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- (73) Patenthaver: **Suntory Holdings Limited, 1-40, Dojimahama 2-chome, Kita-ku, Osaka-shi, Osaka 530-8203, Japan**
- (72) Opfinder: **Ochiai, Misa, c/o Suntory Research Center, 1-1-1 Wakayamadai, Shimamoto-cho, Mishima-gun, Osaka, 618-8503, Japan**
- (74) Fuldmægtig i Danmark: **Budde Schou A/S, Hausergade 3, 1128 København K, Danmark**
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Description**TECHNICAL FIELD**

5 **[0001]** The present invention relates to a polynucleotide encoding an acyl-CoA synthetase homolog and use thereof.

BACKGROUND ART

10 **[0002]** Fatty acids containing two or more unsaturated bonds are collectively referred to as polyunsaturated fatty acids (PUFAs) and known to specifically include arachidonic acid (ARA), dihomo- γ -linolenic acid (DGLA), eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), etc. Some of these polyunsaturated fatty acids cannot be synthesized in the animal body. It is therefore necessary to compensate these polyunsaturated fatty acids as essential amino acids from food.

15 **[0003]** Polyunsaturated fatty acids are widely distributed; for instance, arachidonic acid can be separated from lipids extracted from the adrenal glands and livers of animals. However, polyunsaturated fatty acids contained in animal organs are only in a small quantity and cannot be obtained sufficiently for large supplies when simply extracted or separated from animal organs. For this reason, microbial techniques have been developed for obtaining polyunsaturated fatty acids by cultivation of various microorganisms. Above all, microorganisms of the genus *Mortierella* are known to produce lipids containing polyunsaturated fatty acids such as arachidonic acid and the like.

20 **[0004]** Other attempts have also been made to produce polyunsaturated fatty acids in plants. Polyunsaturated fatty acids constitute storage lipids such as triacylglycerols and are known to be accumulated within microorganism mycelia or plant seeds.

[0005] Acyl-CoA synthetase (ACS) is an enzyme catalyzing the thioesterification of fatty acids and coenzyme A (CoA) and catalyzes the following reaction.

25 Fatty acid + CoASH + ATP $\rightarrow$ Acyl-CoA + AMP + PPi

30 **[0006]** Acyl-CoA produced by ACS is involved in various life phenomena including the biosynthesis and remodeling of lipids, energy production by β -oxidation, acylation of proteins, expression regulation by fatty acids, etc. Furthermore, ACS is reportedly associated with extracellular uptake of fatty acids, intracellular transport of fatty acids, etc. (Non-Patent Documents 1 and 2). In view of the foregoing, it is considered to control the activity of ACS when polyunsaturated fatty acids or the like are produced by utilizing microorganisms or plants.

[0007] In the yeast *Saccharomyces cerevisiae* used as a model eukaryote, six (6) acyl-CoA synthetase genes (ScFAA1, ScFAA2, ScFAA3, ScFAA4, ScFAT1 and ScFAT2) are known (Non-Patent Document 1). The proteins encoded by these genes are different in substrate specificity, timing of expression, intracellular localization and function.

35 **[0008]** Patent Document 1 discloses nine (9) genes as the acyl-CoA synthetase gene (ScACS) derived from *Schizochytrium* sp. Patent Document 1 also discloses an increased production of DPA (n-6) (docosapentanoic acid (n-6)) or DHA when the gene encoding the *Schizochytrium* sp. PUFA synthase system is co-expressed with ScACS, as compared to the case where the co-expression with ScACS is not involved.

40 **[0009]** In addition, acyl-CoA synthetase genes derived from animals and plants are also reported (Non-Patent Document 2 and Patent Document 2).

[Patent Document 1] Japanese Unexamined Patent Application Publication (Translation of PCT Application) No. 2009-529890

[Patent Document 2] PCT International Publication Pamphlet WO 0209295

45 [Non-Patent Document 1] B. B. A. 1771, 286-298, 2007

[Non-Patent Document 2] Exp. Biol. Med., 233 (5), 507-521, 2008

DISCLOSURE OF THE INVENTION

50 **[0010]** Under the foregoing circumstances, it has been desired to isolate a novel gene that increases the amount of the fatty acids produced in a host cell or changes the composition of fatty acids produced, when the gene is expressed in the host cell.

55 **[0011]** As a result of extensive investigations, the present inventors have succeeded in cloning a gene encoding an ACS homolog of lipid-producing fungus *Mortierella alpina* (hereinafter "*M. alpina*") (MaACS), and accomplished the present invention. That is, the present invention provides the following polynucleotides, proteins, expression vectors, transformants, and a method for producing lipids or lipid compositions and foods, etc. using the transformants, as well as foods produced by the method, etc.

[0012] The present invention relates to the embodiments as defined in the claims. Thus, it relates to the following:

EP 2 930 236 B1

A polynucleotide according to any one selected from the group consisting of (a) to (e) below:

- (a) a polynucleotide comprising a nucleotide sequence shown by SEQ ID NO: 56;
- (b) a polynucleotide encoding a protein consisting of the amino acid sequence shown by SEQ ID NO: 57;
- (c) a polynucleotide encoding a protein consisting of an amino acid sequence wherein 1 to 100 amino acids are deleted, substituted, inserted and/or added in the amino acid sequence shown by SEQ ID NO: 57, and having an acyl-CoA synthetase activity or an activity of increasing the amount or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell;
- (d) a polynucleotide encoding a protein having an amino acid sequence having at least 60% identity to the amino acid sequence shown by SEQ ID NO: 57, and having an acyl-CoA synthetase activity or an activity of increasing the amount or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell; and,
- (e) a polynucleotide which hybridizes to a polynucleotide consisting of a nucleotide sequence complementary to the nucleotide sequence shown by SEQ ID NO: 56 under conditions of 5x SSC, 5x Denhardt's solution, 0,5% SDS, 50% formamide at 50°C or 0.2x SSC, 0.1% SDS at 65°C, and which encodes a protein having an acyl-CoA synthetase activity or an activity of increasing the amount or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell.

[0013] That is, the present disclosure is characterized as follows.

[1] A polynucleotide according to any one selected from the group consisting of (a) to (e) below:

- (a) a polynucleotide comprising any one nucleotide sequence selected from the group consisting of the nucleotide sequences shown by SEQ ID NOs: 1, 6, 11, 16, 21, 26, 31, 36, 41, 46, 51 and 56;
- (b) a polynucleotide encoding a protein consisting of any one amino acid sequence selected from the group consisting of the amino acid sequences shown by SEQ ID NOs: 2, 7, 12, 17, 22, 27, 32, 37, 42, 47, 52 and 57;
- (c) a polynucleotide encoding a protein consisting of an amino acid sequence wherein 1 to 100 amino acids are deleted, substituted, inserted and/or added in any one amino acid sequence selected from the group consisting of the amino acid sequences shown by SEQ ID NOs: 2, 7, 12, 17, 22, 27, 32, 37, 42, 47, 52 and 57, and having an acyl-CoA synthetase activity or an activity of increasing the amount or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell;
- (d) a polynucleotide encoding a protein having an amino acid sequence having at least 60% identity to any one amino acid sequence selected from the group consisting of the amino acid sequences shown by SEQ ID NOs: 2, 7, 12, 17, 22, 27, 32, 37, 42, 47, 52 and 57, and having an acyl-CoA synthetase activity or an activity of increasing the amount or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell; and,
- (e) a polynucleotide which hybridizes to a polynucleotide consisting of a nucleotide sequence complementary to any one nucleotide sequence selected from the group consisting of the nucleotide sequences shown by SEQ ID NOs: 1, 6, 11, 16, 21, 26, 31, 36, 41, 46, 51 and 56 under stringent conditions, and which encodes a protein having an acyl-CoA synthetase activity or an activity of increasing the amount or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell.

[2] The polynucleotide according to claim 1, which is either one defined in (f) or (g) below:

- (f) a polynucleotide encoding a protein consisting of an amino acid sequence wherein 1 to 10 amino acids are deleted, substituted, inserted and/or added in any one amino acid sequence selected from the group consisting of the amino acid sequences shown by SEQ ID NOs: 2, 7, 12, 17, 22, 27, 32, 37, 42, 47, 52 and 57, and having an acyl-CoA synthetase activity or an activity of increasing the amount or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell; and,
- (g) a polynucleotide encoding a protein having an amino acid sequence having at least 90% identity to any one amino acid sequence selected from the group consisting of the amino acid sequences shown by SEQ ID NOs: 2, 7, 12, 17, 22, 27, 32, 37, 42, 47, 52 and 57, and an acyl-CoA synthetase activity or an activity of increasing the amount or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell.

[3] The polynucleotide according to [1] above, comprising any one nucleotide sequence selected from the group consisting of the nucleotide sequences shown by SEQ ID NOs: 1, 6, 11, 16, 21, 26, 31, 36, 41, 46, 51 and 56.

[4] The polynucleotide according to [1] above, encoding a protein consisting of any one amino acid sequence selected from the group consisting of the amino acid sequences shown by SEQ ID NOs: 2, 7, 12, 17, 22, 27, 32, 37, 42, 47,

52 and 57.

[5] The polynucleotide according to any one of [1] to [4] above, which is a DNA.

[6] A protein encoded by the polynucleotide according to any one of [1] to [5] above.

[7] A vector comprising the polynucleotide according to any one of [1] to [5] above.

[8] A non-human transformant, into which the polynucleotide according to any one of [1] to [5] above, or the vector according to [7] above is introduced.

[9] A method for producing a lipid or fatty acid composition, which comprises collecting the lipid or fatty acid composition from the culture of the transformant according to [8] above.

[10] The method according to [9] above, wherein the lipid is a triacylglycerol.

[11] The method according to [9] above, wherein the fatty acid is a polyunsaturated fatty acid having at least 18 carbon atoms.

[12] A food product, pharmaceutical, cosmetic or soap comprising the lipid or fatty acid composition obtained by the production method according to [9] above.

[0014] The polynucleotide of the present invention can be used for transformation of an appropriate host cell. The transformant thus produced can be used to produce fatty acid compositions, food products, cosmetics, pharmaceuticals, soaps, etc.

[0015] More specifically, the transformant of the present invention provides an extremely high production efficiency of lipids and fatty acids. Accordingly, the present invention can be effectively used to manufacture pharmaceuticals or health foods which require a large quantity of lipids or fatty acids.

BRIEF DESCRIPTION OF DRAWINGS

[0016]

FIG. 1 shows the correspondence between the cDNA sequence and putative amino acid sequence of MaACS-1.

FIG. 2A shows the alignment between the genome sequence and CDS sequence of MaACS-1.

FIG. 2B is a continuation from FIG. 2A.

FIG. 3A shows the correspondence between the cDNA sequence and putative amino acid sequence of MaACS-2.

FIG. 3B is a continuation from FIG. 3A.

FIG. 4A shows the alignment between the genome sequence and CDS sequence of MaACS-2.

FIG. 4B is a continuation from FIG. 4A.

FIG. 4C is a continuation from FIG. 4B.

FIG. 5 shows the correspondence between the cDNA sequence and putative amino acid sequence of MaACS-3.

FIG. 6A shows the alignment between the genome sequence and CDS sequence of MaACS-3.

FIG. 6B is a continuation from FIG. 6A.

FIG. 7A shows the correspondence between the cDNA sequence and putative amino acid sequence of MaACS-4.

FIG. 7B is a continuation from FIG. 7A.

FIG. 8A shows the alignment between the genome sequence and CDS sequence of MaACS-4.

FIG. 8B is a continuation from FIG. 8A.

FIG. 8C is a continuation from FIG. 8B.

FIG. 9A shows the correspondence between the cDNA sequence and putative amino acid sequence of MaACS-5.

FIG. 9B is a continuation from FIG. 9A.

FIG. 10A shows the alignment between the genome sequence and CDS sequence of MaACS-5.

FIG. 10B is a continuation from FIG. 10A.

FIG. 11A shows the correspondence between the cDNA sequence and putative amino acid sequence of MaACS-6.

FIG. 11B is a continuation from FIG. 11A.

FIG. 12A shows the alignment between the genome sequence and CDS sequence of MaACS-6.

FIG. 12B is a continuation from FIG. 12A.

FIG. 13 shows the correspondence between the cDNA sequence and putative amino acid sequence of MaACS-7.

FIG. 14A shows the alignment between the genome sequence and CDS sequence of MaACS-7.

FIG. 14B is a continuation from FIG. 14A.

FIG. 15A shows the correspondence between the cDNA sequence and putative amino acid sequence of MaACS-8.

FIG. 15B is a continuation from FIG. 15A.

FIG. 16A shows the alignment between the genome sequence and CDS sequence of MaACS-8.

FIG. 16B is a continuation from FIG. 16A.

FIG. 16C is a continuation from FIG. 16B.

FIG. 17 shows the correspondence between the cDNA sequence and putative amino acid sequence of MaACS-9.

FIG. 18A shows the alignment between the genome sequence and CDS sequence of MaACS-9.

FIG. 18B is a continuation from FIG. 18A.

FIG. 19A shows the correspondence between the cDNA sequence and putative amino acid sequence of MaACS-10.

FIG. 19B is a continuation from FIG. 19A.

FIG. 20A shows the alignment between the genome sequence and CDS sequence of MaACS-10.

FIG. 20B is a continuation from FIG. 20A.

FIG. 20C is a continuation from FIG. 20B.

FIG. 21A shows the correspondence between the cDNA sequence and putative amino acid sequence of MaACS-11.

FIG. 21B is a continuation from FIG. 21A

FIG. 22A shows the alignment between the genome sequence and CDS sequence of MaACS-11.

FIG. 22B is a continuation from FIG. 22A.

FIG. 23A shows the correspondence between the cDNA sequence and putative amino acid sequence of MaACS-12.

FIG. 23B is a continuation from FIG. 23A

FIG. 24A shows the alignment between the genome sequence and CDS sequence of MaACS-12.

FIG. 24B is a continuation from FIG. 24A

FIG. 25A shows the alignment between MaACS having relatively high amino acid sequence homology to *S. cerevisiae*-derived FAA protein (FAA: fatty acid activation) and the FAA protein. The single underlined and double underlined sequences denote the ATP-AMP motif and the FACS/VLACS-FATP motif, respectively.

FIG. 25B is a continuation from FIG. 25A.

FIG. 25C is a continuation from FIG. 25B.

FIG. 26A shows the alignment between MaACS having relatively high amino acid sequence homology to *S. cerevisiae*-derived FAT protein (FAT: fatty acid transferase) and the FAT protein. The single underlined and double underlined sequences denote the ATP-AMP motif and the FACS/VLACS-FATP motif, respectively.

FIG. 26B is a continuation from FIG. 26A.

FIG. 27 shows changes with the passage of time in lipid production (FIG. 27A) and arachidonic acid production (FIG. 27B), per mycelia in MaACS-10-overexpressed *M. alpina*.

FIG. 28 shows changes with the passage of time in lipid production (FIG. 28A) and arachidonic acid production (FIG. 28B), per mycelia in MaACS-11-overexpressed *M. alpina*.

BEST MODE FOR CARRYING OUT THE INVENTION

[0017] Hereinafter, the present invention is described in detail. The embodiments described below are intended to be presented by way of example merely to describe the invention but not limited only to the following embodiments. The present invention may be implemented in various ways without departing from the gist of the invention.

[0018] As will be later described in detail in EXAMPLES below, the present inventors have succeeded for the first time in cloning the full-length cDNA of lipid-producing fungus *M. alpina*-derived ACS homolog genes (MaACS-1~12). The present inventors have also identified the nucleotide sequences of genomic DNAs of MaACS-1~12 from *M. alpina* and putative amino acid sequences thereof. The ORF sequences, putative amino acid sequences, CDS sequences, cDNA sequences and genome sequences of MaACS-1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 are SEQ ID NOs: 1, 6, 11, 16, 21, 26, 31, 36, 41, 46, 51 and 56 (hereinafter these sequences are collectively referred to as "ORF sequences of MaACS-1~12"), SEQ ID NOs: 2, 7, 12, 17, 22, 27, 32, 37, 42, 47, 52 and 57 (hereinafter these sequences are collectively referred to as "amino acid sequences of MaACS-1~12"), SEQ ID NOs: 3, 8, 13, 18, 23, 28, 33, 38, 43, 48, 53 and 58 (hereinafter these sequences are collectively referred to as "CDS sequences of MaACS-1~12"), SEQ ID NOs: 4, 9, 14, 19, 24, 29, 34, 39, 44, 49, 54 and 59 (hereinafter these sequences are collectively referred to as "cDNA sequences of MaACS-1~12") and SEQ ID NOs: 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55 and 60 (hereinafter these sequences are collectively referred to as "genome sequences of MaACS-1~12"), respectively. These polynucleotides and proteins may be obtained by the methods described in EXAMPLES below, known genetic engineering techniques, known methods for synthesis, and so on.

1. Polynucleotide of the Invention

[0019] First, the present disclosure provides the polynucleotide described in any one selected from the group consisting of (a) to (g) below:

(a) a polynucleotide comprising any one nucleotide sequence selected from the group consisting of the ORF sequences of MaACS-1~12;

(b) a polynucleotide comprising any one nucleotide sequence selected from the group consisting of the cDNA sequences of MaACS-1~12;

(c) a polynucleotide encoding a protein consisting of any one amino acid sequence selected from the group consisting of the amino acid sequences of MaACS-1~12;

(d) a polynucleotide encoding a protein consisting of an amino acid sequence wherein 1 to 100 amino acids are deleted, substituted, inserted and/or added in any one amino acid sequence selected from the group consisting of the amino acid sequences of MaACS-1~12, and having an acyl-CoA synthetase activity or an activity of increasing the amount and/or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell;

(e) a polynucleotide encoding a protein having an amino acid sequence having at least 60% identity to any one amino acid sequence selected from the group consisting of the amino acid sequences of MaACS-1~12, and having an acyl-CoA synthetase activity or an activity of increasing the amount and/or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell; and,

(f) a polynucleotide which hybridizes to a polynucleotide consisting of a nucleotide sequence complementary to any one nucleotide sequence selected from the group consisting of the ORF sequences of MaACS-1~12 under stringent conditions, and which encodes a protein having an acyl-CoA synthetase activity or an activity of increasing the amount and/or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell; and,

(g) a polynucleotide which hybridizes to a polynucleotide consisting of a nucleotide sequence complementary to any one nucleotide sequence selected from the group consisting of the cDNA sequences of MaACS-1~12 under stringent conditions, and which encodes a protein having an acyl-CoA synthetase activity or an activity of increasing the amount and/or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell.

[0020] As used herein, the term "polynucleotide" means a DNA or RNA.

[0021] As used herein, the term "polynucleotide which hybridizes under stringent conditions" refers to a polynucleotide obtained by the colony hybridization method, plaque hybridization method, Southern hybridization method or the like, using as a probe, for example, a polynucleotide consisting of a nucleotide sequence complementary to any one nucleotide sequence selected from the group consisting of the ORF sequences of MaACS-1~12 or any one nucleotide sequence selected from the group consisting of the cDNA sequences of MaACS-1~12, or the whole or part of a polynucleotide consisting of the nucleotide sequence encoding any one amino acid sequence selected from the group consisting of the amino acid sequences of MaACS-1~12. For the methods of hybridization, there are used the methods described in, e.g., "Sambrook & Russell, Molecular Cloning: A Laboratory Manual Vol. 3, Cold Spring Harbor, Laboratory Press 2001," "Ausubel, Current Protocols in Molecular Biology, John Wiley & Sons 1987-1997," etc.

[0022] As used herein, the term "stringent conditions" may be any of low stringent conditions, moderate stringent conditions and high stringent conditions. The term "low stringent conditions" are, for example, 5x SSC, 5x Denhardt's solution, 0.5% SDS, 50% formamide at 32°C. The term "moderate stringent conditions" are, for example, 5x SSC, 5x Denhardt's solution, 0.5% SDS, 50% formamide at 42°C, or 5x SSC, 1% SDS, 50 mM Tris-HCl (pH 7.5), 50% formamide at 42°C. The term "high stringent conditions" are, for example, 5x SSC, 5x Denhardt's solution, 0.5% SDS, 50% formamide at 50°C or 0.2 x SSC, 0.1% SDS at 65°C. Under these conditions, a DNA with higher identity is expected to be obtained efficiently at higher temperatures, though multiple factors are involved in hybridization stringency including temperature, probe concentration, probe length, ionic strength, time, salt concentration and others, and a person skilled in the art may appropriately select these factors to achieve similar stringency.

[0023] When commercially available kits are used for hybridization, for example, an Alkphos Direct Labeling and Detection System (GE Healthcare) may be used. In this case, according to the attached protocol, after cultivation with a labeled probe overnight, the membrane is washed with a primary wash buffer containing 0.1% (w/v) SDS at 55°C to detect the hybridized DNA. Alternatively, in producing a probe based on the nucleotide sequence complementary to any one nucleotide sequence selected from the group consisting of the ORF sequences of MaACS-1~12 or any one nucleotide sequence selected from the group consisting of the cDNA sequences of MaACS-1~12, or based on the entire or part of the nucleotide sequence encoding any one amino acid sequence selected from the group consisting of the amino acid sequences of MaACS-1~12, hybridization can be detected with a DIG Nucleic Acid Detection Kit (Roche Diagnostics) when the probe is labeled with digoxigenin (DIG) using a commercially available reagent (e.g., a PCR Labeling Mix (Roche Diagnostics), etc.).

[0024] In addition to those described above, other polynucleotides that can be hybridized include DNAs having 50% or higher, 51% or higher, 52% or higher, 53% or higher, 54% or higher, 55% or higher, 56% or higher, 57% or higher, 58% or higher, 59% or higher, 60% or higher, 61% or higher, 62% or higher, 63% or higher, 64% or higher, 65% or higher, 66% or higher, 67% or higher, 68% or higher, 69% or higher, 70% or higher, 71% or higher, 72% or higher, 73% or higher, 74% or higher, 75% or higher, 76% or higher, 77% or higher, 78% or higher, 79% or higher, 80% or higher, 81% or higher, 82% or higher, 83% or higher, 84% or higher, 85% or higher, 86% or higher, 87% or higher, 88% or higher, 89% or higher, 90% or higher, 91% or higher, 92% or higher, 93% or higher, 94% or higher, 95% or higher, 96% or higher, 97% or higher, 98% or higher, 99% or higher, 99.1% or higher, 99.2% or higher, 99.3% or higher, 99.4% or higher, 99.5% or higher, 99.6% or higher, 99.7% or higher, 99.8% or higher or 99.9% or higher identity with the DNA for

any one nucleotide sequence selected from the group consisting of the ORF sequences of MaACS-1~12 or for any one nucleotide sequence selected from the group consisting of the cDNA sequences of MaACS-1~12, or with the DNA encoding any one amino acid sequence selected from the group consisting of the amino acid sequences of MaACS-1~12, as calculated by a homology search software, such as FASTA, BLAST, etc. using default parameters.

[0025] Identity between amino acid sequences or nucleotide sequences may be determined using FASTA (Science 227 (4693): 1435-1441, (1985)), algorithm BLAST (Basic Local Alignment Search Tool) by Karlin and Altschul (Proc. Natl. Acad. Sci. USA, 87: 2264-2268, 1990; Proc. Natl. Acad. Sci. USA, 90: 5873, 1993). Programs called blastn, blastx, blastp, tblastn and tblastx based on the BLAST algorithm have been developed (Altschul S. F. et al., J. Mol. Biol. 215: 403, 1990). When a nucleotide sequence is sequenced using blastn, the parameters are, for example, score=100 and wordlength=12. When an amino acid sequence is sequenced using blastp, the parameters are, for example, score=50 and wordlength=3. When BLAST and Gapped BLAST programs are used, default parameters for each of the programs are employed.

[0026] The polynucleotides of the present invention described above can be obtained by known genetic engineering techniques or known methods for synthesis.

2. Protein of the Invention

[0027] The present disclosure provides the proteins shown below.

(i) A protein encoded by the polynucleotide of any one of (a) to (g) above.

(ii) A protein comprising any one amino acid sequence selected from the group consisting of the amino acid sequences of MaACS-1~12.

(iii) A protein consisting of an amino acid sequence wherein one or more amino acids are deleted, substituted, inserted and/or added in any one amino acid sequence selected from the group consisting of the amino acid sequences of MaACS-1~12, and having an acyl-CoA synthetase activity or an activity of increasing the amount and/or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell.

(iv) A protein having an amino acid sequence having at least 90% identity to any one amino acid sequence selected from the group consisting of the amino acid sequences of MaACS-1~12, and having an acyl-CoA synthetase activity or an activity of increasing the amount and/or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell.

[0028] The proteins described in (iii) or (iv) above are typically naturally occurring mutants of the protein consisting of any one amino acid sequence selected from the group consisting of the amino acid sequences of MaACS-1~12 and include those proteins which may be artificially obtained using site-directed mutagenesis described in, e.g., "Sambrook & Russell, Molecular Cloning: A Laboratory Manual Vol. 3, Cold Spring Harbor Laboratory Press 2001," "Ausubel, Current Protocols in Molecular Biology, John Wiley & Sons 1987-1997," "Nuc. Acids. Res., 10, 6487 (1982)," "Proc. Natl. Acad. Sci. USA, 79, 6409 (1982)," "Gene, 34, 315 (1985)," "Nuc. Acids. Res., 13, 4431 (1985)," "Proc. Natl. Acad. Sci. USA, 82, 488 (1985)," etc.

[0029] As used herein, the "protein consisting of an amino acid sequence wherein one or several acids are deleted, substituted, inserted and/or added in any one amino acid sequence selected from the group consisting of the amino acid sequences of MaACS-1~12, and having an acyl-CoA synthetase activity or an activity of increasing the amount and/or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell" includes proteins consisting of an amino acid sequence wherein, e.g., 1 to 100, 1 to 90, 1 to 80, 1 to 70, 1 to 60, 1 to 50, 1 to 40, 1 to 39, 1 to 38, 1 to 37, 1 to 36, 1 to 35, 1 to 34, 1 to 33, 1 to 32, 1 to 31, 1 to 30, 1 to 29, 1 to 28, 1 to 27, 1 to 26, 1 to 25, 1 to 24, 1 to 23, 1 to 22, 1 to 21, 1 to 20, 1 to 19, 1 to 18, 1 to 17, 1 to 16, 1 to 15, 1 to 14, 1 to 13, 1 to 12, 1 to 11, 1 to 10, 1 to 9 (1 to several), 1 to 8, 1 to 7, 1 to 6, 1 to 5, 1 to 4, 1 to 3, 1 to 2, or one amino acid is/are deleted, substituted, inserted and/or added in any one amino acid sequence selected from the group consisting of the amino acid sequences of MaACS-1~12, and having the acyl-CoA synthetase activity or the activity of increasing the amount and/or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell. In general, the number of deletions, substitutions, insertions, and/or additions is preferably smaller.

[0030] Such proteins include a protein having an amino acid sequence having the identity of approximately 60% or higher, 61% or higher, 62% or higher, 63% or higher, 64% or higher, 65% or higher, 66% or higher, 67% or higher, 68% or higher, 69% or higher, 70% or higher, 71% or higher, 72% or higher, 73% or higher, 74% or higher, 75% or higher, 76% or higher, 77% or higher, 78% or higher, 79% or higher, 80% or higher, 81% or higher, 82% or higher, 83% or higher, 84% or higher, 85% or higher, 86% or higher, 87% or higher, 88% or higher, 89% or higher, 90% or higher, 91% or higher, 92% or higher, 93% or higher, 94% or higher, 95% or higher, 96% or higher, 97% or higher, 98% or higher, 99% or higher, 99.1% or higher, 99.2% or higher, 99.3% or higher, 99.4% or higher, 99.5% or higher, 99.6% or higher, 99.7% or higher, 99.8% or higher, or 99.9% or higher, to any one amino acid sequence selected from the group consisting

of the amino acid sequences of MaACS-1~12, and having the diacylglycerol acyltransferase activity. As the identity percentage described above is higher, the protein is preferable in general.

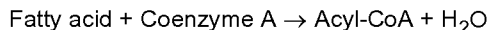
[0031] The term deletion, substitution, insertion and/or addition of one or more amino acid residues in the amino acid sequence of the protein of the invention is intended to mean that one or more amino acid residues are deleted, substituted, inserted and/or added at optional and one or more positions in the same sequence. Two or more types of deletions, substitutions, insertions and additions may occur at the same time.

[0032] Examples of the amino acid residues which are mutually substitutable are given below. Amino acid residues in the same group are mutually substitutable. Group A: leucine, isoleucine, norleucine, valine, norvaline, alanine, 2-aminobutanoic acid, methionine, o-methylserine, t-butylglycine, t-butylalanine and cyclohexylalanine; Group B: aspartic acid, glutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid and 2-aminosuberic acid; Group C: asparagine and glutamine; Group D: lysine, arginine, ornithine, 2,4-diaminobutanoic acid and 2,3-diaminopropionic acid; Group E: proline, 3-hydroxyproline and 4-hydroxyproline; Group F: serine, threonine and homoserine; and Group G: phenylalanine and tyrosine.

[0033] The protein of the present invention may also be produced by chemical synthesis methods such as the Fmoc method (fluorenylmethyloxycarbonyl method), the tBoc method (t-butyloxycarbonyl method), etc. In addition, peptide synthesizers available from Advanced Automation Peptide Protein Technologies, Perkin Elmer, Protein Technologies, PerSeptive, Applied Biosystems, SHIMADZU Corp., etc. may also be used for the chemical synthesis.

[0034] The protein encoded by the polynucleotide of the invention and the protein of the invention are both ACS homolog proteins and considered to have the acyl-CoA synthetase activity since the ATP-AMP motif and FACS/VLACS-FATP motif, which are important for the acyl-CoA synthetase activity, are conserved. As used herein, ATP, AMP, FACS, VLACS and FATP are intended to mean adenosine triphosphate, adenosine monophosphate, fatty acyl-CoA synthetase, very long chain acyl-CoA synthetase and fatty acid transport protein, respectively. Specific amino acid sequences of the ATP-AMP motif and FACS/VLACS-FATP motif contained in the protein of the present invention are shown in FIGS. 25 and 26 at the single underlined and double underlined sequences, respectively. With regard to representative amino acid sequences of the ATP-AMP motif and FACS/VLACS-FATP motif, reference may be made to databases including pfam (<http://pfam.sanger.ac.uk/>), etc.

