatgagaacagcaccaggagttggttctaaaccattcatg
aaagacccactccatgacccagtcacctcccaccaggtcacccctcacaattgaggattataatacaacatgagatttgggg
caggacacaaatccaaaccatatcagatacacattgtgaaatgctcatgatggtcagggtaatttgtatttctatcacctcac
agcgctaccattttattatttttttaaattaaatgcatgagtgagtgtctgatgagaacacctcagatatacccttcagcaa

FIG. 7 (Cont. 24)

caatcatttttataatacagtattaactataggaccattgctgtacgttagatctccagaactcatccaacctgcacaactga
aactgtacaatttaacaaacatcacccgatttccctctcctcccaggtcctgagaccctctattctgctctctactttcaaga
gcttgaatattttagatcccacatgtaaatgagatcatgcagcatttgtctttctgcatctggcttattccactcagcatcat
gtcctccaggcccatccgtgttgttgcaaatgtcagaatttccctcttttcaaagccaaataaaatacagatttatgtataca
cattttctttatacattcatccatttacagtcattaaattattttgcaaatctacactattattaataatcttcaatgaacac
gtctttggcaaagtaatttttatttccttgcatatataataagaaatgggatcaccagattatatgatagctttatttttcaac
ttatcgagtaaccaatcctaccacagtgtattccctttccctcacattcttgccaatatttgtcatctattacatttctgata
ataaccatattaactagtgtgaggtgatatcgcattgtgcttttcatttgaattcctctgataattaggaatgttgagaaacct
tttcgttttctgtttgccatgcatgtatcttctgaaaaaagttatccaggtttttgccctttttttatcagttcatttgttatt
tgctattgaggtatatgggttatttatacatttagatagaccttcttgtcggatacataattacacatagtttttcctgtgct
ttgttgttaaattcaaagaaatcagttccgaattaatggcaggaatttttttgctccatgtgatttatgagtttatggcttc
aggtattatgtccaatattagctgatttttttatatggagttagagaaggcctaattttatttcttttgaatatgaatgccag
ttttacaccattattgaaaagactgtcctttctctactgtgtgctcttggcacacaaaatcaggagagacataatgacaaaag
aaaatatcagatgaatattcctgatgaacatagacctgaaagtcctcaacaaaatactatcaaatagaatccagaagcacttt
aaaatgtaatacatcatggtcaagtgggctttacccctgggatgcaaggctcgttcaatatccacagtaactgtgattcacaa
tgtaaacagaataaaagcaaaaaccatatgattatgtcaatagatactgagaaagcctctggtaggttctaacatccactcat
gataaaaaccctcaacagactagacatcaaagaaacgtacctcagaataatagccatctacagcaaacccacagtcaacacca
tactaaatgagccaattaaaacacttgtctttataaattacccagtctgaggagtttctttatagtgtgagaattgactaata
cagcatccaaataggaaaggaagtcaatccgtccaccttcagcgatgatataattctatacctagaaaatcctaaaaagtctg
ccaaaataattctagaataaacaactttagtaaagtgtcaggatacaaaatcaatggacaaaaattaccagcatttctataag
ccaaccacatccaagctgagagtataatcaagaacaaaatcctatccaacttacagtatccacagagaaaatgaaatgcctgg
gaacacagataacaaacaaggtgaaagatcactacgaggagaactataaagcacagcagaaataaataataaatgatacaaat
aaatgggaaacatttcatgctcatggattggaagaatcaatattgtaaacattgtcataatgcccaaaggaattcacagattc
aatgctatttacataaaactatcatcatcattcttcacagaatcagaaaaaaatctattctaaaatttatatggaaccaaaaa
agaccctgaatagcagaagcaatcctaagcaaaaagaacaatgccagaggcatcatgatactgaccttaaactacaccataat
gtcttgctaacaaaagcagcttggactggtacgatagcagacctgcagaaaaaaaaaaatagatcaaaattgaaaacagaaat
aaagttgcacacctgcaacctttgatctttgacaaggctgacaaaagcaattggaaaaaaaaaatctctgtattcagtaaat
ggttctgggataactggattctggcaggtcttgcagaatgcaagagtgaaggagcctgtccagcttctacctagatttcagat
gttagagagccctgcatgcccaggaagaagcctgctgcagcagtggatccaccacacaaagcctctactagagcattgccaaa
gatggggaaagatggagttggagcccccattcagagtccccactaggacgcttcatagtaaagctgtgggaatgtggccacaa
ccctcaagaccctagaatggtagagctacaggcaacttgcaccctcagcctagaaaagcttccagcacttgactctcacttgt
gaaggcagccccgtggtctgtgcctagcaaacctatagggattggctgcctgaggttttggggacccaccccttgttccagtg
tgccctggttgaagtacataaagtcaagagagattattttgtagtgttaggatttaatatctgcagtgctgggttttatatgt
gtgtgaggcctgttggttgttccactggccaatttatccctttaggattggaattatttacccaatgcctgcaccatcattgc
accttggaagtaaacaactttcatttttaaacttgcaagctcacagctggagggacattgccttaagactcagatgagacttt
ggacattttagttggaggttgatcaacttaacattttgggaactattgaaaaaaggtgattatattttgcagtgtaagaagaa
tatgagaactttgggtctgagagtgcaatgatatcatttaggggttttcccctccaaatgtcatggtgaaatgtgacccacaa
tgttggaggtggggccaactgggtggttttgggtcatgaggagatttttcaggactggcttggcatccaccccatggtaatta
gtgaattcttgctgtattagctactgtgagatttttattgttcaaaaaagtctggcaaccctcctaccctctcatgtcccccct
cctcaccatatgacacagcctcctcccccttgccttccaccatgactgtaagcttcctgaggccctcgcaagaagcagatgc
ttgtgccatgcttctcacacagcctgcagatctgtaagccaaataagcctcttgtctttgtaaatcacttggcctcaggtatt
aatctataccaatgtaaaatagactaatacactgcccaaagcaatatacagagtccatgcaatttatatcaagtaactaatat
aattgattacatatttttaaaaatcctaaaattcatatagaaccaaaaaagggtctgaaaagcaaaagcaatcttgagcaaaa
agaacaaagctggaagtaccgcattccctgacttcaaattacacaacacaaagataacaagaaaggcagcgtggtaatggtag
aaaaaaaatcaagagcccagacatacagccaaatatctacaaccaacggttctttgacaaaactgacaaaaatatacactgga
gaaacaaccctctattcaataagtagtgctgggagaattagatagccttatgcagaagaataaaatgagacttctgtatcatc
atagacacaaattaactgtgaatatggattcaatgtttaaatttataaactcataaaaattcctgaagaaaatctaaaaaaaa
tcctctagacatttgcctaagcaaataaaatatgactaagactgacttcaaaagcaaatgcaatgaaaacaaaattagacaaa
caggattaattgaaacacagattgtctgcatagcaaaagaaataaccaacatggtgaacagacaacctgtgaacagtaaaaaa
aaatttgcaatctattcatcaaagggctaatacatagaatctacaaggaactcaaataagtcaacaagaaataacaaataact
tcattaaagagtgagcaaaaaccagacatttctcaaaagaagacacagacgtggccaaaacaaataaaacatactcagcatca
ccaatcatctgataaatgtaaattacaaacaacatgatatagcatcttccaccagtcacaatggctgttattacaaaataaaaa
acagcaggtgtttggagagaagcataggaaaaataatgcttttatatgcttggtgaaaatataaattagtacaacctctatg
aaaaacaatacagaagtttctcaaagaactaatattagaattaccgtttgtcccagtaatccctcccagtgggtatattcctc
ccaaaaggaaatttttatatcagaaaaagtcacctgcattcctagtgtctttcacagcaacgtgaatagagttgtaggacatt
agcctaaataaaataactcaaaaagatcttctcttttataattggaaagtaaacaatgggtacacatgtacatacataaaaaa
caaaagacactgggaactgcaaaagagggcaaggtgagaggaatgtgagggttaaaaaatcacctactggctccaatgttcac
tagtgggcgatagttacaccagaagcccaaacctcacctttatgaaatatattcatgttacaaaattgcacatgtacaccctg
attctactgaaaaaaacagaaataaaacatgaacagaattgttagactgctagctagatttgtcaacaaagaaaaatgcaaaa
ggagcaattctctgttttggaaccctttctcattttctggtacaattagaaattgtagactaatccctatattctcttctgaa
gccctagcattagccatttctcaaagacatgctggttcctttttttttttttttttttttgagacagggtccagactcactg
caacttccacctcctgggttcaagcgattctcctgtctcagcctcccaagtagctgggattacaggcatgcgccactgtgcct
ggctaatttttgtatttttagtagagacagggtttcgctatgtgggccaggctggtccaaactcctgacctcaaaagatctgc
ccacctcagcctcctaaagtgctggaattacaggtgttagccactgcacctggtcactggtttcttttatagaagaatagtat
taaaaactcaaatcttgattctgggtgtatttttattaatgtgcactcatttcttgtagaaattctcaggtaaaaaatctag
gaagtatgtgttgtgtattaacccatatatacacagacatctaaactatttttatctaatatatgtacctatattatgctaaa

FIG. 7 (Cont. 25)

cttgcaaataaaatgacatgtccaccctaagttaataccacatggatgtttatcgcattccttctatgcctgacactaacctc
ccactccaaccacaaggaaccccatttccccatacgccgtccattctctttgtagtccaattccaagattcctgtggagtgta
acaagatgtgtaagttgtgctcttttgtggaacatcgtcaattggggtacaatgctgatgtgaagtttctttttttctttaatc
ttattgcctacaccatttctgaatctacttagtacctcttttgaattcatacatttgtaatggaattagacattttctatgtt
atctgcattccatcctggaattcctaatcacctatttttaaaaaaaattcttttgaagtaagattgtattagtcagggttccc
tagaggggcagaacaaacaggatatatatacgcacacaggatacacacacacacacacacacacacacacacacacacaca
gagtttattaaggagtattaactcgtatgatcacaaggtcccacaataggccatttgcaagccgaggagcatggaagccagtc
cgagtcccaaagctgaagaacttggagtcccatgttcgagacaaggaagcatccagcacgggagaaagatgtaggctggaagg
ctaagccagtctaatcgtttcatgttcttctgttgttgttgttttttttccctctggccacactggcagctaatgagattgt
accacccagattaagagtgtgtctccctttttgagcccactggctcaaaagttaatctcctttggcaacaccctcacagaccc
acccgggatcaatactttgcacccttcaatctaatcaagttgacactcagtatttagcattacaagtccacccccgtcaacttg
aaaccatacacatctcctgagattatacataatcttcaaacaaagacaataataaagtcataattacacctaatataatacaa
ctttattcgttcaactggaaatgcaccaatccccaatccaaatgctattacatatggtccactcctcaaggacacagccagg
atcatcctatgacttggtgtctagaagactcatgcacttttaatttacctccaatattagactccactttatcacatgcaga
cactgcagaatattttaagacatcgatgtcttatgctgaaaaattcaacagtacataaaattgccttcccaccacagccagtg
gttactactgaataaggatctgccatcccctagggagggtgctatagtggatggtgtgcactgttagtagctatggaaattgat
ccattgtggcaaatggcagcatctttcttttataacattaaaccatattatattgtatacacataccacattgtctttattca
tttgtctgtatgctgaccatcagatagtttccatatcttcgctgttattaacagtgtttcaataaacataggatgcagatatg
tttacaaggtggtaatttcatctacttgggtatactcccagaaacaggatttctggtcatataatatctccagttttaattaa
tttaggacgctttatgttgctttccataattgtggaaatgtagaatggtatagccattatgaaaaacaatttttggttttgagt
tatgatccataaacagcatttgcttatggctctcaatgagagtttctactaaatatgatggaaggccaggaaggattctcacc
ttaaagcttggatggattatgaatttacctcttatttcctaaaagcaaaagtttggaagcatacatgatggaggctgttggca
ggtttcaggatgatctcataaaaggagaatctgctggataaaaatgttgggttttcagttatagacacacctacactcaatat
gaaatgatgaagtcaactgaggatctagaacatgttcacttgaagcaacagcacattctcaaaggaacttattgctccatcac
aagggcgatgaaccttctgaaaccagtaaagtgtgagtgcacagtaagtgataacgttatcacgtttacatgaagtttgtttaa
tgtgccaaaggctggtacagattaatcttacacaaatatatgaaacatatttttccatacatagatatctagaggataatcct
cttagcaaaacttcttcaggttacagaaatctgtgtaagttgtagatctcatggggaactgtctctttataaatactggtctg
tttttcaagtcaggaaaaattatctctgttggagtaggcttccaattgtgtagacttctgaattgcttcttgagttgtaacaa
atgaaccaaaaaatttgactaattggagttttgtggctgtcttaataaaaatttcttataagctttctttcaattatttgaga
ccagttttcctgattttatttttctccaatagataaatttttcacaagatctcaggaaaccacctctctggctctttagtttaa
aagactagcttcttaggaaaagaagcttctttctaacattgaagagctcatttattctgcaaaccatgaagtttgagtctcat
tgtcaagaatcatgaaaatttttactccaatatactgaaagtcatgactcttgaattcaatatttattggcattcacaaaagt
gattcattctcagatgtgtcctatgttgctggcccaacatatcagtgaactgagtatcctcccttagctctctctgtctgtag
cactgagtctacaatcttcagagtcatccatgaaggggagtcctgaggttcatgggattcttgtaaacattcaggtcaacaga
agaaataagcaggattgagggctgccagccatttccacgccattaggaataattaccatctaagtataaaggtctacatcata
cagaataccccacaggataggctgatgcaaaaaattccaaccccacagaggctccacagcaacccttacagttctttcaggga
aggaataatctccaagttaaatgagtcagtaaagctgctctgagctacaggaaaaattggatttggccaggtttgtctgagtt
caacgtgattattatactcagctcctgctccaatctggactgagtacggggaatttaaatgagcctggctgtgtggtttgtta
tatgaaaatctgaactatataaacataaatggcatgtctggactagcatgagggtgagagatcctgggaactccacccccat
actcttatcgccctttcctccaggaacctccaggttctcagggtgagaatccacatagatccctttcatggctctatttctagg
aaaccaaatctctaataaatacacccagactttcttcagacacagaaaccatgggaaaggcatctctagatcctcatctatgt
ggggaaaggtaatccatccccattacaagcccatactagcaggcttcctttatcatgaaaatgggtaaaattagccaatagat
gtaaatttaaagaaaatttcctgtgatgctccagccagaaaagagcaaaaatcagcttcacttctggagacttcccgtatagg
tcacagcccagagaaagaagatcaccacagcattaaaattcagctgtaagaacatgtaatgcttccgtgttccacacattatg
tctcaccagtttagtcaatatggattaaatacgagagtgtggcaatgcacaaactctatctgaggaggaaataggagaaaaat
gttaaggaaaatagaagaattcgacgcctctaataccaggaacttcagcacaaagaaaatgatttcaccttattggcctcaa
atttatttttcctgtggcatctgcagggttccaaagtgagaaaaattaattcactgtgcatgcacttccgaagtgtccacttg
cattctgatatctttacttctatttgcagaaagtagacacatattcagccttagtgccagtgtagggagtgctttccgtgaca
tggataccagaaaaatagggtaaacatagggcccattaatgtgaaaatcagacattgtgtgtgtgtgtttgtgtgtgtgtgcg
tgtgagttgaatagtagagttggagtgggcttctatccacctacaccgcaggtattctcaggtgccataatcaactgcagga
ccctaaaggaaataagagtccccccaaaccccctgaagagtttttgggttcaccgtgtgtccaatgattcagtgcctcttgagc
tctaggaaagggctccccagtgatgcatgagatctttcttggggtctcccctgcagagttcactgggattcctaaggccaattc
agtatttcaaaagatggtgtgagaagcacaggctgtcactaaaggagaattctgagccagggcacagccacttttatacttggc
tggggacactggtaggaatatactctgtgagatcagacaggaacctccttgcaggggcagggcagggctgcaggggcgctca
ggacacacagagcacaggcttccgccccagagcaggtgaaggaggctggggaggggttcctctcagggcctgggacttccttt
aaaaaatctaaaataagtatttcacaaggactgccgatgtttatataaatatcctattcaattgtgagcatttatgaaactcg
atgttgtaatgagaaccacttttacaattggaatttcaaacttccctagacatcttaatagtaagcagctggaggtcaggagg
agatccttttcttataaataagtgcaatttttgggagaaacacactcattcccaaaatagcacattcacatattaaggtctagaa
atgattcgagttgccccctgagacagtcaaatgtgggttctaagtgaggtgcgtgtcctgggggagcttgttctccagtgggg
aagctctgtcaacacagagttcagggatgggtaggggatgcgtggcctctaacaggattacggcttgaacccctcagcttctac
aattgtgtcgtccatgtgtcatgtatttgctctttctcatcctgggtcaggaattgggctattaaatagcatccttcatgaat
atgcaaataactgaggtgaatatagatatctgtgtgccctgagagcatcacccaaaaaccacacccctccttgggagaatccc
ctagatcacagctcctcaccatggactggacctggagcatccttttcttggtggcagcagcaacaggtaacggactccccagt
cccagggctgagagagaaaccaggccagtcatgtgagacttcacccactcctgtgtcctctccacaggtgcccactccaggt
tcagctggtgcagtctggagctgaggtgaagaagcctggggcctcagtgaaggtctcctgcaaggcttctggttacacctttа
ccagctatggtatcagctgggtgcgacaggcccctggacaagggcttgagtggatgggatggatcagcgcttacaatggtaac