[0035] As used herein, the term "acyl-CoA synthetase activity (ACS activity)" is intended to mean the activity of promoting the acyl-CoA-forming reaction through formation of a thioester bond between a fatty acid and coenzyme A (chemical reaction equation below).



[0036] The acyl-CoA synthetase activity can be quantitatively confirmed, for example, by cultivating for a certain period of time host cells, into which the polypeptide of the present invention is introduced, preparing the lysate of the host cells, mixing the cell lysate with a labeled fatty acid (e.g., polyunsaturated fatty acid labeled with a radioactive isotope, etc.) and coenzyme A, reacting them for a certain period of time, then extracting free fatty acids with n-heptane, and quantifying the fatty acyl-CoA which is formed during the above reaction and remained in the aqueous fraction, using a scintillation counter. For details of the method for confirming the acyl-CoA synthetase activity, reference may be made to Black P. N., et al. (J. B. C., 272 (8), 4896-4903, 1997). Alternatively, the acyl-CoA synthetase activity may also be assayed by the method described in "Evaluation of ACS Activity" of EXAMPLE 2, which involves no radioactive label.

[0037] The "activity of increasing the amount of the fatty acids produced in a host cell when expressed in the host cell" is intended to mean the activity that, when the polynucleotide of the present invention or the polynucleotide encoding the protein of the present invention is introduced (transformed) into a host cell and expressed in the host cell, increases the total fatty acid production, as compared to a reference cell (control) derived from the same strain as the host cell in which the polynucleotide described above is not introduced.

[0038] The "activity of changing the composition of the fatty acids produced in a host cell when expressed in the host cell" is intended to mean the activity that, when the polynucleotide of the present invention or the polynucleotide encoding the protein of the present invention is introduced (transformed) into a host cell and expressed in the host cell, changes the amount or ratio of various fatty acids produced, as compared to a reference cell (control) derived from the same strain as the host cell in which the polynucleotide described above is not introduced.

[0039] As used herein, the term "fatty acid" is intended to mean an aliphatic monocarboxylic acid (a carboxylic acid having one carboxylic residue and carbon atoms connected to each other in a chain) represented by general formula RCOOH (wherein R is an alkyl). The fatty acid includes a saturated fatty acid having no double bond and an unsaturated fatty acid containing a double bond(s) in the hydrocarbon chain. The fatty acid is preferably an unsaturated fatty acid, and more preferably, a polyunsaturated fatty acid containing a plurality of double bonds in the hydrocarbon chain. The polyunsaturated fatty acid includes preferably an unsaturated fatty acid having carbon atoms of 18 or more, e.g., an unsaturated fatty acid having carbon atoms of 18 or 20, and examples include, but not limited to, oleic acid, linoleic acid, linolenic acid (γ-linolenic acid, dihomo-γ-linolenic acid, etc.), arachidonic acid, and the like. The polyunsaturated fatty

acids are particularly preferably linoleic acid, γ -linolenic acid, dihomo- γ -linolenic acid and arachidonic acid, more preferably, linoleic acid, dihomo- γ -linolenic acid and arachidonic acid, and most preferably, dihomo- γ -linolenic acid and arachidonic acid.

[0040] In the present invention, the "host cell" is not particularly limited so long as the cell is capable of expressing the polynucleotide of the invention when the polynucleotide is introduced. The cells include cells derived from mammals (excluding human), insects, plants, fungi, bacteria, etc., preferably cells from plants and fungi, more preferably, cells from fungi, and most preferably, lipid-producing fungi or yeast.

[0041] The lipid-producing fungi which can be used are the lipid-producing fungi described in, e.g., MYCOTAXON, Vol. XLIV, No. 2, pp. 257-265 (1992). Specific examples include, but not limited to, microorganisms belonging to the genus *Mortierella* including microorganisms belonging to the subgenus *Mortierella*, e.g., *Mortierella elongata* IF08570, *Mortierella exigua* IFO8571, *Mortierella hygrophila* IF05941, *Mortierella alpina* IF08568, ATCC16266, ATCC32221, ATCC42430, CBS 219.35, CBS224.37, CBS250.53, CBS343.66, CBS527.72, CBS528.72, CBS529.72, CBS608.70 and CBS754.68, etc., or microorganisms belonging to the subgenus *Micromucor*, e.g., *Mortierella isabellina* CBS194.28, IF06336, IF07824, IF07873, IF07874, IFO8286, IFO8308 and IFO7884, *Mortierella nana* IF08190, *Mortierella ramaniana* IFO5426, IFO8186, CBS112.08, CBS212.72, IFO7825, IFO8184, IFO8185 and IFO8287, *Mortierella vinacea* CBS236.82, etc. Among others, *Mortierella alpina* is preferable.

[0042] Specific examples of the yeast include the genus *Saccharomyces*, the genus *Candida*, the genus *Zygosaccharomyces*, the genus *Pichia* and the genus *Hansenula*, and preferably, *Saccharomyces cerevisiae* in the genus *Saccharomyces*. In wild strains of yeast such as *Saccharomyces cerevisiae*, etc., saturated fatty acids or monovalent fatty acids having mainly 18 or less carbon atoms can be synthesized within the cells, but polyunsaturated fatty acids cannot be synthesized therein. For this reason, when yeast such as *Saccharomyces cerevisiae*, etc. is used as a host cell, it is preferred to impart the ability to synthesize polyunsaturated fatty acids to the yeast cells by genetic engineering, etc. The ability to synthesize polyunsaturated fatty acids can be imparted by introducing a gene encoding a protein derived from an organism that already possesses the ability to synthesize polyunsaturated fatty acids and takes part in fatty acid synthesis.

[0043] The "organism that already possesses the ability to synthesize polyunsaturated fatty acids" includes, for example, lipid-producing fungi. Specific examples of the lipid-producing fungi are the same as those given hereinabove.

[0044] Examples of the gene encoding a protein derived from an organism that already possesses the ability to synthesize polyunsaturated fatty acids and "gene encoding the protein that takes part in fatty acid synthesis" include, but not limited to, $\Delta 12$ fatty acid desaturase gene, $\Delta 6$ fatty acid desaturase gene, GLELO fatty acid elongase gene and $\Delta 5$ fatty acid desaturase gene, etc. The nucleotide sequences of $\Delta 12$ fatty acid desaturase gene, $\Delta 6$ fatty acid desaturase gene, GLELO fatty acid elongase gene and $\Delta 5$ fatty acid desaturase gene are available by having access to databases including GenBank, etc. For example, in GenBank, Accession No. AB020033, No. AB020032, No. AB193123 and No. AB188307 are entered to access the respective sequences.

[0045] The genes for fatty acid synthesis-related proteins described above are inserted into appropriate vectors (e.g., pESC (Stratagene), pYES (Invitrogen), etc.), which are then introduced into yeast by the electroporation method, the spheroplast method (Proc. Natl. Acad. Sci. USA, 75 p1929 (1978)), the lithium acetate method (J. Bacteriology, 153, p163 (1983)), and the methods described in Proc. Natl. Acad. Sci. USA, 75 p1929 (1978), Methods in Yeast Genetics, 2000 Edition: A Cold Spring Harbor Laboratory Course Manual, etc.

[0046] Fatty acids can be extracted from the host cells transformed by the polynucleotide of the present invention or the polynucleotide encoding the protein of the present invention in the following manner. A host cell is cultured and then treated in a conventional manner, e.g., by centrifugation, filtration, etc. to obtain cultured cells. The cells are thoroughly washed with water and preferably dried. Drying may be accomplished by lyophilization, air-drying, etc. Depending upon necessity, the dried cells are disrupted using a Dymomil or by ultrasonication, and then extracted with an organic solvent preferably in a nitrogen flow. Examples of the organic solvent include ether, hexane, methanol, ethanol, chloroform, dichloromethane, petroleum ether and so on. Alternatively, good results can also be obtained by alternating extraction with methanol and petroleum ether or by extraction with a single-phase solvent system of chloroform-methanol-water. Removal of the organic solvent from the extract by distillation under reduced pressure may give fatty acid-containing lipids. The fatty acids extracted may be converted into the methyl esters by the hydrochloric acid methanol method, etc.

[0047] The quantity or ratio of various fatty acids may be determined by analyzing the fatty acids extracted as described above using various chromatography techniques. Examples of the chromatography techniques include, but not limited to, high performance liquid chromatography and gas chromatography, and particularly preferably, gas chromatography.

3. Vector of the Invention and Vector-Introduced Transformants

[0048] In another embodiment, the present invention further provides the expression vector comprising the polynucleotide of the invention.

[0049] The vector of the invention is generally constructed to contain an expression cassette comprising:

- (i) a promoter that can be transcribed in a host cell;
- (ii) any of the polynucleotides defined in (a) to (g) above that is linked to the promoter; and,
- (iii) an expression cassette comprising as a component a signal that functions in the host cell with respect to the transcription termination and polyadenylation of RNA molecule.

[0050] The vector thus constructed is introduced into a host cell. Examples of host cells which may be appropriately used in the present invention are the same as described above.

[0051] In these host cells transformed by the vector of the present invention, the ACS activity is more increased, fatty acids are more produced or the quantity or ratio of various fatty acids contained in the cells are changed, when compared to the host cells which are not transformed by the vector of the present invention.

[0052] Examples of the vectors available for introducing into lipid-producing fungi include, but not limited to, pDura5 (Appl. Microbiol. Biotechnol., 65, 419-425, (2004)).

[0053] Any vector is available as the vector used to introduce into the yeast and not particularly limited so long as it is a vector capable of expressing the insert in the yeast cells. The vector includes, e.g., pYE22m (Biosci. Biotech. Biochem., 59, 1221-1228, 1995).

[0054] Promoters/terminators for regulating gene expression in host cells may be used in an optional combination as far as they function in the host cells. For example, a promoter of the histone H4.1 gene, a promoter of the glyceraldehyde-3-phosphate dehydrogenase, etc. may be used.

[0055] As selection markers used for the transformation, there may be utilized auxotrophic markers (ura5, niaD), hygromycin-resistant gene, zeocin-resistant gene, genecitin-resistant gene (G418r), copper-resistant gene (CUP1) (Marin et al., Proc. Natl. Acad. Sci. USA, 81, 337 1984), cerulenin-resistant gene (fas2m, PDR4) (Junji Inokoshi, et al., Biochemistry, 64, 660, 1992; and Hussain et al., Gene, 101: 149, 1991, respectively), and the like.

[0056] For the transformation of host cells, generally known methods may be used. In lipid-producing fungi, the transformation may be performed, e.g., by the electroporation method (Mackenzie, D. A. et al., Appl. Environ. Microbiol., 66, 4655-4661, 2000) and the particle delivery method (the method described in JPA 2005-287403 "Method of Breeding Lipid-Producing Fungus"). On the other hand, the electroporation method, the spheroplast method (Proc. Natl. Acad. Sci. USA, 75 p1929 (1978)) and the lithium acetate method (J. Bacteriology, 153 p163 (1983)) as well as the methods described in Proc. Natl. Acad. Sci. USA, 75 p1929 (1978), Methods in yeast genetics, 2000 Edition: A Cold Spring Harbor Laboratory Course Manual, etc) may be used for the transformation of yeast. However, the method for transformation is not limited to those described above.

[0057] For general cloning techniques, reference may be made to "Sambrook & Russell, Molecular Cloning: A Laboratory Manual Vol. 3, Cold Spring Harbor Laboratory Press 2001", "Methods in Yeast Genetics, A laboratory manual (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY)," etc.

4. Method for Producing the Lipid or Fatty Acid Composition of the Invention

[0058] In another embodiment, the present invention further provides a method for preparing a lipid or fatty acid composition which comprises using the transformant described above.

[0059] As used herein, the term "lipid" is intended to mean a simple lipid including a compound (e.g., a glyceride) which is composed of a fatty acid and an alcohol attached via an ester linkage, or its analog (e.g., a cholesterol ester), etc.; a complex lipid in which phosphoric acid, amino acid(s), saccharide(s) or the like are bound to a part of the simple lipid; or a derived lipid which is a hydrolysate of the lipid and is insoluble in water.

[0060] As used herein, the term "oil and fat" is intended to mean an ester of glycerol and a fatty acid (glyceride).

[0061] The term "fatty acid" is the same as defined above.

[0062] The method for extracting the lipid or fatty acid composition of the present invention is the same as the method for extracting fatty acids described above.

[0063] Fatty acids can be separated from the above fatty acid-containing lipids in a state of mixed fatty acids or mixed fatty acid esters by concentration and separation in a conventional manner (e.g., urea addition, separation under cooling, column chromatography, etc.).

[0064] The lipids produced by the method of the present invention include preferably unsaturated fatty acids, and more preferably, polyunsaturated fatty acids. Preferred examples of the polyunsaturated fatty acids are unsaturated fatty acids having 18 or more carbon atoms, e.g., unsaturated fatty acids having 18 to 20 carbon atoms, and include, but not limited to, oleic acid, linoleic acid, linolenic acid (γ -linolenic acid and dihomo- γ -linolenic acid, etc.), arachidonic acid, etc. Particularly preferred polyunsaturated fatty acids are linoleic acid, γ -linoleic acid, dihomo- γ -linoleic acid and arachidonic acid, more preferably, linoleic acid, dihomo- γ -linoleic acid and arachidonic acid, and most preferably, dihomo- γ -linolenic acid and arachidonic acid.

[0065] The lipids produced by the method of the present invention and the composition of the fatty acids contained in the lipids may be confirmed by the lipid extraction method or fatty acid separation method described above, or a com-

ination thereof.

[0066] The lipid or fatty acid composition obtained by the production method of the present invention can be provided for use in producing, e.g., food products, pharmaceuticals, industrial materials (raw materials for cosmetics, soaps, etc.), which contain oils and fats, in a conventional manner.

[0067] In a still other embodiment, the present invention provides a method for preparing food products, cosmetics, pharmaceuticals, soaps, etc. using the transformant of the present invention. The method involves the step of forming lipids or fatty acids using the transformant of the present invention.

[0068] Food products, cosmetics, pharmaceuticals, soaps, etc. containing the lipids or fatty acids produced are prepared in a conventional manner. As such, the food products, cosmetics, pharmaceuticals, soaps, etc. produced by the method of the present invention contain the lipids or fatty acids produced using the transformant of the present invention. The present invention further provides the food products, cosmetics, pharmaceuticals, soaps, etc. produced by such a method.

[0069] The form of the cosmetic (composition) or pharmaceutical (composition) of the present invention is not particularly limited and may be any form including the state of a solution, paste, gel, solid or powder. The cosmetic composition or pharmaceutical composition of the present invention may also be used as cosmetics or topical agents for the skin, including an oil, lotion, cream, emulsion, gel, shampoo, hair rinse, hair conditioner, enamel, foundation, lipstick, face powder, facial pack, ointment, perfume, powder, eau de cologne, tooth paste, soap, aerosol, cleansing foam, etc., an anti-aging skin care agent, anti-inflammatory agent for the skin, bath agent, medicated tonic, skin beauty essence, sun protectant, or protective and improving agent for skin troubles caused by injury, chapped or cracked skin, etc.

[0070] The cosmetic composition of the present invention may further be formulated appropriately with other oils and fats and/or dyes, fragrances, preservatives, surfactants, pigments, antioxidants, etc., if necessary. The formulation ratio of these materials may be appropriately determined by those skilled in the art, depending upon purpose (for example, oils and fats may be contained in the composition in 1 to 99.99 wt %, preferably, 5 to 99.99 wt %, and more preferably, 10 to 99.95 wt %). If necessary, the pharmaceutical composition of the present invention may also contain other pharmaceutically active components (e.g., anti-inflammatory components) or aid components (e.g., lubricants or vehicle components). Examples of the other components commonly used in a cosmetic or a skin preparation for external use include an agent for acne, an agent for preventing dandruff or itching, an antiperspirant and deodorant agent, an agent for burn injury, an anti-mite and lice agent, an agent for softening keratin, an agent for xeroderma, an antiviral agent, a percutaneous absorption promoting agent, and the like.

[0071] The food product of the present invention includes a dietary supplement, health food, functional food, food product for young children, baby food, infant modified milk, premature infant modified milk, geriatric food, etc. As used herein, the food or food product is intended to mean a solid, fluid and liquid food as well as a mixture thereof, and collectively means an edible stuff.

[0072] The term dietary supplement refers to food products enriched with specific nutritional ingredients. The term health food refers to food products which are healthful or beneficial to health, and encompasses dietary supplements, natural foods, diet foods, etc. The term functional food refers to a food product for replenishing nutritional ingredients which assist body control functions and is synonymous with a food for specified health use. The term food for young children refers to a food product given to children up to about 6 years old. The term geriatric food refers to a food product treated to facilitate digestion and absorption when compared to untreated foods. The term infant modified milk refers to modified milk given to children up to about one year old. The term premature infant modified milk refers to modified milk given to premature infants until about 6 months after birth.

[0073] The form of these food products includes natural foods (treated with fats and oils) such as meat, fish and nuts; foods supplemented with fats and oils during cooking, e.g., Chinese foods, Chinese noodles, soups, etc.; foods prepared using fats and oils as heating media, e.g., tempura or deep-fried fish and vegetables, deep-fried foods, fried bean curd, Chinese fried rice, doughnuts, Japanese fried dough cookies or karinto; fat- and oil-based foods or processed foods supplemented with fats and oils during processing, e.g., butter, margarine, mayonnaise, dressing, chocolate, instant noodles, caramel, biscuits, cookies, cakes, ice cream; and foods sprayed or coated with fats and oils upon finishing, e.g., rice crackers, hard biscuits, sweet bean paste bread, etc. However, the food product is not limited to foods containing fats and oils, and other examples include agricultural foods such as bakery products, noodles, cooked rice, sweets (e.g., candies, chewing gums, gummies, sweet tablets, Japanese sweets), bean curd or tofu and processed products thereof; fermented foods such as Japanese rice wine or sake, medicinal liquor, sweet cooking sherry or mirin, vinegar, soy sauce and bean paste or miso, etc.; livestock food products such as yoghurt, ham, bacon, sausage, etc.; seafood products such as minced and steamed fish cake or kamaboko, deep-fried fish cake or ageten and puffy fish cake or hanpen, etc.; as well as fruit drinks, soft drinks, sports drinks, alcoholic beverages, tea, etc.

[0074] The food product of the present invention may also be in the form of pharmaceutical preparations such as capsules, etc., or in the form of a processed food such as natural liquid diets, defined formula diets and elemental diets formulated with the oil and fat of the present invention together with proteins, sugars, trace elements, vitamins, emulsifiers, aroma chemicals, etc., health drinks, enteral nutrients, and the like.

EP 2 930 236 B1

[0075] As described above, fatty acids can be efficiently produced by expressing the ACS homolog gene of the present invention in host cells.

[0076] Furthermore, the expression level of the gene can be used as an indicator to study conditions for cultivation, cultivation control, etc. for efficient fatty acid production.

EXAMPLES

[0077] Hereinafter, the present invention is described in more detail with reference to EXAMPLES but it should be understood that the invention is not deemed to limit the scope of the invention to these EXAMPLES.

[EXAMPLE 1]

Genome Analysis of *M. alpina*

[0078] The *M. alpina* 1S-4 strain was plated on 100 ml of GY2:1 medium (2% glucose and 1% yeast extract, pH 6.0) followed by shake culture at 28°C for 2 days. The mycelial cells were collected by filtration, and genomic DNA was prepared using DNeasy (QIAGEN). The nucleotide sequence of the genomic DNA described above was determined using a Roche 454 GS FLX Standard. On this occasion, nucleotide sequencing of a fragment library was performed in two runs and nucleotide sequencing of a mate paired library in three runs. The resulting nucleotide sequences were assembled to give 300 supercontigs.

Synthesis of cDNA and Construction of cDNA Library

[0079] The *M. alpina* strain 1S-4 was plated on 100 ml of medium (1.8% glucose, 1% yeast extract, pH 6.0) and precultured for 3 days at 28°C. A 10 L culture vessel (Able Co., Tokyo) was charged with 5 L of medium (1.8% glucose, 1% soybean powder, 0.1% olive oil, 0.01% Adekanol, 0.3% KH₂PO₄, 0.1% Na₂SO₄, 0.05% CaCl₂·2H₂O and 0.05% MgCl₂·6H₂O, pH 6.0), and the whole amount of the pre-cultured product was plated thereon, followed by aerobic spinner culture under conditions of 300 rpm, 1 vvm and 26°C for 8 days. On Days 1, 2 and 3 of the cultivation, glucose was added in an amount corresponding to 2%, 2% and 1.5%, respectively. The mycelial cells were collected at each stage on Days 1, 2, 3, 6 and 8 of the cultivation to prepare total RNA by the guanidine hydrochloride/CsCl method. Using an Oligotex-dT30<Super>mRNA Purification Kit (Takara Bio Inc.), poly(A)+RNA was purified from the total RNA. A cDNA library was constructed for each stage using a ZAP-cDNA Gigapack III Gold Cloning Kit (STRATAGENE).

Search for ACS Homolog

[0080] Using as a query the amino acid sequences of ScFAA1 (YOR317W), ScFAA2 (YER015W), ScFAA3 (YIL009W), ScFAA4 (YMR246W), ScFAT1 (YBR041W) and ScFAT2 (YBR222C), which are ACS from yeast, a tblastn search was performed against the genome nucleotide sequence of the *M. alpina* strain 1S-4. As a result, hits were found in twelve (12) sequences. That is, hit was found on supercontigs containing the sequence shown by SEQ ID NO: 5, SEQ ID NO: 10, SEQ ID NO: 15, SEQ ID NO: 20, SEQ ID NO: 25, SEQ ID NO: 30, SEQ ID NO: 35, SEQ ID NO: 40, SEQ ID NO: 45, SEQ ID NO: 50, SEQ ID NO: 55 or SEQ ID NO: 60. The genes bearing SEQ ID NO: 5, SEQ ID NO: 10, SEQ ID NO: 15, SEQ ID NO: 20, SEQ ID NO: 25, SEQ ID NO: 30, SEQ ID NO: 35, SEQ ID NO: 40, SEQ ID NO: 45, SEQ ID NO: 50, SEQ ID NO: 55 and SEQ ID NO: 60 were designated respectively as MaACS-1, MaACS-2, MaACS-3, MaACS-4, MaACS-5, MaACS-6, MaACS-7, MaACS-8, MaACS-9, MaACS-10, MaACS-11 and MaACS-12.

Cloning of ACS Homolog

[0081] For cloning of the cDNAs corresponding to the MaACS-1~12 genes, screening of the cDNA library described above was performed. Probe labeling was performed by PCR using an ExTaq (Takara Bio Inc.). That is, digoxigenin (DIG)-labeled amplified DNA probes were prepared using a PCR Labeling Mix (Roche Diagnostics) instead of dNTP mix attached to ExTaq.

[0082] Conditions for hybridization were set as follows.

Buffer: 5x SSC, 1% SDS, 50 mM Tris-HCl (pH 7.5), 50% formaldehyde;

Temperature: 42°C (overnight);

Wash conditions: 0.2x SSC, in 0.1% SDS solution (65°C) for 20 mins. x 3

[0083] Detection was performed using a DIG Nucleic Acid Detection Kit (Roche Diagnostics). Phage clones were

EP 2 930 236 B1

obtained by screening and plasmids were excised from the phage clones by in vivo excision to give the respective plasmid DNAs.

[0084] Primers for preparing the probes used for screening of the respective genes, the number of nucleotides in CDS of the respective genes, the number of amino acids in the amino acid sequences deduced from the nucleotide sequences of CDS, and the number of exons and introns by comparison of genomic DNA sequences with CDS sequences are given below.

(1) MaACS-1

Primer ACS-1-1F: 5'-GTCGGCTCCAAGCTTGCAATCC-3' (SEQ ID NO: 61)
 Primer ACS-1-2R: 5'-GGACAGCTCCAGCACTGTGGTAAAG-3' (SEQ ID NO: 62)
 cDNA (SEQ ID NO: 4)
 CDS (SEQ ID NO: 3): 1857 bp
 ORF (SEQ ID NO: 1): 1854 bp
 Amino acid sequence (SEQ ID NO: 2): 618 amino acids (see FIG. 1)
 Number of exons: 5, number of introns: 4 (see FIG. 2)

(2) MaACS-2

Primer ACS-2-1F: 5'-GACCACGGGATTCCCCAAGGCTGC-3' (SEQ ID NO: 63)
 Primer ACS-2-2R: 5'-CTTGGTCGCGCTTGTTCCTGGCCAC-3' (SEQ ID NO: 64)
 cDNA (SEQ ID NO: 9)
 CDS (SEQ ID NO: 8): 1929 bp
 ORF (SEQ ID NO: 6): 1926 bp
 Amino acid sequence (SEQ ID NO: 7): 642 amino acids (see FIG. 3)
 Number of exons: 8, number of introns: 7 (see FIG. 4)

(3) MaACS-3

Primer ACS-3-1F: 5'-TACAGCTTTGTTGCTGTCCCCATC-3' (SEQ ID NO: 65)
 Primer ACS-3-2R: 5'-GATGATGGGTGTGCTTGCAAAGATC-3' (SEQ ID NO: 66)
 cDNA (SEQ ID NO: 14)
 CDS (SEQ ID NO: 13): 1653 bp
 ORF (SEQ ID NO: 11): 1650 bp
 Amino acid sequence (SEQ ID NO: 12): 550 amino acids (see FIG. 5)
 Number of exons: 9, number of introns: 8 (see FIG. 6)

(4) MaACS-4

Primer ACS-4-1F: 5'-AACCCAAAGCTGCGCCAGGCTGTCC-3' (SEQ ID NO: 67)
 Primer ACS-4-2R: 5'-TTACAGCTTGATTCTTTTGATGG-3' (SEQ ID NO: 68)
 cDNA (SEQ ID NO: 19)
 CDS (SEQ ID NO: 18): 2067 bp
 ORF (SEQ ID NO: 16): 2064 bp
 Amino acid sequence (SEQ ID NO: 17): 688 amino acids (see FIG. 7)
 Number of exons: 7, number of introns: 6 (see FIG. 8)

(5) MaACS-5

Primer ACS-5-1F: 5'-GTCGTGCCCCGATGCGGAGACGC-3' (SEQ ID NO: 69)
 Primer ACS-5-2R: 5'-TCAGTGATCCCGTTATACATCAG-3' (SEQ ID NO: 70)
 cDNA (SEQ ID NO: 24)
 CDS (SEQ ID NO: 23): 1980 bp
 ORF (SEQ ID NO: 21): 1977 bp
 Amino acid sequence (SEQ ID NO: 22): 659 amino acids (see FIG. 9)
 Number of exons: 6, number of introns: 5 (see FIG. 10)

(6) MaACS-6

EP 2 930 236 B1

Primer ACS-6-1F: 5'-GCGTCCCCCTCTATGATACATTG-3' (SEQ ID NO: 71)
 Primer ACS-6-2R: 5'-GTGGGATGCAGGACGGCAACATCG-3' (SEQ ID NO: 72)
 cDNA (SEQ ID NO: 29)
 CDS (SEQ ID NO: 28): 1980 bp
 ORF (SEQ ID NO: 26): 1977 bp
 Amino acid sequence (SEQ ID NO: 27): 659 amino acids (see FIG. 11)
 Number of introns: at least 5 (see FIG. 12)

(7) MaACS-7

Primer ACS-7-1F: 5'-GGATGCCGAACAACAGCGCGTGG-3' (SEQ ID NO: 73)
 Primer ACS-7-2R: 5'-GCACCCTCCTCAGAAACAGCCCTC-3' (SEQ ID NO: 74)
 cDNA (SEQ ID NO: 34)
 CDS (SEQ ID NO: 33): 1827 bp
 ORF (SEQ ID NO: 31): 1824 bp
 Amino acid sequence (SEQ ID NO: 32): 608 amino acids (see FIG. 13)
 Number of exons: 5, number of introns: 4 (see FIG. 14)

(8) MaACS-8

Primer ACS-8-1F: 5'-CAGTCGAGTACATTGTCAACCACG-3' (SEQ ID NO: 75)
 Primer ACS-8-2R: 5'-GCGGTTCAAGAGGCGAGGCACAGC-3' (SEQ ID NO: 76)
 cDNA (SEQ ID NO: 39)
 CDS (SEQ ID NO: 38): 2079 bp
 ORF (SEQ ID NO: 36): 2076 bp
 Amino acid sequence (SEQ ID NO: 37): 692 amino acids (see FIG. 15)
 Number of exons: 8, number of introns: 7 (see FIG. 16)

(9) MaACS-9

Primer ACS-9-1F: 5'-GTTTCATCTTCTGCTGGCTGGGTCTC-3' (SEQ ID NO: 77)
 Primer ACS-9-2R: 5'-GTTGCGTTGTTACGCGGCAATCC-3' (SEQ ID NO: 78)
 cDNA (SEQ ID NO: 44)
 CDS (SEQ ID NO: 43): 1851 bp
 ORF (SEQ ID NO: 41): 1848 bp
 Amino acid sequence (SEQ ID NO: 42): 616 amino acids (see FIG. 17)
 Number of exons: 5, number of introns: 4 (see FIG. 18)

(10) MaACS-10

Primer ACS-10-1F: 5'-ATGGAAACCTTGTTAACGGAAAG-3' (SEQ ID NO: 79)
 Primer ACS-10-2R: 5'-TCAGCAAAGATGGCCTTGGGCTGG-3' (SEQ ID NO: 80)
 cDNA (SEQ ID NO: 49)
 CDS (SEQ ID NO: 48): 2076 bp
 ORF (SEQ ID NO: 46): 2073 bp
 Amino acid sequence (SEQ ID NO: 47): 691 amino acids (see FIG. 19)
 Number of exons: 8, number of introns: 7 (see FIG. 20)

(11) MaACS-11

Primer ACS-11-1F: 5'-GTCAAGGGCGAGACTCGCATCC-3' (SEQ ID NO: 81)
 Primer ACS-11-2R: 5'-CGGTGACGATGGTCATGGACTGC-3' (SEQ ID NO: 82)
 cDNA (SEQ ID NO: 54)
 CDS (SEQ ID NO: 53): 2043 bp
 ORF (SEQ ID NO: 51): 2040 bp
 Amino acid sequence (SEQ ID NO: 52): 680 amino acids (see FIG. 21)
 Number of exons: 3, number of introns: 2 (see FIG. 22)

EP 2 930 236 B1

(12) MaACS-12

Primer ACS-12-1F: 5'-GCGAGACCCGCATCCGCCGCTCC-3' (SEQ ID NO: 83)

Primer ACS-12-2R: 5'-GACCGTCCTCGCCCAGGGTGTCTG-3' (SEQ ID NO: 84)

cDNA (SEQ ID NO: 59)

CDS (SEQ ID NO: 58): 2043 bp

ORF (SEQ ID NO: 56): 2040 bp

Amino acid sequence (SEQ ID NO: 57): 680 amino acids (see FIG. 23)

Number of exons: 3, number of introns: 2 (see FIG. 24)

Sequencing Analysis

[0085] The identity between the CDS nucleotide sequences of 12 ACS homologs from *M. alpina* is shown in TABLE 1 and the identity between the amino acid sequences is shown in TABLE 2. MaACS-11 and MaACS-12 showed high identity of 80.2% in the nucleotide sequence and 84.3% in the amino acid sequence.

TABLE 1 Sequence identity among CDS nucleotide sequences of ACS homologs from *M. alpina*

	MaACS-1	MaACS-2	MaACS-3	MaACS-4	MaACS-5	MaACS-6	MaACS-7	MaACS-8	MaACS-9	MaACS-10	MaACS-11	MaACS-12
MaACS-1	-	51.3	42.9	45.4	44.7	46.6	46.0	45.6	69.5	44.7	46.2	45.8
MaACS-2		-	43.4	46.8	46.9	45.7	46.5	44.6	52.5	44.9	44.9	44.0
MaACS-3			-	38.0	38.2	38.9	43.7	37.5	42.8	41.5	39.0	39.1
MaACS-4				-	50.4	51.6	43.8	57.7	44.2	47.0	49.7	49.3
MaACS-5					-	70.8	44.7	53.0	44.9	46.6	48.9	47.2
MaACS-6						-	46.2	53.0	45.2	47.9	49.2	49.4
MaACS-7							-	44.2	45.9	42.3	45.0	44.6
MaACS-8								-	44.3	48.1	50.7	50.8
MaACS-9									-	42.7	46.2	47.8
MaACS-10										-	51.8	52.1
MaACS-11											-	80.2
MaACS-12												-

TABLE 2 Sequence identity among amino acid sequences of ACS homologs from *M. alpina*

	MaACS-1	MaACS-2	MaACS-3	MaACS-4	MaACS-5	MaACS-6	MaACS-7	MaACS-8	MaACS-9	MaACS-10	MaACS-11	MaACS-12
MaACS-1	-	366	11.8	13.9	15.1	15.8	18.0	14.8	71.9	13.5	14.6	15.0
MaACS-2		-	11.0	14.0	15.4	15.0	17.2	13.2	37.0	12.3	12.7	13.8
MaACS-3			-	21.7	21.5	20.8	13.1	21.1	10.5	17.7	18.5	17.9
MaACS-4				-	37.5	37.5	17.0	50.9	15.4	22.8	29.8	29.5
MaACS-5					-	77.9	17.0	41.2	16.4	25.2	29.1	29.8
MaACS-6						-	16.6	39.8	16.6	25.3	29.9	29.4
MaACS-7							-	15.5	17.0	15.3	16.2	16.7
MaACS-8								-	15.2	24.9	27.8	28.6
MaACS-9									-	14.1	14.5	14.7
MaACS-10										-	32.8	32.6
MaACS-11											-	84.3
MaACS-12												-

EP 2 930 236 B1

[0086] Using as query sequences the putative amino acid sequences for the CDS sequences of MaACS-1~12, BLASTp search was performed against the amino acid sequences registered in GenBank. The proteins having the amino acid sequence which matched the putative amino acid sequences of MaACS-1~12 with highest score and the identity between these proteins and the putative amino acid sequences of MaACS-1~12 are shown in TABLE 3. The identity of the putative amino acid sequences of MaACS-1~12 with the amino acid sequences of *S. cerevisiae*-derived acyl-CoA synthetases are also shown in TABLE 4.

TABLE 3 Sequence identity between the amino acid sequences of *M. alpina*-derived ACS homologs and known amino acid sequences

	identity(%)	gi	
MaACS-1	41.8	71014575	Putative protein from <i>Ustilago maydis</i>
MaACS-2	35.4	71014575	Putative protein from <i>Ustilago maydis</i>
MaACS-3	23.5	71895089	Chick ACS long-chain family member 5
MaACS-4	36.9	115487304	Putative protein from <i>Oryza sativa</i>
MaACS-5	42.5	168065128	Putative protein from <i>Physcomitrella patens</i>
MaACS-6	40.9	13516481	Long-chain acyl-CoA synthetase from <i>Arabidopsis thaliana</i>
MaACS-7	45.7	120612991	Putative protein from <i>Acidovorax avenae</i> subsp. <i>citrulli</i>
MaACS-8	40.0	13516481	Long-chain acyl-CoA synthetase from <i>Arabidopsis thaliana</i>
MaACS-9	37.8	67538044	Putative protein from <i>Aspergillus nidulans</i>
MaACS-10	33.2	171682488	Putative protein from <i>Podospora Anserina</i>
MaACS-11	48.8	169854433	Putative protein from <i>Coprinopsis atramentarius</i>
MaACS-12	45.1	156045509	Putative protein from <i>Sclerotinia sclerotiorum</i>

TABLE 4 Comparison of amino acid sequences of *M. alpina*-derived ACS homologs and amino acid sequences of *S. cerevisiae*-derived ACS

	ScFAA1	ScFAA2	ScFAA3	ScFAA4	ScFAT1	ScFAT2
MaACS-1	13.8	15.3	13.6	13.5	29.8	18.1
MaACS-2	12.5	13.6	13.4	13.5	26.3	17.5
MaACS-3	15.8	14.0	15.0	14.8	13.6	12.9
MaACS-4	26.3	28.3	23.9	24.2	14.0	16.0
MaACS-5	25.6	28.2	25.5	25.8	13.2	18.6
MaACS-6	25.3	28.4	25.8	25.5	13.0	18.1
MaACS-7	16.5	17.5	16.0	16.9	16.6	20.6
MaACS-8	23.0	28.0	21.3	22.8	12.2	14.8
MaACS-9	15.6	15.5	14.3	14.7	30.1	18.3
MaACS-10	30.8	20.6	30.6	30.6	14.0	14.2
MaACS-11	39.6	22.6	37.3	38.7	12.9	15.8
MaACS-12	41.3	22.3	39.8	39.0	14.4	16.2

[0087] FIG. 25 shows the alignment between MaACS from MaACS-1~12, which have relatively high amino acid sequence homology to the *S. cerevisiae*-derived FAA proteins, and the FAA proteins. FIG. 26 shows the alignment of the ACS homologs having relatively high amino acid sequence homology to *S. cerevisiae*-derived FAT proteins. The regions of the ATP-AMP motif and FACS/VLACS-FATP motif, which are important motifs for the ACS activity, are highly conserved in both groups shown in FIGS. 25 and 26.

Construction of Expression Vector

[0088] Vectors for expressing MaACS-1, MaACS-10, MaACS-11, MaACS-6, MaACS-8 and MaACS-9, respectively, in yeast were constructed as follows, using the expression vector pYE22m (Biosci. Biotech. Biochem., 59, 1221-1228, 1995).

[0089] The plasmid containing SEQ ID NO: 29, which was obtained by screening MaACS-6, was digested with restriction enzymes BamHI and XhoI. The resulting DNA fragment of approximately 2.1 kbp was ligated to the DNA fragment obtained by digestion of vector pYE22m with restriction enzymes BamHI and Sall using a Ligation High (TOYOBO) to give plasmid pYE-ACS-6.

[0090] Using the plasmid containing cDNA of MaACS-8 as a template, PCR was performed with the primers below using ExTaq (Takara Bio Inc.). The thus amplified DNA fragment was cloned by a TOPO-TA Cloning Kit (Invitrogen).

Primer EcoRI-ACS-8-F: 5'-GGATCCATGCCTTCCTTCAAAAAGTACAACC-3' (SEQ ID NO: 85)

Primer SmaI-ACS-8-R: 5'-CCCGGGCAAAGAGTTTCTATCTACAGCTT-3' (SEQ ID NO: 86)

[0091] The nucleotide sequence of the insert was verified and the plasmid containing the correct nucleotide sequence was digested with restriction enzymes EcoRI and SmaI. Using a Ligation High (TOYOBO), the resulting DNA fragment of approximately 2.1 kbp was ligated to the DNA fragment obtained by digesting vector pYE22m with restriction enzymes EcoRII and SmaI to give plasmid pYE-ACS-8.

[0092] Using the plasmid containing cDNA of MaACS-9 as a template, PCR was performed with the primers below using ExTaq (Takara Bio Inc.). The thus amplified DNA fragment was cloned by a TOPO-TA Cloning Kit (Invitrogen).

Primer EcoRI-ACS-9-F: 5'-GAATTCATGGTTGCTCTCCCACTCG-3' (SEQ ID NO: 87)

Primer BamHI-ACS-9-R: 5'-GGATCCCTACTATAGCTTGGCCTTGCC-3' (SEQ ID NO: 88)

[0093] The nucleotide sequence of the insert was verified and the plasmid containing the correct nucleotide sequence was digested with restriction enzymes EcoRI and BamHI. Using a Ligation High (TOYOBO), the resulting DNA fragment of approximately 2.0 kbp was ligated to the DNA fragment obtained by digesting vector pYE22m with restriction enzymes EcoRII and BamHI to give plasmid pYE-ACS-9.

[0094] Using the plasmid containing cDNA of MaACS-1 as a template, PCR was performed with the primers below using ExTaq (Takara Bio Inc.). The thus amplified DNA fragment was cloned by a TOPO-TA Cloning Kit (Invitrogen).

Primer EcoRI-ACS-1-F: 5'-GGATCCATGTATGTGCGCTCCAAGCTTGC-3' (SEQ ID NO: 89)

Primer Sall-ACS-1-R: 5'-GTCGACTCAAAGCCTGGCTTGGCGCTGACG-3' (SEQ ID NO: 90)

[0095] The nucleotide sequence of the insert was verified and the plasmid containing the correct nucleotide sequence was digested with restriction enzymes EcoRI and Sall. Using a Ligation High (TOYOBO), the resulting DNA fragment of approximately 1.9 kbp was ligated to the DNA fragment obtained by digesting vector pYE22m with restriction enzymes EcoRI and Sall to give plasmid pYE-ACS-1.

[0096] Using the plasmid containing cDNA of MaACS-10 as a template, PCR was performed with the primers below using ExTaq (Takara Bio Inc.). The thus amplified DNA fragment was cloned by a TOPO-TA Cloning Kit (Invitrogen).

Primer ACS-10-1F: 5'-GGATCCATGGAAACCTTGGTTAACGGAAG-3' (SEQ ID NO: 91)

Primer KpnI-ACS-10-R: 5'-GGTACCTAGAAGTCTTCCACATCTCCTC-3' (SEQ ID NO: 92)

[0097] The nucleotide sequence of the insert was verified and the plasmid containing the correct nucleotide sequence was digested with restriction enzymes EcoRI and KpnI. Using a Ligation High (TOYOBO), the resulting DNA fragment of approximately 2.1 kbp was ligated to the DNA fragment obtained by digesting vector pYE22m with restriction enzymes EcoRI and KpnI. Plasmid pYE-ACS-10 was obtained by screening for the orientation that the GAPDH promoter of vector pYE22m was located at its 5' end of CDS of MaACS-10.

[0098] Using the plasmid containing cDNA of MaACS-11 as a template, PCR was performed with the primers below using ExTaq (Takara Bio Inc.). The thus amplified DNA fragment was cloned by a TOPO-TA Cloning Kit (Invitrogen).

Primer SacI-ACS-11-F: 5'-GAGCTCATGCCAAAGTGCTTTACCGTCAACG-3' (SEQ ID NO: 93)

Primer BamHI-ACS-11-R: 5'-GGATCCTTACTTGGAGCCATAGATCTGCTTG-3' (SEQ ID NO: 94)

[0099] The nucleotide sequence of the insert was verified and the plasmid containing the correct nucleotide sequence was digested with restriction enzymes SacI and BamHI. Using a Ligation High (TOYOBO), the resulting DNA fragment

EP 2 930 236 B1

of approximately 2.0 kbp was ligated to the DNA fragment obtained by digesting vector pYE22m with restriction enzymes SacI and BamHI to give plasmid pYE-ACS-11.

Expression in Yeast

Acquisition of Transformants

[0100] The yeast *S. cerevisiae* EH13-15 strain (*trp1*, *MAT α*) (Appl. Microbiol. Biotechnol., 30, 515-520, 1989) was transformed with plasmids pYE22m, pYE-MaACS-6, pYE-MaACS-8 and pYE-MaACS-9, respectively, by the lithium acetate method. The transformants were screened for the ability to grow on SC-Trp agar medium (2% agar) (per liter, 6.7 g Yeast Nitrogen Base w/o Amino Acids (DIFCO), 20 g glucose, 1.3 g amino acid powders (a mixture of 1.25 g adenine sulfate, 0.6 g arginine, 3 g aspartic acid, 3 g glutamic acid, 0.6 g histidine, 1.8 g leucine, 0.9 g lysine, 0.6 g methionine, 1.5 g phenylalanine, 11.25 g serine, 0.9 g tyrosine, 4.5 g valine, 6 g threonine and 0.6 g uracil).

Cultivation of Yeast

[0101] One each from the transformants obtained using the respective plasmids was provided for the following cultivation experiment.

[0102] One platinum loop of the yeast was plated on 10 ml of SC-Trp and cultured with shaking for preincubation at 30°C for a day. After 1 ml of the preincubation was added to the SC-Trp medium, main cultivation was performed by shake culturing at 30°C for a day.

Analysis of Fatty Acids in Mycelia

[0103] The yeast culture broth was centrifuged to recover the mycelial cells. After washing with 10 ml of sterile water, the mycelial cells were again centrifuged, recovered and lyophilized. The fatty acids in the mycelial cells were converted into the methyl esters by the hydrochloric acid-methanol method followed by extraction with hexane. After hexane was removed by distillation, the fatty acids were analyzed by gas chromatography.

[0104] The fatty acid production per medium is shown in TABLE 5. In the strains transformed by ppYE-MaACS-6, pYE-MaACS-8 or pYE-MaACS-9, the fatty acid production per medium was increased as compared to the control which was transformed by pYE22m.

TABLE 5 Fatty Acid Production by Transformant per Medium

	Control	MaACS-6	MaACS-8	MaACS-9
Fatty acid production (mg/L)	135	159	196	187

Expression in Arachidonic Acid-Producing Yeast

(1) Breeding of Arachidonic Acid-Producing Yeast Strains

[0105] To breed arachidonic acid-producing yeast strain (*S. cerevisiae*), the following plasmids were constructed.

[0106] First, using the cDNA prepared from *M. alpina* strain 1S-4 as a template, PCR was performed with ExTaq using the primer pair of $\Delta 12$ -f and $\Delta 12$ -r, $\Delta 6$ -f and $\Delta 6$ -r, GLELO-f and GLELO-r, or $\Delta 5$ -f and $\Delta 5$ -r to amplify the $\Delta 12$ fatty acid desaturase gene (GenBank Accession No. AB020033) (hereinafter " $\Delta 12$ gene"), the $\Delta 6$ fatty acid desaturase gene (GenBank Accession No. AB020032) (hereinafter " $\Delta 6$ gene"), the GLELO fatty acid elongase gene (GenBank Accession No. AB193123) (hereinafter "GLELO gene") and the $\Delta 5$ fatty acid desaturase gene (GenBank Accession No. AB188307) (hereinafter " $\Delta 5$ gene") in the *M. alpina* strain 1S-4.

$\Delta 12$ -f: 5'-TCTAGAATGGCACCTCCCAACACTATTG-3' (SEQ ID NO: 95)
 $\Delta 12$ -r: 5'-AAGCTTTTACTTCTTGAAAAAGACCACGTC-3' (SEQ ID NO: 96)
 $\Delta 6$ -f: 5'-TCTAGAATGGCTGCTGCTCCAGTGTGAG-3' (SEQ ID NO: 97)
 $\Delta 6$ -r: 5'-AAGCTTTTACTGTGCCTTGCCCATCTTGG-3' (SEQ ID NO: 98)
GLELO-f: 5'-TCTAGAATGGAGTCGATTGCGCAATTCC-3' (SEQ ID NO: 99)
GLELO-r: 5'-GAGCTCTTACTGCAACTTCCTTGCTTCTC-3' (SEQ ID NO: 100)
 $\Delta 5$ -f: 5'-TCTAGAATGGGTGCGGACACAGGAAAAACC-3' (SEQ ID NO: 101)
 $\Delta 5$ -r: 5'-AAGCTTTTACTCTTCCTTGGGACGAAGACC-3' (SEQ ID NO: 102)

[0107] These genes were cloned with the TOPO-TA-Cloning Kit. The clones were confirmed by their nucleotide sequences. The clones containing the nucleotide sequences of the $\Delta 12$ gene, $\Delta 6$ gene, GLELO gene and $\Delta 5$ gene were designated as plasmids pCR-MA $\Delta 12$ DS (containing the nucleotide sequence of the $\Delta 12$ gene), pCR-MA $\Delta 6$ DS (containing the nucleotide sequence of the $\Delta 6$ gene), pCR-MAGLELO (containing the nucleotide sequence of the GLELO gene) and pCR-MA $\Delta 5$ DS (containing the nucleotide sequence of the $\Delta 5$ gene), respectively.

[0108] On the other hand, the plasmid pURA34 (JPA 2001-120276) was digested with restriction enzyme HindIII. The resulting DNA fragment of approximately 1.2 kb was inserted into the HindIII site of the vector, which was obtained by digesting pUC18 vector (Takara Bio Inc.) with restriction enzymes EcoRI and SphI, then blunt ending and self ligating said vector. The clone in which the EcoRI site of the vector was located at its 5' end of URA3 was designated as pUC-URA3. Also, the DNA fragment of approximately 2.2 kb, which was obtained by digesting YEp13 with restriction enzymes Sall and XhoI, was inserted into the Sall site of vector pUC18. The clone in which the EcoRI site of the vector was located at its 5' end of LUE2 was designated as pUC-LEU2.

[0109] Next, the plasmid pCR-MA $\Delta 12$ DS was digested with restriction enzyme HindIII, followed by blunt ending and further digestion with restriction enzyme XbaI. The resulting DNA fragment of approximately 1.2 kbp was ligated to the DNA fragment of approximately 6.6 kbp, which was obtained by digesting vector pESC-URA (STRATAGENE) with restriction enzyme SacI, blunt ending and further digesting with restriction enzyme SpeI. Thus, the plasmid pESC-U- $\Delta 12$ was obtained. The plasmid pCR-MA $\Delta 6$ DS was digested with restriction enzyme XbaI, followed by blunt ending and further digestion with restriction enzyme HindIII. The resulting DNA fragment of approximately 1.6 kbp was ligated to the DNA fragment of approximately 8 kbp, which was obtained by digesting the plasmid pESC-U- $\Delta 12$ with restriction enzyme Sall, blunt ending and further digesting with restriction enzyme HindIII, thereby to give the plasmid pESC-U- $\Delta 12$: $\Delta 6$. This plasmid was partially digested with restriction enzyme PvuII. The resulting fragment of approximately 4.2 kb was inserted into the SmaI site of pUC-URA3 to give the plasmid pUC-URA- $\Delta 12$: $\Delta 6$.

[0110] Also, the plasmid pCR-MAGLELO was digested with restriction enzymes XbaI and SacI. The resulting DNA fragment of approximately 0.95 kbp was ligated to the DNA fragment of approximately 7.7 kbp, which was obtained by digesting vector pESC-LEU (STRATAGENE) with restriction enzymes XbaI and SacI. Thus, the plasmid pESC-L-GLELO was obtained. The plasmid pCR-MA $\Delta 5$ DS was digested with restriction enzyme XbaI, followed by blunt ending and further digestion with restriction enzyme HindIII. The resulting DNA fragment of approximately 1.3 kbp was ligated to the DNA fragment of approximately 8.7 kbp, which was obtained by digesting the plasmid pESC-L-GLELO with restriction enzyme ApaI, blunt ending and further digesting with restriction enzyme HindIII, thereby to give the plasmid pESC-L-GLELO: $\Delta 5$. This plasmid was digested with restriction enzyme PvuII and the resulting fragment of approximately 3.2 kbp was inserted into the SmaI site of pUC-LEU2 to give plasmid pUC-LEU-GLELO: $\Delta 5$. The *Saccharomyces cerevisiae* strain YPH499 (STRATAGENE) was co-transformed by the plasmid pUC-URA- $\Delta 12$: $\Delta 6$ and plasmid pUC-LEU-GLELO: $\Delta 5$. The transformants were screened for the ability to grow on SC-Leu,Ura agar medium. Among the transformants thus obtained, random one strain was designated as the strain ARA3-1. By cultivating the strain in a galactose-supplemented medium, the strain became capable of expressing from the GAL1/10 promoter the $\Delta 12$ fatty acid desaturase gene, the $\Delta 6$ fatty acid desaturase gene, the GLELO gene and the $\Delta 5$ fatty acid desaturase gene.

(2) Transformation into Arachidonic Acid-Producing Yeast and Analysis

[0111] The ARA3-1 strain was transformed by plasmids pYE22m, pYE-ACS-1, pYE-ACS-10 and pYE-ACS-11, respectively. Transformants were screened for the ability to grow on SC-Trp,Leu,Ura agar medium (2 % agar) (per liter, 6.7 g Yeast Nitrogen Base w/o Amino Acids (DIFCO), 20 g glucose and 1.3 g amino acid powders (a mixture of 1.25 g adenine sulfate, 0.6 g arginine, 3 g aspartic acid, 3 g glutamic acid, 0.6 g histidine, 0.9 g lysine, 0.6 g methionine, 1.5 g phenylalanine, 11.25 g serine, 0.9 g tyrosine, 4.5 g valine and 6 g of threonine). Random four strains from the respective plasmid-transfected strains were used for the subsequent cultivation.

[0112] These strains were cultivated at 30°C for a day in 10 ml of the SC-Trp,Leu,Ura liquid medium described above. One milliliter of the culture was plated on 10 ml of SG-Trp,Leu,Ura liquid medium (per liter, 6.7 g Yeast Nitrogen Base w/o Amino Acids (DIFCO), 20 g galactose and 1.3 g amino acid powders (a mixture of 1.25 g adenine sulfate, 0.6 g arginine, 3 g aspartic acid, 3 g glutamic acid, 0.6 g histidine, 0.9 g lysine, 0.6 g methionine, 1.5 g phenylalanine, 11.25 g serine, 0.9 g tyrosine, 4.5 g valine and 6 g threonine) and then cultivated at 15°C for 6 days. The mycelial cells were collected, washed with water and then lyophilized. After the fatty acids in the dried mycelial cells were converted to the methyl esters by the hydrochloric acid-methanol method, the analysis of fatty acids was performed by gas chromatography. The ratio of each PUFA to the total fatty acids in the control strain transformed by plasmid pYE22m, and in the strains transformed by each ACS homolog from *Mortierella* is shown in TABLE 6.

TABLE 6 % Ratio of PUFA in ACS homolog expression strains from *Mortierella*

	control	MaACS-1	MaACS-10	MaACS-11
18:2	7.23 ± 0.11	8.15 ± 0.29	14.87 ± 0.28	10.57 ± 0.30
18:3(n-6)	0.38 ± 0.01	0.44 ± 0.04	1.67 ± 0.10	0.92 ± 0.07
DGLA	0.41 ± 0.01	0.42 ± 0.02	0.30 ± 0.17	0.33 ± 0.03
ARA	0.42 ± 0.01	0.63 ± 0.04	0.47 ± 0.10	0.75 ± 0.10
Average ± Standard Deviation				

[0113] As shown in TABLE 6, the ratio of fatty acids could be modified by expressing the ACS homolog from *Mortierella*. Particularly in the MaACS-11 expression strain, the ratios of arachidonic acid, linoleic acid and γ -linolenic acid were increased by about 1.8 times, about 1.5 times and about 2.4 times, respectively, as compared to the control strain. In the MaACS-1 expression strain, the ratio of arachidonic acid was increased by about 1.5 times, as compared to the control strain. Further in the MaACS-10 expression strain, the ratios of linoleic acid and γ -linolenic acid were increased by about 2 times and about 4 times, respectively, as compared to the control strain.

[EXAMPLE 2]

Construction of Expression Vector

Expression Vector for Yeast

[0114] The vector pYE-ACS-12 for expressing MaACS-12 in yeast was constructed as follows. Using a plasmid containing the cDNA of MaACS-12 as a template, PCR was performed with the following primers using KOD-Plus-(TOYOBO).

Primer Eco-ACS-G-F: 5'-GAATTCATGACAAAGTGCCTCACCGTCG-3' (SEQ ID NO: 103)

Primer Sma-ACS-G-R: 5'-CCCGGGACTTAGGCCGTTCCATAAAGCTG-3' (SEQ ID NO: 104)

[0115] The amplified DNA fragment was cloned using a Zero Blunt TOPO PCR Cloning Kit (Invitrogen). The nucleotide sequence of the insert was verified and the plasmid containing the correct nucleotide sequence was digested with restriction enzymes EcoRI and SmaI. Using a Ligation High (TOYOBO), the resulting DNA fragment of approximately 2 kbp was ligated to the DNA fragment obtained by digesting vector pYE22m with restriction enzyme BamHI and then blunt ending with a Blunting Kit (TAKARA Bio) and further digesting with EcoRI, to give plasmid pYE-ACS-12.

Expression Vector for *M. alpina*

[0116] The vector for expressing MaACS-10 and MaACS-11 in *M. alpina* was constructed as follows.

[0117] First, pUC18 was digested with restriction enzymes EcoRI and HindIII and an adapter obtained by annealing oligo DNA MCS-for-pUC18-F2 with MCS-for-pUC18-R2 was inserted therein to construct plasmid pUC18-RF2.

MCS-for-pUC18-F2:

5'-AATTCATAAGAATGCGGCCGCTAACTATTCTAGACTAGGTGACGGCG CGCCA-3' (SEQ ID NO: 105)

MCS-for-pUC18-R2:

5'-AGCTTGGCGCGCCGTCGACCTAGTCTAGAATAGTTTAGCGGCCGCATTC TTATG-3' (SEQ ID NO: 106)

[0118] Using the genome DNA of *M. alpina* as a template, PCR was performed with the primers Not1-GAPDHt-F and EcoR1-Asc1-GAPDHt-R using KOD-Plus-(Toyobo). The amplified DNA fragment of about 0.5 kbp was cloned using a Zero Blunt TOPO PCR Cloning Kit (Invitrogen). After the nucleotide sequence of the insert was verified, the DNA fragment of about 0.9 kbp obtained by digesting with restriction enzymes NotI and EcoRI was inserted into the NotI and EcoRI site of plasmid pUC18-RF2 to construct plasmid pDG-1.

Not1-GAPDHt-F: 5'-AGCGGCCGCATAGGGGAGATCGAACC-3' (SEQ ID NO: 107)

EcoR1-Asc1-GAPDHt-R: 5'-AGAATTCGGCGCGCCATGCACGGGTCCTTCTCA-3' (SEQ ID NO: 108)

[0119] Using the genome of *M. alpina* as a template, PCR was performed with the primers URA5g-F1 and URA5g-

EP 2 930 236 B1

R1 using KOD-Plus- (Toyobo). The amplified DNA fragment was cloned using a Zero Blunt TOPO PCR Cloning Kit (Invitrogen). After the nucleotide sequence of the insert was verified, the DNA fragment of about 2 kbp obtained by digestion with Sall was inserted into the Sall site of plasmid pDG-1. The plasmid that the 5' end of URA5 gene inserted was oriented toward the EcoRI side of the vector was designated as the plasmid pDuraG.

URA5g-F1: 5'-GTCGACCATGACAAGTTTGC-3' (SEQ ID NO: 109)
URA5g-R1: 5'-GTCGACTGGAAGACGAGCAGC-3' (SEQ ID NO: 110)

[0120] Subsequently, PCR was performed with KOD-Plus- (TOYOBO) using the genome of *M. alpina* as a template and the primers hisHp+URA5-F and hisHp+MGt-F. Using an In-Fusion (registered trade name) Advantage PCR Cloning Kit (TAKARA Bio), the amplified DNA fragment of about 1.0 kbp was ligated to the DNA fragment of about 5.3 kbp amplified by PCR with KOD-Plus- (TOYOBO) using pDuraG as a template and the primers pDuraSC-GAPt-F and URA5gDNA-F, to give plasmid pDura-RhG.

hisHp+URA5-F:
5'-GGCAAACCTTGTCTATGAAGCGAAAGAGAGATTATGAAAACAAGC-3' (SEQ ID NO: 111)
hisHp+MGt-F:
5'-CACTCCCTTTTCTTAATTGTTGAGAGAGTGTGGGTGAGAGT-3' (SEQ ID NO: 112)
pDuraSC-GAPt-F: 5'-TAAGAAAAGGGAGTGAATCGCATAGGG-3' (SEQ ID NO: 113)
URA5gDNA-F: 5'-CATGACAAGTTTGCCAAGATGCG-3' (SEQ ID NO: 114)

[0121] Using the plasmid pDura-RhG as a template, the DNA fragment of about 6.3 kbp was amplified by PCR with KOD-Plus- (TOYOBO) using the primers pDuraSC-GAPt-F and pDurahG-hisp-R.

pDurahG-hisp-R: 5'-ATTGTTGAGAGAGTGTGGGTGAGAGTG-3' (SEQ ID NO: 115)

[0122] Using the plasmid containing cDNA of MaACS-10, the DNA fragment of about 2.1 kbp was amplified by PCR with KOD-Plus- (TOYOBO), using the primers below.

Primer ACS-10+hisp-F:
5'-CACTCTCTCAACAATATGGAAACCTTGGTTAACGGAAAGT-3' (SEQ ID NO: 116)
Primer ACS-10+MGt-R:
5'-CACTCCCTTTTCTTACTAGAACTTCTCCACATCTCCTCAATATC-3' (SEQ ID NO: 117)

[0123] The resulting DNA fragment was ligated to the 6.3 kbp DNA fragment described above using an In-Fusion (registered trade name) Advantage PCR Cloning Kit (TAKARA BIO) to give plasmid pDuraRhG-ACS-10.