FIG. 7 (Cont. 26)

acaaactatgcacagaagctccagccagagtcaccatgaccacagacacatccaccagcacagcctacatggagctgaggag
cctgagatctgacgacacggccgtgtattactgtgcgagaga
cacagtgtgaaaacccacatcctgagggtttcagaaacccc
agggaggaggcagctgcactgaatttgaggagattacagggcttacaatgtttaaagttgtttagaaaatgagctgagcaatt
gaggaatgtgagtaatggaaacatggatgcactctatataggaaatgtttctttcaacagtcaccctatatgcaaaattcaga
atggtaaaggcagcaatcagtgaggctgacgcaaatattcccatggaggccttgtgcagacataccgtttttaaaatcagata
gataaataatttggaacaagattgctggtaacgtggctaagactaaatatgattcctaaaaactggccaaaatctattccaaa
ttgtctctgccactcctttacataaatgtattaaaaagtagttttaagaccacagcaaaattggacagaaggtgcagagagt
tctcatgtgcccctgcttcaccatgcacaggctttcccactgtcaccatcctgccccagagtcatcaataagttacaatggat
gaacttacatgggcggattggttctttcctcttctggtggtctcttggcataccaagcccaaattatcttgaagcaccatagg
ttctactgtaatgcctaaccttgtttttactctagtttgctactttaaatttcccttttttgtctccttaattgccagcc
atgtttcccatatgaatagactctcccctggctgggaaagctgggcaaactccatttgaccttttgatttataagacattaagg
gctccttacccaaccctcttcttcaaggaattaacctgtgtaagcagatcctcagcatttcaaaggagcccaattaactgata
aggtactggaacaaacaatgtatgaagttcccaggatttttctcaaagagataacaacataaagccttgagttcatgcccagc
atagcatcatatctaactataatgaaggatttagagccctgcacctggtaacgttgctttttgtaaccatttgtcttttaaat
tgtttatctctctgtaaccatttgcttcttttgattcttgcatgtttttacttctgtagaattattgtatttgagttcccctc
ccctcctaaaccaagatataaaagttaatcaagccccttcctcggggccgagagaattttgagcgttagccatctcttcggc
agccggcttaaataaaggactcttaatttgtctcaaagtgtggcgttttctctaactcgtttgggtataacactacaagtggg
ttcctgggaatgatgccagttcagaggaaaagtgggtggggctattcatatttgggctctttttagaagattcataaaacag
atattttcctatacgttctgtgactcctgatttactatcccttcccagagggtaaggtccctaagtgttttgcggtatatcca
tgtctatggaaagaaagcaagttctggtgaatcccgtaaggaatgtcctttgatgagaagtggagaccttggtcatgaggcac
atcatgtatgattttctataattccgttagattcactgtaattttgggggtgtcctgtggaatgggtcttctgtgtccctgc
atgttcagctatatctgtgtggtgccacttacacttaatgagatgagattcctgctgcttgtatcaggtcactggtgatctct
gaagctgcttctggtttctgctttaatatgtaaagagcatgtcaaacatcacccacattcttacaataataaaagcctggaaa
attgattatcaataatttcttgaatctgttgaagaaatgaaattgcagggaaaaccaggacccccaaaactagaaagacatta
aaatagagataatcagactgatggatcaaagttctgtggcaataagataccaaatttataaacaaggcctaaagtcatggatta
agtcactcacccctacacttaaaaaaatgactgtactgtaacttccacagggctttttgttttctgtagcacctaaacaagc
actggttctgaggtaagcatattaaaacatttgcagctcatggaactccaaacgtggtaactgaccctctcccacaagccata
aatagagctttgtttggacaagagacagatttcagtaactgtcttctgagaagagactactgaccatgaacttgtcctggcaa
tttacagagactgtgcagtgtgtgtctttctgcctctgcacaaagccctttgatgaacagggcccgattgtcattcatttag
ttcttaagtcctcatccccaaagcaaacactaaatgcatgtaacatgtgtgtttgcttattagacatgagagcctgcccacta
tgtgaacatcaacaagatccttctatagcctgctgagtgtgtacacttggccaatccatttgcatgaattcatttctcctctt
tccctctcttgaagtgcctgctcactgtctctgtgggaggctttgcttcccagcctgttaaggtggctgtcctgcagctttaa
ccatttctcagaagtaaagtctcctttctaaatttataaattatgtgactgttccgttgaaagtgcaagctggtgggaacagt
tacatggtaattcggtaaattgctggtggacaggtgtggacagggataggtaagaactcctgggggctgcacaccccacact
tcgatggaatttccctccagaaacttctgggttctcaggatgataatccaaacagattccttcatggctctgtcatcaggaga
gctactctcttgataaatatgctcagaacttcctccagacaagatcctacagagaaaaaatgcttttcaagatcctctattct
atgtgaggggaaggtattcttttccatcccaggcagtttcatcttagccttcctgtgtcataaaaaggtcaggttcaagacaa
taatatgtggatgctgcagccaggaggggggagtagaagacggaggaaaatcagctgcaccactggagactccttgtaaaggg
cacagtctagagaaaaaacatcaagaaaacattgaaatcaatttccagtacatatactgctcccctgcccaccacatcacctc
ttcaccagtatgatcaatctggattaaagagaaaagtgtggcaatgcacagactctgtccaaggactagaccttagggaaacc
aaaggcagagggagaggaaaagttaaggacagtgaagcggtttaaagcctctgagaccaacagcttcaggaccaaggccacgg
ccctctgtcaatggccttagatttacctctcacggggcatccacagggttcccaggtgagaacaggcaaaaacaaggtgaag
acactttccaaatctccagcagtactgagcttgctttagctctgtttgaagaaacaaaacaacaacaacaaacaacaacaacc
gcaaatataaccaggattaaggtcagtgttggaagcacttttattaatttttttaaatttttttatttctcagatggggtcttg
ctctgtctcccaggctggagtgcagtggtgcggctctggctctgcaacctccacctcctggggtcaagcaatcctccacccta
gcctcccaagtagctgggattacaggtgcatgccacggcgcccagttaatttttgtatttttttagtagagacagtgttttcc
atgttggtcaggctggtctcgaactcctgacctcaggtgatccgcccaaattgccctcccagagtcctgggattacaagttaa
ttgagttaataaagctgttctgaactatgaaaaacattagtttgctcccagatttcttgatttcagtttgattattatattc
agctgctgccctaatatgtttgagcatgttactatttaaatgaccctggctgtttgatttgttatatataaatctaaactaaa
acaacttaaaggacaggtttgtactattattaggatgagatattctgggtgcccctcatttgctccatgaacctccacatttt
taatttagaattcacataaattccttgtgagttgtgtcagtcatcgagagacctaatctctaacacctttacccagaaccttc
tccagatagaccacccacaggaagaacatttatagtaatttatctacatggtggaaggtacttcactgccattgtagaaccct
cttcccagccttcctttatgaggcaaatgattgccagtatggtaagattgaacaaaaggatgtgccagtagggtaagattgag
caaaaatagtcctgagatcctgcagacagggaaggacgtaatagacaaatatcagctttattagaggagactccttgtaaagg
tcatagccaagaaaaagaagacaaaatcactgagattaaattctaagaatcttggtccagttcaatcaagccatcaacagcca
ggtggcttcagtggccactatgcatattacccccatgcctaaatgttctggcttgtacaaagagcttctctgtaaattgcacat
tgccatagtggaagatggcatgggagattttgtgacaaacacttaaggtgcaataatagctatttttccttttatcatgacaat
atgtggcatgcttctagattcatttcatgccaaagaagttcctcagaagggtaaggaaatggagaatcttacacggtccaatg
cagtccccaagaagggactttgaatggacagttacactggttactacgatgtgtctctgaccttctcaggatcgaagatagtc
atgagtatcaaggtggagatggtctaggtgagagaaaggaagtagtgttcttagaagatggtatgccaagataagcctgacta
tctctcctcttccagttcctgcaacttcatattgcctgattgagtcacttgcctatggtggtaatgacatcagcaatgcaata
aattctctggtggctttatatctggtttataacatgggagatgtttcctcaagagtggtgatgccagtgtggcttctgctctc
tggtggtgttggaatctgcattagtctgtgggtttggaggaaggagattcagccatggggaagaatctgacactctcacaccc
tctgtgccttcggtactggactgctcctgcctcactatggtgattgcatcagatattgcctccccaccagacaacacgttaa
catggctccttgtacctggctttaaccaagaaagttgtcgacttgactcttcgtgacattgtatagcctggttttgtcacaatc
tttatttcgggaattatcagtgctgccatcttggctgtcttcaagtatgtcatcctcacagtgtgaagctgtttgacattaac

FIG. 7 (Cont. 27)

attttttgtcaatgtttgggactaccttacatattccggctcagttcaaaatgagctatgtaatgtagccaggtttccactgag
ttccactttgcttcttggctgtctattcctgcgcaagtttctatgtattttgtatcaggcttcaattccattatgtttaaaat
gttgtctctaaagataaacaaagatttttttaaaacaaccaaacatgcagccatttgaccgagtgtggtctgcattgttagtc
tcaccatcttctgccctaacaagcaccgaatctaacaacacaaatatcatggaagctttccttggagtagctcctgtaattag
aatcattgtattctgccctcctgtcagtggtggaacgttctattggcacatgtggaaacctcttagagggacgagtttctttg
aacacaataaaatttttaagttaggaataacttatttgaaagcaattcattgaaggttattgctaagaagttagaaacagtctt
ttggcagtcatttcttcaagatgtatggcagtgtgggagggatatataaagtggaataggaacttgggctagttaaatggaat
agcctccaatgttaatctgtttacctttttaactgaatgaaaaagcctatagttgtaagaaaagaaaaaaaacacaatcctcac
acattccctcccatcagcattgaagatgagtgtggcaatgcagagactctatatagggaggagaacatagggaaatgcaaag
acaatgggagaaaaaagtcaaggacagtagagcaactggaagcttctgacaccaacagcttgatgaacagggtcactcaaccc
ttggtggacacagagtcacttctcttagggaaactgcagtattctcaggtgacaatatgcaaacatgatgaatgtacacttgc
tacgtctccagttgtgtactgttttccttacttctgtttggagaaggaagtcatatactcaggtctagtatccgtgtagaggg
tgctcaccatttgcaagatactaggaaaaatggcaagttagaggcccactgttgtaaaaatcaaccagttctgtgtgtgtgtg
tgtgtgtgtgtgtgtgtgtgtgttatagaaaaagaagacatggagtgggcattgatccacaagtatatatacctacaggta
ttcttagatgtaatattcaattgcaggagaccaaacaagataaagcatccccccaaaaccccttgaaaatttttgtgctcactat
gtgtccactgattaaatgtatcctgagctccagggaagggctccccgatggtttcttagagttcactgggtctcctaaggtca
atgttttcaaaagatggtgtcagtaacatatggtgtcactgaaggagcattttaaactagggcatgacctcttcctatagccc
tagagacactgagagagaaatcctctgtgagcccagatggaaacctccatgcagggcagaggcagtgctgcaggggcgccca
ggacccacccagaacaggctccagccccagagctggtgcacaggaggctgcagaggggatttctcccagaattgagtgttgtt
ttattgaaaaccaaaaaattataacatgttaaaattagaattttgcaaagactatttctattatctctatacatttagaaata
aacaaatcaacaattcagtgagaaccacatttaaaaggcaaaattgttacttgtttgagatattttcctagtaaaaagatgaa
gaacagggatggttttattaaatcaaaaggtacacatttcagaagacgcagagatcccaagagtaagactgcagacagcaaag
cctagaaagggcggaggctgtccatgtgccatgtcctgtgtgagtcaccttcttagtggagaagttctcccttcacaaagttt
tgggcatataaagggaaacacgacattaaataagaacgaggacttgtacctcagcatcccacagttgtgtggttcatgtgaga
tctatttttctctttctcatgctggatcaagggtaaggctatgaagtagtagttctcgtgaatatgcaaatcacctgaggtgaa
cactacagatatgtctgtgccctgagagcatcacccaataaccacacaccacaaagacactcgctgagaagagcaaccctaag
acacataattgtcagattcaccaaggttgaaatgaaggaaaaagttttaagggcaaccagagttgtgccatggcacagtgttg
tgccatgtcctttctctgttttcttgcctgtttatttatgtcagatgtgccacctacatggaataaggtcagaattctgcctc
cagtaacacatcaaaggtgaccttcgattgtacttttggtttatgctccaaaatattgattataaaattcatcaccgtcatat
tttatgtcaaaataaatctgcataatctgaatgtcagtacattttggaatctattaaataactgaaattgcaagaaatattac
ccactccaaaaactggagagatgggcatgtccagaatggcagttagcacttgcttacctggtgcagaaactgcagaagccaca
agctgttgagggcacttacatggtaaccactacggacgtctgaaagacaaatgtggactcggtaaatgtgaccgttccagagg
gtcttatacttctaaggtttctggactttctctccagaaacctccagattctaaaatatacaatccaaataaatttccgatgg
gtcagaattgaagatgaaatgaagatgattaattacagagaaatataccaggagcccacttcaaaagcttctaaagggaatga
cttttccagaaccttatcctatgtgaaggaagacaaatctcccattccagattctcccccattcttccattattatatgaatg
agtaaagttagccaaaaggggtaagacgtacataaatagtccaaggaggccgaaacctcaaaagggagtaacagccaaaaatg
agcttttccccctggagatgctttgtcaaggtcacagcccagaagaggaagcctattgaatctctaggtttccattggaagaac
aggcagtgcttacctgcactgcacaatccattctaactaggatgatggctatggattaaagatgaaagtgtggcaatgcacag
actccatctgaggagaacacagaaatactaagacaatggcagagggtgagacaaagacagtagagcaatgtgaagcctctgac
atcgtgatttttaagaccaacatcttgtaaatgccatcatagttctcagcttcttttattatgggacctttgctggtttccta
gctgagaaagtgaaaataacaacctgcatggacttcccaagtctccacctgtatcctgtttgctttagatctctaggagaaga
aagtcagataactgggcctggtgtcagtgtaggaggcacttcctaaaagccacatattaggagaagggaaaatgtgtgttatt
ggaatagtggatatggagtgggctttcatttgaatgtatctgcacctgctagtattctcagatgcaacattcaactgcaagag
cccagtgaagaaacatggcactcgcaaatctcttgtaagttttgtcttcattttggttccactaatgaagtgaatctggagc
ttcagggaaggggctcctcctgtgtcattgaatccttgctctgggtctccctgcagagttcaataggtttagtaaggctaat
caattgtttcaagagatggtgtcagcagcatatggtgtcactgaaggagtattctacactagcacacagccatttcatgctgg
gctagagaagcctgggggaaatgatttgaagtctcagcaaggaacctccttgcaaggcaggggctgggctgtcgggggcaccg
agcaggtgagtcagaaatcaatatgtaaagatgaggacctatggatatgaattgaaaatatataaatacttcaaaaaattcca
gtaaattgagtccaaaattaaccccaaattattcaaaacacaaattccttgacaattattttgggagcagtgagttcataaag
aattcaaaactactgtttcagcttctgattcttattgttcctgagatgagaaaatcatctctaatcacacatcacacagcaaa
tctgtaaacaagagtgtttctatggaagatcctgggggatctgaacaccaggcaggtgctggagaccctgtttcaggagcgcc
cagcagatctcagagggacctgctggtcactcacgtgggacatcagcagtaacttttctcagtcaccagtcagctgtgctggtg
actgatggacccaggacagaaccaaggcacctcctcagtgtcatggagagtgatggttccagaaatcatccaggtgctctctg
tgcttataaaatgtaggttcactgtgaggagcatgttctgaggggattgttctgtgaaaggacctctgttcatgagtgttca
taaatggagcagggcatgcatttcctcaaacaggaatagcgcttggaccatcagcatctcactcttgtaaatctgatgtgtca
tttatcttcccttttattattgaccaggctttgcgctatgaaatgctctgtctcatgaatatgcaaataacctgagatcca
ctgaggtaaatttggatgtctgtgccctgagagcatcacccaacaaccacatccctcctctatagaagcccctgagagcacag
ctcctcaccatggactgtacctgggggatcctcttcttggtggcagctgccacaggtaaggggctcccaagtcctagtgatga
ggagggattgagtccagtcaaggggctttatcatctcctcccttctcctcacagatgtccattcccaggttcagctgttg
cagcctggggctgaggtgaagaagcctgcgtcctcagtgaaggtctcctgccaggcttccagatacaccttcaccaaatactt
tacacagtgggtgcgacagggccctggacaagggcatagtggttgggatgcatcaaccccttacaatgataacacacactacgc
acagaagttccggggcagagtcaccattaccagtgacaggtccgtgagcacagcctacatggagctgagcagcctgagatctg
aagacatggtcgtgtattcctgtgtgagagacacagtgcgaaaacccacatcctgagagtgtcagaaaccccaggaaggaggc
acctgtgctgacacagaggagatgacaaagattattagattaaagattttcttagaaaatgacactaagtcattaaagaaaag
gaacaatattaatgtgtatttgagaaattttaattatttgagagatttttcatacagcatttattctgtaaacaaatttcaat
gattacagaatgaatcaaattaatgaaactaatacagaacttcctctgaaggtatctttgtaaacattaatttcttaatcagt