[0124] Using the plasmid containing cDNA of MaACS-11 as a template, the 2.1 kbp DNA fragment was amplified by PCR with KOD-Plus- (TOYOBO) using the primers below.

Primer ACS-11+MGt-R:
5'-CACTCCCTTTTCTTATTACTTGGAGCCATAGATCTGCTTGA-3' (SEQ ID NO: 118)
Primer ACS-11+hisp-F:
5'-CACTCTCTCAACAATATGCCAAAGTGCTTTACCGTCAAC-3' (SEQ ID NO: 119)

[0125] The resulting DNA fragment was ligated to the 6.3 kbp DNA fragment described above using an In-Fusion (registered trade name) Advantage PCR Cloning Kit (TAKARA BIO) to give the plasmid pDuraRhG-ACS-11.

Evaluation of ACS Activity

[0126] The yeast EH13-15 was transformed by plasmids pYE22m, pYE-ACS-5, pYE-ACS-8, pYE-ACS-10, pYE-ACS-11 and pYE-ACS-12, respectively, and random two transformants obtained were cultivated as follows. One platinum loop of the mycelial cells were plated on 10 ml of SC-Trp medium and cultivated with shaking for preincubation at 30°C for a day. After 1 % of the preincubation was added to 100 ml of the SD-Trp medium, main cultivation was performed by shake culturing at 28°C for a day.

[0127] The crude enzyme solution was prepared as follows. The mycelial cells were collected by centrifugation, washed with water and temporarily stored at -80°C. The mycelial cells were suspended in 5 ml of Buffer B (50 mM sodium sulfate buffer (pH 6.0), 10% glycerol and 0.5 mM PMSF). The mycelial cells were then disrupted with a French press (16 kPa, 3 times). Centrifugation was carried out at 1,500 xg at 4°C for 10 minutes and centrifuged. The supernatant obtained

EP 2 930 236 B1

was used as the crude enzyme solution.

[0128] The ACS activity was determined by the following procedures based on the description of a reference literature (J.B.C., 272 (8), 1896-4903, 1997). The reaction solution contained 200 mM Tris-HCl (pH7.5), 2.5 mM ATP, 8 mM MgCl₂, 2 mM EDTA, 20 mM NaF, 0.1% TritonX-100, 50 µg/ml fatty acids, 50 µM CoA and 100 µl of the crude enzyme solution (suitably diluted in Buffer B), and was made 500 µl in total. The reaction was carried out at 28°C for 30 minutes. After completion of the reaction, 2.5 ml of stop solution (isopropanol : n-heptane : 1 M sulfuric acid (40: 20: 1)) was added and the mixture was thoroughly agitated. Furthermore, 2 ml of n-heptane was added thereto. After thoroughly mixing them, the mixture was centrifuged to recover the upper layer. Further 2 ml of n-heptane was added to the lower layer and treated in the same manner to recover the upper layer. The upper layers recovered were combined and evaporated to dryness using a centrifugal concentrator. Then, 50 µl of 0.2 mg/ml tricosanoic acid (23: 0) was added thereto as an internal standard. The fatty acids were converted into the methyl esters by the hydrochloric acid-methanol method, followed by fatty acid analysis using gas chromatography. The amount of the fatty acids, which were changed to acyl-CoA and thus distributed into the lower layer by the procedures above, was calculated from the amount of fatty acids detected. The results are shown in the table below. The ACS activity is expressed as the amount of fatty acids distributed into the lower layer by the procedures above, per weight of the protein in the crude enzyme solution. The control is the strain transformed by pYE22m and the others are the transformants in which the expression vectors of the respective genes were introduced.

TABLE 7 ACS Activity on Palmitic Acid

	MaACS-5		MaACS-10		MaACS-11		MaACS-12		Control	
	#1	#2	#1	#2	#1	#2	#1	#2	#1	#2
mg/mg·protein	0.26	0.20	0.41	0.34	0.49	0.43	0.31	0.40	0.11	0.12

[0129] When palmitic acid was used as substrate, MaACS-5, MaACS-10, MaACS-11 and MaACS-12 showed the ACS activity of approximately 2 to 4 times the control.

TABLE 8 ACS Activity on Oleic Acid

	MaACS-10		MaACS-11		MaACS-12		Control	
	#1	#2	#1	#2	#1	#2	#1	#2
mg/mg·protein	0.25	0.20	0.25	0.16	0.16	0.18	0.09	0.11

[0130] When oleic acid was used as substrate, MaACS-10, MaACS-11 and MaACS-12 showed the ACS activity of approximately twice the control.

TABLE 9 ACS Activity on Linoleic Acid

	MaACS-5		MaACS-8		MaACS-10		MaACS-11		MaACS-12		Control	
	#1	#2	#1	#2	#1	#2	#1	#2	#1	#2	#1	#2
mg/mg·protein	0.47	0.42	0.42	0.38	524	5.67	3.46	3.20	0.95	0.78	0.14	0.14

[0131] When linoleic acid was used as substrate, MaACS-5, MaACS-8 and MaACS-12 showed the ACS activity of several times (approximately 3, 3 and 6 times, respectively) the control, whereas MaACS-10 and MaACS-11 showed the ACS activity of several tens times (approximately 40 and 20 times, respectively) the control.

TABLE 10 ACS Activity on γ -Linoleic Acid

	MaACS-5		MaACS-8		MaACS-10		MaACS-11		MaACS-12		Control	
	#1	#2	#1	#2	#1	#2	#1	#2	#1	#2	#1	#2
mg/mg·protein	0.26	0.28	0.16	0.31	0.63	0.59	0.90	0.75	0.52	0.63	0.07	0.09

[0132] When γ -linoleic acid was used as substrate, all of MaACS-5, MaACS-8, MaACS-10, MaACS-11 and MaACS-12 showed the ACS activity of approximately 2 to 10 times the control.

EP 2 930 236 B1

TABLE 11 ACS Activity on Dihomo- γ -Linoleic Acid

	MaACS-10		MaACS-11		MaACS-12		Control	
	#1	#2	#1	#2	#1	#2	#1	#2
mg/mg·protein	4.98	4.21	2.75	2.98	2.04	1.86	0.09	0.05

[0133] When dihomogamma-linoleic acid was used as substrate, all of MaACS-10, MaACS-11 and MaACS-12 showed the ACS activity of several tens times (approximately 60 times, 40 times and 30 times, respectively) the control.

TABLE 12 ACS Activity on Arachidonic Acid

	MaACS-10		MaACS-11		MaACS-12		Control	
	#1	#2	#1	#2	#1	#2	#1	#2
mg/mg·protein	8.12	7.19	2.73	2.87	1.08	0.87	0.13	0.03

[0134] When arachidonic acid was used as substrate, MaACS-10, MaACS-11 and MaACS-12 showed the ACS activity of several tens times (approximately 90 times, 30 times and 10 times, respectively) the control.

[0135] As above, MaACS-10, MaACS-11 and MaACS-12 in particular showed a higher activity on polyunsaturated fatty acids of 20 carbon atoms such as dihomogamma-linoleic acid or arachidonic acid.

Arachidonic Acid Uptake Activity of ACS-Expressed Yeast

[0136] The yeast EH13-15 was transformed by plasmids pYE22m, pYE -ACS-10, pYE -ACS-11 and pYE -ACS-12, respectively, and random two transformants obtained were cultivated as follows. One platinum loop of the cells were plated on 10 ml of SC-Trp medium and cultivated with shaking for preincubation at 30°C for a day. After 100 μ l of the preincubation was added to 10 ml of the SC-Trp medium in which 50 μ g/ml of arachidonic acid was supplemented, main cultivation was performed by shake culturing at 25°C for a day. The mycelial cells were collected, lyophilized and subjected to fatty acid analysis. The ratio of arachidonic acid taken up into the mycelial cells to the added arachidonic acid was determined. The results are shown in TABLE 14. The control is the strain transformed by pYE22m and the others are the transformants in which the expression vectors of the respective genes were introduced.

TABLE 13 Dry Mycelial Weight

	Control		MaACS-10		MaACS-11		MaACS-12	
	#1	#2	#1	#2	#1	#2	#1	#2
%	36.63	37.81	65.86	66.64	61.53	61.35	63.64	67.06

TABLE 14 Ratio of Arachidonic Acid Taken Up into Mycelia

	Control		MaACS-10		MaACS-11		MaACS-12	
	#1	#2	#1	#2	#1	#2	#1	#2
mg/10ml	15:30	15.80	19.60	18.10	16.70	17.40	16.80	16.20

Acquisition of M. Alpina Transformants

[0137] Using as a host the uracil-auxotrophic strain Δ ura-3 derived from M. alpina strain 1S-4 as described in PCT International Publication Pamphlet WO 2005/019437 entitled "Method of Breeding Lipid-Producing Fungus"), transformation was performed by the particle delivery method using the plasmids pDUraRhG-ACS-10 and pDUraRhG-ACS-11, respectively. For screening of the transformants, SC agar medium was used (0.5% Yeast Nitrogen Base w/o Amino Acids and Ammonium Sulfate (Difco), 0.17% ammonium sulfate, 2% glucose, 0.002% adenine, 0.003% tyrosine, 0.0001% methionine, 0.0002% arginine, 0.0002% histidine, 0.0004% lysine, 0.0004% tryptophan, 0.0005% threonine, 0.0006% isoleucine, 0.0006% leucine, 0.0006% phenylalanine, and 2% agar).

Evaluation of M. Alpina Transformants

[0138] The transformants obtained were plated on 4 ml of GY medium and cultured with shaking at 28°C for 2 days. The mycelial cells were collected by filtration, and RNA was extracted with an RNeasy Plant Kit (QIAGEN). A SuperScript First Strand System for RT-PCR (Invitrogen) was used to synthesize cDNA. To confirm expression of the respective genes from the introduced constructs, RT-PCR was performed with the following primer pairs.

ACS10-RT1: 5'-GTCCCGAATGGTTCCT-3' (SEQ ID NO: 120)
 ACS10-RT2: 5'-AGCGGTTTTCTACTTGC-3' (SEQ ID NO: 121)
 ACS11-RT1: 5'-AACTACAACCGCGTCG-3' (SEQ ID NO: 122)
 ACS11-RT2: 5'-CGGCATAAACGCAGAT-3' (SEQ ID NO: 123)

[0139] In the transformants that overexpression was confirmed, one transformant each was plated on 10 ml of GY medium (2% glucose and 1% yeast extract) and cultured with shaking at 28°C at 300 rpm for 3 days. The whole volume of the culture was transferred to 500 ml of GY medium (2 L Sakaguchi flask) and shake cultured at 28°C and 120 rpm. Three, seven, ten and twelve days after this day, 5 ml each and 10 ml each were taken and filtered. After the mycelial cells were dried at 120°C, fatty acids were converted into the methyl esters by the hydrochloric acid-methanol method and analyzed by gas chromatography. The fatty acid production and the amount of arachidonic acid produced, per dried mycelial cells were monitored with the passage of time. The transformant host strain Δ ura-3 was used as control. The results are shown in FIG. 27 (MaACS-10) and FIG. 28 (MaACS-11).

[0140] As shown in FIGS. 27 and 28, when MaACS-10 and MaACS-11 were overexpressed in *M. alpina*, both the amount of fatty acids and the amount of arachidonic acid per mycelia were increased as compared to the control.

INDUSTRIAL APPLICABILITY

[0141] The polynucleotide of the present invention is expressed in an appropriate host cell to efficiently produce fatty acids, in particular, polyunsaturated fatty acids. The fatty acids produced in host cells according to the present invention can be used to produce fatty acid compositions, food products, cosmetics, pharmaceuticals, soaps, etc.

[Sequence Listing]

[0142] Furthermore, the present disclosure relates to the following items:

1. A polynucleotide according to any one selected from the group consisting of (a) to (e) below:

- (a) a polynucleotide comprising any one nucleotide sequence selected from the group consisting of the nucleotide sequences shown by SEQ ID NOs: 1, 6, 11, 16, 21, 26, 31, 36, 41, 46, 51 and 56;
- (b) a polynucleotide encoding a protein consisting of any one amino acid sequence selected from the group consisting of the amino acid sequences shown by SEQ ID NOs: 2, 7, 12, 17, 22, 27, 32, 37, 42, 47, 52 and 57;
- (c) a polynucleotide encoding a protein consisting of an amino acid sequence wherein 1 to 100 amino acids are deleted, substituted, inserted and/or added in any one amino acid sequence selected from the group consisting of the amino acid sequences shown by SEQ ID NOs: 2, 7, 12, 17, 22, 27, 32, 37, 42, 47, 52 and 57, and having an acyl-CoA synthetase activity or an activity of increasing the amount or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell;
- (d) a polynucleotide encoding a protein having an amino acid sequence having at least 60% identity to any one amino acid sequence selected from the group consisting of the amino acid sequences shown by SEQ ID NOs: 2, 7, 12, 17, 22, 27, 32, 37, 42, 47, 52 and 57, and having an acyl-CoA synthetase activity or an activity of increasing the amount or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell; and,
- (e) a polynucleotide which hybridizes to a polynucleotide consisting of a nucleotide sequence complementary to any one nucleotide sequence selected from the group consisting of the nucleotide sequences shown by SEQ ID NOs: 1, 6, 11, 16, 21, 26, 31, 36, 41, 46, 51 and 56 under stringent conditions, and which encodes a protein having an acyl-CoA synthetase activity or an activity of increasing the amount or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell.

2. The polynucleotide according to item 1, which is either one defined in (f) or (g) below:

- (f) a polynucleotide encoding a protein consisting of an amino acid sequence wherein 1 to 10 amino acids are

EP 2 930 236 B1

deleted, substituted, inserted and/or added in any one amino acid sequence selected from the group consisting of the amino acid sequences shown by SEQ ID NOs: 2, 7, 12, 17, 22, 27, 32, 37, 42, 47, 52 and 57, and having an acyl-CoA synthetase activity or an activity of increasing the amount or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell; and,

(g) a polynucleotide encoding a protein having an amino acid sequence having at least 90% identity to any one amino acid sequence selected from the group consisting of the amino acid sequences shown by SEQ ID NOs: 2, 7, 12, 17, 22, 27, 32, 37, 42, 47, 52 and 57, and an acyl-CoA synthetase activity or an activity of increasing the amount or changing the composition, of the fatty acids produced in a host cell when expressed in the host cell.

3. The polynucleotide according to item 1, comprising any one nucleotide sequence selected from the group consisting of the nucleotide sequences shown by SEQ ID NOs: 1, 6, 11, 16, 21, 26, 31, 36, 41, 46, 51 and 56.

4. The polynucleotide according to item 1, encoding a protein consisting of any one amino acid sequence selected from the group consisting of the amino acid sequences shown by SEQ ID NOs: 2, 7, 12, 17, 22, 27, 32, 37, 42, 47, 52 and 57.

5. The polynucleotide according to any one of items 1 to 4, which is a DNA.

6. A protein encoded by the polynucleotide according to any one of items 1 to 5.

7. A vector comprising the polynucleotide according to any one of items 1 to 5.

8. A non-human transformant, into which the polynucleotide according to any one of items 1 to 5, or the vector according to item 7 is introduced.

9. A method for producing a lipid or fatty acid composition, which comprises collecting the lipid or fatty acid composition from the culture of the transformant according to item 8.

10. The method according to item 9, wherein the lipid is a triacylglycerol.

11. The method according to item 9, wherein the fatty acid is a polyunsaturated fatty acid having at least 18 carbon atoms.

12. A food product, pharmaceutical, cosmetic or soap comprising the lipid or fatty acid composition obtained by the production method according to item 9.

SEQUENCE LISTING

[0143]

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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20 <213> Mortierella alpina

<400> 34

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EP 2 930 236 B1

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<211> 2076

50 <212> DNA

<213> Mortierella alpina

<400> 36

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2076

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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<211> 2079

EP 2 930 236 B1

<212> DNA

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<400> 38

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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<400> 42

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Lys Arg Gly Asp Ile Val Ser Leu Phe Met Leu Asn Arg Pro Glu Phe
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EP 2 930 236 B1

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EP 2 930 236 B1

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<211> 1851

<212> DNA

<213> Mortierella alpina

<400> 43

EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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<212> DNA

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EP 2 930 236 B1

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EP 2 930 236 B1

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<400> 46

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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<212> PRT

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<400> 52

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EP 2 930 236 B1

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EP 2 930 236 B1

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Ala Asp Gly Thr Leu Ser Val Ile Asp Arg Lys Lys Asn Leu Val Lys
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Leu Ser His Gly Glu Tyr Ile Ala Leu Glu Lys Leu Glu Ser Val Tyr
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Lys Ser Thr Ala Tyr Cys Asn Asn Ile Cys Val Tyr Ala Asp Ser Met
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Gln Asn Lys Pro Val Ala Leu Ile Val Ala Ser Glu Pro Arg Ile Leu
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Glu Leu Ala Lys Ala Lys Gly Leu Glu Ser Arg Asp Phe Ala Val Leu
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Cys His Asp Lys Val Ile Ile Lys Ala Val Leu Asp Ala Cys Leu Ala
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Thr Ala Lys Lys Ala Gly Leu Lys Pro Ala Glu Leu Leu Gln Gly Val
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<211> 2043

EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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 Cys Gly Leu Arg Lys Phe Gly Val Glu Pro Lys Asp Lys Leu Thr Val
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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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<212> DNA

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<400> 129

EP 2 930 236 B1

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EP 2 930 236 B1

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<212> DNA

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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EP 2 930 236 B1

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REFERENCES CITED IN THE DESCRIPTION

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PATENTKRAV

1. Polynukleotid i overensstemmelse med et vilkårligt blandt (a) til (e) nedenfor valgt kendetegn:

- 5 (a) et polynukleotid, der omfatter en nukleotidsekvens ifølge SEQ ID NO: 56;
- (b) et polynukleotid, der koder for et protein, som består af aminosyresekvensen ifølge SEQ ID NO: 57;
- (c) et polynukleotid, der koder for et protein, som består af en aminosyresekvens, hvori 1 til 100 aminosyrer er fjernet, erstattet, indsat og/eller tilføjet i aminosyre-
- 10 sekvensen ifølge SEQ ID NO: 57, og har acyl-CoA-syntetaseaktivitet eller aktivitet til forøgelse af mængden eller ændring af sammensætningen af de i en værtscelle producerede fedtsyrer, når det udtrykkes i værtscellen;
- (d) et polynukleotid, der koder for et protein, der har en aminosyresekvens med mindst 60% identitet med aminosyresekvensen ifølge SEQ ID NO: 57 og har
- 15 acyl-CoA-syntetaseaktivitet eller aktivitet til forøgelse af mængden eller ændring af sammensætningen af de i en værtscelle producerede fedtsyrer, når det udtrykkes i værtscellen; og
- (e) et polynukleotid, der hybridiserer til et polynukleotid, som består af en nukleotidsekvens, som er komplementær til nukleotidsekvensen ifølge SEQ ID
- 20 NO: 56 under betingelserne 5x SSC, 5x Denhardt's opløsning, 0,5% SDS, 50% formamid ved 50°C eller 0,2x SSC, 0,1% SDS ved 65°C, og som koder for et protein med acyl-CoA-syntetaseaktivitet eller aktivitet til forøgelse af mængden eller ændring af sammensætningen af de i en værtscelle producerede fedtsyrer, når det udtrykkes i værtscellen.

25

2. Polynukleotid ifølge krav 1, som er det ene eller det andet i (f) eller (g) nedenfor definerede:

- (f) et polynukleotid, der koder for et protein, som består af en aminosyresekvens, hvori 1 til 10 aminosyrer er fjernet, erstattet, indsat og/eller tilføjet i aminosyre-
- 30 sekvensen ifølge SEQ ID NO: 57, og som har acyl-CoA-syntetaseaktivitet eller aktivitet til forøgelse af mængden eller ændring af sammensætningen af de i en værtscelle producerede fedtsyrer, når det udtrykkes i værtscellen; og
- (g) et polynukleotid, der koder for et protein, som har en aminosyresekvens med mindst 90% identitet med aminosyresekvensen ifølge SEQ ID NO: 57 og har
- 35 acyl-CoA-syntetaseaktivitet eller aktivitet til forøgelse af mængden eller ændring

af sammensætningen af i en værtselle producerede fedtsyrer, når det udtrykkes i værtsellen.

3. Polynukleotid ifølge krav 1 omfattende nukleotidsekvensen ifølge SEQ ID NO: 56.
- 5
4. Polynukleotid ifølge krav 1, der koder for et protein, som består af aminosyresekvensen ifølge SEQ ID NO: 57.
5. Polynukleotid ifølge et hvilket som helst af kravene 1 til 4, som er DNA.
- 10
6. Protein, der kodes for af polynukleotidet ifølge et hvilket som helst af kravene 1 til 5.
7. Vektor omfattende polynukleotidet ifølge et hvilket som helst af kravene 1 til 5.
- 15
8. Værtselle, i hvilken polynukleotidet ifølge et hvilket som helst af kravene 1 til 5 eller vektoren ifølge krav 7 er indført.
9. Fremgangsmåde til fremstilling af en lipid- eller fedtsyresammensætning, som omfatter opsamling af lipid- eller fedtsyresammensætningen fra kulturen af transformanten ifølge krav 8.
- 20
10. Fremgangsmåde ifølge krav 9, ved hvilken lipidet er en triacylglycerol.
11. Fremgangsmåde ifølge krav 9, ved hvilken fedtsyren er en flerumættet fedtsyre med
- 25
- mindst 18 carbonatomer.

Figure 1

1 GCTCTTTTTCGTCTCTTTGCCACCCCACTCTGCTGTGCCTCTCCACTCCCCCTGCCCTGCCAACGTTCTTCTGTCACTTTGCACAGCAGTATCTCC
 101 TCTGATCTCGCTGRTTATATTCCTCTAATCTCGTTTGGTTATATTCCTCTGATCTCGCTGGTTATATTTCTTACAGATAGGATGCTGTCCCTGCAGT
 M D A V P A V .
 201 TGCTGCTGGGCCATCCCGCAGGCATGTATGTGGCTCCAAGCTTGCAATCCCCCTGATGTCAAGTTAGCTAAAGCCCTAGTCAAGTGCACCAAGCTAGGT
 . A A A A I P A A M Y V G S K L A I P R D V K L A K G L V S A K L G
 301 TACAGTCTCTACGAGACGACTCGATCAATATCTCTTATCGTTTGAAGAGACCTGTAGAAGCACCTCATCCGCCAAGCTTTGGTCTTTGAAGGCA
 Y R S Y E K N D S I N I S Y R F E E T C K K H P H R E A L V F E G K .
 401 AATCGTACACCTTCCAGGACATCCAGCGAGAATCGAATAGGTGGGACACTGGCTGTGTCAAAGGCGTCAAGCGAGGAGAGATCGTGTGCTCTTCAT
 . S Y T F Q D I Q R E S N R V G H W L L S K G V K R G E I V S L F M .
 501 GCAAAATAAGCCAGAGTTTCTCTTCTTCTGGCTTGACTCAACAAGATCGGCGTAGCGGAGCATTCAACACCAACCTCTCGGGCAAAACCTCTGACG
 . Q N K P E F L F W L G L N K I G A T G A F I N T N L S G K P L T
 601 CACTCATTGCTACCGGACAGCATCCATTCTGATTATGGATGCGGAACCTGCCGACCCCATTTATAGTGTCTCTGATGAAGTCTTGCAGATGGGATATC
 H S L R T A T A S I L I M D A E L P T P I V S V L D E V L E M G Y Q .
 701 AGATATATTCCCTACGGAGGATCCAGCAACAGGCTTTGCTACACAAGTTGAACCTTCTCAATCTCGGATGCGGCTTGCCCAAGAGCTCTGCGAAGGAA
 . I Y S Y G G S Q Q H A F A T Q V E L S Q I S D A A L P K S L R R K .
 801 AACCACTGCAAAATGATATTGCCATGTTGATTACACCTCCGGAACGACGGGTTGCCCAAGCTGGACGGTTCTCCCATGCTCGAGGCAACGTTGCCCGCA
 . T T A N D I A M L I Y T S G T T G L P K A G R F S H A R A N V A A
 901 CTTTCTGGACGCTCTTCTACCACTTCAGCGAAAACCGGCTGTACATCGCTTGCCTCTTTACACAGTGTGAGGCTGTCTTGGAAATATGCTGCG
 L F W T S F Y H F S E K D R L Y I A L P L Y H S A G A V L G I C V A .
 1001 CCTGGGTACCGGTGCTACGGTGGTCTCTGGCGGCAAGTTTCAACTACTTCTCTGGGACGAAATGCCAGCGGCCAACAAGGTCAACCGTATCCAGTATAT
 . W V T G A T V V L A R K F S T T S F W D E C R A N K V T V I Q Y I .

Figure 1 (cont.)

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1101 TGGAGAAATCTGCCGATACCTTACTGAATGCTCCTCTCCTTGGACAAGACACACCATCCGAATGGCGCATGGCAACGGCATCGCTCCGGATGTA
    . G E I C R Y L L N A P P S P L D K T H T I R M A H G N G M R P D V

1201 TGGACACAGATTCAGAGATCGTTTCGGCATCCCTTTGATCGGAGAAATGGTATGCAAGCACTGAGGGCACCGGAATCTTGACAAACTATAACACAGGACCCA
    W N R F R D R F G I P L I G E W Y A S T E G T G I L T N Y N T G P N .

1301 ATGGCGCTGCTGCGATAGGATACAGAGGCTCCTTGGCCAGAACTGTGATAAGGCTCTGAAGATTGGGAAGTTGGACATCCAAACCGAGGAACCTTATTGG
    . G A G A I G Y R G S L A R T V D K G L K I A K F D I Q T E E L I R .

1401 TGACAAAATGGTCGATTCGATTGAGTGTGTCGACATGAGCCCGGCGAGCTCTTGACAATGATTGATTCAAGTATCCCACTCGCGCTTTCOAAGGTAC
    . D K N G R C I E C V A D E P G E L L T M I D S S D P T R A F Q G Y

1501 CATAAAATGCAGGTGCAAACTCCAGAAAGTCTCCAGGATGCATTCACTGTGGCGACCAATACTTTCGTACTGTGACATCCCTTCGTCCGACCGCTG
    H K N A G A N S K K V V Q D A F S V G D Q Y F R T G D I L R R D A D .

1601 ATGGCTATTCTATTTTGGGATCGTGTGGAGATACTTTCGGCTGAAATCTGAAACGTGTCAACTGCGGAGGTTTCTGAGGTGCTCTCAGCATACCC
    . G Y F Y F G D R V G D T F R W K S E N V S T A E V S E V L S A Y P .

1701 GGAATGCATCGAGGTCAACGTTTATGGGTTCAAGTCCCTGGACACGACGGCGGCGGATGGCTGCCATTGTCTCAAGGACACCATGAACTGGGAT
    . D C I E V N V Y G V Q V P G H D G R A G M A A I V S K D T M N W D

1801 AGTTTCGCCAAGTTTGCACTCAAAAATCTGCCGAAGTACTCTGTGCGGATTTTCATCCGCAAGGTCCCAAGATGGAGATTACGGGAACGTTCAAGCAAC
    S F A K F A L K N L P K Y S V P I F I R K V P E M E I T G T F K Q R .

1901 GAAAGTTGAACGTGAACGAGGCGATGGACCCGAGCAAGATCAAGACGAAATGCTGTGGATGGGCACCTCCCTACCGGCCCTTCAAGAGGCGCA
    . K V E L V N E G M D P S K I K D E M L W L D G H S Y R P F K E A E .