FIG. 7 (Cont. 28)

gctgtaagtattttggaacacagacacaaaatcacattttaagtctgcatttatgtctattaaaaatgccaaaaaaatctcct
tttgtgcatgtagcattttgaattcccaccatcaatgcatgatagttcttggttttccacattcatattgtcatgtatcctta
tgagaattgtgtgttttaaccaatctagtaggtgagtaatgggatctaatttttatttaaatgcacatgtccctccaaaagtt
catatttaacaatttttcctataacttctgttgagacgcctctcctgacattcggttcatttttaactgcattgcttcatttcga
ttcattgcaagttgacttgcatattgtttataaaagtcatttcacaaattaaaagaattcatttcacaaatatgtgacttgga
agtattttctccaagtctgtggctgtctttattcccttatcagtgtgtattgcagaaacatatgtgtgtgtatgtgtctgtgt
gtgtatgtgtctgtttgtacgaatttagactcaaaaacatgtaaaattgcattcattcatagatgatgtatttggcaatatat
atgaagtctcattataaaatacactaatagtgattatttttccatgtctctcaactcaggccacaatcaactcatgagtgtt
taaacttcatctacttgattggaggactatccatttcagatatttggaatacttctgtaaggaaatgtgttcatcttcccaat
atttatttatataatcatctattaatatgtgtattggtttatgaatatatatttcatactctgaagaagatccatgctatatt
attcatttttatcgttcaaatcaccacagctttattaggtcctgggagctcatttaatttggatcctgtatccttacagcacac
ctcatccttttgtttttgaatacttccctgtttccttgtattacaataaattctaagctcatttttctatattaccttttttgt
acatagaattagcctttttttctaaagattgcttgtttctaatgttaacgaatagcagtaaaataaaaaaaattgtgataccgt
gtataattacttctaggacctctcaacctactggcctagtagacgtgcatgtttatatgaacccatgtttgtggacgcatcaa
aactatttatgtaactaatcttctgtaactttattatattaaaaatgagaacacactggtctcctgacccaactatgctacca
catggacctttctagccttccttcttgactgtccataaccacccactgcaaagtgaggaatcctatcctaccaactgccttа
ttattacctagttgcacaattttaggacacatgcatagcggtatcagaaatgtaaagctcattggaaatatatttatctacta
gaatagagtgttatgtgtagtttctttacattttaaacttatagaatttcctcatttccaaagttaattagattagcaacttc
attttctactttctttagtgaagtcatttcaattacattatataatatcatttatttgaaattcggtataaaccaaaactata
gtcaagtaaacagatagaggatattcaaggaacttagagagtgagtattaaataagtacaaatggcactgtttaagaatagta
aaattatttttagtgatataaaatggttgagacacgatgcagttaatttgtctaaactcataaatgtgtgatggaaaatataa
acctaaatatatacaatttttgtaaaaagtatttagcagttcattaaccccaggattaaatgcagactgtatcaagttatcta
ataacttatttggtgagggtggggatgtcatgagatgcatgcaaaaaagaatgaagtaatttttcctcatttgcgtttaagatg
ttaccattcactaaagacctttaatttaaaaaaaatcaatttttctacgtgacccaggtttttttcttcctgacgagcaaataac
ccagataattcttttctttccttggttgagaaagatttttccccaaacttcagctcagttcaggcacacactgtccctgaatgg
gcatttaccctcagatgggtaacacacctgtcaacatggggactcttctgtcagacaaacacacctttactcacgtggattct
tccctcagaccaacacacaagtccccacatggactctttcctcagaccaccacatatgtccttacatttactctttcctctag
taatgacatttcctcatgtggactcttgtctcagacaaacaaacatgtctgcatgtgaactcttcactctgataagtacaaat
atttccacagtgactgtttcctgacacaagcacatatatccaatgttgaactgttttatggcaaaatgatctcaagataataa
ttataaaatccctcctgacaaggtgtagatctgcatttttttattgtaccttaactttgccttattgtcaagaacaatagttt
gcagctctatatgcaccgattagagattggtgtccatttttctctggaaatgtatttttatattcttactggatgtatttttt
gataatgtttgctactgtgaagatacctgaacagggtccacactagaaaataaaaaagactaatcggcagattaaccctgtgc
atccagacccacgagtcctttgatcctgccccctgaaatggagacacagaggacagatgagcaatgctgagcggtgcaccca
agaccacaaaaagaaagacaaggaaatgtgtcccctccctcctcatgaaaggcagctcatccctgttccttcaggccctgg
tgaggagccaacccatgtctgttcccttcctcggtgtccacaccgtggggtctgccctgatttgggcttcccttctcatcacc
ctcaatattagtgtcccttgtgaatcaggtccagctgcggctgctccacatggggccgttcttccatttcctctgtgtttgca
gaagtcctgtgtgaaatttactgatagagtcaggggggaaaattgtacagcccagtggttcactgagactctcatgcaaagcc
tctgatttcaccttactggctacagcatgagcttggtccagcaggcttcatgacagggattggtgtgggtggaaacagtgag
tgatcaagtgggagttctcagagttactctccatgagtacaaataaattaacagtcccaagcgacacctttтcatgtgcagtc
taccttaaagggaccaaactgaaagtcaaggacaaggccttgtaatactgtgagagacacaggagagggaatatctgcgtgag
cccagacagaaaaatctctgcaggaagacaggagggagctgcatggtagatgctcctcagaaccaccagggcaccttggggac
aacctgggggcactcagaaccaccagggtgtgcttaggaccacgggacactcaggatattaggggtgctcaggatcacgagg
gggcgctcatgacaccaggggacactcagaatcacaaggggcgctcaggacacgagggtttgcccgggaccaccagcaggca
ctcaggtcaccaggggtgctcaggaccaccaggggcgctcaggacaccaggggcgctcagaaccaccaggggcgctcag
gacacctgggggcgctcagaagcatcaggggtgctcaggatatcagagtgccctcagtaccacgaggggcgctcatgacacc
aggggcactcagaaccaccaggggcgctcagtacacggggttctcttaggaggcagctccaaatcagaagcctgagaggct
gtggttttcttttaaaccttggtgattcccgacctggtcaagcaaaagtcttccccaggatctctcaccatttcttccttgta
agtccatgattacttttacctacaaaacattaacttagaacaggaatttaattcaacttttaatgctgcatatttttccaagta
atactagcaatgatctctcaggacaatttttacaataggttatttatatatttttcttgattaaaaataatactattattaaaa
tagtaaagttataaaaatcacacctgtaatcccagcactttgggaggctaaggcaggcagatcacttgagctcaggactttta
gaacagcctggcagcacagtgaggtctttttctatatatatatatgtaaaataataataataataataaatacctgggtatggt
tccacctgtggtagcagctacttgaaaggctgaggcaggaggatcccttaagcctgggaggttaatgctgcagtgagctgtga
ttgtgccactgcactccagcctcgttgacagagtgagaccctatttaaagaaaatgtataccctcaatacaaactgtttcaat
gattagagttttgtatttttgtgctgtaatagtcaaacaattgtacatgtttttttaacattaactcagcatatacatggtatt
ttgtttatttttctttcatctgctgtttttggaaattaaacacgactttaaatgctcttgttctccatttttggttggcttcag
gtgtcctgtttttcagactatttctccatcttccctttctctttgaaagtattttacttttcctcagtctccatgaaggaaaaa
gaaagtccctttactttctgacctccaagtctgttgaatcagttcccttctcttcataatcactgaagccaaccaagtttaga
ggataatggttctccttagaatatgctcgtctacctgcagactctctgccctaactcacccttttccagggtcctgcagacca
tctcctcgtttccctaagtaccacagagtgggctctgcagctcctgctgccctctgtgtgctcagccctggggctcactagtg
ttttgatgatcaagtccaaatccccatgtgcttggaccctctgagaccaccctctaggaagatgccattgtgagtgagccctg
aaaatcatggactgtgttcagtttcatattcctggatgttctctgttgtaaaggaatattgacaaataaatactagagtttgt
attgaatattcatgccaaaaaagtttttttaaaaatttttcaaatgaaacaattttatcttgcctagtttgaaaactacaatct
aaatttaacaaataatgtaatacaacgtttgtcctattagttattcaatttattaaaaacagactgatatttaaagttaatac
cattgcacatttgagtgacatatttggcaagaacagcatttacattcagctttaacaaaacatgtatttatatatatttgtct
ttttagtattggaataggcagacatacacgtagaagagcattattttctactacaacctcaaactgcaaacacaatttaaatt
caattaagtaataaaaaaaatatgaaacaaatgggtgtgctgttttggtgtttagatatacattcacttttgcatgggcacat

FIG. 7 (Cont. 29)