2001 GCATACTAGAGTGTGTCAGCGGCAAGCCAGGCTTTGACGAATAAAATTATTTCGTTTTTCCTCGTTGAAAAA
    . H T R V V S G K A R L

```

Figure 2A

1	ATGGATGCTGTCCCTGAGTTGCTGCTGGGCAATCCCGGAGGCAATGATGTGGCTCCAGCTTGCAATCCCGGTGATGTCAAGTTAGCTAAAGGCG	100
genome CDS	ATGGATGCTGTCCCTGAGTTGCTGCTGGGCAATCCCGGAGGCAATGATGTGGCTCCAGCTTGCAATCCCGGTGATGTCAAGTTAGCTAAAGGCG	
101	TAGTCAGTGCCAAGCTAGGTTACAGGTGCTAGGAGAAAGCACTCCGATCAATATCTCTTATGTGTTTGAAGAGAGCTGTGAAGAAGCAACCTTCATGCGGA	200
genome CDS	TAGTCAGTGCCAAGCTAGGTTACAGGTGCTAGGAGAAAGCACTCCGATCAATATCTCTTATGTGTTTGAAGAGAGCTGTGAAGAAGCAACCTTCATGCGGA	
201	AGCTTTGGTGTTTGAAGGCAAAATGTTACACCTTCCAGGACATCCAGGAGGTAAACAAGAAAACAATTGTCCAAAGTCACAGTCGAAAGCATCCGAAATT	300
genome CDS	AGCTTTGGTGTTTGAAGGCAAAATGTTACACCTTCCAGGAGGTAAACAAGAAAACAATTGTCCAAAGTCACAGTCGAAAGCATCCGAAATT	
301	TTTACTCAAGATAAATTGCGATCATGCGCAACACACCCCTCCGTCGATTTTCACTAACCTTCGACTTGGATGTAGATTCGGAATAGGGTGGGACACTGGCTGT	400
genome CDS	TTTACTCAAGATAAATTGCGATCATGCGCAACACACCCCTCCGTCGATTTTCACTAACCTTCGACTTGGATGTAGATTCGGAATAGGGTGGGACACTGGCTGT	
401	TGTCAAAGGGCTCAAGCGAGAGAGATGGTGGCTCTTCATGCAAAATAGCCAGAGTTTCTCTTCTTCTGGCTTGGACTCAACAAGATGGGGCTAG	500
genome CDS	TGTCAAAGGGCTCAAGCGAGAGAGATGGTGGCTCTTCATGCAAAATAGCCAGAGTTTCTCTTCTTCTGGCTTGGACTCAACAAGATGGGGCTAG	
501	GGGAGCATTTCATCAACAGCAAGCTCTCGGGCAAACTCTGAGCCACTGATTTGGTTACGGCGACAGCATCCATTCTGATTATGGATGGGGAACCTGGGACG	600
genome CDS	GGGAGCATTTCATCAACAGCAAGCTCTCGGGCAAACTCTGAGCCACTGATTTGGTTACGGCGACAGCATCCATTCTGATTATGGATGGGGAACCTGGGACG	
601	CCGATTTATAGTGTCTCGATGAAGTCTTCAGATGGGATATCAGATATAATTCCTACGGAGGATCCAGGCAACACGGCTTTTCTACACAAGTTGAACTTT	700
genome CDS	CCGATTTATAGTGTCTCGATGAAGTCTTCAGATGGGATATCAGATATAATTCCTACGGAGGATCCAGGCAACACGGCTTTTCTACACAAGTTGAACTTT	
701	CTCAAAATCTCGGATGGGCTTGGCCAAAGAGTCTGGCAAGGAAACCACTGCAATGATATTGCCATGTTTCATTTACAACCTCCGGGAACGAGGTTTGGC	800
genome CDS	CTCAAAATCTCGGATGGGCTTGGCCAAAGAGTCTGGCAAGGAAACCACTGCAATGATATTGCCATGTTTCATTTACAACCTCCGGGAACGAGGTTTGGC	

Figure 2A (cont.)

genome	801	CAAAGCTGGACGGTTCCTCCATGCTCGAGGCAACGGTAGGATTATACCCCGCTCTCCCGCCCTTTTTCATTTGCTGTGAAGTTATTAGCTG	900
CDS		CAAAGCTGGACGGTTCCTCCATGCTCGAGGCAACGGTAGGATTATACCCCGCTCTCCCGCCCTTTTTCATTTGCTGTGAAGTTATTAGCTG	
genome	901	TTCCACTAGCATATTGACTCATATTACAGTTCTTCTTTACACGTGGGATCCAGTTGGCGACTTTTCTGGAGGCTTTCTACCACTTCAGCGAAAAGAG	1000
CDS		TTCCACTAGCATATTGACTCATATTACAGTTCTTCTTTACACGTGGGATCCAGTTGGCGACTTTTCTGGAGGCTTTCTACCACTTCAGCGAAAAGAG	
genome	1001	CGCTGTACATCGCTTGGCTTCTTTACACAGTGTGAGGCTGCTGGGATATGCTGGCTGGGTCAACCGTCTACCGTCTGCTGCTGGCGGCAAGT	1100
CDS		CGCTGTACATCGCTTGGCTTCTTTACACAGTGTGAGGCTGCTGGGATATGCTGGCTGGGTCAACCGTCTACCGTCTGCTGCTGGCGGCAAGT	
genome	1101	TTTCAACTACTTCTTCTGGGACGAATGACGGGCAACAAAGTCAAGTCAAGTATATGGAGAAATCTGCGGATACTTACTGAATGCTCTCTCTTC	1200
CDS		TTTCAACTACTTCTTCTGGGACGAATGACGGGCAACAAAGTCAAGTATATGGAGAAATCTGCGGATACTTACTGAATGCTCTCTCTTC	
genome	1201	TCCCTTGGACAGACACACACATCCGATCCGATGGCGCATGGCAAGGATGTAATGGAGATTCAGAGATTCGTTTCGGCATCCCTTTTGATC	1300
CDS		TCCCTTGGACAGACACACACATCCGATCCGATGGCGCATGGCAAGGATGTAATGGAGATTCAGAGATTCGTTTCGGCATCCCTTTTGATC	
genome	1301	GGAGAAATGGTATGCCAAGCCTGAGGGCAACCGGAATCTTGACAACTATAACACAGGACCCCAATGGCGCTGGTGGATAGGATACAGAGGCTCTTGGCCA	1400
CDS		GGAGAAATGGTATGCCAAGCCTGAGGGCAACCGGAATCTTGACAACTATAACACAGGACCCCAATGGCGCTGGTGGATAGGATACAGAGGCTCTTGGCCA	

Figure 2B

genome	1401	1500
CDS	GAACCTGTGCGATAGGGCTCTGAAGATITGGAAAGTTGCGAGTCCAAACGAGGAACCTTATTCCTGACAAAATGGTGGATGCAATTCAGGTAAAGTTGACAGT GAACCTGTGCGATAGGGCTCTGAAGATITGGAAAGTTGCGAGTCCAAACGAGGAACCTTATTCCTGACAAAATGGTGGATGCAATTCAG	
genome	1501	1600
CDS	ATTAAGTTGAACATATTCCACAGTAACCTTTGTCTTGGGTGTCGAAATACTGACTACTTCTTGTATGCGCCCTTCAAGTGTGTCGACAGTACGCGCGCGG TGTGTCGACAGTACGCGCGCGG	
genome	1601	1700
CDS	AGCTCTTGACAAATGATTGATTCAGGTGATCCACATCCGCTTTCCAGGGTACCATAAAATGCAGGTGCAAACTCCAGAAAGTGTGTCAGCATGCAATT AGCTCTTGACAAATGATTGATTCAGGTGATCCACATCCGCTTTCCAGGGTACCATAAAATGCAGGTGCAAACTCCAGAAAGTGTGTCAGCATGCAATT	
genome	1701	1800
CDS	CAGTGTGGTAGCTGTAATCTTCAACCTTGGTGCTTCAACAGCAAACTTTGTGATGCGGCTGACTCGATGACCCCTGCTGCTACATTTTCTAGGCGA CAGTGTGG	1900
genome	1801	1900
CDS	CCAACTACTTTCGTACTGTCACATCTTCGTGCGGACGCTGATGGCTATTTCTATTTTGGCGATGCTGTGTGGAGATACTTTCCGCTGCAAAATCTGAAAG CCAACTACTTTCGTACTGTCACATCTTCGTGCGGACGCTGATGGCTATTTCTATTTTGGCGATGCTGTGTGGAGATACTTTCCGCTGCAAAATCTGAAAG	
genome	1901	2000
CDS	GTGTCAACTGCGGAGGTTCTGAGGTGCTCTCAGGATACCGGACTGCTGAGGTCAAGCTTTATGCGCTTCAAGTCCCTGCGACACGACGCGCGCGCGCAG GTGTCAACTGCGGAGGTTCTGAGGTGCTCTCAGGATACCGGACTGCTGAGGTCAAGCTTTATGCGCTTCAAGTCCCTGCGACACGACGCGCGCGCGCAG	
genome	2001	2100
CDS	GCATGGCTGCGCATTTGCTCCAAAGGACACCATCAACTGCGGATAGTTTGGCGAAGTTTGCACCTCAAAAATCTGCGGAAGTACTCTCTGTGCGGATTTTTCATCCG GCATGGCTGCGCATTTGCTCCAAAGGACACCATCAACTGCGGATAGTTTGGCGAAGTTTGCACCTCAAAAATCTGCGGAAGTACTCTCTGTGCGGATTTTTCATCCG	
genome	2101	2200
CDS	CAAGGTCCACAGATGGAGATTACGGGAAGTTTCAAGCAACGAAAGGTTGCACTGGTGAACGAGGCGATGGACCGACCAAGCATCAAGAGACCAAAATCTCTG CAAGGTCCACAGATGGAGATTACGGGAAGTTTCAAGCAACGAAAGGTTGCACTGGTGAACGAGGCGATGGACCGACCAAGCATCAAGAGACCAAAATCTCTG	
genome	2201	2278
CDS	TGGTTGGATGGGCACTCTACCGGCGCTTCAAGAGCGGAGCATCTAGAGTGGTCAAGCGGCAAGCGGCTTTGA TGGTTGGATGGGCACTCTACCGGCGCTTCAAGAGCGGAGCATCTAGAGTGGTCAAGCGGCAAGCGGCTTTGA	

Figure 3A

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1  ATCCGCCCATCGCGCTCTCTTGGCCACTGATCTCAAGCGTGATCCAAAGGTGATTCTTAGCCGCACTCAGCCAGCTACTTAGAACTCTACCCACATATCC
101  CTTATTGATACAATGGCTCCGCTCGCTGCACTCGCGCCGCGCTCTGGCGGCGAGGATACTATCTCAATGGCAAGTACCAAACTACTAAGGACTTGGCGGCTTG
      M A S T K S L R T W R L
201  TTGGCGTTGGTCTCCATGCACGCCAAAGACTTGAAGCCTTGGTCAGAAATCGGCACTCCAGTCTTTACAACAGGTTCCAGGAACAATGCCAGATCCGGCC
      F A L V S M H A K D L R P W S R I G T A V F T T G S R N N A R S G L
301  TTCTCTGTGGCCCTGTGTTTGAGAACAGCTCTTACACCTGGAGAGACTTGGAGCTGGGTCCAAACAGGATGGCCCATTTGGTTGTCTCAAGGAATC
      · S L L P L F L R T R L T P G E T W S W R P T G W P I G L L L K E S
401  CAAAAAAGCAGCGCTGTGGCGATGATGATGAATACTCGCTCTGTTTCATTATCACTGGCTGGCAATGCTCAAGATCATGGTTGTACCTGCTTTTATC
      · K K K E R V A M M H N S P L F I I T W L A M L K I M V V P A F I
501  AATAACCAGATTCCAGGACCTGTCTGTGTTTCATTCTCTTAAGTGGCCGACGCCAAGTTCTCTGTGTCGATTACGAGTTGGCACTGTCACAAAGT
      N N Q I A G P V L V H S L K V A D A K F L L F D Y E L A P V I Q K S
601  CGCTCAATGAGATCAAGGACATGGTTACAACTCTACACTGTACACCCAGGATCAAGTTCTAGGTCAACTTTACGCCAATCTGCCCGAGGCTGCTCG
      · L N E I K D M G Y N L Y T V T P K D Q V L G Q L Y A N L P E A A R
701  TCAGGTGTGGATGAGGCTCCTTCATTCTTTGGTTATGTGAAATGGCAGAACCTCAGTACCGAAGTTTTCGAAACGAGAGTGTCTCAGGAGGTGGTGATC
      · Q V L D E A P S F F G Y V E W Q N L S T E G F S N E S R Q E V V I
801  TCCGACCCCGCAGCGCTTGATTACACCCAGCGGACCCAGCGGATTCCCGAAGCTGCTATCATGGACCATGGACGTTGCCAATTTGGCTTGATCTCTTATG
      S D P A A L I Y T S G T T G F P K A A I M D H G R C N L A S I S Y G
901  GCACCTATCGCGCATCAAAACCCAGAGAACAGTTTACATCACATTTCGGCTCTATCATCTCTGCTGGAGCCATCATTTGGTCTGGGCCAGAGCTTCACGAG
      · T L C G I K P E N K V V I T L P L Y H S A G A I I G L G Q S F T S
1001 CGGATGCACCATTTGTGCGCGCAAGTTCTCGGTGACAAAGTTTTCGGCTGATTGGGTGAGTACGACGTAACATTTTCAGTACATTTCGCGGAACTC
      G C T I V L A R K F S V T K F W R D C V E Y D V T H F Q Y I G E L

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Figure 3A (cont.)

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1101 TCCGCTACCTTCTAAATGCCCCGAAAGTCCACTGGACAAGGCATAGGTTCCGATGGGTTTGGCAACGGAATGCCCGCGATGTTTGGCCAAAGT
    C R Y L L N A P E S P L D K R H K V R M A F G N G M R P D V W A K F .
1201 TTCAGCAACGATTCAATATCCCCATTATTGTTGAGTACTAAGCCATGAGCGAAGCAATGTCCTTTTGAATGTGGCCAGCAACGCGCAACCAAGG
    . Q E R F N I P I I V E Y Y A M S E G T S S L L N V A R N K R D Q G .
1301 TCCGCTGGGATTCCGTGGCCCGTGTGAGGGCCTTGACGCCCTTCACTGGTCAAGGTGACTTTGACACGAGGAGCTGATCCGCGATTAAGAAG
    . A V G F R G P V V R A L T P P V Q L V K V D F D T E E L I R D K K
1401 ACGGACTTTCCGTCTATGCCAGCCTGCTGAGATTGAGAACTGGTACCGTAGCCGACAAAGACCACTGGCGCAGCTATGCTGGTATTTCAATC
    T G L C V L C Q P G E I G E L V T L A D N K T T G A R Y A G Y F N Q .
1501 AGCAGAGCTTTCOAAGGCAAGCCTGCTCCAGAACCTGCTAGTAAGGACACATCTACTTCCGGACCGGTGACCTCTTGTACTCCAAGGACCACTACTG
    . P E V S K A R L V Q N V V K D D I Y F R T G D L L Y S K D Q Y W .
1601 GTACTTTGCTGATCCGCGAGGACACGCTACCGGTGGAAGGAGAGAGCTGTGACACCGAGATTGACAGACACTATCGCGCGTGTTCAGGGCGTGGCT
    . Y F A D R A G D T Y R W K G E N V S T A E I A D T I G R V E G V A
1701 AGTTGACTGTTTATGGCGTATCGGTCCCGGGCATGGATGGACCGCGGGCATGGCTTTGGTCTCAAGAACTCGATTGTGCAGATGGCAGGTGGA
    S C T V Y G V S V P G M D G R A G M A A L V L K N S I V Q M A G G S .
1801 GCCAGGCAAGTTCCATGTGATGAGGCTGCCCTGAACCGCTTTTTCGTCAGTTCAGCAAGGATGTGCTCAAAAACCTGCCCGCGTATGCGATTCCCTCG
    . Q A K F H V D E A A L N A F L R D L S K D V V K K L P A Y A I P R .
1901 GTTCTTGGGATTTCAGAGCAGGAACCTGAGACACCGGCAAGTTCAAGACAGAGTGGACCTGAGAGGAAGGTTTCACCTCGGTAAAGCTCAAG
    . F L R I A E Q E L E T T G T F K N K K V E L K K E G F D L G K V K

```

Figure 3B

```
2001  GAGCGGCTGTACTGTGGACACCCAGGGTGAATATGCCCCCTTTGGCGCTGCCGAGAACGACGAGATCCTCCGACGAGCCGCTGTCTTTGACCGGATGT  
      E R L Y W W T P K G E Y A P F G V A E N E Q I L A G R A R L  
2101  TTGTCAATGAAGTCATCGGCATCATCATCAAAAAAAAAAAAAAAAAAAAA
```

Figure 4A

genome CDS	1 ATGCAAGTACCAAAATCACTAAGGACTTGGGGCTTGTTCGGCTTGGTTCATGCAAGCAAAAGGTATGAACGATCGACTTGGGGGACGCACTCTGTCTCA ATGGCAAGTACCAAAATCACTAAGGACTTGGGGCTTGTTCGGCTTGGTTCATGCAAGCAAAAGGTATGAACGATCGACTTGGGGGACGCACTCTGTCTCA	100
genome CDS	101 ATGTGATTGCTTGTTCNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN 200 ATGTGATTGCTTGTTCNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN 200	200
genome CDS	201 NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN 300 NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN 300	300
genome CDS	301 NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN 400 NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN 400	400
genome CDS	401 NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN 500 NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN 500	500
genome CDS	501 CGAATGTGGGACGGAAOCTAATTTTTCGGTGGCTTTAGGTTTGTTCAGCGTTCTTTTGAGCTGATATCTTTTGGCCACTCTTGCATACCTTA 600 CGAATGTGGGACGGAAOCTAATTTTTCGGTGGCTTTAGGTTTGTTCAGCGTTCTTTTGAGCTGATATCTTTTGGCCACTCTTGCATACCTTA 600	600
genome CDS	601 GACTTGAGGCTTGGTGGAGATCGGACTGCGAGTCTTACAACAGTTCCAGGAACAATGCCAGATCCGCCCTTCTCTGTTGCCCTTGTTTTGAGAA 700 GACTTGAGGCTTGGTGGAGATCGGACTGCGAGTCTTACAACAGTTCCAGGAACAATGCCAGATCCGCCCTTCTCTGTTGCCCTTGTTTTGAGAA 700	700
genome CDS	701 CAGCTCTTACACCTGGAGAGACTTGGAGCTGGGTATGTGCACTAGCAATTTTTCGACGCTGATCTGCTGATAGAGGACATACATTAAATAAT 800 CAGCTCTTACACCTGGAGAGACTTGGAGCTGGGTATGTGCACTAGCAATTTTTCGACGCTGATCTGCTGATAGAGGACATACATTAAATAAT 800	800
genome CDS	801 TGATATCATTTTGTCTGTGCACTGCTCTATTCGATATACAGCTGCAACAGGATCGTAAGTTGGCAACTGCATACAGTACTTGTGCTCTTTATCA 900 TGATATCATTTTGTCTGTGCACTGCTCTATTCGATATACAGCTGCAACAGGATCGTAAGTTGGCAACTGCATACAGTACTTGTGCTCTTTATCA 900	900
genome CDS	901 TGGTTACTCAGGCTTCATTGCGCTCAATGTTTCCTTTGAACCTAGCCCATTTGGTTTGTCTCAAGGAATCCAAAAGAGGAGGCTGTGGCGATGATCA 1000 TGGTTACTCAGGCTTCATTGCGCTCAATGTTTCCTTTGAACCTAGCCCATTTGGTTTGTCTCAAGGAATCCAAAAGAGGAGGCTGTGGCGATGATCA 1000	1000

Figure 4A (cont.)

genome CDS	1001 1100 TGCATAACTGGCTCTGTTTCATTATCACTGGCTGGCAATGCTCAAGATCATGGTTGTACCTGCTTTTATCAATAACAGATTCCAGGACCTGTTCTGGT TGCATAACTGGCTCTGTTTCATTATCACTGGCTGGCAATGCTCAAGATCATGGTTGTACCTGCTTTTATCAATAACAGATTCCAGGACCTGTTCTGGT
genome CDS	1101 1200 TCATTCTCTTAAAGTGGCGACGCCAAGTTTCTCTCTGTTGATTAACGATTGGCACTGTCAATCCAAAGTGGCTCAATCAGATCAAGGACATGGGTTAC TCATTCTCTTAAAGTGGCGACGCCAAGTTTCTCTCTGTTGATTAACGATTGGCACTGTCAATCCAAAGTGGCTCAATCAGATCAAGGACATGGGTTAC
genome CDS	1201 1300 AATCTCTACACTGTCAACCCAGGATCAAGTTCTAGGTCAACTTTAAGCCCAATCTGCCCCAGGCTGCTGTCAAGTGTGGATCAGGCTCCTTCATTCT AATCTCTACACTGTCAACCCAGGATCAAGTTCTAGGTCAACTTTAAGCCCAATCTGCCCCAGGCTGCTGTCAAGTGTGGATCAGGCTCCTTCATTCT
genome CDS	1301 1400 TTGGTTATGTGCAATGGCAGAACCTCAGTAACGAAGGTTTCTGGAACGAGAGTGTCTCAGGAGGTGGTGTATCTCCGACCCCGCAGGCTTGATTACACCCAG TTGGTTATGTGCAATGGCAGAACCTCAGTAACGAAGGTTTCTGGAACGAGAGTGTCTCAGGAGGTGGTGTATCTCCGACCCCGCAGGCTTGATTACACCCAG

Figure 4B

1401	CGGACCAACGGGATTTCCCAAGGCTCTATCATGGAACATGGACGTTTCAACGCTGTAAGCAATCGCATAGGATCGATAGCGCTGAATCGCTCGCGAGTGGGA	1500
1501	TGCAAAATGGTCGAGATGCTTACCAATTATCGTGGTGTGCCCTTTTATAGTGGCTTCGATCTCTTATGGCACCTCTATGGCGGATCAAAACAGAGAACAAAGGT	1600
1601	TTACATCACAATTGCCGCTCTATCATTTCTGCTGGAGGTACGTCCTTCCATCTCACCGCTCAACATCTCTTAAGGAGTTTGATCCTCTTCTTACACTCAATTA	1700
1701	CTTCCTGGGCATGGGAACAAGCCATATTGCTCTGGCCAGAGCTTTCACAGGGGATGCAACCATTTGCTGGCGGCAAGTTCTCGGTGACAAAGTTTTCG	1800
1801	GGGTGCAATTGGTTGAGTACACAGTAACTCATTTTGAGGTTACAAGTCTCTATCCAATGGTCTACATACCGTCTTGTGTAATTTTCAACGGGCAACCGCCACTA	1900
1901	ACCGCTTTTATATGTATACCGGCACTACATTTGGGCAACTCTGGCGCTAGCTTCTAAATGGCCCCGAAAGTCCAGCTGGACAAAGGCCATTAAGTTTCGGAT	2000
2001	GGCGTTTGGCAACGGAAATGGCCCCGGATGTTTGGGCAAAAGTTTCAGGAAGGATTCATATGCCCATTAATGCCCATTAATGTTTGGTACTACTACGGCATGAGCGGAAGCA	2100
2101	TGCTGGCTTTTGAAATGTTGGCCAGGAACAAGCGGACCAAGGTGGAGTGGGATTCGGTGGCCCCGCTGGTGGAGTTATGGGGCATCTGGGGCTTTAGTTCCT	2200
2201	CGTGTCAATGTTTCATTATACATCTTCAGCTCAACTTTTGGCCGCTGCTTTTTCCTTTTCAATTTTGTTCCTACTAGGGCTTGACGGCTCCGGTTCA	2300
2301	CTGGTCAAGTGGACTTTTGACACGGAGGAGCTGATCCCGATAGACAAGAGGGAGCTTTGGTCCCTATGGCAGCTTGGTGGAGATTGGAGAACTTGGTCAACGG	2400

Figure 4B (cont.)

genome CDS	2401	2500
	ITAGCGACAAACAAGACGACTGGCGCAGCTATGCTGGGTATTTCATGAGCCAGAGGTTCGAAAGCAAGGCTGGTCCAGAAACGTGGTAGTGAAGGACGA ITAGCGACAAACAAGACGACTGGCGCAGCTATGCTGGGTATTTCATGAGCCAGAGGTTCGAAAGCAAGGCTGGTCCAGAAACGTGGTAGTGAAGGACGA	
genome CDS	2501	2600
	CATCTACTTCGGACGGGTGACCTCTTGTACTCCAGGACCACTACTGGTACTTTGCTGATCGCGCAGGAGACACCTACCGGTGGAAAGGAGAGAACGTC CATCTACTTCGGACGGGTGACCTCTTGTACTCCAGGACCACTACTGGTACTTTGCTGATCGCGCAGGAGACACCTACCGGTGGAAAGGAGAGAACGTC	
genome CDS	2601	2700
	TCGACAGCCGAGATTCCAGACACTATCGGCCGTGTTCAGGGCGTGGCTAGTTGTACTGTTTATGGCGTATCGGTCCCGGGCATGGATGGACCGCGCGGCA TCGACAGCCGAGATTCCAGACACTATCGGCCGTGTTCAGGGCGTGGCTAGTTGTACTGTTTATGGCGTATCGGTCCCGGGCATGGATGGACCGCGCGGCA	
genome CDS	2701	2800
	TGGCTGCTTTGGTGCTCAAGAACTCGATTGTGCAGATGGCAGGTGGAAGCCAGGCCAAGTTCCATGTGGATGAGCGTGGCTGAACCGCGTTTTCGGTGA TGGCTGCTTTGGTGCTCAAGAACTCGATTGTGCAGATGGCAGGTGGAAGCCAGGCCAAGTTCCATGTGGATGAGCGTGGCTGAACCGCGTTTTCGGTGA	

Figure 4C

genome CDS	2801 CTTGAGCAAGGATGTGGTCAAAATACTGCGGGGTATGCCATTCTCGTTCTTGGCATTTGCAGACAGGAACTCGAGACGCGGCACGTTCAAGAAG CTTGAGCAAGGATGTGGTCAAAATACTGCGGGGTATGCCATTCTCGTTCTTGGCATTTGCAGACAGGAACTCGAGACGCGGCACGTTCAAGAAG	2900
genome CDS	2901 AAGAGGTGGACCTGAACAGGAAGGTTGACCTCGGTAAAGTCAAGGAGCGGCTGTACTGTGCACACCCAAAGGTTGAATATGCCCCCTTTTGGGCTGG AAGAGGTGGACCTGAACAGGAAGGTTGACCTCGGTAAAGTCAAGGAGCGGCTGTACTGTGCACACCCAAAGGTTGAATATGCCCCCTTTTGGGCTGG	3000
genome CDS	3001 CGGAGAACGACGAGATCCTCGGAGGACGGCTCGTCTTTGA CGGAGAACGACGAGATCCTCGGAGGACGGCTCGTCTTTGA	3041

Figure 5

1 GCCTACTTTGGGCTGGCTCATCGACCCAAAGGAGCAATGGAAAGGATGCTCTTACCATGCTTTGACCATGGCCATGGCCATGGCTGGCTTGGT
 M E T D A L T I A L T I A I A I V L A L V .
 101 CAAATTCAAGCAAAAGAGCCCTGACCTGCATCCGCTCCTGCTCGGGCAGCAATCGTCTGTCAAGCCCATTCGGAACGAGGGGAGTCCGTTATCCATAGA
 · K F N E K E P D L H P L L L G Q Q S S V T P I R N E G E S V I H R
 201 TCCAAACCGTGCACACGGGACACTGCTGACGAAGCGCCCGAGCGAGAAATCAAGACTCTGCACGATGTCTGGCAGACTGGAGCAGCTGTCAACCCAG
 S K T V P H G T L L T K R P S E K I K T L H D V W Q T G A A V N P A .
 301 CCGGCCGATCGTTGATGTTTATGCTCCAGAACCGAGTTTGGCTTATCGAGGCCAGCTATGAGCAAGTCAATAGGAGGATTGGGGCTTCGGAACAGGTTT
 · G R S L M F M L Q N Q F A F I E A T V E Q V N R R I G G F G T G F .
 401 CGTGAAGCAACAGGGCTAAAGCCAAAGCAGACACACAGTAGGAATCTTTATGCCCTACTCTCAAGAATCGTTCCCTTCCGCCAGGAGGCATCTCTATCGA
 · V K A T G L K : P K T D T P V G I F M P Y S Q E S F V A Q A F Y R
 501 TACAGCTTTGTTGCTGTCCCATCCATGATCTGAGGAACAAGCAACCTCTTGGTGAGGTAGTACAGCAGACCAAGTCAAGGCCATCATAGTCTCACAA
 Y S F V A V P I H D L R N N D L L V E V V D Q T K L K A I I V S Q K .
 601 AGTGCTCCCGTTATTGCTGCAATCTCTGAAGGAGTCTCCACCATCAAGACAATCATATGCGCAGCAATCTACATCTCACAGGAGCAGCTGGAATGGC
 · V L P L L L Q S L K E C P T I K T I I M A G I Y I S Q E Q L E M A .
 701 AGCAGCATGGAGTAAGCTGCTCAAAATTGGCGGCACTGGAAATATGAGGGATCCTCGACTCTGATGAGCGCTGTTACGCCCTGATCCGGAGCATGTTGCC
 · A Q H G V K L L K F A A V E Y E G S S T L M E P V Q P D P E D V A .
 801 ATGATCAACTATAACAAAGTGGTCTTGGCTCTCGAAAGGGGTGATGCTTACCCATGCCAAGCTGATCGGGCGATGACTGCCCTTCAAGGAGTCACTTC
 M I N Y N T K S S S L S K G V M L T H A N L I A A M T A F T E S L P .
 901 CGGCAAAAGCGTTTCTCCAGCAAGATGCTTCTCTCATTTTCCATGGAGATGTCATCTCTCTTCTTCATGTGACCGCCCATCATCTCTGATGGG
 · A K K R F S S K D R L L S H F S N G D V I S V F M S S A I I L M G .
 1001 AGGTCTTTGGTCTTCCATCTGGTTTCATGAAGACGTTTTCATGATTTCCCAAGCTTCTGCAACACGATCTTTTCCAGCACACCCCATCATCTCTGGAA
 · G S L V F P S G L M K N V L H D S Q A S A P T I F A S T P I I L E

Figure 5 (cont.)

1101 AAGATTACGAAGCACTTCAGTTGACGTATGCCAAGCCTCCATGTTACGGCGCGCTTTCCTGCCAAATTGGCCATACTTCAAGCTGGAGCAATCACTA
 K I H E A L Q L T Y G Q G S M F R R G F A A K L A I L Q A G R I T T ·
 1201 CAACAAGCCTATCGGACTTGATTGGACTGGGCGAGTCCGCAACCTTGGTGGAAAGTTGCAATGGTTGTAAACAACACATCCTAOCACACCTGAGAC
 · T S L W D L I G L G E V R S K L G G K V R M V V T T H P T K P E T ·
 1301 CCTGGATTATATCAGAGCGCGCATGGGCATCCATGTCATTACCACTTACGGCAGGACAGACAGTGGGGCATTGTACACGCCCGCAACATGCTGGATTAT
 · L D Y I R A A M G I H V I T T Y G R T E T S G I V T A R N M L D Y
 1401 GCCAAGCACCTCATTAGGACCAACAGTGGTTCGAACGAGTTAAGCTTGTGGACGATGTTGCAGCTGGCTTTACAAGTGCAGACGAGCCCAACCCAC
 A N A P H L G P P V G C N E V K L V D D V A A G F T S A D E P N P R ·
 1501 GAGCGAGATCCTTATCCGAGGCCCAATGTGATGAAGTTATTACAAGAACGCCGTGCCACTTCAACGGCTATCGATGAGGAAGGTGGTTCCATTG
 · G E I L I R G P N V M K G Y Y K K P G A T S T A I D E E G W F H S ·
 1601 AGGAGAGCTGGGCACATTCCACTCCAAAGGCACCTTTAGACGTGTTGGGCAAGAGAAGACGAAAGTCTCCAGTTGGATCACCCGTATGAAAGGAGATG
 · G E L G T F H S N G T L D V L G K K K K T K S A V G S P S
 1701 CTGCATGTGCTACAGAATATAAAAGCGAGAAGATAGCTTCGGTAACCACTCAAAAAAATAAAAAA

Figure 6A

genome	1	ATGGAAGGGATGCTCTTACCATCGCTTTGACCATCGCCATCGCCATCGTCTGCTTTGGTCAATTTCACGAAACAGAGCTTCAGCTGCATCGCTCG	100
CDS		ATGGAAGGGATGCTCTTACCATCGCTTTGACCATCGCCATCGCCATCGTCTGCTTTGGTCAATTTCACGAAACAGAGCTTCAGCTGCATCGCTCG	
genome	101	TGCTCGGGCAGCAATCGTCTGTCAAGCCCATTCGGAACGAGGGCGAGTCGGTTATCCATAGATCCAAACGGTGCACACGGGACACTGCTGACGAAGCG	200
CDS		TGCTCGGGCAGCAATCGTCTGTCAAGCCCATTCGGAACGAGGGCGAGTCGGTTATCCATAGATCCAAACGGTGCACACGGGACACTGCTGACGAAGCG	
genome	201	CCCGAGCGAGAAATCAAGACTCTCCAGATGTCTGGCAGACTGGAGGAGCTGTCAACCCAGCCGGCGGATCGTTGATGTTATGCTGCAGAACCCAGTTT	300
CDS		CCCGAGCGAGAAATCAAGACTCTCCAGATGTCTGGCAGACTGGAGGAGCTGTCAACCCAGCCGGCGGATCGTTGATGTTATGCTGCAGAACCCAGTTT	
genome	301	GGTTTATCGAGGTAAGATGGACCGGCTGTAGTAACCCCGCTGTCTCTTGAGCAATATCGCAGGAGTCTCACCATTAGAGGATTTCATTCTCCTTGGCATA	400
CDS		GGTTTATCGAGG	
genome	401	CGCCACGTATGCTAACGTGTGATTCCGGTAGCCCTTCTCTGTGTGAAGATGGGTGATGTGGATCTCTAACAGATCTTGGTTCAATGGTGACACAGAGCA	500
CDS		CCACGTATG	ACCA
genome	501	AGTCAATAGGAGGATTGGCGGCTTCGGAAACAGGTTTGTGAAGCAACAGGGCTAAGCCCAACAGCGACACAGCAGTACCTTTATGCGCTACTCT	600
CDS		AGTCAATAGGAGGATTGGCGGCTTCGGAAACAGGTTTGTGAAGCAACAGGGCTAAGCCCAACAGCGACACAGCAGTACCTTTATGCGCTACTCT	
genome	601	CAAGGTACGGAAACAAGCGGTGAGTACTGATCCAGCAAGCATAGGAGTGAACCGGAGTGAGCCACCTGTTTGACCTTGCACCGCGCTCTTTACTGTA	700
CDS		CAAG	
genome	701	GAATCGTTGGTTGCCAGGAGGCAATCTATGATACAGCTTTGTGTGTCGCCATCCATGATGATCTGAGGAACAAGACCTCTTGGTGGAGGTAGTAGAC	800
CDS		AATCGTTGGTTGCCAGGAGGCAATCTATGATACAGCTTTGTGTGTCGCCATCCATGATGATCTGAGGAACAAGACCTCTTGGTGGAGGTAGTAGAC	

Figure 6A (cont.)