gtatgtgtctttgctgggctgttgtgtatgtatgtgtgtttgtagaaccatgaagttttcaaatacatcattaaatgacatag
ttatattaatcttggccaggcatggtggctcaagcctgtaatcccagcactttgggaatcttaggcaggcagatcacctgggg
tcaagggtttgagaccagcctggtcaacagggtaaaaccccgtctctactaaaaatacaaaaattagccaggtattgtggcac
aagcctttagtcccagtgtggcagggaaatgtggggtcggaaatcccacacagagtttctactggtataccacctagtggagc
tgtaagaagaaagccactgccctccagaacccagaatggtagatccactgacagcttgcaccatgtttctggaaaaaccacat
accctcaatgccagctcgtgaaagcagccaggagggagactgtgccctgcaaaagtttttttaaaactttcatttgaaaagtt
ttaaaaaagttctgtcacaggggcagaacttcccaagaccatgtgaacccacttgttacatcaggtaacctggatttgagaca
tggagtcaaagaagattattttggaacattaagatttgacttcccagctggatttcagacttgcatgggacctgtagtttgga
ccaatttctccatttggaatggctgtatttacacaatgcctgaactcccattctttctaggaagtaactgacttggtttttat
tttacaggctcatagatggaagagacttgcctcatctcaaatgagaccttggactgtggacttttgagttaaggctcaaatga
gttaagactttggcagactcttgaacaggcatgattggttttgaaatgcgacagcaatcattactctagaggaccacacgtga
agtgcaacaagcaggcgcagaagacaagtgattcgtgatttcactgtagtttgtttaaatggtagactcacagaagtagaata
gaatgttggttaccaggggctggaggggtggactggaaaaggagagattgtggtcaaagtgtaaaatgttccagttagacaga
aggagtaagttacagtgttctaatgcacaagatggaaaatatggctgtgaatgcattatatatttcaaaatggctaaacatgc
aaatgttaaaatttttttcccactaagaaattatacaggtcgggagcgggggctcacacttgtaaacccagcactttcggaggc
cgaggtgggtggatcacaaggtcaggagttcaagaccagacttgccaagatggtgaaaccctgtctccactaaaaacacaaaa
attagccaggcgtggtgttcaccacaggagaattgcttgaagcaaaggctgcagtgagccaagatcataccactgcactccaa
ccggggtgacagagtgagactcagtctcaaaaaaaaaaaagaaatacatttatgaggtgctggatatgttaaatagcttgatt
aacaattccataatgtatgcatgtatgatagcatgtgtgaatggacctgtatgaaggtgaggtgccctggtcacgtgacagtg
aggtgacttgggggaggtgtaaggttacctgggggtatgtgtgcggtgaacttgggcacatgtgaggtgacccacggtgcatg
tgtggtggcctgggtgcgtgtgaggttacctggacatgtatgaggtgacatggggaattcgtgaggtgacttggatatgtatg
atgtgacctcaggcatgtgtgaggtgacctggccgacgtgtgaggtgacctgggggacgtgtgaggtgacatggggaatgtgt
gaggtgacctgcgggaatgtgtgaggtgacctgcgagcattccaggtgacctgggggtgtgtgagcttagcaggagtgtgtg
tgaggtgacatggggtatatgtgaggtgacccccctgacgtgtgaggtgacctgagcacatgtgaggtcacctaaggcacatc
tgagttgacctgggggatgtgtgaggtgacctagggaaatgtatgagctgacaaagggcatgtgtgcagtgacctgggtgcat
gtgaggtgacctggtgcatgtgttagtttacctgggggatgtgtgaggtgaacaggggcaggtgtgaagtgcctgaggaatgc
atgaggtgacctggtgcatgtgtgtggtgacctagcagatttacgaggtgacctgcgggatgtgtgaggtgaatagggacttg
tgtgaggtggccacaggaatgtgtgaggtgacctgggggatgtgtaaggtgacattgggggatgtgtgaggtgactcagggcac
atgtgaggtgacctgggggatgtgcaaggtcaccttgggtgagtgtgaggtgaccttgggggatgtgcaaggtcacactgtgtg
agtgtgaggtcatctgggatatttcaaacttcgtaaggaaagcctgcaacagtatatggcactaaaagcttcacactccaaca
ccgttaatgcgcacatcctcaaggaactctaagtgtttccaggttagcttaaatgccatggagcgacacctgccccaggcaca
ctcatatatgcatcctgggtctccctatcaaccctatcctcaaatttcagtttatgtttgctccatgatatcaactctgat
atgttgaaggttttttttttctttttatttgtagttgttcaggtttgctatttcactctcattactctgggctcagtcctctcc
tcaggtgtcccacttcagagcttgctatataataggagacatgcaaataggaccctccctttctgatgaaaagcagcgcagc
ctgaccctgcagccctgggagagaagccccagccctgggattctcaggtgtttctattgggtcaacagcaataaacaaattac
catggaatttgggctgagctgggtttttcttgctggtattttaaaaggtgattcatggagaactaaggatattgagtgagtgg
acatgagtgagagaaacagtggatatgtgtggcagtttctgaccagggtgtctctgtgtttgcaggtgtccagtgtgaggtgc
agctggtggagtctgggggaggcttggtacagcctgggggtccctgagactctcctgtgcagcctctggattcaccttcagt
aacagtgacatgaactgggcccgcaaggctccaggaaaggggctggagtgggtatcgggtgttagttggaatggcagtaggac
gcactatgtggactccgtgaagcgccgattcatcatctccagagacaattccaggaactccctgtatctgcaaaagaacagac
ggagagccgaggacatggctgtgtattactgtgtgagaaatcctgtgaggggacacaagtgcgagcccagacacaaacctcct
gcaggaacactgggcgaaatcagctgcaggggtgctcagggcccactcatcagagtcaaccccagagcaggtgcacatggag
gctgggtttgtttcctgtcaggatttgggacttcctctgcttctgacagtttccctagggaaactctttaattttagatttc
tgtgcccaccaatgtcatctctacatatatttttttaaatcattataatacgaggactcattctcacatgcacaatatgtata
ttgccacctacgggaatgaaaactcctcaaccatggtcaccagcatcagagttgtgaggaagctcaggggtgcctggtgagtc
ttctccagtcagactcaggacagtaacctcaatgggattccctgactagaatggcttttagggatttcgattacagccaagag
agaggctggaccaggttcagtgtcatgtaggacctcacagattttatgtatgacatttctcctgacaataaagtatgcaaatg
agtatcagtcactgatctggtgcttcctgactttcatttttagtggttctcgcttttccatttgattttcctgctttctggat
aaaaggatgttgtccctgtggtctaaatccctggggctcaagccctttccctggagcttaggtggggctcaggctgtgactcc
tgcagccattgggagaggctgctgagacttttcttctctctcattgttcaggatactccactctgttttctggagacgcgtctg
agaacgcgtgtggccattagtaatgagggcacaagcttctttggtcaaaatggggtgaggatgtggaattgatcctgtgctgt
gtaaactgtcacagagtcaccttcttcaccagtagtgttagaagagcttgtaaaatttgtcggaatccaactggagtcccctg
tgttcaaaccctgacaaatggagctgggggaaggccatggatggaagcttctcatgcacataccctgagaacaagacctagct
ttataacactccaaaaaaccacaaattgaacaaaggcaaccacaacaataaaagaattacttatatccctgagaacaagagct
agctttataacactcagaataaccacaacaacaaaataattacttatatacctaacaacaagagctagctttttaacactcgg
aaaggccacaatcttgcacaaggcaaccacaacaatgaaagaattacttctgtgaaaatatctgcacagcaactgcctatcca
accttacactgatgtcaaccttgttattgatgcttctagcccaggatcgtcctcatcaaaatgtcattcagatcctgcctatg
aaaaaaattgtgtttttcagtgcactcatgttctagtaaagccctcagagaccctctccttcacctgtgctgtctctggattt
ccaatcataaccagtacttcctcctggagctgtatctgccagccccagggaagaagctgaagtgggtcaggtgtgtaggtca
cgaggaaacacacagtgcaacccgcttctcaagagtccagtcaccacctccagatccacattcagaaaacagtttttcctaca
gctgagctacccgcacaatgagtaaaccaccatggatttttatacaaaagacacagaaggggaggtcattgtgaggccagaca
caaacctccctgcagggaagctcaggacaccaggggtgctcagacaccaagggctctcaggacacatcaaggcaggtgcaag
aggggaaaaaaggtgctggaggtgggggtttttcatcactgtcatattttactctccactatatttattctaatgtatattatt
ttattattagacaatgatatttatataaatatatagccatacgtaggtgcaccaagttgtcctttccatcttatgtggacctt
gtccattaggacgaagtccctgtatgtatttgagcacctcataagttatggttaattatgtaggatctctcacttttttctgtg
tcccttcctccctcctctctcacacacaaactgacacccacaaagagttctacaactttaattacctgatgcgttgaagaaaa

FIG. 7 (Cont. 30)

tttactgaagtgcagctttttcagtttaactgctgttcatgttgatgtaggaataagaacattgtctttctcaactgtgtagc
tctctaagctgagtagcacctttatttataatacccagatactgaaagcaatccaaatattgatcagcaggttaagcagtaaa
cactttgttctaaattcgttcacttgaataatacccactgttcaaacaagtacggctggaaatgctcaacaagggtaaattca
caagtacttatgaagagtaacataagccaaagaaatacaagtacatacatacagttccacttttataaatttttataaaatgaa
aactaatctaaagttacataatgaaaaccagtagttggccgtggacatggtatgagaagggaaggtgtaggaagtggcaatta
caggacaacgagaggaaatttttgaggataatttttttctgtattgagaaaggttatggttatgtcattatttgtcaaattgtac
acattaagtgaagattattactttctaatttcgacttcttaaaatactacaaatttaaacatatataatttggtagaaaagga
gttagagatggataaaatatatgagaaataaaaaagaaaatctcagaacgatggcataaggattcaaccatcaaactaaataa
attttaaatttctcaacacagaattatagattcataaaaccagctcctggattcattgattttgtggaattgatttacatgtc
tttatctccttcagttctgctctgatgttaggtatttcttctcttctgctagcttgtgaatttgctcttgcttctttagttct
tcaaattgtgatgttagggtgtcagttttagatctttcctgctttctcttgtagacacctagtactataaatttccctctaca
cactgctttaaatgtgtcctgaagattctcatatgttgtgtctttgttctcattggtttcaaagatcatctttatttctgcct
tcatttctttatttacccagtagacattcaggaacaggttttccagtttccatgtagttgtgcagttttgagtgaatttcttc
atcctgagttctaatttgattattgcacttgtggtctgacagactgtttgttatgatttctgttcttttgcatttggcgagga
gtgtattacttccaattatgtggtcagttttagaatatgtgcgatgaggtgctgagaagaatgtatattctgtttgacttgggg
tggagagttctgtagatatctattaggtctgcttcaagtcctgaatatccttgttaattttctgtctcgttgatctgtctaat
attgacagcggggtgttaaagtctcccactcttgttgtgtgggagtctaagtctctttgtaggtctctaaggacttcctttat
gaatcggggtgctcctgtatttggtgcatatatatttaagatatttagctcttcttgttgcattgatccctttaccattatgc
aatgcctttctttgtctcttttgatctttttttggtttaaaatgttttatcagagattaggattgcaactcctgcttttttttt
ttttttgctttccatttgcttagcaaatattcctccatccctttattttgagcctatgtgtgtctttgcatgtgagatgggtc
tcctgaatagagcacatcaacaaaataaatagacagctagccagattaataaagaagaaaagagagaagaatcaaataaatgc
aataaaaagtaatgtaggggatatcactactgatcccaccgaaatacaaactaccatcagagaatactataaatgcctctatg
caaatatactagaaaatctagaagaaatgcataactgcctggacacatacaccgtccaaagtctaaatcaggaagaagtcaaa
tccctgaatagaacaataacaaattctgaaattgaggcagtaattaatagcgtacaaaccaaaaaaaaagtccgtgaccagat
ggattcacagctgaattctaccagaggtacaaagaggaactggtaccattccttctgaaactatttcaaacaatagaaaaaga
gggactcctccctaactcttttatgaagccagcatcatcctgataccaaaacctggcagagacacaacaaaaaaaagaaaag
ctcaggccaatatccctgatgaacatcaatgcaccaattctcaataaaatactggcaaaccaaatccagcagcacatcaaaaa
gcttatccaccacgatcaagtgggcttcatccctgggatgcaaggctggttcaacatatgcaaaacaataaatgtaatccatc
acctaaacagaagcaatgacagaaaccacataatcatctcaaaagatgcagaaaaggacttcaacaaaattcaacacccctc
atgctaaaaactcaatgctctaggtattgatggaatgtatctcaaaataataaaagctatttatggcaaacccacagccaata
tcatacagaatgggcaaaaactggaagcatttacttttgaaaaccagcacaagacaacgatgcctctctcaccactccaattca
acgtagtattgagagatctggccagggtaatcaggcaagagaaagaaataaattgtataaaaataggaaaagaggaagtcaga
ttgtctctgtgtgcagatgacatgattgtatatttagaaaacccccatcgtctcagcccaaaatctccttaagctgataagcaa
cttcaacaaagtctcaggatacaaaatcaatgtgcaaaaatcacaagcatttctataacccaataacagaaaaacagagagcc
aaatcatgagtgaactcccactcaaaattgctacaaagaaaataaaatacctaggaatagaacttacaagggatgtgaaggat
ctcttcaaggagaactgcaaaccaccgctcaaagaaataagagaggacccaaacaaatggaaaaacattccatgctcatgaat
aggaagaataaacatcatgaaaatggccatactgcccaaagcaacttatagattgaatgctatccccatcaaactaccaatga
ctttcttcacagaattggaaaaaactatttttaaagttcatatggaaccaaaaatacatcctgcatagccatgacaatcctgag
caaaaaaaaaaacaaagctggaggcatcatgctacctgacttcaaactatactacaaggctacagtaaccgaaacagcatggt
attggtaccaaaacagacatatagaccaatggaacagagcagaggcctcacaaataacaccacacatctacaaccatctgaac
tttgacaatcttgacactaacaaacaatggggaaagaattccggaactatttaataagtggtgttgggaaaactggcgagcca
tatacagaaaactgaaactggacccccttccttacaccttatacaaaaactaactcaagatggatgaaagacttatccagacct
gaaaccataaaaatcctagaagaaaatctaggcaataccatccaggacataggcatgggcaaagacttcaagtctaaaacacc
aaaagtaatggcaacaaaagctaatactgacaaatgagatataattaaaggaaagtgcttctgcacagcaaaagaaactatca
tcagaatgaacaggcacctacagaatgggagatttttgcaatctatccatctgacaaagggctaatatccagaatctacaaca
aatttacaagaaaaaaaaacccatcaaaaagtaggtgaaggatatgaacagacatttctcaaaagaagacatttatgcagcca
gcaaacatgaaaaaaccctcctcatcactggtcattagagaaatgcaaatcaaaaccacaatgagataccatctcacaccagt
tagaatggtgaccattaaaaagtcaggaaacaacagatgctggagaggatgtggagaaatagtaacatttttacactgttggt
gggagtgtaattaagttcatccattgtggaggacagtgtggcgattcctcaaggatctagaactagaaataccatttgaccca
gcaatcccattacttggtatgtaccccaaggattataaatcattctactacaaagacacattgcggcaccattcccaatagca
aagacttgaaaccaacccaaatgtccatcaataatagactggataaagaaaatgtggcacatatacaccatggaatactatgc
agccataaaaaaggattagttcatgtcctttgcagggacatggatgaagctggaaaccatcattctcagctaactaacagaag
aacagaaaaccagacaccgctgttctcactcgtaagtgggagttgaaccatgagaccaggtggacacagggaggggaatatca
cacactgaggcctgttgggaggtaaagggctaggggagggatagcattaggagaaatacctaaggtagacggcaggttgatgg
gtgcagcaaaccaccatggcgtgtgtatacctatgtaacaaaactgcacattctgcacacgtaccccagaacgtaaagtatca
tttaaagaaaggattacatattccattaaatatatatgagaaatcagagactcctgaatatacacatgaatacacactgggtc
tacctatatttttagggaaacactagaatacagcaaaataatgtcatgattttattaaaaaggggggtttatcaaaccacacc
aggcatgtccagctctgtcctggagctggttcagggaacaggtgggtcctgtgtttgggagccatgacaacaagctcacagcg
tcagttctagttgaaacctcaaaaaggcaaagggatctcaactaaaatatcatgtggatgtcacatctgtgggtgctgcatac
tccccgatgtgaatatggaaaggttaattacctcttgaactctctgccgagattagtgctggtctctcaggaacacccaaaa
tggctcgatagagccagaaagcagactggctcagggtttttgtgatggtttcgtcgtgggtcagagtgaggcttcccacgcac
aggaaggggattgtacagtgcgaaacacccactggtgtcaaatgaggaagctcccgcaattcctaactagattcacattgtgt
gataaaagacacacaatagacataacttcatggtcggatatcacaaaatgccgttaaaagatgtggtaaaaaggcaactttaa
atttttagtcattggagtgcgtacaacacaaaaatcattttcaatatttgtaacacatgcatgcaataggacaaaggtatgtg
atgagggtaaaatctcgaaagtgtgaatcttccagctaccaagtcgtagggtaataactgatgtgtgctgagggaggaaacca
tcacgccatagtgctaatggtataacccttggtgaagagagttcaatattttattgaagttttcataatttttatttaaagat