801	AGACCAAGCTCAAGGGCATCATAGTCTCACAAGGTGCTCGGTTATTCGTGCAATCTCTCAAGGAGTGTCCAAACCATCAAGACAATCATCATGCGCAGG	900
genome		
CDS		
901	AATCTACATCTCACAGGAGCAGCTGGAAATGGCAGGCACAGCATGGAGTAAGCTGCTCAAAATTCGGGGCAGTGGAAATATCAGGGATCTCTGACTCTGATG	1000
genome		
CDS		
1001	AATCTACATCTCACAGGAGCAGCTGGAAATGGCAGGCACAGCATGGAGTAAGCTGCTCAAAATTCGGGGCAGTGGAAATATCAGGGATCTCTGACTCTGATG	1100
genome		
CDS		
1101	GAGCCTGTTCAAGCTTGGTATGTGAAGCAAAAGTCAAGGAAATGCGGTTGCTTGATGTTGGCTGGCATGTTTGAACCAACGACCTCTTTTAATAGATCC	1200
genome		
CDS		
1201	GGAGGATGTTGCCATGATCAACTATAACACAAGTGGTCTTCCGATGGATGCTTGTGTTTTCAGTGGTAGTGTTCATAGCGGGCATGGAGATGATTGA	1300
genome		
CDS		
1301	GGAGTCACTTCCGGCAAAAAGCGTTTCTCCAGCAAGATCGTCTCTCTCAATTTTCCAAATGGAGATGTCATCTCTCTTCACTGAGCGCCAT	1400
genome		
CDS		

Figure 6B

genome	1401	CATCTGATGGGAGGTTCTTTGGTCTTTCCATCTGGTTTGATGAAGAAGTTTTCGATGATTCGCCAAGCTTCTGCCAACAGATCTTTGCAAGGTACAAG	1500
CDS		CATCTGATGGGAGGTTCTTTGGTCTTTCCATCTGGTTTGATGAAGAAGTTTTCGATGATTCGCCAAGCTTCTGCCAACAGATCTTTGCAAG	
genome	1501	ATGTTCCAGTGTGATCTGTGGATTGTCCTGGTTATTTCATGTGCAAGATACTTACGGGGCTGTTCOCATTTATTTTTCACCCCTCTAGCACACCCATCATCC	1600
CDS		CACACCCATCATCC	
genome	1601	TGGAAAGATTACGAAGCACTTCAGTTGACGTATGGCCAAAGGTCCATGTTCAGGGCCGGCTTTGCTGCCAAATTGGCCATACTTCAAGCTGGACGAAT	1700
CDS		TGGAAAGATTACGAAGCACTTCAGTTGACGTATGGCCAAAGGTCCATGTTCAGGGCCGGCTTTGCTGCCAAATTGGCCATACTTCAAGCTGGACGAAT	
genome	1701	CACTACAACAAGCCTATGGGACTTGATTGGACTGGGGAGGTCCGACGAACTTGGTGGAAAGGTTCGAAATGGTTGTACAACACAGTAACTCTCCTTTT	1800
CDS		CACTACAACAAGCCTATGGGACTTGATTGGACTGGGGAGGTCCGACGAACTTGGTGGAAAGGTTCGAAATGGTTGTACAACACAG	
genome	1801	TTACCATGGGGCTTACGTACTTGCAGCATGATATTTCGAAGATACTAACACTCTTTTTCATCAGGCTCCTGTAGTCTACCAAACTTGACAAGCTGGATT	1900
CDS		ATCCTACCAAACTTGACAAGCTGGATT	
genome	1901	ATATCAGAGCCCGGATGGGCATCCATGTCTATTACCACTTACGGCAGGACAGAGAGCTGGGGCATTTGTGACAGCCCGCAACATGCTGGATTATGCCAACGC	2000
CDS		ATATCAGAGCCCGGATGGGCATCCATGTCTATTACCACTTACGGCAGGACAGAGAGCTGGGGCATTTGTGACAGCCCGCAACATGCTGGATTATGCCAACGC	
genome	2001	ACCTCATTTAGGACCAACAGTGGGTTGCAAGAGGTTAAGCTTGTGGAGCATGTTCAGCTGGCTTTAGAACTGACAGAGCCCAACCCACGAGCCGAG	2100
CDS		ACCTCATTTAGGACCAACAGTGGGTTGCAAGAGGTTAAGCTTGTGGAGCATGTTCAGCTGGCTTTAGAACTGACAGAGCCCAACCCACGAGCCGAG	
genome	2101	GTAAGGAGTGCATATCTCTTCTGCTTCATGGGGCATATAAAGGCTCAATGGCGTTGATTCTACTCTAACAGCGTTATTTTATTTGTTCAACAATATTTT	2200
CDS			

Figure 6B (cont.)

2201	GTGCCTAGATCCTTATCCGAGGCCCCCAATGTGATGCAAGGTTATTACAGAGCCGGTGCACCTTCAAACGCTATCGATCAGGAAGGGTGGTTCCATTG	2300
genome	ATCCTTATCCGAGGCCCCCAATGTGATGCAAGGTTATTACAGAGCCGGTGCACCTTCAAACGCTATCGATCAGGAAGGGTGGTTCCATTG	
CDS		
2301	AGGAGAGCTGGGCACATTCCACTCCAGCGGCACCTTAGACGTTTGGCCAGAGAGAGAGCAAGTCTGTCAGTTGGATCACCGTCATCA	2391
genome	AGGAGAGCTGGGCACATTCCACTCCAGCGGCACCTTAGACGTTTGGCCAGAGAGAGAGCAAGTCTGTCAGTTGGATCACCGTCATCA	
CDS		

Figure 7A

1 CACAGGCTCAGTTGGCTCTGACCCGAGCCCACTCCGACCTCTGCTCTCATCTCTCCCTTGCTCTGCTCTTCAAGGTCTAACAGCATCAAC
 101 ATCAGCATCAGCATCAAGCTTCTCATCTCCCTCGTCTAAATCTCTGAAGAGTTGGCTTTGGCAATTCCAGCAATGTCCCTGACACAGAGCCGAGTCC
 M S L D Q N A Q S
 201 GTTGAGCTCCGAGCACCCGCAACCCAGGCGAGAGGCACTCTATCCGCCCAAGGCTTCGAGATGCGCTTCTCCCGCTCCACCCAGACAGCCGACACA
 V E L P G T R Q P G Q T G I Y R R K G F E N A L L A V P P S R P H I
 301 TCAAGACCATCTAAGATGGCTTCCAGCACCGGACTGAAGCTTAATCCCAACGAGCTGCGCTGGGAGCGGAGTGTAGACCGGCTGACGACACCTTTGG
 K T I Y D A F Q H G L K L N P N G A A L G S R V Y D P V T D T F G
 401 AGGCTATGCTCGGCAGACGTAATGCACAGGTGAACGACGATCACTGCTTGGCAGTGGATTGCTCAAAATTCATAAGCAGCTCCATGCTCTTGGCACC
 G Y V W Q T Y A Q V N D R I T R F G S G L V K I H K D V H G L A T
 501 GTGGCCAGAAAGTGGTCTCTGGGAATCTGGGCCATCAACCCAGGAGTGGACCATGGCTCCGAGGCTTCTCGGCCCTACAACTGGTCTCGGTGGGTC
 V G Q K W S L G I W A I N R P E W T I A S E A C S A Y N L V S V G L
 601 TTACGATACTTTGGACCCGAGGCTGTGACTTATGGCATTAATCAGCGTCACTGCTCTATTGCTTACAAAGTGTGGATCATATGGCAGCGCTGCTGA
 Y D T L G P E A V T Y G I N H A E C S I V V T S V D H I A T L L N
 701 CGAATCTTCCAAGATGCCCTGGGCTCAAAATCATCATCAGCATGGATGACCTGATCTGGGAGAGCAGGCCAGGACTGGCTCCGACCCGACCATCCTC
 E S S K M P G L K I I I S M D D L D T G R A G P G L A P T G T I L
 801 AGGACTTACGCTCAGGACAAAGGGTACTACTTTATGATTTGGTCTGAGGTGAAGCGCTGGTATTCAGCATGACGAAAGCATAGCCACCAACCTCCT
 R T Y A Q D K G V L L Y D W S E V E A V G I Q H G R K H T P P T S S
 901 CCGACGCATATAGATCTGCTATACGAGGAGACAGGCTTCCAAAGGTGGCATTTTGAOCATGCAAACTTGATGGCCCTTTTGGCCCTCCAGTGA
 D A V T I C Y T S G T T G L P K G A I L T H G N L I A L L A S S D
 1001 TGTGGCCACACCAAGTCTGGCTGACGATTGCTCATCAGTTTCTTGGCCCTGCCCTCAGCTCTTTGGTCCGGTCACTGAGGCTCTTGGCGATGGCGCCGAGA
 V A T P V L A D D C L I S F L P L P H V F G R V M E L F A M A A G
 1101 GGAAGATTGGCTACAGACGGGAGATCCTTTGGGTCTCTTGGAGGACGCTCCGACCTAAAGCCCTCCATCTTCCGCCCTGTGCCACAGACTGCTGAACC
 G K I G Y S T G D P L R L L E D V S H L K P S I F P A V P R L L N R

Figure 7A (cont.)

1201 GCGTGATGCCAAGGTGTATGCGGCACTGTTGGAGGCGCTGGACTCAGAGGGGACTGGCGGCAAGGAGATTGGCCACCAAGCTCACCATTGAGACA
 . V Y A K V Y A A T V G A P G L T G A L A R R G L A T K L T N L R E .
 1301 GGGCAAGGTTTCACCAACCCATTGTGGACCGAATCCTCTTCTCAAGCTCAAGCAACCGCTCGCGCGCAATGTGAGACTGATGTTGACTGCTCCGCT
 . G K G F H H P L W D R I L F S K V K Q A L G G N V R L M L T A S A
 1401 CCCATCTCGGCCGAGATCTTGGAAFTGCTCCGTGCGCTTCTCTGCTGCGAGTCTGTGGAGGCATATGGACAGACTGAGCGCGGTGGAGCGGCCACAAACA
 P I S A E I L E F V R V A F C C E V V E A Y G Q T E G G G A A T N T .
 1501 CCGTGATTGGCGAGACCGAGGCTGGACACGTGGTCCTCTCTCAAGCTTGTTCGAGATCAAACTGGTGATGTACCCGAGCTGAACCTACTTTGGGACCGA
 . V I G E T E A G H V G P P Q A C C E I K L V D V P E L N Y F A T D .
 1601 TAAACCATTCCTCGTGTGAGATTGTGTCCGTGGACCGGTGTCATTCCTGTTATCTCAAGGATGAGGCCAAGACCAAGGAGACCATTTGATGAGGAG
 . K P F P R G E I C V R G P G V I P G Y L K D E A K T K E T I D E E
 1701 GCGTGGCTGCACTCGGGCGGATATCCCCATCATGATGGCAAGGACCGTTACCATCATTTGACAGGAAGAAGACGTGTTCAAGCTGAGCCAGGAGAAAT
 G W L H S G D I A I M S G K G T V T I I D R K K N V F K L S Q G E Y .
 1801 ACATCCCGGAGAGAACATTGAAGGCGGTTTCCTCTCCAGGTTCCATTCAATCAACAATTCCTGGTGCAACCGGACTGACCGAGAGCTGTTTGGTGGC
 . I A A E N I E G R F L S K V P F I Q Q I L V H G D S T E S C L V A .
 1901 CATCTTGATCCACAGCGCTCAGGCTTCATCCCTTTGTGAACAAAGTGTGAGAACGTCATCTTCAACCTGAGATCTTTCAGCGCTACAGGAAGATC
 . I L I P E P E A F I P F V N K V L E N V N L Q P G D L A A Y R K I

Figure 7B .

2201	GTTAACACCCAAAGCTGCGCAGGGCTGTCTCAAAGAGCTGATCAAGCGCTGCACAAGATGCTGGATTGAAGCGCTTTTGAGATTCCAAGCGCATCCTCC V N N P K L R Q A V L K E L I K A G K D A G L K G F E I P K A I L L .
2101	TGCAATCTGAGGCATTCAOAGTCGAAAAGACAAGATGACCCGACCTTTCAGAATCAAAGACACCCTGTGTCACAGCTTAOCOGGAGCAACTGACAGC . E S E A F T V E N D K M T P T F K I K R H P V V Q A Y R E Q L T A .
2201	OCTCTACAAGAAATCCATCAAAGGAATCCAAAGCTGTAAAGAAACCCTTAGAAOCTGGCGTGCTGCCAGCAATTAAAAAAGAGAGATATTACT . L Y N E I H Q K E S K L *
2301	CTCACAGCTAAAAAAAAAAAAAAAAAAAAAAAAAAAA

Figure 8A

genome CDS	1 ATGTCCCTCGACAGAACGCCAGTGGTTGAGCTCCAGGACCCGGCAACAGGCCAGAGAGGTAACACAGGGCCAGCAGTACTGACACCGCTTTTTCAT 100 ATGTCCCTCGACAGAACGCCAGTGGTTGAGCTCCAGGACCCGGCAACAGGCCAGAGAGGTAACACAGGGCCAGCAGTACTGACACCGCTTTTTCAT
genome CDS	101 TAAGTTCCAAACCCACAGTCTTGGACATGGGGGAGACCTGCTGTGTACTGTGATTACACCCCGGGCCCGCTTCCCTTCTGCTGCTTGACCCGT 200 TAAGTTCCAAACCCACAGTCTTGGACATGGGGGAGACCTGCTGTGTACTGTGATTACACCCCGGGCCCGCTTCCCTTCTGCTGCTTGACCCGT
genome CDS	201 GTGACACCCCGCAAACTGCTCAGCTCTTCTGGCTGACCAACCTTCAATTCACTGACATGACCTTGGCATCTATGCGCCAAAGGCTTGGAGATGCGCTTCTG 300 GTGACACCCCGCAAACTGCTCAGCTCTTCTGGCTGACCAACCTTCAATTCACTGACATGACCTTGGCATCTATGCGCCAAAGGCTTGGAGATGCGCTTCTG AGGCATCTATGCGCCAAAGGCTTGGAGATGCGCTTCTG
genome CDS	301 GCGTCCCAACCCAGCAGACCGCACATCAAGACCATCTAAGATGCTTCCAGCAGGACTGAGCTTAATCCCAAGGAGCTGCCCTGGGACAGCGAGTGT 400 GCGTCCCAACCCAGCAGACCGCACATCAAGACCATCTAAGATGCTTCCAGCAGGACTGAGCTTAATCCCAAGGAGCTGCCCTGGGACAGCGAGTGT
genome CDS	401 ACGACCCGGTCAACGACACCTTTGAGGCTATGTCTGGAGAGCTATGCAAGGTGACGACCGCATCTGCTGGCAGTGCATTTGCTCAAAATTCA 500 ACGACCCGGTCAACGACACCTTTGAGGCTATGTCTGGAGAGCTATGCAAGGTGACGACCGCATCTGCTGGCAGTGCATTTGCTCAAAATTCA ACGACCCGGTCAACGACACCTTTGAGGCTATGTCTGGAGAGCTATGCAAGGTGACGACCGCATCTGCTGGCAGTGCATTTGCTCAAAATTCA
genome CDS	501 TAAGAGTCCATGGTCTTGCCACCGTGGCCAGAGTGGTCTCTGGCAATCTGGCCATCAACGACCGAGTGCACCATCGGCTCGAGGCTTCTCTG 600 TAAGAGTCCATGGTCTTGCCACCGTGGCCAGAGTGGTCTCTGGCAATCTGGCCATCAACGACCGAGTGCACCATCGGCTCGAGGCTTCTCTG TAAGAGTCCATGGTCTTGCCACCGTGGCCAGAGTGGTCTCTGGCAATCTGGCCATCAACGACCGAGTGCACCATCGGCTCGAGGCTTCTCTG
genome CDS	601 GCTACACCTGGTCTCGGCTCTTACCATACTTTGGACCGAGGCTGACCTTATGGCATTAAACGCTGAGTGTCTATTTGCTGTAACAAGTG 700 GCTACACCTGGTCTCGGCTCTTACCATACTTTGGACCGAGGCTGACCTTATGGCATTAAACGCTGAGTGTCTATTTGCTGTAACAAGTG GCTACACCTGGTCTCGGCTCTTACCATACTTTGGACCGAGGCTGACCTTATGGCATTAAACGCTGAGTGTCTATTTGCTGTAACAAGTG
genome CDS	701 GTAGGACATGAGCCATAGGACACCGCTAAAAAAACAATGCTTCTCATGACAGTATCGATAGTAAGTTATTCTTGGCGCTTGATGTTCTTA 800 GTAGGACATGAGCCATAGGACACCGCTAAAAAAACAATGCTTCTCATGACAGTATCGATAGTAAGTTATTCTTGGCGCTTGATGTTCTTA
genome CDS	801 GTGGATCATATCGCCAGCTGCTGAACGAATCTTCCAGATGCTGGGCTCAAAATCATCATCAGCATGGATGACCTCGATACTGGGACAGCAGGCGCAG 900 GTGGATCATATCGCCAGCTGCTGAACGAATCTTCCAGATGCTGGGCTCAAAATCATCATCAGCATGGATGACCTCGATACTGGGACAGCAGGCGCAG GTGGATCATATCGCCAGCTGCTGAACGAATCTTCCAGATGCTGGGCTCAAAATCATCATCAGCATGGATGACCTCGATACTGGGACAGCAGGCGCAG
genome CDS	901 GACTGGCTCCACCGGACCATCTCAGGACTTACGCTCAGGACAAAGGGTACTACTTATGATTTGCTGAGGTTGAAGCGCTCGGTATTTCAGCATGG 1000 GACTGGCTCCACCGGACCATCTCAGGACTTACGCTCAGGACAAAGGGTACTACTTATGATTTGCTGAGGTTGAAGCGCTCGGTATTTCAGCATGG GACTGGCTCCACCGGACCATCTCAGGACTTACGCTCAGGACAAAGGGTACTACTTATGATTTGCTGAGGTTGAAGCGCTCGGTATTTCAGCATGG

Figure 8A (cont.)

genome CDS	1001 ACGAAAGCATACGCCACCAACCTCTCTCGACGCATATAAGATCTGCTATACACGCGGACACACAGGCTTGCCAGTAAATATGTTGCTTTTATTGCCAAGCA ACGAAAGCATACGCCACCAACCTCTCTCGACGCATATAAGATCTGCTATACACGCGGACACACAGGCTTGCCCA	1100
genome CDS	1101 TACAGTGTGCCGATATTTTCAATGTTCAATTGCTCTCATTAGATGCATGACACTTATCATTTACTTAAGCGACTTTCTTTGGCGTTTCATAGAAAGGTGCC AAAGGTGCC	1200
genome CDS	1201 ATTTTGACCCATGGAACCTTGATCGCCCTTTTGGCTCCAGTGTCTGGCCACACACACAGTGTGCTGACGATTGCTCATCAGTTTCTTGCCCTCTGCTG ATTTTGACCCATGGAACCTTGATCGCCCTTTTGGCTCCAGTGTCTGGCCACACACACAGTGTGCTGACGATTGCTCATCAGTTTCTTGCCCTCTGCTG	1300
genome CDS	1301 ACGTCCTTGGTGGGTCATGAGGCTCTTGGGATGGCCGAGGAGAAAGATTGGCTACACACGGGAGATCCTTTGGCTCTCTTGGAGGAAGTCTGCGCA ACGTCCTTGGTGGGTCATGAGGCTCTTGGGATGGCCGAGGAGAAAGATTGGCTACACACGGGAGATCCTTTGGCTCTCTTGGAGGAAGTCTGCGCA	1400

Figure 8B

genome CDS	1401 CCTAAAGCCCTCCATCTTCCCGCTGTGGCCAGACTGCTGAACCGCGTGTATGCCAAGGTGTATGCCGCAACTGTGTGGAGCGCTGGACTCACAGGGCA CCTAAAGCCCTCCATCTTCCCGCTGTGGCCAGACTGCTGAACCGCGTGTATGCCAAGGTGTATGCCGCAACTGTGTGGAGCGCTGGACTCACAGGGCA	1500
genome CDS	1501 CTGGGCGCAAGGATTTGGCCACCAAGCTCACCAATTTGAGAGAGGCAAGGTTTCCACCAACCATTTGCGGAACGAAATCCTCTTCTCAAGGTCGAAGG CTGGGCGCAAGGATTTGGCCACCAAGGTCACCAATTTGAGAGAGGCAAGGTTTCCACCAACCATTTGCGGAACGAAATCCTCTTCTCAAGGTCGAAGG	1600
genome CDS	1601 AAGCGCTCGCGGCAATGTGAGACTGATGTGACTGTAAGTGTGCTTTTGGAMAGTAATCAAGTTTATGTAAACCCCGCCCCCCCCCTTGTGTTTATA AAGCGCTCGCGGCAATGTGAGACTGATGTGACTG	1700
genome CDS	1701 AACATTAAATGTTGTTACTGTGTGCTAGCCTCGGCTCCCATCTCGGCGGAGATCTTGGAAATTCGTCGGTGTGGAAATTCGTCGGTGTGGAGGCTGGAGGCG CCTCGGCTCCCATCTCGGCGGAGATCTTGGAAATTCGTCGGTGTGGAAATTCGTCGGTGTGGAGGCTGGAGGCG	1800
genome CDS	1801 ATATGGACAGACTGAGCGGCTGGAGCGGCGCACAAACACCGTGAATTTGGGAGAACGAGGCTGGACAGCTGGTCTCTCAAGCTTGTTCGAGATCAAA ATATGGACAGACTGAGCGGCTGGAGCGGCGCACAAACACCGTGAATTTGGGAGAACGAGGCTGGACAGCTGGTCTCTCAAGCTTGTTCGAGATCAAA	1900
genome CDS	1901 CTGTGATGTACCCGAGCTGAACCTACTTTGGCAACCAATAACCAATTCGCTCGTGTGAGATTTGTGTCCGTGGACCCGCTGCAATTCCTGTGTTATCTCA CTGTGATGTACCCGAGCTGAACCTACTTTGGCAACCAATAACCAATTCGCTCGTGTGAGATTTGTGTCCGTGGACCCGCTGCAATTCCTGTGTTATCTCA	2000
genome CDS	2001 AGGATGAGGCCAAGACCAAGGAGACCATTTGATGAGAGGCTGGCTGCACTCGGGGATATGGCCATCATGAGTGGCAAGGCAAGGCTTACCATCATTTGA AGGATGAGGCCAAGACCAAGGAGACCATTTGATGAGAGGCTGGCTGCACTCGGGGATATGGCCATCATGAGTGGCAAGGCAAGGCTTACCATCATTTGA	2100
genome CDS	2101 CAGGAAGAGAGAGCTTCAAGGTAAACAAACAGTGGGCTCTCCACAGATCTGTAGCGGCTTTTTCGCGGCACAGTACACTGAACCAACCCCTGTTT CAGGAAGAGAGAGCTTCAAG	2200
genome CDS	2201 GCTTTGTTCTCTCACTAGCTCAGCCAGGAGATACATGGCGCAGAGACATTTCAAGGGGTTTCTCTCCAGGTTCCATTCATCCAAACAAATTCCTGG CTCAGCCAGGAGATACATGGCGCAGAGACATTTCAAGGGGTTTCTCTCCAGGTTCCATTCATCCAAACAAATTCCTGG	2300
genome CDS	2301 TGCACGGGACTCGACCGAGAGCTGTTTGGTGGCATCTTGTATCCAGAGCCCTGAGGCTTCATCCCTTTGTGAACAAAGTGTCTGAGAAAGTCAATCT TGCACGGGACTCGACCGAGAGCTGTTTGGTGGCATCTTGTATCCAGAGCCCTGAGGCTTCATCCCTTTGTGAACAAAGTGTCTGAGAAAGTCAATCT	2400

Figure 8B (cont.)

genome CDS	2401	TCACCTGGAGATCTTGCAGGCTACAGGAAGATCGTTAACAAOCCAAAGCTGGGOCAGGCTGTCTCAAGAGCTGATCAAGGCTGGCAAGCATGCTTGA TCACCTGGAGATCTTGCAGGCTACAGGAAGATCGTTAACAAOCCAAAGCTGGGOCAGGCTGTCTCAAGAGCTGATCAAGGCTGGCAAGCATGCTTGA	2500
genome CDS	2501	TTGAAAGGCTACGACAGAACTCTCTTTGCTACCGTAGCGGAGGCCACTAGAGTTGAGGTGATACAGATCCACAAAAAATACTAAACAATC TTGAAAG	2600
genome CDS	2601	TCCTCTCAAAACTTGGTGTCTCTTGTACCAACAGCTTTGAGATTCCAAAGGGATCTCTCTGAAATCTGAGGCATTCAAGCTCGAAAAACGACAAGATGA GCTTGAGATTCCAAAGGGATCTCTCTGAAATCTGAGGCATTCAAGCTCGAAAAACGACAAGATGA	2700
genome CDS	2701	CCCGGACTTCAAGATCAAAAGACACACCTGTGTCTGCTCCAGGCTTACCGGAGGCACTGACAGGCTCTACAGCAATCCATCAAAAGGAATCCAAAGCTGTA CCCGGACTTCAAGATCAAAAGACACACCTGTGTCTGCTCCAGGCTTACCGGAGGCACTGACAGGCTCTACAGCAATCCATCAAAAGGAATCCAAAGCTGTA	2800

Figure 8C

2801
A A A
genome CDS

Figure 9A

1 TTTT TTTT TTTT TTTT TCTCTCTCCAAAGCCCTTTTCAACCCCTTCTACTCGGCTCGTACTCAAGGCTCAAGTCCACACTCTCGTCTCTTAGCCTGCTGCATTCA
CGATTCAATTCCTCTCTCGACTCCAGCATCGCTACTCCCTCTGCTACTCTTTCACCATGACGACCCCAATTTGTACTCCATCGAAGCTGGCAGGCACGCCACAG
ATTCCGGGGCAGGGCAAAACCTCGGGCAGCGTTCTCAGCCGACAGAAACTCGTCCAGAGCTATCAGTCTTTCAAGGGGACGGCTCCATCAACACTCTAT
IPGEGGKPRRSVLSPLSKLVQSYQSFKGDSITTLTY
ATGAGAACTTTTGGAGGCGATCCAGCGCTCAGAGGAGGACAGTTTCTCGACACGCGCCCATCGTGTGATATGTAGCTCAGCGCTACGAATCGGCTAAG
ENFLEGIQRSEGGELGHRPIVDNVAPPYEWLS
CTACAGCGCGTTACGAAACGTGTCCGCCAAGCTTTGGCGCTGTCTCATCCAGCTGGGCTGAAAGTCGACTCGAAGCTTTGGCATCTTTTCCATCAACAGG
YTRVQERVANFGAGLILQLGLKVDNSNFGIFSNR
CCGGAATGGACAATGAGTGAAGTGGAGGCTACATGTACAACTTTACATCTGTGCGGCTTTAGCAGACTCTGGGCGGCTCGGGCATCGAATACATCGTTA
PEWTMSLELAGYMYNFTSVPLLYDTLGVSAIEYIVN
ATCAGACGAGATGGACACCATCATCGCGTGGCTGATAAAGCCTCGATCCTGTTAAACATGAATCAACTCTCGGACACTCAAGAACATTGTGCTTAT
QTEMETIIASADKASILLNMMKSTLPTLKNIVVM
GGGCTGCTCGAAGACGCGCTGTTCTGAGGGTAGGAAATGGATATCCACATCGTTGCGTGGAGTCAGCTGGAACGGATCGGCTTCAACAACCCCGG
GSL EDALVVEGREMDIHIVAWSDV ERDGGFNPPA
CCAGCAACCCCTCCAAACCGGACGAGCTGGCCACCATCTGCTACAGTCAAGAACACCGGGACACCAAGGGCGGCAATCCTGACCCACAAAACCTTG
PANPPTPDVATATICTYTS GTTSGTTPKGAILTLTKNFV
TGGCTGGCCTTGCCCTGTTCCATATGATGGCAAGCACCACCAAAAGTTTTTCATCCCTCGAGCGTTGACACTCACATATCTTACCTGCCCTGGCACATGT
AGLASFSFHMMAKHKQKFFIPSSVDTHISYLP LAHV
GTTGAGCGTTTGTCTCAGGCTGTATGATTTCTGGCCGAGCTGGGATTGGGTATTACCAAGGAGACACTTTGAAGCTACTCGATGATGTGGGCATCTTG
FERLSQAVMISGAARIGVYVQGGDTLLKLLDDDVAIL

Figure 9A (cont.)

1101 CAGCCACCATCTTTGTGCGTTCCAGCACTCTTTAAGAGATTACAGAGTTCTAGCAGGTGTGAAGCAAGCGGCTCTCCAGCTTCTTAT
 Q P T I F V S V P R L F N R I Y D K V L A G V K A K G G L A A F L F .
 1201 TCAACCGCGCTTTTGAACCAAGAGCGCTAATTTGAACCGCGGTATCCTGGAGCAGCCATCTGGGATCGACTGGTATTTGGTCCAATTCGTCCGCACT
 . N R A F E T K K A N L K R G I L E H A I W D R L V F G A I R A R L .
 1301 CGGTGGCAAGTTAAGCATATTGTCTCAGGATCAGCCCTATAGCCCGGACGCTCATGGATTCTCTGGCATTTGCTTCAGTCCGCGAGCTTTATGAAGGG
 . G G K V K H I V S G S A P I A P D V M D F L R I C F S A D V Y E G
 1401 TATGACAGACGAGCAGGCTGCTGCTTTGTGTATCAGCTACAGAGGTGACTTGACCTGGGTCAAGTGGGACCCCTCAGCTGTGCTCGAAGTGAAGC
 Y G Q T E Q A A G L C M S Y R G D L T S G Q V G P P Q L C V E V K L .
 1501 TCAGAGACGTTCCGGACATGCCACTACACAAGCCAGCAAGCCCTCGCCCTCGCGGGAGATCATGCTTCGAGGCCATTGCTTTCAAGGCTATTACAA
 . R D V P D M H Y T S Q D K P R P R G E I M L R G H S V F K G Y Y K .
 1601 GGCTCCAAAGCAACAGAGGAGACACTGACCGCACAGGATGGCAAGCACTGGAGACGTTGGTGAATCGGACGAGCTTGGCCGCTTGGTGGTGTGTCGAC
 . A P K Q T E E T L D A Q G W A S T G D V G E W D E R G R L V V I D
 1701 CGTGTCAAAAACATTTTCAAGTTGGCTCANGGGAATACATTGCACTGAAAGATCGAAGCGTCTCTGGCCAAACACTACCTTGTCCGCCAGGTCCTTIG
 R V K N I F K L A Q G E Y I A P E K I E A V L A K H Y L V A Q V F V .
 1801 TCTAGCGAGACTCCTTCCAAGCGACATTGGTGGAGTTGCTCCCGATGCGGAGAGGCTAAAGCCTTGGCCGATGACCATGGCCCTGGAGGCAAGAG
 . Y G D S F Q A T L V G V V P D A E T L K P W A D D H G L G G K S .

Figure 9B

```
1901 CTATGAGAACTATGGGCTCATCCCGCTGTCAAGAAACTTTCTGAAGGAGCTCAAGAGTTTGGTGTGATAATGATCTGAAGGCTTTGACATATTG  
    . Y E E L C A H P A V K E T L L K E L K E F G R E N D L K G F E I L  
2001 AAGAACATTTCATGTACGGGGGAGCAATTCTCAATTGAGATGATCTTTTGACACCCACATTTCAAGCTGAAGAGACACACCCGGAAGAGAGTACATCG  
    K N I H V T A E Q F S I E N D L L T P T F K L K R H T A K E K Y I A  
2101 OCCAGATTGAGCTGATGTATAACGGGATCCACTGAAGAGTCTAGCCAAAGCAGATCTTTTATTACTGTCTGTTAAAAAACTACTCTAACCATCAAAA  
    . E I E L M Y N G I H *  
2201 AAAAAAAAAAAAAA
```

Figure 10A

genome CDS	1 ATGACCAACCAATTTGTACTTCATCGAAGTGGCAGGCGACGCCACAGAGATTCCGGGGAGGGCAAACTCGGGGAGGGTTCTCAGCCGAGACAACACTGGTCC ATGACCAACCAATTTGTACTTCATCGAAGTGGCAGGCGACGCCACAGAGATTCCGGGGAGGGCAAACTCGGGGAGGGTTCTCAGCCGAGACAACACTGGTCC 100
genome CDS	201 AGAGCTATCAGTCTTTCAAGGGGACGGCTCCATCACCACCTCTATATGAGAACTTTTGGAGGGCATCCAGGCTCAGTACTGACAOCCACATGGTCA AGAGCTATCAGTCTTTCAAGGGGACGGCTCCATCACCACCTCTATATGAGAACTTTTGGAGGGCATCCAGGCTCAG 200
genome CDS	301 GGCAGACTTCTCCACATGACACCGGTTTCTCTATTAAAGTTATCCCTTGGCCGCTTTGGCTTTGTGTGTTAAAGATGTGCTTAATCATAGAGGAG ACCGAG 300
genome CDS	401 GAGAGTTTCTCGGACACCGGCCCATGCTGGATTAATGTAGCTCAGCGTACGAATGGCTAAGCTACACGGCGTTTCAGGAAGCTGTGGCAACTTTTGGCGC GAGAGTTTCTCGGACACCGGCCCATGCTGGATTAATGTAGCTCAGCGTACGAATGGCTAAGCTACACGGCGTTTCAGGAAGCTGTGGCAACTTTTGGCGC 400
genome CDS	501 TGCTCTCATCCAGCTGGGCGCTGAAAGTGGACTGGAACTTTGGCATCTTTTCCATCAACAGGCGGAAATGGGTGAGTGCAGTGGCAGGATCCTTTTCTTT TGCTCTCATCCAGCTGGGCGCTGAAAGTGGACTGGAACTTTGGCATCTTTTCCATCAACAGGCGGAAATGG 500
genome CDS	601 TATGAATGGGCGGTTGGAGTCTAGATTCCATGATGGCTGGGTTGGACCGGCTCGGGCCCCAACCAACAACGTGTGGGAAACCCCAACCGACTCTA 600
genome CDS	701 ATAGAACTCCGTTCCCTCTGATTTTGGGAGCGAACAATACTATTAACTGTAGACAATGAGTGAAGTGGAGGCTACATGTACAACTTTACATCTGTGGCGCTT ACAATGAGTGAAGTGGAGGCTACATGTACAACTTTACATCTGTGGCGCTT 700
genome CDS	801 TAAGACACTCTGGGCGCTCGGCCATCGAATACATCGTTAATCAGACGAGATGGAGACCATCATCGTGGCTGATAAAGCCTGATCTGTGTTAAACA TAAGACACTCTGGGCGCTCGGCCATCGAATACATCGTTAATCAGACGAGATGGAGACCATCATCGTGGCTGATAAAGCCTGATCTGTGTTAAACA 800
genome CDS	901 TGAATCAACTCTGGGACACTCAAGACATTTGTGTTATGGGCTCGCTCGAAGACGCGCTGTTGTGAGGGTAGGGMAATGGATATCCACATCGTTGC TGAATCAACTCTGGGACACTCAAGACATTTGTGTTATGGGCTCGCTCGAAGACGCGCTGTTGTGAGGGTAGGGMAATGGATATCCACATCGTTGC 900
genome CDS	1001 GTGGAGTGAAGTGGAGCGGATGGCTTCAAGAAACCGGCGAGCGAACCTTCAACACCGGACGAGCTCCACCTCTGCTACAGCTCAGGAAACCC GTGGAGTGAAGTGGAGCGGATGGCTTCAAGAAACCGGCGAGCGAACCTTCAACACCGGACGAGCTCCACCTCTGCTACAGCTCAGGAAACCC 1000

Figure 10A (cont.)

genome CDS	1001 GGGACACCAAGTAACCTTAAGATGTCGATATGAGAAATCTCTAAATGTGGCATGCCAGCTTGAAATGAGAAATTCACCTCTCATAGACACTTGTGTCC 1100
genome CDS	1101 TTTCTCAAGTCACTCACCCTCTCTTCATTTTATCTTACGTGTATGTGTATGTAGGGGGCCAAATCTCTGACCCACAAAACTTTGTGGCTGGCCTTGGCCTGTT 1200
genome CDS	1201 CCATATGATGGCAAGCACCACCAAAAGTTTTCATCCCTCGAGCGTTGACACTCACAATCTTACCTGCCCTTGGACATGTGTTCCAGCGTTTGTCTCAG 1300
genome CDS	1301 GCTGTTATGATTTCTGGCAGCTGGATTGGGTATTACCAAGGAGACACCTTTGAAGCTACTCGATGATGCGGATCTTTCAGGCCACCATCTTTGTGT 1400

Figure 10B

genome CDS	1401 CCGTTCCAGCAGCTCTTTAACAGGATTTACGACAGGTTCTAGCAGGTGTGAAGCCAAAGGGCGGCTCTGCGAGCTTTCTTATTTCACGCGGCTTTTGAAAC CCGTTCCAGCAGCTCTTTAACAGGATTTACGACAGGTTCTAGCAGGTGTGAAGCCAAAGGGCGGCTCTGCGAGCTTTCTTATTTCACGCGGCTTTTGAAAC	1500
genome CDS	1501 CAAGAAAGGCTAATTTGAAACGGGTATCTCTGAGCAGCCCATCTGGCATGCACTGGTATTTGGTGCAATTCGTGCGCACTCCGTGCGCAAGTTAAGCAT CAAGAAAGGCTAATTTGAAACGGGTATCTCTGAGCAGCCCATCTGGCATGCACTGGTATTTGGTGCAATTCGTGCGCACTCCGTGCGCAAGTTAAGCAT	1600
genome CDS	1601 ATTGCTCAGGATCAGCCCTATAGCCCGGAGCTCATGGATTTCCTTGGCATTTGCTTCAGTGGCGACGTTATGAAGGCTATGACACAGCAGCAGCAGG ATTGCTCAGGATCAGCCCTATAGCCCGGAGCTCATGGATTTCCTTGGCATTTGCTTCAGTGGCGACGTTATGAAGGCTATGACACAGCAGCAGCAGG	1700
genome CDS	1701 CTGCTGGTTTGTTGTTATGAGCTACAGAGGTGACTTGACCTGGGTCAAGTGGGACCCCTCAGCTGTGCGTGAAGCTCAGAGACGTTCCGGACAT CTGCTGGTTTGTTGTTATGAGCTACAGAGGTGACTTGACCTGGGTCAAGTGGGACCCCTCAGCTGTGCGTGAAGCTCAGAGACGTTCCGGACAT	1800
genome CDS	1801 GCACCTACACAGCCAGGACAGCCCTGCGCCCTGCGGGGAGATCATGCTTCGAGGCGATTCAGTTTTCAGGCTATTACAGGCTCCAAAGCAAACACAGAG GCACCTACACAGCCAGGACAGCCCTGCGCCCTGCGGGGAGATCATGCTTCGAGGCGATTCAGTTTTCAGGCTATTACAGGCTCCAAAGCAAACACAGAG	1900
genome CDS	1901 GAGACACTGGACCCACAGGGATGGGCAAGGTATGGTTTGTGCACCAACTATTTCGTCAATTACGCTTAACACTGCTGTGTCATCAGCCCGCATCTGACT GAGACACTGGACCCACAGGGATGGGCAAG	2000
genome CDS	2001 AAGGTCACATTGTAACGGACATAGCACTGGAGAAGTTGGTGCAATGGACGAGCGTGCGCGCTTGGTGGTGATGCAACGCTGTCAAAACATTTTCAAGTTG CACTGGAGAAGTTGGTGCAATGGACGAGCGTGCGCGCTTGGTGGTGATGCAACGCTGTCAAAACATTTTCAAGTTG	2100
genome CDS	2101 GCTCAGCGGAATACATTGCACCTGAAAGATGGAAGCCGCTCTGGCCAAACACTACCTTGTGCGCCAGGCTTTGTCTACGCGAGACTCCTCTCCAGCGA GCTCAGCGGAATACATTGCACCTGAAAGATGGAAGCCGCTCTGGCCAAACACTACCTTGTGCGCCAGGCTTTGTCTACGCGAGACTCCTCTCCAGCGA	2200
genome CDS	2201 CATTTGGTGGGAGTTTGCTGCGCGATCGGAGACGGCTTAAGCCTTTGGCCCGATGACCATGGCTTTGGAGCGCAAGAGCTATGAAGAACTATGCGGCTCATCC CATTTGGTGGGAGTTTGCTGCGCGATCGGAGACGGCTTAAGCCTTTGGCCCGATGACCATGGCTTTGGAGCGCAAGAGCTATGAAGAACTATGCGGCTCATCC	2300
genome CDS	2301 CGCTGTCAAAGAAACCTTGTGTAAGGAGCTCAAGAGTTTGGTGTGAAATGATCTGAAAGGCTTTGAGATATTGAAGAACTATTCATGTAACGGGGAG CGCTGTCAAAGAAACCTTGTGTAAGGAGCTCAAGAGTTTGGTGTGAAATGATCTGAAAGGCTTTGAGATATTGAAGAACTATTCATGTAACGGGGAG	2400

Figure 10B (cont.)

genome	2401	CAATTCTCAATTGAGAAATGATCTTTTGGTGGAGTGGGACCCGACACAGTTTCAGAGTCAAGGATCGTATATTAACTAAGCCCTTGCTTTGGT	2500
CDS		CAATTCTCAATTGAGAAATGATCTTTTGGTGGAGTGGGACCCGACACAGTTTCAGAGTCAAGGATCGTATATTAACTAAGCCCTTGCTTTGGT	
genome	2501	AGACACCCACATTCAAGCTGAAGAGACACACACCCGCGAAGAGAGTACATCGCGGAGATTGAGCTGATGTATACCGGATCCACTGA	2586
CDS		AGACACCCACATTCAAGCTGAAGAGACACACACCCGCGAAGAGAGTACATCGCGGAGATTGAGCTGATGTATACCGGATCCACTGA	

Figure 11A

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1  TTTCCTCACCCTTCCCTCCGCTCTGCTGCACACTCCTCTCTGGCTTATACCATCCACCCCTCTAGCCCGCGCCACTTCGCCCGCCCAACCTCATCCGACTC
101 ACACCGCAATGGCTACTCAAAATGTACTCGGTGGTGGTCCCAACAGCCCGGACATTCGCCGGGAGGCAAGCCCGCGGTAGTGTCTTTGTCAGACAA
    M A T Q M Y S V V V P N S P D I P G E G K P R R S V L C P D K
201 GCTCCTGGAGAACTACCCCTCAGTGAAGCAGGCTCAAGCATCAGACCTGTACGAGAACTTCCAGAAGGTGTTCTCCGTTTCAGGGGGGGCCCATTTT
    . L L E N Y P S V K A G S T I T T L Y E N F Q E G V L R S G G A H F
301 TTGGGCCATCGTCCCATTTGTGAATGGCCAGCCTCAGGCTTACAAGTGGCAGTCTGTATGCGATGTACAGAAGCGTGTADGCACTTCCGGCGCTGGCCTGG
    L G H R P I V N G Q P Q A Y K W Q S Y V D V S K R V T H F G A G L A
401 CTCATCTCCGCTTGTCTCCAAAGCAAAAGCTTTGGAAATTTCTCTATCAACCGGCTGAGTGACCATGAGTGAGCTTGGCTGCTATATGCACAACTACAC
    . H L G L S P K Q N F G I F S I N R P E W T M S E L A G Y M H N Y T
501 CAGCTCCCCCTCTATGATACATTTGGGAGTGGCCGGATCGAGTATATCGTTAACCACTGAGATGAGATCATTCATTGCTTCGTCGCACAAAGCTTCT
    . S V P L Y D T L G V A A I E Y I V N Q T E M Q I I I A S S D K A S
601 ATCATCTCCACATGAATCAGCACTTCCAAACGTTCCAGCAATTTGCTCATGGGGAAATTTACTGACGCTCTGTCGCACAGGTAAGGAGCTCAACA
    I I L H M K S A L P T V Q T I V V M G E F T D A L V A E G K E L N I
701 TCAACATTTGTATCCTGGACCGATGTGGAAGAGCGGCTGTGAGCGGCTGTGAGCGGTGCACCCACAGCGGAGGATATCGCTACCATCTGTTACAC
    . N I V S W T D V E K S G L E R P V E A V H P T A E D I A T I C Y T
801 ATCTGAACCACTGGAACGCCAAAGGTGCTATCTTGACCCACAGAACTTTGTGCACTATCGCTTCATTCACATGATGCAAAAGCATGCGAGGTTTC
    . S G T T G T P K G A I L T H K N F V A T I A S F H M M A K H G R F
901 TTCAATCCCTCGGCTGCCGACACACATGTATCTTACCTGCCCCCTTCCACAGCTTTGAGCGCTTTGCCAGCGTGTATGATCTCGGGCGCTCGCGGTA
    F I P S P A D T H V S Y L P L A H V F E R L C Q A V M I S G A A R I
1001 TTGGTTACTACCAAGAGATAGCTGAAGCTGCTGGACATGTTGCGCTCTGATCCACCACTTTTGGCTCGCTGCTCTTTAAGCGTATCTA
    . G Y Y Q G D T L K L L D D V A V L H P T I F A S V P R L F N R I Y

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Figure 11A (cont.)

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1101 CCACAAGGTGCTTCTGGGTC AAGGCCAAGGTTGGTATCGCGGCTTCTTGTTAACGGGCATATAATTCCAGAAGGCCAACTTGGAAAGGCGCTA
    . D K V L A G V K A K G G I A A F L F N R A Y N S K K A N L R K G V

1201 CTTGAGCATCGCTCTGGGACAAGCTGCTCTTTGGACGATTCGGCGCGCTTGGGTGGCAAGCTTAAGCACATCTGTTCAGGATCTGCGCCCATCTCTC
    L E H P L W D K L V F G A I R A R L G G K V K H I V S G S A P I S P .

1301 CTGATGTGATGGATTTCCTCCGCATCTGCTTCAGCGCTGATGTGTATGAGGATATGCCACAGACAGCCAGGATTAAGTATGAGCTATCGCGG
    . D V M D F L R I C F S A D V Y E G Y G Q T E Q A A G L S M S Y R G .

1401 TCATTTCACCTCAGGACAGGTTGGCCACCTCAACTCTGCACAGAGCTCAAGTTGAAGGACATCCCTAGTATGAACATATACAGCGCGGACAAGCCTTTC
    . D L T P G Q V G P P Q L C T E V K L K D I P S M N Y S S A D K P F

1501 CCGGTCGAGAAATCATGCTTCGGCGGAAACTCTGTGTTCAAGGGCTATTACAAGCAACCAAGCACACTGAAGAACATTTGGATGCTGACGTTGGTCCA
    P R G E I M L R G N S V F K G Y Y K A P K Q T E E T L D A D G W S S .

1601 GTACCGGAGACGTTGGACAGTGGATGCCAAGGCGCTCTGGTGTGATTCGCGCTCAAGAACATCTTCAAGTTGGCGCAAGGAGAATATATTGGCGC
    . T G D V G Q W D A Q G R L V V I D R V K N I F K L A Q G E Y I A P .

1701 TGAAGAATCGAGGCTGTCTCGCCCAAGCACTTCCTGTTGCCACAGATTTTGTCTATGGCAGCTCGCTCCAGGCCACCAATTTGCCGGTGGTTGCCCT
    . E K I E A V L A K H F L V A Q I F V Y G H S L Q A T I V A V V V P

1801 GATGCTGAGACGCTCAAGTTGTGGGCTAAAGAAAACAGCTGGTGCACAGCTTACGAGGAGCTGTGGGCTCTCCCTCAGCTTCGCACACCCCTCCAAA
    D A E T L K L W A K E N K L G D K S Y E E L C A L P Q L R T T L Q K .