FIG. 7 (Cont. 31)

gccatttttcaacatactcagatgattgtgagtgccattgattctgtatcgtatgaacaatggcaataccttccatgtttaca
taatattaaaaaccacgttaagactgaatatttggtgtcatggtgcatcacgttattctagcttccatactagttgttttatt
tgtttgttttctcctttgttggcatttggtttcgaattcatatgtcaggtctctataatgtaggaatttatttaaaagtgtct
ttttttgtccattttgatggggcttccaggagacgtaagaacctcctctgcttgcaacacattttaaaattacacactaatgt
agaacatctgtatttaatcctggtttttagttaattgacaagctctaataagtgaagtaacttctccattctgggctgatttt
acatcaggtataggaatatatcctaggtgaaagtttgtaccagtaatatgaattattaggtaataacctccacctttatgatt
tacatgttattcatcaagaaatagtgttaaatcaggagtctcaatgaaagtattacctaagggatatacaaaatatattgcta
atctacataaaacagatgtgaacacactcttagtatccagccatgtttcctgtcaaccacacagtaactttgacttcacttgg
gacttgttctaattttcaaattagttacttattaatcttaatgcttctagatattatgtgtgactattttagcagagagtgaa
gaaagacagcctaggccgactaaacaatgaggaaaatcacaacctgatgaaacaggaagcctctggatgtgagtggctccagg
attgaataatttgacaactcatgtacccaggaagtttcttttctcaatttccacactgatgcatccagaaagtcagcttcac
ccccaggtgactcccataatgcagtgacatggtgacaatattcccatggtcacatacgtattttatatattggctggaaaag
gggcagagacagttctgcaatttctcctctgaaggaccaggaacacctcaacagaccacctccctgccccatgactagaact
gcaccacgtgcccacatggacactcatccctgatggggataagaagactccattgatgaggccgactattttagcatataaat
tagtaaagactgatataaaggtttcaacaactaattgaagtctgttcttctatgtccaccagagactatagatgctccagcga
tatcttgttttctttgctgcgtgactgtgtctcttctccttgttccatcctccagagaatctctttcagctcccacaggtgc
attcctctgttacatgtaactgacaattgataaattagtggaagcccttacactaaaggaagagtctctgacctcatcttggt
ccatattcctagaaaggcattgtgcccgtaagtctgggtgtgaccttctgagtgttcctgaccctcctccagaggagatgctc
atctgtgtgttcttgtccctttcactggggtagaaccaccctgtttcccccaggtgttccctcccacagctccagtgttccgc
atcagtgtcatcacctcccagatctgctgccctgccctgcagactaaagctctgattccataagaaggagagttatgtctcaa
cagaacttcgtggcagtgacctctgttcccatctcaattcctgaggggttgcaccagtgcccctagggtactggttttggtgg
ttcccctgcaaagtaatttttggttctgtagtggatataagggagtcgagtctgaatgcctttcaaaaatgggggctcttgtt
ctctcccagacagacactttgggaaaggaagattttgtgactgccccttttttgggaaagggattcaagaggatagaaaagc
tcttcagtatgtggtcccttagaatttcaaactacaacaagcttaccatattcagtttcaagcaatcccatatatatttgtat
ttttatctttaacagactatatttcatatgccagactctgccttaggtaatctcatatgctggctttgttactctctacaaga
acttgcttcttgttaaatttaagatttttttttaacttcagttatcctaagcattcagaaatttgcaaaatttcatcttgactg
tttatctgttattgttgatgtagttgtaagaaataaagaatatatatccctcatttatgtacattttcaagtcgagtagtaga
tttttagtactaccagagtaataaaataatttgaacattgttaagctgcttaacagaaaatcaaattatggtaaatttgttca
atggaatactacacaacatttataataaataattgtctgatacatgcaacaagaaggtaaaatatctaagtatttttgctgag
taaaataaaccagacaaatgagaagatttaccatataatttcatttatataaattctggaaaataaaaactgaacttacttaa
gtaatataacaacaaggtaaaatatctaagtattgatgttcaggaaaataaagcaaatgaataagaatatgtactatgttatt
ccatttttaataaactctgataaattaaattgaatctacagcaatataaagaagaacagaatttaccatttggggaaatggtag
aagaagggaagaggaaaggaggaggaatatagaagaatgagagggaaattttgtgaattttctggttcaccttggtaactagg
atggttacatcaggtttatcaattgtacactttaaatatgtgaagtttattatcagtaaactgaaatttataaaatttattac
cagcaaacaaatgaaaacttgcacaagaaataagtgacataaagatagaaaaaatattaaatttcagaaacacctaataattt
atcttcgtgaaccctagttctcaccatatttttaggtgaatgctagaatgcagcaaaattacacatgctctcaatacagaaag
tgggtttcacaaaccacactaggcatgctcagctctgtcctggagttgggttagggagtaatatagggccagtggatgaggag
cacaggcctagatactggggctcactaacctcaggtatgagctcttagatacatacaaagccccctccacgcatgggtttactt
ccccatctgtaaattgagaaaccattgacccctaaaaatatgatttacacaaatatgtaaaaatgtaagagagtgattagtgc
aaagtgtttatcacagcacaatttcataacaagacagcaagttttccaaacagcatcattgtcattagattcctgcagggcat
cattaccttatctgggccctgccctctgttcaggcatcccaccccagagcttgctatatagtaggtgacatgcaaataggcc
ctccctctcctgatgaaaaccagcccagtcctgaccctgcagctctgggagaggagccccagccttgggattcccaagtgttt
tcattcagtgatcaggactgaacacagaggactcaccatggagtttgggctgagctggattttccttgctgctattttaaaag
gtgatttatggagaactagagagattaagtgtgagtggacgtgagtgagagaaacagtggatatgtgtggcagtttctgatct
tagtgtctctgtgtttgcaggtgtccagtgtgaggtgcagctggtggagtctgggggaggcttggtaaagcctgggggtccc
ttagactctcctgtgcagcctctggattcactttcagtaacgcctggatgagctgggtccgccaggctccagggaagggctg
gagtgggttggccgtattaaaagcaaaactgatggtgggacaacagactacgctgcacccgtgaaaggcagattcaccatct
aagagatgatttcaaaaaacacgctgtatctgcaaatgaacagcctgaaaaccgaggacacagccgtgtattactgtgccacag
acacagtgaggggaggtcagtgtgagcccggacacaaacctccctgcagggcgcgcggggccaccaggggcgctcgtgacc
cactgagggcgggacaggtcccaggagcaggtgccgggagaggtttcctttctcctcagctggaaaagtcaggtttatcttcg
caggactctggagtcttctaggctgtgatattttgttacttatatttattatgaattttatcattaatacttaaatttttagta
attattaacattctacatattattatttttaagtatatacttcaagaaataaacattcctaattgcataataattattgt
aacataattattgtaacatataattatatcctaaatgcataataattattgtaacaatcacattctcattttgtatttgaatt
ttcatatttatttttactaagattttaattttaatataaaatatttttctacaattgtctgttttccatttttgtgagataaaa
ttagcatatacaaaaatgcacagattctccaggtacagttagagggtttcaggcaaatgtgcacatacttgtctacagcagct
aagtgagggtgaggaacaggtgaggtccatctccccacaaagtgtcctcttagtgcttccagttagttctcacataaggattt
ttttttatttcaactttataatttagatacagagggttcatgtgtggatttgttacatgggattactgagtgatgctgaggtt
tggaatacagatttcttcacccctccctccatggtctagcagtccacagtgtctgttgctcccatatttatgtctatgtgtg
ctcaatgctgaggtcccacttacaagaatatgtggtgttcagttttatttcctgaattaatttgtttaggattaagaactcc
agctccatttgttttgctgcaaaggacatgatttcattctttcttatggctgtgtagtattatatattttacatgtaacacat
tttatatatccactctaccattgatgtgcatctgggctgatctttgtctttgccactgtgaataacacagcaataaacataca
catgcatgtgtctctttggtagaattatttgtttaccttgtagtgtataccctgtaataggatagctggttcatataatatct
ccatttttaagtttttgagaaatctccagtctgctttccaaagtgggtggactaatttatattcccattaacagtgtgtaagt
gctttcttttcaccacagccccatcagtatccattggtttttgacttttagtgataaaaatttgagtggtgtgaggctgcac
acctacaaccatatgatctttgataaggctgacaaaaaaacaagaaatgagaaaggaattccctgttccataaatggtgctgg
gacaactagctggccacacgacaaagattgaaactggatgtctgctttcaacatatataaaaattaactcaaaattgataaaa

FIG. 7 (Cont. 32)

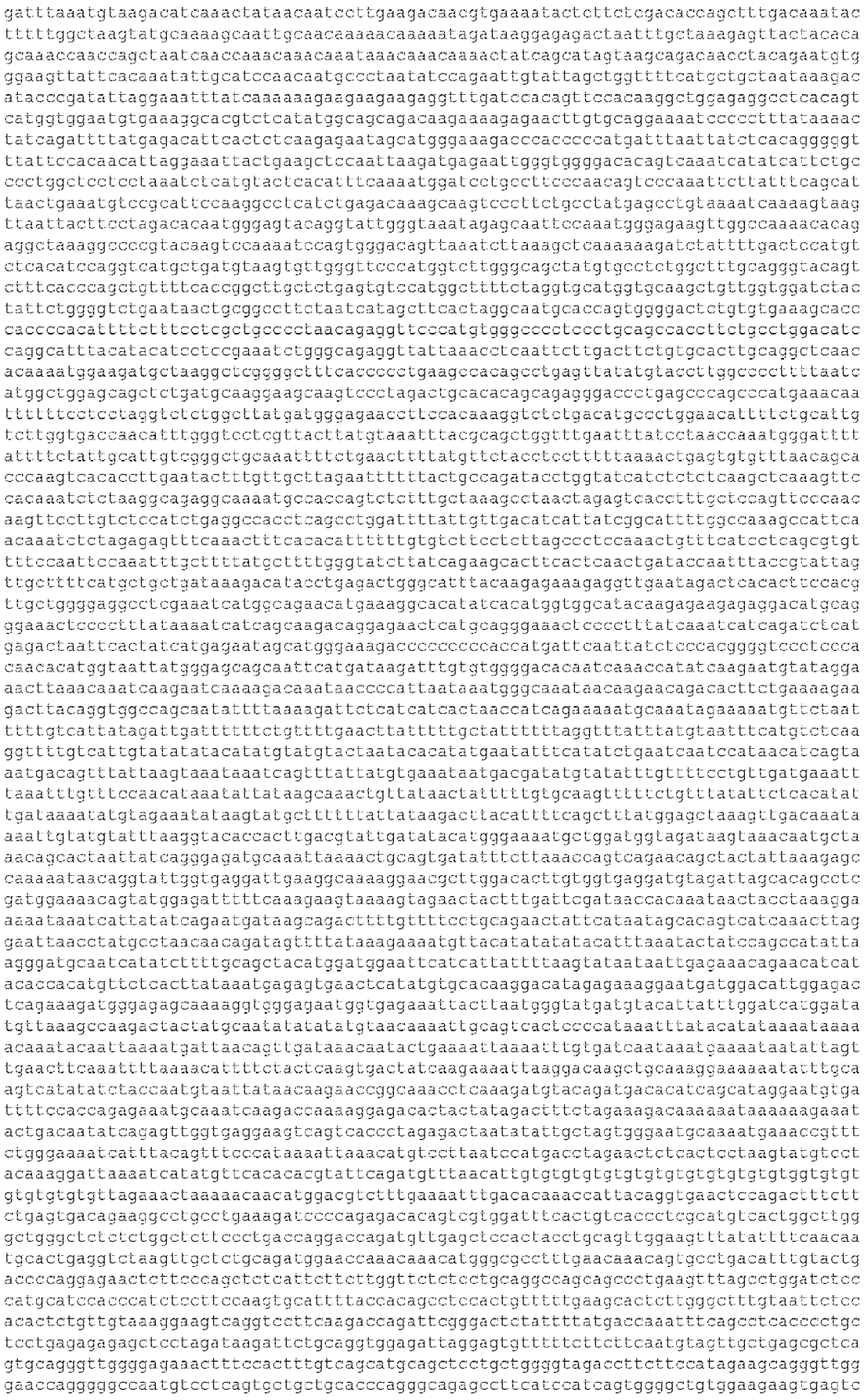


FIG. 7 (Cont. 33)

tctggttctcagtagctcttgtccagaactgagcctctgcagcatgttctgtcggccccagtgtcctggccctaaggagcag
catcctaaaatgggagctagcatatttgagaataacaacacctacacattcagaagctctttggctttctttccagctaatat
aatttcctttttttttgtgtagcaacctgtacacacgcatattgatgcatacagacctatgacacttttttctcgataagtaaa
aaattattgatcactgtgatcttttctccaagttcaccatttccctgaaggtgagcacaggtccttctgcatgtgttcaaaca
aaaggcccagagactacctggtaagtgaggtgctcacctggttctggatgtttggtctgtctcctcccctctgttgccccaca
caaggtcagcccactctttccaggtccgaagaagagagcacaggtttgtcctgattatatgactcacccagcttctgatgact
ctcctgttgccagcgtccatggcctcagtgaaggtctcctgcaaagctctggatacaccttcgccagctacgacattcactgt
gtgtgacaggcccctggataagggtttgaatggatggtagggagctactctggcaatggtaacacaggctatgcacagaagtt
tcagggcagagtcaccatgaccagggacacgtccacgagcacagcctacatggagctgagcagtcagagatctgaggacatag
atgtgtactactgtgcgagacacacagtgtgaaaacccacatcctgagagagtcagaaatcctgagggaggtggcagcagtgc
taggcttgagagatgacagggatttttatttgctttaaaggctttttttagaaagcgaggttaattcattacagaaaaaaggaa
aatagaaatgtgtatggactctaattatgtgggaaattttccatacaacttttgttctctaagcaaaattcagggagtggaaa
acaaatcaaattaataaacctgataaaagaattcctctgaaaatttagtgtgagcataagtttttgaatgggtgttgtaaata
ttttggaacacagctgctagatcacattttaactctacacttatctccattatataaaatatcaaaatgttttaatgttttcc
attttgtgcaattataatttttgtgttataatcacattttaacactttaactctacacttatctccattatataaaatatcaaa
atgttttaatgttttccatttcgtgcaattataattttgtgttcatgccagcaatgcatgatagatcttgttcttccgcatcc
tcattgccatttggcactaagagtattgtgtattttaatattctaatagattagtagtgatagctcattgctgtttaaatgca
catatttctaattaaaattttgtatttaattatttttatataattgtgatgaagtgtctcgtatggtatttggattatttttta
ttgcattgtttctttttgatcagttgtaagtttccttatatacccattatataagtcactcacaaagttaacaaaaaattgat
taacaaatatgtgttttacaagtgtattctccaaattgttgttgtcgttttactcccatatcagtgtctgtgggagaaaaata
tttatatacatatatatgtgtgtgtgcatatatatatatatatatatatagtgtgtgtgtgtgtaaacttagataaaataatt
atttcataaatcatactttggcatcatatctaaaaactaattatgaattccactaacaggatttttctcttgtctccaatct
caggccacaatcacagcataagcatttaaatttctcctatttgatgagaagattattaacttaagatgtttagaattcttctg
aatggaaggtgccttttttctaattttctgtattcaataatctgttaatatcagtattggctcatgaatgtttatttttttact
atggagaagatctagtgctacattatttatttttatcgctcaaatcaccacagctttttttttaggttctgtgagctcatttagt
ttggattctgtatttttacagcatgccccatcctttgttttgatcacttccctatttcctggtattacaagaaatactaag
ctcattatctctattatctttccacacatagaatcagttatttctccaaggattactggtccctgatattaaagaattatat
taaaacacaaaattatgatgttggatgtgtgttgttaatgtactgtcagtgtttctagaatctctaagctaacaggcctag
aaaatgtgtatgtgtatattaacccatgttaactgacccatctaatctatttatgtatccaatcttctgtatgtttattgcat
caaactttagaacactggtatctacaatctactatgatgatacatgaatgtttcaagccttccttccttgcctgtccatacca
cctactgcaaagtgaggaacccctcccatcatttgccgttcattcaatttgttgtacaattttagaatatatgcgtcgtggta
ttagaattgttaacttgtaccctgttggaagtatgtttattgactagaataaagtgtttaagtgcagtttctttatacttta
gacttacagaacaccctgagttctaagttatataggtgagaaactttatgtgccaccttcttcagtgaggttatttgaaatat
gttgtatacattttatttgacattctgtaaaagacaaaactgtagatgtcataaatatatgaggattttctagaaatttagag
agagggtatgcattaggagaaacaggtactgtttgcaaacagtgaaatttttttatgatctgcagtagtgaacacatgacacaa
tttgttaattctcacaattttatgatgtaaactgtgaatctaaatatatacaacttacaaaattatgtagcacatcatgaaca
tgcaaagtgtacaaaaataaaatatcaaatacatttacaccgcgtgggcagggaattgcatgagatgcaggcaacaaagaatg
aagtaaccttccccatttgcacataagatgtttccattcacaagagacctttcttttatcaggttcatgtgcaaccaagtttc
cctgctgacaagcatttaagccagatgattcgcaacttcctttgactgagaaagatttccctcaaacttcagctcagtgcagg
cacacaccatctctgaatgggcatttaccatcagacaatgcccacacctgtccccacatggaccttccctcagacaaacaaa
cacatcctcaggttgactcttcctcagacaagcacccctgtcttcatgtgaactcttcctcagataagcacacatgtcccc
acattgacttttcctcagacaagcacatatagctgacaacgaacagttatgtggcaaaatgagctcaggatagtggtaatta
tggactccagctctgatagtttgtagaaattgtcatttttaaaattctgactgaagactttccttttattgtagaagacagtcc
tttacagctctaattgcacagcctacagacaggagtccatttcctctgggcaaggtttatttttatttgtttactgtacttat
ttgttgataaatattgatactacaaagatagcctatagggtccacatacgagaaaaaaagagtaatgggcagatcaaccctgc
aaatccagtcccaggagtctttgaccctgccctccctggaatccagagacagagatgggaagaggcctgctgagcagtgcact
catgtccccagggagaaagacatggaaatgaggcccctcctctgcaaatgaaaagtagctcatcccctgttcctgtagatcct
ggtgaggagccatcccacatctgtgccctcctcagtgtccacaccatggggtctgtgcagatctgggctgctcttgtcatca
ctctcaatgttcaggttccccgtggatcaggccctgctgtggctgttgcctctgtgttttcagaagtcccctgtgaagttaac
taatggagttagacagagaaatactacagaccaggaattctgccttttctgcaaagcctctggattcactttcactgaaaaca
gcataagcttgatccagcaggcttcatgacaggggtgggtgtgggtaataacaataattcaaatagaagttctcagtgggact
ctccttgagtaaaaagatgattaacaatcctcaaatacactcagttcaggagattctctttttaagatgattaacctgagagct
caggaaaagtccgtgtattactttgagggacacagtgagggacatctgtgtgaactcagacaccaacctccctgcagggaga
caggaggggactgcctggtagatgcttctcagaaccaccaggggtgctcaggacatcaggggcactcagaaccatcagggg
atgctcaggacaccagagggcactcaggacactgggggggggtgtcactcagaaccaccaggggcactcaggacactgggg
ggggggtcactcagaaccaccaggggcgctcaggacactgcgggggggggggggggtcactcaaaaccaccaggggcg
ctcaggacactatgaggggggtggtcactcaaaaccaccaggggcgctccggacacggtggtgaggggtagctcaggatag
caggggtgctcagaaccaccaggggcgctcaggacactgggggggggggtcactcagaaccaccaggggacactcaggaca
ctggtggcgggggggggggggtggtcactcagaaccaccaggggcactcgagacaccagggagccctcaggacactagggg
gagctcagaaacaccaaagggcaatcaagacaccaggggatctcagaaccaccaggaggtgctcaggacaccaggggtctct
gaaccactaggggagattaggaccccaggggctcagaaccactaggggttttcaggagaccaggggcgctcaggacacc
aggggcgatagggacaccaggtggttcagaaccactagagtgtgctgagaaccaccaggggtgctcagaaccccaggggct
gctaaggacaatagggagtgctgagaaccaccagtgggcgctcaggacaccaggggatctcagaatcaccaggctgtgctca
ggacaccgggggtgctcaggacctccaggagcgcacacgacacaaaggatagctcaggacctacaggggcgatcagaacgc
cagggtgcgttgaggacaacaagggctcacaggacacaacgacgtgcttagtaaaccgggggacactcacaaccaccgggg
tactcaggacaccaggggtgcccaggaaaccagggagcactgaggacaccactgctcccttaggaggcagctccacatcagg

FIG. 7 (Cont. 34)

tccctgagtgggagcagggaggagggttcctcttgtatcttgccactaacatgttgggagtttttctgcttcctttgtggttt
caattattggctgattcttcggtacaaagcagagcaagtataaagctctgctttcttggattatgtaatgtttttggctttgg
atgctaccagaattacattgtactttgagaggattcattcatggtgtgtgcaatagtgaatgaaacctgtaattttagggtg
gctttgaaagctatgttaggtgtggctgagggcagtttacaggaaatggtcatcactatagaaggctactcatttctttgcac
atttgcgtaagcaattgtagtttatgaattaaaaactgcctgttttcttggtccttttttcttaaatggtcccactctaagggc
agtaatgtaatcaagctgtgtttcaaagatctgcaatcaagttaagtctgtttaatgaaatgctttgtaaagaaaatgtacat
ctatttttagagtcacctttacatttacattgctttacaaatattaatttggtaaatttagtctcataattatcttcagta
attaaaaatcttaaagtcatgtcatgttaaattaagtaatcctaggcttctcactgtgaattagggttactaaaaattagaat
agtaagagagtataatcaatttatggtgaagtttattaagaaagatgaagatatgttttttgcttaaaaatattttgttttcc
agtttacagggcctttctactggttttaagatgacaaccactgtttacatctgacccttttttgttgaacatctgttgagttt
ctattgatattccacagctagagttttaaagtaaaagctctagtatctttgtattagtgtgaatgtgtgcttgtatgtattat
gtacatatatatatatttttgttatgtgttatggctacaaggtacaaaattgactttaaaataaataactattttaaattaa
gtcaatgagccctaatgcatctgaagtacatgtaacttaaataaatatgtaataaataagctggcttcaaaattattggtaaa
ataaaattggaaatattttaacaattattagaatacctcatagtttatatcaattgatcaagtgattttatatttaaaatcac
agctagatattatatggtgtgaaacatttctatgaagattataaaattattaacctagttaaaaccagaatgatctttgtaat
ttgacaaataagatgtttaatactgttgttttaataaaaaacaggtaaatagttattggaaatacaatcatttatttaataag
aattttacttaggtaaacacctgaaattcatgggttataatatgggtaacagggaaaaaacttaaaggatgagtattactgt
tttcataaatgatctaggtaagctatttaaaaaataaattaggttaatgtaacaaaataaaccttttaaataaacttgttcta
caatttaaaaatctaaagtttaattaaataatagatattaactaaatgtttaggtcattactaattgttttaaaaaatgtata
ctataagaaaatatttttgtaaaaaatttgttcttacagaaagattttatttaattcagaggttacttataaaacatcctaaa
cataaccagtaaataagagagatgccactgcactccagcctgggtgacagagcaagattctgtctcaaaaaaaaaaaaagaaa
agaaatttttagacatagaggagtacttttggtatgaaaggttaaaataaaaaaaaataatttttatatgagaaagaatcttgt
aacttttttatcctaaaataaaaatgactttatttaagaaacagtgatgtttagaataaaactatatgctcaagtatgccataa
gcgttttgtgtaagtcaaactaaggtttgtaaaaagttaattaattaaaataacttcatattatgaagttgactataattaaa
aaggaagtatttataatagtctttatagatttgtagagatctggctttcatataaaaatatataaatatactaaagattggtt
aggaatgaaaaattgtgcttaaagtattgatttactcaataaaattataagatattttaatttttttaacccaaaagtttaact
cttactgcatcttgccagttttatttttattctctttttgagaaggcttgagaggatctcaaatttttcatgagctcctctaaca
tttttttttcttacagcagttagcctctaacgatgttaacttctaactgttgttagcttctaactgctattattgcctgatgct
aaaaatcttttatattaaagttcttaataaaatgttttatttcaatatagtattctgcactcttgggttttttttaaatgtcta
tatttgtctatggaaccaaaatcttcacttgtaatccaagacacattcttcctatgtctaattaatcaaatactttgtttcat
tagagttgacttgcaggttatctgcatggatttccccacagggaaacacagtcacactgctgaaggtgtttttttcccatttgg
taactggcataaaacaaatttttatattttcttgaaatacttcctctgtagctgtttttaagtttttcaactacttaggaatac
tgagattttgagaaaatataaattattgttattacgttaatgtaactatctggcataactttttaaaggacttgtcctgctaca
ttactgatctttgattcctaggtctaaaaaggatacacaacactttgggaggcttcagagggtggatctcctgagggcaggag
ttagagacgaacctggccaaaaaggcacaatctcatttttaataaaaaatacaaaaattagctgggcgtggtggcgggcgcagg
taatcccaactacttgggagcctgaggcagggagaattgcttgaacctgggaggcagaggttacagtaagccgagattacacc
actgcactccagcctgggtgagactctgtctcaggaaaaacaaataaatacaataaaaataaaaaagacaccgagtcttgcta
aattttaaactctgacagcaattgaagccccatctagagatgtggaagaaaatgacaataaaaattaatcacacacttaagac
acaaggccggaaaattgaatctactcaaccactccaggcccagggactgttacagaagaagcggtttgtaagattgtaaaagc
taattttgaaagatgaaattacttgagagtttctttatacagtaaacattaatattaaaggcacactaatgccaggctagtag
ctgggccatgtgtcagattgacaagggtttcttgaagaattaatccacttttttaatttgaaaaacttataaaagtttataaga
gatcatttgaaattaaattttatggtaaaagtaattataatgtaatagatttatttttcagaattgagagacagttttaacttt
ctctcatgctgttcttataaggggctattgtttagaaaattaattcttctctttgaaaaataaaagtttttgctttctttcaa
aatcactgagttctcactgggctaaataaataacttacattacagcaatctgtaatcctatttttgtaatatcaagcattgtaa
acttttgatatttgacaaacttcacaaaataaaattctaaattcagtcatttgacctcattattctttttatgatattaggtcc
ccaaagccaaaattaaacatattcagcttatttggtataattaaaatatgcaggaagcaatgtcaaatttgcaaaagtgttta
actttggactatatttaaataaatgtggactatataattggactatatttatataaattaaagagtatatttttccaaaattgt
atgagattcaagtgatttgatatgtcttagtatatttttatcagtagtatttatgattattatgtaaaatttctgtttattgcc
agaaataagcaaatcttctcctcaattctgtctttaaccatggctattctaaaacttcagtcatccacagttggtgttttact
ttgattctttatcaggtggcttatagtaatctatagaattttgaggagtactcaaatatacgattgtgacaatttttataaatt
gtgccattggtatagagattaaaacttccatgactctcattgatacctgattcatttatgatgattgttaatctaatattaag
caggacaggacttaattgcatgaactgaattgacagaagactgaaattgttttatggcttattctttaatgcatttgctaat
tacttatgttctgttttttcagaatcaggaaaagtttgtcttttaagctcttcacagttgttaacaattgagtatggtatact
ttactgataaaaaaatataaaacataatatcttcttatttacataatttctccaaaatttggaaactgtgagtattcttatatc
aaaatagttatttgcataggttcaataaaaacctgctttcttccataacagggcacaattggagacaatggtcattttactaa
ggctttaacttgaattatatattttcagatttacttttataaaatgaatctaacctggagagctgataaagccccttgggaaaa
ctggcatgcacatttttttttttttacagggccccgaactgtagtaagtaaacaatttaatttctgacagacccaggactccc
aggttttcttggaaacttgaaaaaagagaaagtaacccaattcacatagctatctggtggcacagataaaatattggctgggc
ttgaagattttaaagattctacccttgattccttataaaaaatttccagcaaagtcaatttatggaataaaattggcctatg
tacaaacaaaaaatagaaaacaaaaagagagctaatatgttaaagggttactttggctggcatcttatacaaaaaaaccaggg
ccaagtctcataagcctaaaactgattttacaaatagattagtcctactatgattttgtgtctaataaaattggggaattata
gagagaaatattatttcaaaataaactatagtgcatcagttaatagattttaaccttgtccacttgcttttcaatttatatta
ttttctacaatttggactgaattttaaagcgtatctttgcacgagtctccaaaataatgttttcagttatttccctttttaaa
tatttttcctggcttgaaatcagcagaagttaaactgtgctttcttacagctagacaatgtaaattctaaaagaaaacaaaat
caatgatatggtttggctccgtgtccctacccaaatctcaccttgtattgtaataattcacacattgcaagggtggaatgagg
tggagataattgaatcataggggctgttttcttcatgcttttctcctgttagtgagtgagttctcacaagatttgataatttt

FIG. 7 (Cont. 35)

atgaggggcttccctcttcacttaacacttctctctcctgcagtcatgtgaaatagcatgtgtttgctacccctttcatcatg
attgtaagtttttgtggcctccccagccatgcagaactgtgagtcaattaaacctatttttctttaaaaattacccagcctc
gtgtatgtccttatagcaacctgaaaatggactgatacaagcaacttaactacatacgaagtctccttttgtacctgcctatt
gtgaagagaaaataaatcttgagaccccaaaatcactaagctaaagagaagagtccagctggtgtaataggagatagaaagaa
attatttaggtagatagttaggatgaaagagtctctggcaaaacttttcttctcacaagaattagctcagaaataacttcttt
tctaatcagacacagttcaaagagatcacttctaacaaagagcagcctgaaagatcgggctgtaaaacatagataaacaactc
tggcagagagggtatttctgtgtgtaatcaccaaagttcacatacataggatgggtcccaataaaaacattgggtcttaatga
gcacattcctttccttttctggggtcacactgagataggaaagctgttagcttgcacggggtttgggatgcctccagctgcaa
ggaggtaccagggacctggcatggaaactcctcccccctttttcagcacatgcatggtggaaggagataaggaacgtggagca
gaccaagctaagtccccacctgcataataaaagcatgagatggggctgccagagacttcgctctctgcagatggcacacctgg
tcctgcttttgcaccttatgttgataagaagccatctccccacgagcacatttataaaaatccttacgttgataagatactgt
ctccccacgagcacatttataaaaatccttacattttactgcggcacagcaacccatctgggacccttttctgtgacagagaga
ttttttttccttttacacattaaatttctgctctaacctcactctttgtgtgtctgtgtccttgattttcatagccacgacac
aaagaaccctttggtgatattccagataacaaaggtgctttactggagagggctttgggcaacctgcctcccattctattcaaa
gtgattcctctgaggcccacacgagacagatacatatctgattgcttcctcttcagtatcatttatgaaaaaatgaagattca
ctaagtctgactaaattgtggattcagtggtaggctgataaaggacttaaaataatgcaacctactgtgtcttatctacttct
aaactgcaaaaccccctttcaatttgtcctgtcttgaaggaaaaaaaatgtacattttacatatattgattgatgtctcatgt
ctctctaaaatgtataaaatcaagctgtacttcaatcgccttgggcacatgtctcaggacttcctgaggctggtcatgggtgg
gttcttaactttggcaaaataaatgtattagtctgttctcctgctactaataaaaacataaccaagcctgggtaatttataaa
gcaatgaggtttaatggacttatagttccacatggctgggaatgcttcaaaatcatgtcaggaaagcaagggacatcttacat
ggtggcagacaagagagagcttgcacaggggaactcccttgataaaaccatcagatctaatgggacttattcactatcatga
gaacagcatgggaaagtgctgacttactgcaggagaactacataattttatattttcctatatgcttctttttcattacacat
gtaaattttcataccatccaaatttcccttacccagcttttcctctttatatattgaaagccctaaaaattgtctttgggga
atggcactaaccacacacagtttctgtgattacttttatttttcttccaggcatgtcctggaaagacataatttccttgggga
aaattaattttaatttgattaagatctgtctcagaaaccttcggtttacactaggaaagatcccaaattaggagccaattact
gtaaaaatcagccataccactctgtgagtgtgtgtgtgtgtggcgggggtgtatatgtgtgtgtacatgcatgttttcattt
ctgtgggctttaagccatgtagttctctctgcgaagatactatttggcatgaccttgaatagagaattgtaagagaaataag
aggctcctatgaattatccgaaagtttctggactcaccatgtatcttgactgtgtcattgcatctgacagtcccagggaagtg
actctctggtggtttcatgaatctgtgcttgggctctctctgcagtttactgggtatagtaatgacaaatcactgtttcaaga
gacaatttcgaaagcattagatgctgctgagagaggattatgaaccaggggacagcccctttcattctgggggagcgacattgg
gagaatatgctctgtgagcccaaacagcttcctcccctgcagggtgagggcagagctgcaggacaggcccagaacccactcaa
cacagatgtcagccctggagctgctgcagaggagtctgaggagaaaatttttaccagcacctgaattacacttatttcaaacaa
aaatgcatgtcctgtgagtgtttgtttccctattggaggagttctgtactcatgaagttctggacatgccagcggacaaatat
cagtaaacaaacatcagaacttgaacctcagcttcccactgttgcattctccatgtgtcatctctattatttctcatgctaga
tcaggtatttagctatgaaatattccagctaattaacgtgtaaatagcttgaagtctactgagttaaatacatatattttctc
ttgtttttgccaggtgttccctcccacacctccaatagtctccactattatcatcatcttctagatcttctgcgatgccctgg
agattaaggatttgattccatgacagagaggaggtgcatttcgatggaactttggtgaaaaccttggtctttatcccatttcc
tctgggggctccaccagtgcctctggaatcatggtttcagtggcttgcccctgcatggtaggtcattcctttattctgtagtgc
tgatgagggaggtgggtctgaacgcatttcagtagtatgggctctccttctgtctcagacactttgggaaaggaaaatttttc
tgagcgtcctcattctagaacaaagggattcaattgtataggaatgctgaaaatagaaaaccttcagccaaattaaggttaat
aagattaattgagcaatggatgattcatgaattgggcagcccccagaatcacagcagattcaaagagacttcagtgcagtcac
ggggtggaagaagatttatagattagaaaaatgatgtacagaaatcagaagtgaggtacagaaacagctggattggttacagg
ttgcttttgtcttatttaaacaaggtgtgcaccctcaagagtgtacgagtggttgaggtatggctgctggaattggccaagac
tccgctgttgttacaggcgcatgctccgaagttggcttttcaatctcgtccacctattcaggtaggttacagtttgtccacaa
ggactcaaacacagaagtacggagtccttttcaggccatatttaattcactttatcagtgcccttcagtatgtggttcctgag
aatttcacatgacaacacgtttaccacactggaatttaagcaatccaacacgtttgtagctttgtcttgtaatgggctatatt
tcatgtggcagcctcggcctcagtttagctaacactatggcttcatttctctctacaagaactcatttcttccaagatttcca
tgttcctgaaaggaaaataaaccctttgggacccccatatcactaagccaaagggaagtcaagctgaaaattgtttggggcaaa
cccacctccattctttccctaaaatgagagctactaaggtttttaaaagctacagacctccttcaaaatttgaccacaagtaa
aatccttgtggacccaggacagagagagtcatttctctgctcatgtaagtcaaacgcatacctgattgctccctgtgctctac
tgtttcactaaatcagactaaggcctacgtgactattcctgtaaattgtgcattcagttaaaggctaatcagaaactcaaata
atgcaaccatttctctcaaacctacctatgatctagaagccctctcccccacttcaagttgtcctgccttttctgaactaaatca
atgtacatctgatatatatatattgattaatgtctcatgtctccctaaattgtataaaaccaagctgtgcccacaagcttggg
cacatgtcgtcagcactccctgaggctgtgtcacaggcatgtccttaatcttggaaattgaacttcctaaatctattgagatt
agtctcagatactctttggtttacaggtttgttttttatttcataacttcaattatttgacatgctaaagaaaatttgccaaat
agcgcattctcttgtttatgtgttattgttgttgcaaaaataatatatttttatatataatttatcatctatgtacattaccaa
attgagtagcagatttattagtaagacccaaagtaatgaaaagttcagataccaattagcaacttagaaaaacaaattatgct
acatttgtttgctgaaatgctacctattatttataaaaaataaacaatacaacataaaaggtttaattctcagtatttctatt
gagaaaaataagccaaatagatgagtacatactatattatttcattcttataaattctagagaataaaaactagtctaaagaa
atatgaaaacatcagtacttttataaagaaatggtagaagaaaaggagaaaaacaaaaatatatctataaaagagcaagagga
attctgaggtgagttgacttgtcaccttcttgaaaatagagactttctttatcaaaatttactattgtacaggttaaatatgt
gaatttttatcatctgtcaattaaaactcataaaatttattacaagtaaacaagtgaaatttttagacaaaaaagggatgataag
aaggaacaaataaatacattaaatgtcagatacaccaaaaatgtatctgcctgacgcctagttgtctctgtatttttaggtaa
atgcagcaaaatcacacaggttgtcgtggcaggaagtggattctgcaaaccacactaggccgtttatctctgtcctgtagttg
gttcagagcaactgaggccagctgtgaggcgcataggcccaggtactaggactcactcatgccagatataagccctgagacac
gtacatagcccctccatgtgtgggttcacttttacatctgtacatgaagaaaccactgactcctaaataacatcatctataca

FIG. 7 (Cont. 36)

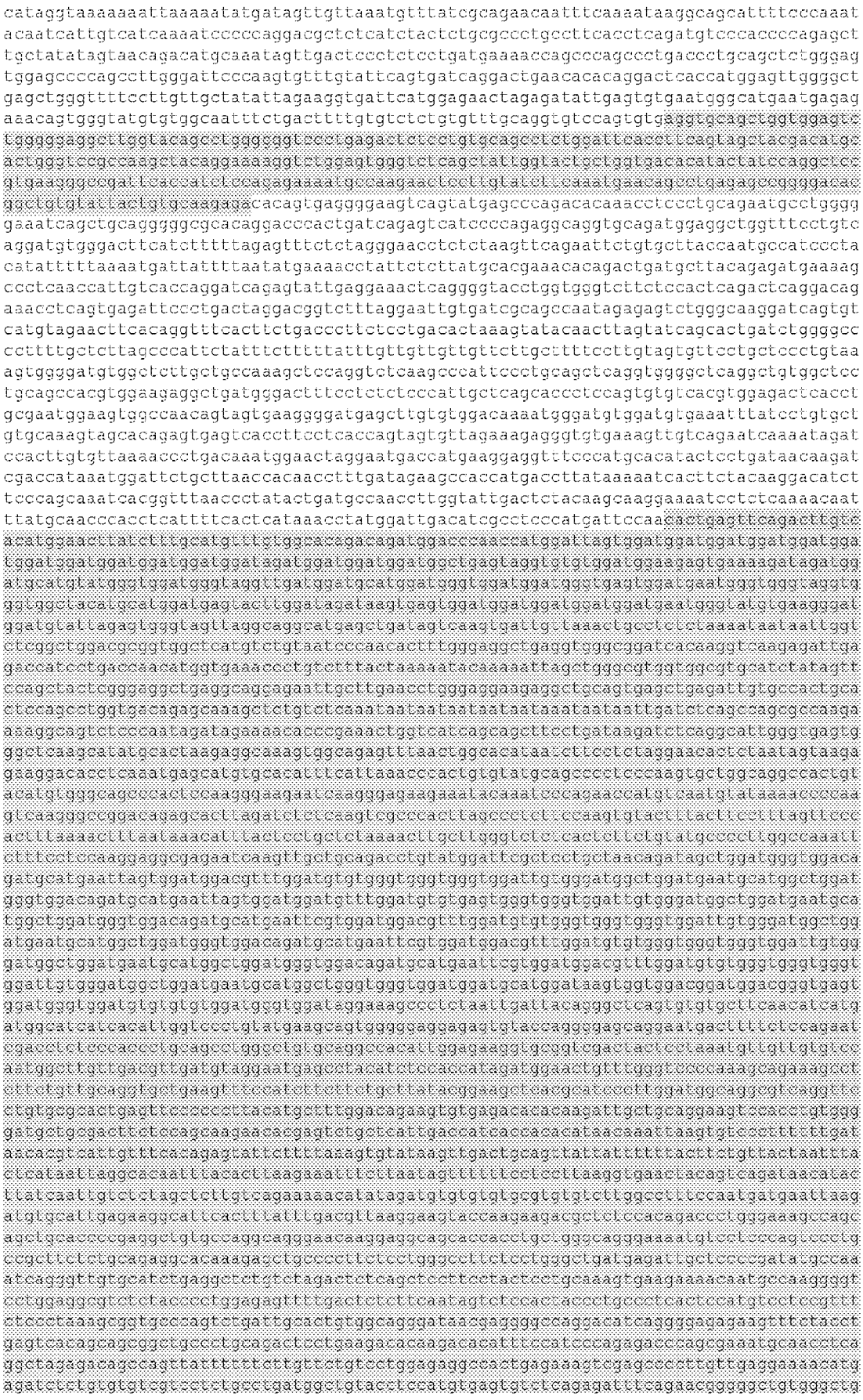


FIG. 7 (Cont. 37)

tggtgtccgcttgtgactcatctctttgttcttgtccctgagtgtcctgcatcagatgcagctactggagtcatgcccaggg
ctggtgaggtcctcacagacctctgggcctggacccagcagccctctgggaaggcgctgggcacctcagctccagggcagc
acacacttcagcccagccttttctgggccaactctccatctgtagagacacatccaaggcccagttatccctgcagctgagctc
cgtgatggccaagggcagggccgcacattcccgtgggagacagaatggggacctcagcgtgagcccagacacaaacctccctg
cagggaagcacaagaccaccaggcggcgctccagaccacacagcggccccagaaqcaggttttaggggqcggggcagacgtgt
ccgcgttgagtcaggtcattggttttacttttcctgaqcaaacggcctctgccaaggactcactgcacctctcacctccacag
ttgtttttttttttttttaatcaccctgtagagttttgctagctaatttagacattgaggagtgcttcatacttcctgggc
ctctgcttgcagaaacatagcaattgtaaggaggcacgtgggaaagccccggcccggtgacccgggggatgctgctgtggccc
tggcaagagggcgtcgggccgcagtaacaaaggtgcagacggctctcagcctgcgcccgcggagtacaacacataaggctgt
aacctaacgaaaaaagaatcgcagtgcaactgtcctgcatttgagtttgtgatcagttttgccctttgtctttaacaggttct
aacataaaattttgaatgttggttcaagccctgtgggtaaaatgcacttacccacattcctttaaacaaatagaacactgaggt
ggaaatgttttgaaaaagtagttttcagacatttggaaacaagcatcacaggatcataacccctgagaaaagaaaaacaaatg
aacgaatcctgtattgcctgaaagcagctgccaggacacacggaaaggcttagtgagctgagcggacagagagcagagttca
aggcagcagcagcccgaggggaggagcaccggggagcaggctgctgtgcagccaggatgggccgggtggggcgggggggaaa
cagctggagacttgccgcagggaggcggatcccccaggtttggggctgagaaccgacttatgcctgacttatgcctgcatgaa
aagaaactactcgatatcagggggaaatcaccagaaacctgtggacccaaaaccacacagagcctacacaaggaaagcattgt
ttgtgttctcccagccagggtggaaagaccttgagatatgtaaagcttcaagcaatcttccgaagtaatctcgtgagtagtgg
tgccacattaattcaggactaaaggctgctctgaactgaacctaagaaatgctcaagtgtagcctggagcccgggtgcagtg
gctcacacctgtaatcccagcactgtgggaggccgaggcaggcggatcacttgaggtcaggactttgagaccagcctggccaa
catggcaaaacctgtctctactaaaaaacacaaaaattagctgggcgtggtggcagatgcctgtaatcacctcccacctggacc
cttccttgatacatcagaattacaactagagatgagattgggtggggacacagagccaaaccgtatcacataggaacctaaa
aggataataaagtaggaaaacttcccacatcagtaaccctttatccgatagtaatcccaatctgcaaagtaaaactgtgtgat
tttactaagataacggaatcttctctacagaaggactttccagtgcaaaagctccccacccctcaccatgaaatgcacgtgacc
atttccaatttgtgtaaagtcctcagttagtactgagacttcggaaggttagaaatccctttgctcatgctgcatggtccgga
tgagatgtaagaatcattagctaatagacatgcaacagcttttgtgtgaaagatgttatgagacatttaaggtatttgcttgt
gattactaagcattcattgtatcattggagcacatgtgctttataccctggagaaatttccagtaattgaattgctgggttga
atgggatttgatttggattaaatttaaactatagatttattttagggaaaacaggcatcttaattatgttattgggggccc
ttgctcccagagctcccaagatggtgcaggccgcttccaaaatgaccgcaggccacttccaagatggtggcaagccttcatgt
tctctgaccttggggttcttggcctcacggattccaaggaatggaagcttgggccatgcagtgagtgttatagctctatagaa
gccgtgggtcacggaagagaaccgtcgaacccagtgactagtgttcagctcgactaggacgaacccaggcacttagccgtgca
ggaacaatggcgagcatttggcccgatcgagagtggcaatgggcgcctcgctggatcaggagcacagcggataccctgatgga
tccggagggatggaagccagcggtgcgtctcccacgggggcaaacagcagtggtggacggtgagCGTACG
gttatctatgctgtctcaccatagagaatattacctatttcagaatgtatgtccatgattcgccgggtaaatacatataatac
acaaatctggcttaataaagtctataatatatctcataaagaagtgctaaattggctagtgctatatatttttaagaaaattt
cttttgactaagtccatatcgacttttgtaaaagttcactttagcatacatatattacacgagccagaaattgtaacttttgcc
taaaatcacaaattgcaaaatttaattgcttgcaaaaggtcacatgcttataatcaacttttttaaaaatttaaaatactttt
ttatttttttatttttaaacataaatgaaataatttatttattgtttatgattaccgaaacataaaacctgctcaagaaaaaga
aactgttttgtccttggaaaaaaagcactacctagtggatcctctagagtcgacctgcaggcatgcaagcttgagtattctat
agtgtcacctaaatagcttggcgtaatcatggtcatagctgtttcctgtgtgaaattgttatccgctcacaattccacacaac
atacgagccggaagcataaagtgtaaagcctggggtgcctaatgagtgagctaactcacattaattgcgttgcgctcactgcc
cgctttccagtcgggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgaaccccttgcggccgcccgggccgtcg
accaattctcatgtttgacagcttatcatcgaatttctgccattcatccgcttattatcacttattcaggcgtagcaaccagg
cgtttaagggcaccaataactgccttaaaaaaattacgccccgccctgccactcatcgcagtactgttgtaattcattaagca
ttctgccgacatggaagccatcacaaacggcatgatgaacctgaatcgccagcggcatcagcaccttgtcgccttgcgtataa
tatttgcccatggtgaaaacgggggcgaagaagttgtccatattggccacgtttaaatcaaaactggtgaaactcacccaggg
attggctgagacgaaaaacatattctcaataaaccctttagggaaataggccaggttttcaccgtaacacgccacatcttgcg
aatatatgtgtagaaactgccggaaatcgtcgtggtattcactccagagcgatgaaaacgtttcagtttgctcatggaaaacg
gtgtaacaagggtgaacactatcccatatcaccagctcaccgtctttcattgccatacggaattccggatgagcattcatcag
gcgggcaagaatgtgaataaaggccggataaaacttgtgcttatttttctttacggtctttaaaaaggccgtaatatccagct
gaacggtctggttataggtacattgagcaactgactgaaatgcctcaaaatgttctttacgatgccattgggatatatcaacg
gtggtatatccagtgatttttttctccattttagcttccttagctcctgaaaatctcgataactcaaaaaatacgcccggtag
tgatcttatttcattatggtgaaagttggaacctcttacgtgccgatcaacgtctcattttcgccaaaagttggcccagggct
tcccggtatcaacagggacaccaggatttatttattctgcgaagtgatcttccgtcacaggtatttattcgcgataagctcat
ggagcggcgtaaccgtcgcacaggaaggacagagaaagcgcggatctgggaagtgacggacagaacggtcaggacctggattg
gggaggcggttgccgccgctgctgctgacggtgtgacgttctctgttccggtcacaccacatacgttccgccattcctatgcg
atgcacatgctgtatgccggtataccgctgaaagttctgcaaagcctgatgggacataagtccatcagttcaacggaagtcta
cacgaaggttttgcgctggatgtggctgcccggcaccgggtgcagtttgcgatgccggagtctgatgcggttgcgatgctga
aacaattatcctgagaataaatgccttggcctttatatggaaatgtggaactgagtggatatgctgtttttgtctgttaaaca
gagaagctggctgttatccactgagaagcgaacgaaacagtcgggaaaatctcccattatcgtagagatccgcattattaatc
tcaggagcctgtgtagcgtttataggaagtagtgttctgtcatgatgcctgcaagcggtaacgaaaacgatttgaatatgcct
tcaggaacaatagaaatcttcgtgcggtgttacgttgaagtggagcggattatgtcagcaatggacagaacaacctaatgaac
acagaaccatgatgtggtctgtccttttacagccagtagtgctcgccgcagtcgagcgacagggcgaagccctcgagtgagcg
aggaagcaccagggaacagcacttatatattctgcttacacacgatgcctgaaaaaacttcccttggggttatccacttatcc
acgggatatttttataattatttttttttatagtttttagatcttcttttttagagcgccttgtaggcctttatccatgctgg
ttctagagaaggtgttgtgacaaattgccctttcagtgtgacaaatcaccctcaaatgacagtcctgtctgtgacaaattgcc
cttaaccctgtgacaaattgccctcagaagaagctgttttttcacaaagttatccctgcttattgactctttttttatttagtg

FIG. 7 (Cont. 38)

tgacaatctaaaaacttgtcacacttcacatggatctgtcatggcggaaacagcggttatcaatcacaagaaacgtaaaaata
gcccgcgaatcgtccagtcaaacgacctcactgaggcggcatatagtctctcccgggatcaaaaacgtatgctgtatctgttc
gttgaccagatcagaaaatctgatggcaccctacaggaacatgacggtatctgcgagatccatgttgctaaatatgctgaaat
attcggattgacctctgcggaagccagtaaggatatacggcaggcattgaagagtttcgcggggaaggaagtggttttttatc
gccctgaagaggatgccggcgatgaaaaaggctatgaatcttttccttggtttatcaaacgtgcgcacagtccatccagaggg
ctttacagtgtacatatcaacccatatctcattcccttctttatcgggttacagaaccggtttacgcagtttcggcttagtga
aacaaaagaaatcaccaatccgtatgccatgcgtttatacgaatccctgtgtcagtatcgtaagccggatggctcaggcatcg
tctctctgaaaatcgactggatcatagagcgttaccagctgcctcaaagttaccagcgtatgcctgacttccgccgccgcttc
ctgcaggtctgtgttaatgagatcaacagcagaactccaatgcgcctctcatacattgagaaaaagaaaggccgccagacgac
tcatatcgtatttcctccgcgatatcacttccatgacgacaggatagtctgagggttatctgtcacagatttgagggtggt
tcgtcacatttgttctgacctactgagggtaatttgtcacagttttgctgtttccttcagcctgcatggattttctcatactt
tttgaactgtaatttttaaggaagccaaatttgagggcagtttgtcacagttgatttccttctctttcccttcgtcatgtgac
ctgatatcgggggttagttcgtcatcattgatgagggttgattatcacagtttattactctgaattggctatccgcgtgtgta
cctctacctggagtttttcccacggtggatatttcttcttgcgctgagcgtaagagctatctgacagaacagttcttctttgc
ttcctcgccagttcgctcgctatgctcggttacacggctgcggcgagcgctagtgataataagtgactgaggtatgtgctctt
cttatctccttttgtagtgttgctcttattttaaacaactttgcggtttttgatgactttgcgattttgttgttgctttgca
gtaaattgcaagatttaataaaaaaacgcaaagcaatgattaaaggatgttcagaatgaaactcatggaaacacttaaccagt
gcataaacgctggtcatgaaatgacgaaggctatcgccattgcacagtttaatgatgacagcccggaagcgaggaaaataacc
cggcgctggagaataggtgaagcagcggatttagttggggtttcttctcaggctatcagagatgccgagaaagcagggcgact
accgcacccggatatggaaattcgaggacgggttgagcaacgtgttggttatacaattgaacaaattaatcatatgcgtgatg
tgtttggtacgcgattgcgacgtgctgaagacgtatttccaccggtgatcggggttgctgcccataaaggtggcgtttacaaa
acctcagtttctgttcatcttgctcaggatctggctctgaaggggctacgtgttttgctcgtggaaggtaacgaccccccaggg
aacagcctcaatgtatcacggatgggtaccagatcttcatattcatgcagaagacactctcctgccttttctatcttggggaaa
aggacgatgtcacttatgcaataaagcccacttgctggccggggcttgacattattccttcctgtctggctctgcaccgtatt
gaaactgagttaatgggcaaatttgatgaaggtaaactgcccaccgatccacacctgatgctccgactggccattgaaactgt
tgctcatgactatgatgtcatagttattgacagcgcgcctaacctgggtatcggcacgattaatgtcgtatgtgctgctgatg
tgctgattgttcccacgcctgctgagttgtttgactacacctccgcactgcagttttcgatatgcttcgtgatctgctcaag
aacgttgatcttaaagggttcgagcctgatgtacgtattttgcttaccaaatacagcaatagtaatggctctcagtccccgtg
gatggaggagcaaattcgggatgcctggggaagcatggttctaaaaaatgttgtacgtgaaacggatgaagttggtaaaggtc
agatccggatgagaactgtttttgaacaggccattgatcaacgctcttcaactggtgcctggagaaatgctctttctatttgg
gaacctgtctgcaatgaaattttcgatcgtctgattaaaccacgctgggagattagataatgaagcgtgcgccttgttattcca
aaacatacgctcaatactcaaccggttgaagatacttcgttatcgacaccagctgccccgatggtggattcgttaattgcgcg
cgtaggagtaatggctcgcggtaatgccattactttgcctgtatgtggtcgggatgtgaagtttactcttgaagtgctccggg
gtgatagtgttgagaagacctctcgggtatggtcaggtaatgaacgtgaccaggagctgcttactgaggacgcactggatgat
ctcatccctttttctactgactggtcaacagacaccggcgttcggtcgaagagtatctggtgtcatagaaattgccgatgg
gagtcgccgtcgtaaagctgctgcacttaccgaaagtgattatcgtgttctggttggcgagctggatgatgagcagatggctg
cattatccagattgggtaacgattatcgcccaacaagtgcttatgaacgtggtcagcgttatgcaagccgattgcagaatgaa
tttgctggaaatatttctgcgctggctgatgcggaaaatatttcacgtaagattattacccgctgtatcaacaccgccaaatt
gcctaaatcagttgttgctctttttttctcaccccggtgaactatctgcccggtcaggtgatgcacttcaaaaagcctttacag
ataaagaggaattacttaagcagcaggcatctaaccttcatgagcagaaaaaagctggggtgatatttgaagctgaagaagtt
atcactcttttaacttctgtgcttaaaacgtcatctgcatcaagaactagtttaagctcacgacatcagtttgctcctggagc
gacagtattgtataagggcgataaaatggtgcttaacctggacaggtctcgtgttccaactgagtgtatagagaaaattgagg
ccattcttaaggaacttgaaaagccagcaccctgatgcgaccacgttttagtctacgtttatctgtctttacttaatgtcctt
tgttacaggccagaaagcataactggcctgaatattctctctgggcccactgttccacttgtatcgtcggtctgataatcaga
ctgggaccacggtcccactcgtatcgtcggtctgattattagtctgggaccacggtcccactcgtatcgtcggtctgattatt
agtctgggaccacggtcccactcgtatcgtcggtctgataatcagactgggaccacggtcccactcgtatcgtcggtctgatt
attagtctgggaccatggtcccactcgtatcgtcggtctgattattagtctgggaccacggtcccactcgtatcgtcggtctg
attattagtctggaaccacggtcccactcgtatcgtcggtctgattattagtctgggaccacggtcccactcgtatcgtcggt
ctgattattagtctgggaccacgatcccactcgtgttgtcggtctgattatcggtctgggaccacggtcccacttgtattgtc
gatcagactatcagcgtgagactacgattccatcaatgcctgtcaagggcaagtattgacatgtcgtcgtaacctgtagaacg
gagtaacctcggtgtgcggttgtatgcctgctgtggattgctgctgtgtcctgcttatccacaacattttgcgcacggttatg
tggacaaaatacctggtgatccgccaacaaatactaccttttatcttgctcttcctgctctcaggtattaatgccgaattgttt
catcttgtctgtgtagaagaccacacacgaaaatcctgtgattttacattttacttatcgttaatcgaatgtatatctattta
atctgcttttcttgtctaataaatatatatgtaaagtacgctttttgttgaaatttttttaaaccttgtttatttttttttct
tcattccgtaactcttctaccttctttatttacttctaaaatccaaatacaaaacataaaaataaataaacacagagtaaat
tcccaaattattccatcattaaaagatacgaggcgcgtgtaagttacaggcaagcgatccgtctaagaaaccattattatcat
gacattaacctataaaaataggcgtatcacgaggccctttcgtctttgcgatcgcacaccgcagggtaataactgatataatt
aaattgaagctctaatttgtgagtttagtatacatgcatttacttataatacagttttttagttttgctggccgcatcttctc
aaatatgcttcccagcctgcttttctgtaacgttcaccctctaccttagcatcccttccctttgcaaatagtcctcttccaac
aataataatgtcagatcctgtagagaccacatcatccacggttctatactgttgacccaatgcgtctcccttgtcatctaaac
ccacaccgggtgtcataatcaaccaatcgtaaccttcatctcttccacccatgtctctttgagcaataaagccgataacaaaa
tctttgtcgctcttcgcaatgtcaacagtacccttagtatattctccagtagatagggagcccttgcatgacaattctgctaa
catcaaaaggcctctaggttcctttgttacttcttctgccgcctgcttcaaaccgctaacaatacctgggcccaccacaccgt
gtgcattcgtaatgtctgcccattctgctattctgtatacacccgcagagtactgcaatttgactgtattaccaatgtcagca
aattttctgtcttcgaagagtaaaaaattgtacttggcggataatgcctttagcggcttaactgtgccctccatggaaaaatc
agtcaagatatccacatgtgtttttagtaaacaaattttgggacctaatgcttcaactaactccagtaattccttggtggtac

FIG. 7 (Cont. 39)

gaacatccaatgaagcacacaagtttgtttgcttttcgtgcatgatattaaatagcttggcagcaacaggactaggatgagta
gcagcacgttccttatatgtagctttcgacatgatttatcttcgtttcctgcaggtttttgttctgtgcagttgggttaagaa
tactgggcaatttcatgtttcttcaacactacatatgcgtatatataccaatctaagtctgtgctccttccttcgttcttcct
tctgttcggagattaccgaatcaaaaaaatttcaaagaaaccgaaatcaaaaaaaagaataaaaaaaaaatgatgaattgaat
tgaaaagcgtgtg

FIG. 7 (Cont. 40)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2018/014568

A. CLASSIFICATION OF SUBJECT MATTER
INV. A01K67/027 C07K16/00
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A01K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data, BIOSIS, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	WO 2014/141189 A1 (UNIV ERASMUS MEDICAL CT [NL]; KINGDON CRAIG R [GB]) 18 September 2014 (2014-09-18) page 6 - page 20; claims 12, 16 -----	1-8,11, 12,14, 21,27-33 9,10,13, 15-20, 22-26
X	Dimiter S. Dimitrov ET AL: "Therapeutic Antibodies: Current State and Future Trends - Is a Paradigm Change Coming Soon?" In: "Methods in Molecular Biology", 10 December 2008 (2008-12-10), Humana Press, Inc., US, XP055462641, ISSN: 1064-3745 vol. 525, pages 1-27, DOI: 10.1007/978-1-59745-554-1_1, tables 1.1-1.5 ----- -/--	28,33-35

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 March 2018	09/04/2018

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Deleu, Laurent

1

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2015/179535 A1 (REGENERON PHARMA [US]) 26 November 2015 (2015-11-26) paragraph [0108] - paragraph [0109]; examples 1,2	28,33
X	WO 2014/093908 A2 (OMT INC [US]) 19 June 2014 (2014-06-19) cited in the application	28,33
Y	paragraph [0092] - paragraph [0111]; claims 1-15 paragraph [0128] - paragraph [0153]	9,10,13, 15-20, 22-26

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2018/014568

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2014141189 A1	18-09-2014	EP 2967012 A1	20-01-2016
		US 2014356907 A1	04-12-2014
		WO 2014141189 A1	18-09-2014
WO 2015179535 A1	26-11-2015	AU 2015264189 A1	17-11-2016
		CA 2949438 A1	26-11-2015
		CL 2016002934 A1	03-11-2017
		CN 106414496 A	15-02-2017
		EA 201691877 A1	31-03-2017
		EP 3145539 A1	29-03-2017
		JP 2017524339 A	31-08-2017
		KR 20170005133 A	11-01-2017
		PH 12016502064 A1	19-12-2016
		SG 11201608567Y A	29-11-2016
		US 2015337029 A1	26-11-2015
		US 2017340728 A1	30-11-2017
		WO 2015179535 A1	26-11-2015
		ZA 201607047 B	27-09-2017
WO 2014093908 A2	19-06-2014	AU 2013358958 A1	09-07-2015
		CA 2895144 A1	19-06-2014
		CN 104994729 A	21-10-2015
		EP 2931030 A2	21-10-2015
		JP 2016505257 A	25-02-2016
		KR 20150094720 A	19-08-2015
		SG 11201504676V A	30-07-2015
		US 2015113668 A1	23-04-2015
		US 2017174770 A1	22-06-2017
		WO 2014093908 A2	19-06-2014