1901 AGGAGTTGGCTACTTTTGGCAAGAATCGGATCTGAAGGCGCTTTGAGATTCTTAAGAACATTCATGTTAICTCCGAGCAGTTTTCATTTGAGAAGCATCT
    . E L A T F G G K E S D L K G F E I P K N I H V I S E Q F S I E N D L .

```

Figure 11B

2001 TTGACCCCCACCTTCAAGCTGAAGACACATGCTGCGCAAGAGAACTATAACCCCGAAATCGACCCCATGTATGCAAGAAATCGCTTAATATAAATAATGG
- L T P T F K L K R H A A K E K Y N A E I D R M Y A E I A

2101 TTGTACTCAATATATAAAAAAAA

Figure 12A

[illegible]

Figure 12A (cont.)

801	ATGTGGAAAGAGCGGCTCTTGAGCGGCTGTGGAGCGGCTGACACAGCGAGGATATGGCTACCATCTGTACACATCTTGAACCACTTGAAGCGG	900
genome		
CDS	ATGTGGAAAGAGCGGCTCTTGAGCGGCTGTGGAGCGGCTGACACAGCGGAGGATATGGCTACCATCTGTACACATCTTGAACCACTTGAAGCGG	
901	AAAGTAAGTCAAGATCATTAATGGTGAGCGCTCCATTCCTTGGACTGAACAGTCTACTCAGCAGGTTCTTGGTTTACATGGCCAGAGGTGCTA	1000
genome		
CDS	AAAGTAAGTCAAGATCATTAATGGTGAGCGCTCCATTCCTTGGACTGAACAGTCTACTCAGCAGGTTCTTGGTTTACATGGCCAGAGGTGCTA	AGGTGCTA
1001	TCCTGACCCACAGAAGAACTTTGCTTGGCACTATCGCTTCATTCACACATGATGGCAAGCATGGCAGGTTCTTCATTCCTTGGCTGGCGACACACATGTATC	1100
genome		
CDS	TCCTGACCCACAGAAGAACTTTGCTTGGCACTATCGCTTCATTCACACATGATGGCAAGCATGGCAGGTTCTTCATTCCTTGGCTGGCGACACACATGTATC	
1101	CTAOCCTGCCCTTGCCACAGCTCTTGAGCGGCTTTTGCCAGGCTGTATGATCTCGGCGGCTGGCGGTATTTGGTTACTAOCAGGAGATACGCTGAAGCTG	1200
genome		
CDS	CTAOCCTGCCCTTGCCACAGCTCTTGAGCGGCTTTTGCCAGGCTGTATGATCTCGGCGGCTGGCGGTATTTGGTTACTAOCAGGAGATACGCTGAAGCTG	
1201	CTGGAGCATGTTGGCGTCCGCAATCCACCAATTTTGGCTGGTCTCTTTAACGGTATCTACGACAGGTTGCTTGGGTCAAGGCCAAGG	1300
genome		
CDS	CTGGAGCATGTTGGCGTCCGCAATCCACCAATTTTGGCTGGTCTCTTTAACGGTATCTACGACAGGTTGCTTGGGTCAAGGCCAAGG	
1301	GTGGTATCGCGGCTTCTTGTTTAACGGCGCATATAATTCACAGAGGCCAATTTGGAAAGGGGCTACTTGAGCATCCGCTCTGGGACAAAGCTGCTT	1400
genome		
CDS	GTGGTATCGCGGCTTCTTGTTTAACGGCGCATATAATTCACAGAGGCCAATTTGGAAAGGGGCTACTTGAGCATCCGCTCTGGGACAAAGCTGCTT	

Figure 12B

1401	genome	1500
	CDS	TTGAGCGATTTCGGCGCGCTTGGTGGCAAGTTAAGCACAATGTTGTCAGGATCTGCCCCCACTCTCTGATGATGATTTCTCTCGGCATCTGCTTC
		TTGAGCGATTTCGGCGCGCTTGGTGGCAAGTTAAGCACAATGTTGTCAGGATCTGCCCCCACTCTCTGATGATGATTTCTCTCGGCATCTGCTTC
1501	genome	1600
	CDS	AGCGCTGATGTGTATCAGGATATGCCACAGCGAAGNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
		AGCGCTGATGTGTATCAGGATATGCCACAGCGAAGNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
1601	genome	1700
	CDS	NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
		AACTGTGCACAGAGGTCAAGTTCAAGGACATCCCTAGTATGAACCTATACGACGCGGACAAGCCCTTCCGCCCTGGAGAAATCATGCTTCGGCGAAACTC
1701	genome	1800
	CDS	NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
		TGCTTCAAGGGCTATTACAAAGCACCAGGACACTGAAGAACATTGGATGCTGACGGTTGGTCC
1801	genome	1900
	CDS	NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
1901	genome	2000
	CDS	NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
		AGTACCGGAGACGTTGGACA
2001	genome	2100
	CDS	GTGGGATGCCAAGCGCGTCTGGTGGTCAATGATGGGTCAAGACATCTTCAAGTTGGCGCAAGGACAATATATTTGGCGCTGAAAGATCGAGGCTGTCT
		GTGGGATGCCAAGCGCGTCTGGTGGTCAATGATGGGTCAAGACATCTTCAAGTTGGCGCAAGGACAATATATTTGGCGCTGAAAGATCGAGGCTGTCT
2101	genome	2200
	CDS	CTGCCAAGCACITCTTGGTGGCCAGATTTTGTCTATGGGCACTGCTCCAGGGCCACCATTGTGGGGTGTGTGGCTGATGCTGAGAGCCTCAAGT
		CTGCCAAGCACITCTTGGTGGCCAGATTTTGTCTATGGGCACTGCTCCAGGGCCACCATTGTGGGGTGTGTGGCTGATGCTGAGAGCCTCAAGT

Figure 12B (cont.)

genome	2201	2300
CDS	TGTGGGCTAAGAAAACAAGCTGGGTGACAAGTCTTACGAGGAGCTGTGGCTCTCCCTCAGCTTGGCAGCTTGGCAGCAACCTCCAAAAGGAGTTGGCTACTTTTGG TGTGGGCTAAGAAAACAAGCTGGGTGACAAGTCTTACGAGGAGCTGTGGCTCTCCCTCAGCTTGGCAGCAACCTCCAAAAGGAGTTGGCTACTTTTGG	
genome	2301	2400
CDS	CAAAGAAATCGGATCTCGAAGGCTTTGAGATTCTTAAGAAACATTCATGTATCTCGAGGAGTTTCAATTGAGAAAGATCTTTTGGTGAGTGTGCTTCCG CAAAGAAATCGGATCTCGAAGGCTTTGAGATTCTTAAGAAACATTCATGTATCTCGAGGAGTTTCAATTGAGAAAGATCTTTTGG	
genome	2401	2500
CDS	AGTATGAACCACTGTGTGGTATGTAACTTGGCATTTCTGAAGCTAACTCTCGGTAACCTTCTACTTCAATTGTGAATTCTCTCTTGTGGCATACAGACG ACC	
genome	2501	2581
CDS	CCCACCTTCAAGCTGAAGAGACATGCTGCCAAAGAGAAAGTATTAACGGGAAATGGACCGCATGTATGAGAAATGGCTTAA CCCACCTTCAAGCTGAAGAGACATGCTGCCAAAGAGAAAGTATTAACGGGAAATGGACCGCATGTATGAGAAATGGCTTAA	

Figure 13

1 GGCACGAGGCTCTACTCTCCATTGCGCCACTCACTCAATTGCGCCCTCTGTCCATCACCGGCATTGCTGGTGGCGCCTTCGCGCACTCCACTCTTCTTTCA
 101 TTCCCTTCTTTACAACGGCCATCTCCCTCGCTCTGGCTTCTCCATCCAGGCTAACATGCACATCTGAATGCCACAAGACCATTCTCCAGGCTGTC
 M H I L N A T R P F S R L S
 201 TCCAACCGTAAGGAGACCTTGGCTAGGACTGGCGCCAGACGGCCCTTATGCTATCCGCGCAGACGAGCCAGCTCCTAGGCTGTGCATATGTCGAGGCAACC
 P T V R R P W L G L G Q T R P Y A I A Q T E A S P R L S Y V R G T
 301 ACGTCGGCACCCAGCTATGGAGGATCCCATCGGTGCTACTGGACAGGCTGCTCAATGCTACGCTGACCGCCTCGGACTTGTCTGTCGAAGCAGGAGC
 T V G T Q L C E D P I G A Y W D R V V N R H G D R L G L V V K H E Q
 401 AGGACCTGCACCTGGACCTTCGGTCAGTTTGGCGGCCAGGTTGATAGCCTCTGCCGTGGGCTCTATGAGTCTGGCTTGGGAAAGGCTGATCGACTGCTGT
 D L H W T F R Q F G G Q V D S L C R G L Y E S G L R K G D R L A V
 501 CTGGATCCCGAACACAGCGGCTGGCGCAGCTCCAGTAGCTACTGCCAAGTCTGGCATCATCTGCTAACTCTCAACCCCTGGCTACCGGAGGCAAGAG
 W M P N N S A W A T L Q Y A T A K S G I I L V T L N P A Y R R Q E
 601 CTACTGCAGACATTGCTTTGGTCGAGTCAAGTCATTGGTCTATGTGCCAAGTCTAAAGACTTCGAATTATAGCGAGATGTTGCTGACCTCTCTACCCAG
 L L Q T L S L V E C K S L V Y V P S L K T S N Y S E M L L D L L P E
 701 AACTCCAGTACCGAGTCGCCAATCAGCTCTTGACCGAGAGCTACCCCTCACTTCGTCAAGTCATCGTGTTCACAAATGGCTCGCAAGTCCCAGACACAGC
 L Q Y Q S P N Q L L T E K L P S L R Q V I V F D N G S Q V P E T A
 801 AAATTGAAGGATTGACAAAGTATCAGGATTTGTTGATCAAGATCCCTCGACCCGCTGTCGACGGAGCTCTTGAAAAGCAACGGCTTCGCTATCCACAAC
 K L K G L T K Y Q D L L I K N P S T A V D G A L E K E R L A I D N
 901 AGGATATCATCAATCTCCAGTTTACTACGGAACTACAGGCCCTTCCCAAGGGCGTCTCGCTGTCGATCGAAACATCTTGAATAACGGCATTCATATTG
 R D I I N L Q F T S G T T G L P K G V S L S H R N I L N N G I H I G
 1001 GAGATAACATGCGCACTGACGGAAAGGATTGCTTTGTCGCCCGCTCTTCACCTGCTTTGCACTGCTGCTGCGAAGCTTGGCTGCAATGACCCCA
 D N M R L T E K D L L C C P V P L F H C F G L V L A S L A A M T H

Figure 13 (cont.)

1101 TGGCGCAGGAATTATTACCCCTTCGCAGTCCCTTTGATGCTGAGGCCACACTGAGGGCTGTTCTGAGAGGGTGTCTACAGCGCTGCATGCGGTGCGGACT
 · G A G I I Y P S Q S F D A E A T L R A V S E E G A T A L H G V P T
 1201 ATGCTGTTGGAAGAGATGAACCCACCTTTCCAAAGTACAACTTTCCACACTTCGGACAGGAATTGCACCTGGATCCCTGTGCCCATTTGAGGTCA
 M L L E E M N H P N F A K Y N L S T L R T G I A A G S P V P I E V M
 1301 TGAAGAAGTGCAGACAAAGATGAACCTGAAGGAGCTGACTATCTGTTACGGCATGCCGAGACCTCGCCCGTGTCTTCAATGACACTCACAAACGGATGA
 · K N V Q T K M N L K E L T I C Y G M T E T S P V S F M T L T T D E
 1401 ATTACGGCATCGATCTGAGACTGTTGACCAATTATGCCACATCTCGAGGCCAAAGTCGTCAACCTGAGACGGAGAGACTTTGCCAGTGAATTCATCA
 · L R D R C E T V G R I M P H L E A K V V N P E T G E T L P V N S S
 1501 GGAGAGTTGTGCACGCCGGGTATGCTGTGATGGAGGGTGGTTACTGGCGATCCAGGAGGACAGATGCAGTGGTGGACAAGGATGGCTGGATGCCACA
 G E L C T R G Y A V M E G G Y W R S Q E Q T D A V V D K D G W M H T
 1601 CTGGCCACACTGCCGTGCTCGATGACCGTGGCTTTTCAGGATCCAGGACATCAAGGACATGGTATCCAGGAGCGCAAAAATCCATCCTGTAGA
 · G D T A V L D D R G F C R I D G R I K D M V I R G G E K I H P V E
 1701 GGTCCGAACTGTCTCTTTGAGATGGACGGCGTCAAGACCTGTCTGTGATTGGCGTTCCCGACACAGCGGTATGCGGAGCAGGTGTGTGGCTGGATCTCG
 · V E N C L F E M D G V K N V S V I G V P D K R Y G E Q V C A W I S
 1801 ACCAAGCAGCGGAAGACCGTCACTCTGGAGGCAGTGCAAAAGTTCTGTAGGGCAAGATTGGCCACTACAAGGTGCCCGGTATGTGTTGTGGTGGAGT
 T K D G K T V S L E A V Q K F C E G K I A H Y K V P R Y V V V E S
 1901 CCAATGAGTTCGGACTACCCCTCGGCAAGATCCAAAGAATGTGATGGCGAGCTGACCAAGGCAAGCTGCAGCTGCCCTTGATGGTACTAGGATAT
 · N E F P T T P S G K I Q K N V M R E L T K A K L Q L P
 2001 GGAGCCGACGAAGTAATAAGCGGTATGCTGGCATGGCCCAAGATCTGAGCCCTGCGGTGAGTGCATTCTAGTACGCCATTAG

Figure 14A

1	ATGCACATTCTGAATGCGCACAGAACAATCTCCAGGCTCTCTCCAAACCGTTAAGGAGACCTTGGCTAGGACTCGGCGACAGCGCGCCCTTATGCTATCGCGG	100
genome		
CDS		
101	AGACCGAGGCCAGTCTTAGGCTGTCTATATCTCCAGGCAACAACCGTGGCAACCACTATGCGAGGATCCCATATGGTTGGTACTTGGGACAGGGTCTGTCAA	200
genome		
CDS		
201	ITGGTCAAGGTCAACCGCTCGGACTTGTGTGTCAGGACGAGGACCTGACCTGGACCTTCCGTCAGTTTGGCGGCGACGGTTGATAGCCCTCTGCGGTGG	300
genome		
CDS		
301	CTCTATGAGTCTGGCTTGGAAAGGCTGATGAGCTGGCTGTTATGTACACTCTGCTGGCTGAAGCGCTTGAAGGGAATAAATCTGTATTGAACCCCGCGCC	400
genome		
CDS		
401	GCTGCATTAGCGTGGTTTCAACATTTGGCTAAATTTTCTCTTCCCTGGCTCTTGGCGATGCAACACAGTGTCTGATGCGGAACAACAGCGCGGTGGGCGCA	500
genome		
CDS		
601	CGCTCCAGTATGCTACTGCCAAGTCTGGCATCTTCTGGTAACTCTCAACCTCGGTATGTACTGCAATGCTAATATCACTATCGGCTCGGCTCAAAAAATA	600
genome		
CDS		
701	TGCTTTTTCAGGTGTTTACTTATCTTCCTCGCGTTCTCTATAACAGGTAACCGGAGGCAAGAGCTACTGCGAGACATTTGCTTTGGTTCGAGTGCAGAGTCATTTGG	700
genome		
CDS		
801	CTCTATGTGCAAGTCTAAGACTTCCGAATTTATAGGAGAGATGTTGGTCCAGCTTCTTAACAGAACTGACGTACCGCAATACAGTCTTTGACCGAGAA	800
genome		
CDS		

Figure 14A (cont.)

801	900	
genome		
CDS		
		GCTAACCCTCAGCTTGGTGAAGTCATGGTGTTCGACATGGCTGCCAAGTCCAGAGAGAGAGCAAAATTGAAGGATTGACAAAGTATCAGGATTTGTTGATG
		GCTAACCCTCAGCTTGGTGAAGTCATGGTGTTCGACATGGCTGCCAAGTCCAGAGAGAGAGCAAAATTGAAGGATTGACAAAGTATCAGGATTTGTTGATG
901	1000	
genome		
CDS		
		AAGAAATCCCTCGACCCCTGTGGACGGAGCTCTTGAAGAAGAAAGCCCTGGCTATCGACAGAGGGATATCATCAATCTCCAGTTTACTAGCGGAACCTACAG
		AAGAAATCCCTCGACCCCTGTGGACGGAGCTCTTGAAGAAGAAAGCCCTGGCTATCGACAGAGGGATATCATCAATCTCCAGTTTACTAGCGGAACCTACAG
1001	1100	
genome		
CDS		
		GCCTTCCCAAGTATGTGTCAGAAATTGAACCTTGACACCGGATGCGATTAATGAGCTTCAACCAACCTTGTCTCGACACCGCTCTTGCAATACTATG
		GCCTTCCCAAG
1101	1200	
genome		
CDS		
		CTCCAAATTTTAGGGGGCTCTCGCTGTGGCATGGAAACATCTTGAATAAAGGCAATTCATATTTGGAGATTAACATGGGACTTGACGGAAAGGATTTGCTTTG
		GGCGTCTCGCTGTGGCATGGAAACATCTTGAATAAAGGCAATTCATATTTGGAGATTAACATGGGACTTGACGGAAAGGATTTGCTTTG
1201	1300	
genome		
CDS		
		CTGCGCGGTCCCGCTCTTTTCACTGTCTTTGGACTGTGTGGCAAGCTTTGGCTGCAATGACCCATGGCGCAGGAATTAATTACCTTTGCCAGTCCCTTTGAT
		CTGCGCGGTCCCGCTCTTTTCACTGTCTTTGGACTGTGTGGCAAGCTTTGGCTGCAATGACCCATGGCGCAGGAATTAATTACCTTTGCCAGTCCCTTTGAT
1301	1400	
genome		
CDS		
		GCTGAGGCGACACTGAGGGCTGTTTCTGAGGAGGGTGTCTACAGCGCTCGATGGGTGGGACTATGCTGTGTGCAAGAGATGAACACCCCAACTTTGCCAA
		GCTGAGGCGACACTGAGGGCTGTTTCTGAGGAGGGTGTCTACAGCGCTCGATGGGTGGGACTATGCTGTGTGCAAGAGATGAACACCCCAACTTTGCCAA

Figure 14B

genome	1401	1500
CDS	AGTACAACCTTTGACACACTTGGACAGGAATTGACAGCTGGATGCTGTCGACATTCAGGTTCATGAAGAAGTGCAGACAAAGATGAACCTGAAGAGCT AGTACAACCTTTGACACACTTGGACAGGAATTGACAGCTGGATGCTGTCGACATTCAGGTTCATGAAGAAGTGCAGACAAAGATGAACCTGAAGAGCT	
genome	1501	1600
CDS	GACTATCTGTTAAGGCATGAOCAGACCTGGGCTGCTCTCATGACACTCACAACGAATGAATTAGGGATCGATGTGAGACTGTGGAOGAATTATG GACTATCTGTTAAGGCATGAOCAGACCTGGGCTGCTCTCATGACACTCACAACGAATGAATTAGGGATCGATGTGAGACTGTGGAOGAATTATG	
genome	1601	1700
CDS	CCACATCTGAGGCGCAAGGTAAACGGCTGTCAGCCTGGTGTTCATAATTTTGTCTTGAATCTCGGTGGTCTGTCTTAATTTTGGGTACATTGCTTGC CCACATCTGAGGCGCAAG	
genome	1701	1800
CDS	ACAATACCGTAGTCTGTCACCTGAGAGGGAGAGACTTTGCCAGTGAATTTCACAGGAGAGTTGTGCACCGGGGTATGCTGTGATGGAGGGTGGTTA TGGTCAACCTGAGAGGGAGAGACTTTGCCAGTGAATTTCACAGGAGAGTTGTGCACCGGGGTATGCTGTGATGGAGGGTGGTTA	
genome	1801	1900
CDS	CTGGGATGCCAGGACAGACATGTCAGTGGTGGACAGATGGCTGGATGCCACATGGGACACTGGCTGGTGGATGCCACATGGGACACTGGCTGGTGGATGCCAGGATC CTGGGATGCCAGGACAGACATGTCAGTGGTGGACAGATGGCTGGATGCCACATGGGACACTGGCTGGTGGATGCCACATGGGACACTGGCTGGTGGATGCCAGGATC	
genome	1901	2000
CDS	GACGAGGCATCAAGGACATGGTGTATGAGGAGGCGCAAAATCCATCTGTAGAGTGCAGAACTGTCCTTTTGTAGATGGAGCGGTCAAGAACGTGT GACGAGGCATCAAGGACATGGTGTATGAGGAGGCGCAAAATCCATCTGTAGAGTGCAGAACTGTCCTTTTGTAGATGGAGCGGTCAAGAACGTGT	
genome	2001	2100
CDS	CTGTGATTGGGTTCCGACAAAGCGGTATGGGAGAGGCTGTGCTGGTGGATCTCCACCAAGGACGGAGACGGTTCAGTCTGGAGGCAGTGCACAAAGTT CTGTGATTGGGTTCCGACAAAGCGGTATGGGAGAGGCTGTGCTGGTGGATCTCCACCAAGGACGGAGACGGTTCAGTCTGGAGGCAGTGCACAAAGTT	
genome	2101	2200
CDS	CTGTGAGGGCAAGATTGCGCACTACAGGTGCGGCTATGTGGTTGTGGTGGATGCAATGAGTTCGACCTACCGGCTGGGCAAGATGCCAAAGAAAT CTGTGAGGGCAAGATTGCGCACTACAGGTGCGGCTATGTGGTTGTGGTGGATGCAATGAGTTCGACCTACCGGCTGGGCAAGATGCCAAAGAAAT	

Figure 14B (cont.)

2201	GTGATGCGCGAGCTGACCAAGCGGAGCTGCGAGCTGCTTGA	2242
genome		
CDS	GTGATGCGCGAGCTGACCAAGCGGAGCTGCGAGCTGCTTGA	

Figure 15A

1 TGCTTTCTCTGTCACCGCTCCTCTTCCCATTCCTCCGCTCCTCCGTTCCCTAATCAGTTTCTCAGACCGCTGTCCATTGCTCTGGGCTCCACA
 101 CACACCCCACTCTCCCTTGACAAATACCTTATCCAGATCAAGACAGATGCCCTTCTTCAAAGAAGTACAACTCCAGACGACAGAGTGTGAGCTCCCTGGC
 M P S F K K Y N L D K Q S V E V P G
 201 ACTCGGAAGCCTGCGGCTTACAGCCACTACAGACATGCGGCTACGGGATGCTCTCTGTCAACAACATCCGTGAGGCGCCCTCATATCGAAACTCTTTACG
 T R K P G A S G H Y R H A A Y G D A L V T N I R E A P H I E T L Y D
 301 ACATGTGCAGAACTCTGTACAAGTATGGGCGCAATGACTTTTGGGTCACGCTCCCTTCAACACTGTTCGCCACAGCTATGGTGGCTACAGTTGGGA
 . M W Q N S V T K Y G G N D F L G H R P F N T V A Q T Y G G Y S W E
 401 GACGTACCGCCAGATTAAACCAGGCGTTAATGCGTTCCGACAGGCTATCATGCAACCTGCAACGAGGTGATCCCTGGCAACCGGACAGCTTAACCGCTGGCG
 . T Y R Q I N Q R V N A F G S G I M H L N E V I L G N R Q L N R W A
 501 TTGGGCATCTGTGCCACCGCTGCGCTGAGTGGTTTATTACGAGATGAGCTGCAACCTGCTACAACCTCATTTCTTTGCCATTGTACGACACCCCTTGGAC
 L G I W S H G R P E W F I T E M S C N C Y N L I S V A L Y D T L G P
 601 CTGATGCAGTCGAGTACATTGTCAACCGCGGAGATTGAGATTGTGTCTCAAGTGGCAACCATATGCGCTCTTTGGTCGAGAACCGCGAGAACGCTCCC
 . D A V E Y I V N H A E I E I V S S A N H I A S L L E N A E K L P
 701 CAAGCTCAAGGCCATTGTGAGCATGGATGCTCTTCAAGATACCGTCCGCTCCGCGGCGCCACCTCTGCGGACAGAGTTCTTCTGCTGCGGTGGGTGCACAA
 . K L K A I V S M D A L H D T V P V P G A T S A A Q V L R A W G A Q
 801 AAGGCATCAAGGTCTATGACTTTAAGGAGATTGAGTCCTCGGTCCGAGTTCCCTCGCAAGCACCTGCTCCACCGCTGATGAGGTGGCTCCATCT
 K G I K V Y D F N E I E S L G A E F P R K H L P P T A D E V A S I C
 901 GCTACACTTCGGGCAACCGGTACGCTAAAGGAGCCATGCTCACCCACAGAACTTTGTGTACTCTTGTGTACCAACCGGACGGCATGCTTCTCAG
 . Y T S G T T G Q P K G A M L T H R N F V A T V G T N R E G M L L T
 1001 CCAGGACGAGCTTTTGATCAGTTTCTTGCCCTTGCGCTCACATTATGGACCGGCTCATTCACACTTCTCGATGTACAGGGTGGCAAGATTGGTTACTTC
 . E D D V L I S F L P L A H I M G R V I D T C S M Y S G G K I G Y F
 1101 CGTGGAGATATTCTTTGCTTCGAGGAGGTTGCTCAGTCGCTCCACAGATTCTTCCAGCTGTGCCCTCTTCAACCGGATTTATGCCAAGCTCG
 R G D I L L L L E D V A E L R P T F F P A V P R L L N R I Y A K L V

Figure 15A (cont.)

```

1201 TTGCTCTACCAATTGAGGCCCCCGGTTTGGTGGTGCCCTTGGCCGGTGTGGCCGCCAAGATGGCCAACTTGTCTCCGCAAGGGTGTCAACCA
    . A S T I E A P G L V G A L A R R G V A A K M A N L A A G K G V N H .

1301 CCGTCTCTGGGACAGACTGCTGTTCAACAAGGTCAAGATGGCCCTGGTGGTTCAGGTTCATCCTGACTGGATCTGGGCCCATTTGCCAAGGAGGTT
    . A L W D R L L F N K V K M A L G G R V Q V I L T G S A P I A K E V

1401 CTCAGCTTCTTGAGAAATTGCTTTGCGATGCGTGGTTTTCAGGGAATACGCTCCACTGAGGGCATGGCTACCGCACCATCACAATGGCTGATGAGTACA
    L S F L R I A F G C V V L E G Y G S T E G M A T A T I T M A D E Y I .

1501 TTCTGGTCACATTGGCTGCGCTGCTGGATGGAGCTCAAGCTGGTGGATGTGGCCGGATGAACCTCTCTACCGACCGCCCTACCCCGCTGG
    . P G H I G C P R A G C E L K L V D V P A M N Y L S T D Q P Y P R G .

1601 AGAGATCTGGATCCGTGGTCACACTGTTTCAAGGATACCTTCAAGGACGAGAGAACACTAGTGAGACTATCGACTCTGAAGGCTGGCTCGCTACCGGT
    . E I W I R G D T V F K G Y F K D E K N T S E T I D S E G W L A T G

1701 GATATTGGATTGTGGATAAGCGTGGATGCTTTACGATCATTGACCGCAAGAGAACATCTTCAAGTTGGCCACAAGGTGAATACATTGCTCTCGAAAGA
    D I G F V D K R G C F T I I D R K K N I F K L A Q G E Y I A P E K I .

1801 TTGAGAACGCTCTTGGGGCCAGCGTGCATCTTGTCCAGCAGATCTATGTTCAATGGTGATTCGGCTTGAGTCCACCTTGGTGGCAGTTCTTATTCCCGAGCC
    . E N V L G A R C N L V Q Q I Y V H G D S L E S T L V A V L I P E P .

1901 CGAGACCTTCCCTGCGCTTCGCGAATGCCATTGCTGGTCCGCTCACCTGCTGAGATGTTGAGGGTTTCAACAAGCTGTGCCAAGATCCCAAGGTCAAG
    . E T F L P F A N A I A G A S V T A G D V E G L N K L C Q D P K V K

```

Figure 15B

```
2001 ATCGCGGTTCTGAAGGAGTTGAGAGCGCGGAAAGCGCGTGGGATTCGAGTTGTAAGCGTGTCCACTTGACACCGGATGCATTCTCGG
    I A V L K E L E K A G K A G A M R G F E F V K R V H L T T D A F S V .
2101 TCGACAACGGCATGATCAGACCTACCTTCAAGGTCCGTCGCCACAAAGTAGCCAGCATTTTCAGGGAGCAAAATCACGGCCCATGTATAAGGAGATCAATGC
    . D N G M M T P T F K V R R P Q V A E H F R E Q I T A M Y K E I N A .
2201 CTGACCCCTGTTGCCAAGCTGTACATACAAACCTCTTTGCCCTTATTACCTTTGAATAGAAAGGTGACACGTTGTTGATTCACACAAAAA
    . S T P V A K L
2301 AAAAA
```

Figure 16A

genome CDS	1 ATGCTTCCTTCAAAAAGTACAACCTCGACACGACAGTGTTCAGGTCCTCGGACTCGGAGGCTTCCGGCTTCAGGCAAGTTTGATAGTGGCTCATGAG ATGCTTCCTTCAAAAAGTACAACCTCGACACGACAGTGTTCAGGTCCTCGGACTCGGAGGCTTCCGGCTTCAGGCAAGTTTGATAGTGGCTCATGAG	100
genome CDS	101 ATGCAACTGTTGGGCCACGCTACCATGAACTAGTGGCTAATGCAGATTCTCTATTGCTTTCAACCTTCTCAGAGCTACAGACATGCCGCCCTAAGG GCCACTACAGACATGCCGCCCTAAGG	200
genome CDS	201 CGATGCTCTTGTCAOCCAAACATCCGTGAGGCCCTCATATCGAACTCTTTAGACATGTGGGAGAACTGTAAAGTTGATTCCCGAGGACCTCGGAAATCTT CGATGCTCTTGTCAOCCAAACATCCGTGAGGCCCTCATATCGAACTCTTTAGACATGTGGGAGAACT	300
genome CDS	301 TACTGGATCTGTCTCACAAGAAAGACTCACACTCTGCTCTCCACAATTACCTTGTAACTTCAGCTGTGACAAAGTATGGCGCAATGACTTTTGGGTG CTGTGACAAAGTATGGCGCAATGACTTTTGGGTG	400
genome CDS	401 ACCGTCCCTTCAACACTGTTGCCAGACCTATGGTGGCTACAGTTGGGAGAGCTACGCCACAGATTAAACAGGGTTAATGGCTTCGGCAGCGGTATCAT ACCGTCCCTTCAACACTGTTGCCAGACCTATGGTGGCTACAGTTGGGAGAGCTACGCCACAGATTAAACAGGGTTAATGGCTTCGGCAGCGGTATCAT	500
genome CDS	501 GCACTGAACGAGGTGATCCTCGGGAACCGCCAGCTTAAACCGTGGGGTTGGGCATCTGGTCCACAGCTCCGCTGAGTGGTTCAATTACGGAGATGAGC GCACTGAACGAGGTGATCCTCGGGAACCGCCAGCTTAAACCGTGGGGTTGGGCATCTGGTCCACAGCTCCGCTGAGTGGTTCAATTACGGAGATGAGC	600
genome CDS	601 TGCACCTGCTACAACCTCATTTCTGTTCATTGTACACACACCTTGGACCTGATGAGTCCAGTACATTGTCAACCAACCGCCAGATTGAGATTGTGTCT TGCACCTGCTACAACCTCATTTCTGTTCATTGTACACACACCTTGGACCTGATGAGTCCAGTACATTGTCAACCAACCGCCAGATTGAGATTGTGTCT	700
genome CDS	701 CAAGTGGTAAGTGGCTTTTCTTTTCTATTGGCGGCTGCTGCTGCACTGAAACTATAATGTTTCTGATCTCCCTTTTGTGTACCTCT CAAGTG	800
genome CDS	801 CCTTTCCATCAACTCTTTGTAATTATTCGCGGCAATTGACTCTATATGCACCAACCATATCGCTCTTTGCTGAGAAACCGCCAGAGCTCCGCCAA CCAAACCATATCGCTCTTTGCTGAGAAACCGCCAGAGCTCCGCCAA	900
genome CDS	901 GCTCAAGGCCATTGTCAAGCATGGATGCTCTTCAGATACGGTCCCGTCCCGGGCCACCTCTCGCGCACAGGTCTTCTGCTGGGGTGCACAAAG GCTCAAGGCCATTGTCAAGCATGGATGCTCTTCAGATACGGTCCCGTCCCGGGCCACCTCTCGCGCACAGGTCTTCTGCTGGGGTGCACAAAG	1000

Figure 16A (cont.)

genome CDS	1001 GGCATCAAGGCTATGACCTTTAAGAGATTGAGTCCCTCGGTCCGAGTTCCCTGCCAAGCACCTGCCTCCACCGGCTGATGAGTGGCTCCATCTGCT GGCATCAAGGCTATGACCTTTAAGAGATTGAGTCCCTCGGTCCGAGTTCCCTGCCAAGCACCTGCCTCCACCGGCTGATGAGTGGCTCCATCTGCT	1100
genome CDS	1101 ACACTCCGGCACCAACCGGTCAGGCTGTAAGTGTGTTTCCCTTCACTGAGGATGTCCGCTGAGGATGCAATTTTCTGATTGAAACTTCCCATCTAACAT ACACTCCGGCACCAACCGGTCAGGCT	1200
genome CDS	1201 CGCTTGATCTATACAAAGGAGGCAATGCTCACCACAGAAACTTTGTGCTACTGTTGTATCCGAAACCGGAGGAGATGCTTCTGCACCGAGGACGCTTTT AAGGAGGCAATGCTCACCACAGAAACTTTGTGCTACTGTTGTATCCGAAACCGGAGGAGATGCTTCTGCACCGAGGACGCTTTT	1300
genome CDS	1301 GATCAGGTATACTCATCTTGAAGCTGATCAATGACACCGGATGTACAAACCGGACGATGCGAGGAGATCTACAAATGCCGGAATGGCTCAGCTCCGGTTTAC GATCAG	1400

Figure 16B.

genome CDS	1401 AATTACACACTTCTAGTTTCTTGGCTCAGATTATGGGAGGCGTCAATGACACTTCTCGATGTACAGGGTGGCAAGATTGGTTACTTCCGGTG TTTCTTGGCCCTTGGCTCAGATTATGGGAGGCGTCAATGACACTTCTCGATGTACAGGGTGGCAAGATTGGTTACTTCCGGTG	1500
genome CDS	1501 GAGATATTCTTTTGGCTTCTCGAGGAGCTTCTCAGCTGGTCCACATTTCTTCCAGCTGTGCTCGCTCTTGAACCGCAATTTATGCCAAGCTGGTTGG GAGATATTCTTTTGGCTTCTCGAGGAGCTTCTCAGCTGGTCCACATTTCTTCCAGCTGTGCTCGCTCTTGAACCGCAATTTATGCCAAGCTGGTTGG	1600
genome CDS	1601 CTCTACCAATTGAGGCCCCGGTTTGGTGGGTCCCTTGGGCGGTGGCGGTGGTCCAGCTGTGCTCGCTCTTGAACCGCAATTTATGCCAAGCTGGTTGG CTCTACCAATTGAGGCCCCGGTTTGGTGGGTCCCTTGGGCGGTGGCGGTGGTCCAGCTGTGCTCGCTCTTGAACCGCAATTTATGCCAAGCTGGTTGG	1700
genome CDS	1701 CTCTGGACAGACTGCTGTTCAACAGGTCAAGATGGCGCTGGGTGGTGGTTCAGGTTCATCTCTGACTGGATCTGGGCCAATTTGCCAAGGAGGTCTCA CTCTGGACAGACTGCTGTTCAACAGGTCAAGATGGCGCTGGGTGGTGGTTCAGGTTCATCTCTGACTGGATCTGGGCCAATTTGCCAAGGAGGTCTCA	1800
genome CDS	1801 GCTTCTTGAGAAATGCTTTCCGATGGGTGGTTTGGAGGGATACGGCTCCACTGAGGGCATGGCTACCGCACCATACAAATGGCTGACTAAGTGAAAGCT GCTTCTTGAGAAATGCTTTCCGATGGGTGGTTTGGAGGGATACGGCTCCACTGAGGGCATGGCTACCGCACCATACAAATGGCTGACTAAGTGAAAGCT	1900
genome CDS	1901 AGTTATTTTATTGAATGTCTGGAGCCTGTGGACTGTAGATTTCATCTAACCATTTACTAATCTTTTCAAAATAGTCAGTACATTCTCTGGTCACATT TGGAGTACATTCTCTGGTCACATT	2000
genome CDS	2001 GGCTGGCCCTGCTGCTGGATGGAGCTCAAGCTGGTGGATGTGGCGGATGCACTAOCCTCTCTACGGACAGGCCCTACCCCGTGGAGAGATCTGGATCG GGCTGGCCCTGCTGCTGGATGGAGCTCAAGCTGGTGGATGTGGCGGATGCACTAOCCTCTCTACGGACAGGCCCTACCCCGTGGAGAGATCTGGATCG	2100
genome CDS	2101 GTGGTGACACTGTTTTCAAAGGATACTTCAAGGACAGAGAACACTAGTGAGACTATGCATCTGCAAGCTGGCTGGCTACCGGTGATATTGGATTTCG GTGGTGACACTGTTTTCAAAGGATACTTCAAGGACAGAGAACACTAGTGAGACTATGCATCTGCAAGCTGGCTGGCTACCGGTGATATTGGATTTCG	2200
genome CDS	2201 GGATAAGCGTGGATGCTTTACGATCAATTGACCGCAAGACAGACATCTTCAGGATATGAGCAAAAGTGGGATTCATCTGATCTGTTCTCTCTGCTTTTC GGATAAGCGTGGATGCTTTACGATCAATTGACCGCAAGACAGACATCTTCAGGATATGAGCAAAAGTGGGATTCATCTGATCTGTTCTCTCTGCTTTTC	2300
genome CDS	2301 CGGTTAAGGAATTCGGCTCATACTAACGTTCTCTGCTCAATGGTTTGCATGTATTATAGTTGGCACAGGTGAATACATTGCTCTGAAAGATTTCAGAACG TTGGCACAGGTGAATACATTGCTCTGAAAGATTTCAGAACG	2400

Figure 16B (cont.)

genome CDS	2401	2500
	TCTTGGGCGCAGCCCTGCAATCTTGCCAGCAGATCTATGTTTCATGGTGATTGGCTTCAGTCCACCTTGGTGGCAGTTCCTATTCCCGAGCCCGAGACCTT	
	TCTTGGGCGCAGCCCTGCAATCTTGCCAGCAGATCTATGTTTCATGGTGATTGGCTTCAGTCCACCTTGGTGGCAGTTCCTATTCCCGAGCCCGAGACCTT	
genome CDS	2501	2600
	CCTGGCCCTTCGGCAATGCCAATTCCTGGTGGCTGGCTCACTGCTGGAGATGTTGAGGGTTTGAACAAGCTGTGCCAAGATGCCAAGGTCAAGATCGCGGT	
	CCTGGCCCTTCGGCAATGCCAATTCCTGGTGGCTGGCTCACTGCTGGAGATGTTGAGGGTTTGAACAAGCTGTGCCAAGATGCCAAGGTCAAGATCGCGGT	
genome CDS	2601	2700
	CTGAAGGAGTTGGAGAGGGCGGAAAGGGCGGTGGATGGCGGATTCGGATTCGTGAAGGGTGTCCACTTGACCAAGGATGCATTCTGGGTGGACAACG	
	CTGAAGGAGTTGGAGAGGGCGGAAAGGGCGGTGGATGGCGGATTCGGATTCGTGAAGGGTGTCCACTTGACCAAGGATGCATTCTGGGTGGACAACG	
genome CDS	2701	2800
	GCATGATGACACCTACCTTCAAGGTCCGTCCGCCACAGTAGCCGAGCATTTTCAGGGAGGCAATTCACGGGCATGTATAGGAGATCAATGCCCTGGACCCG	
	GCATGATGACACCTACCTTCAAGGTCCGTCCGCCACAGTAGCCGAGCATTTTCAGGGAGGCAATTCACGGGCATGTATAGGAGATCAATGCCCTGGACCCG	

Figure 16C

2801	2816
TTGTTGCCAAGCTGTAG	TTGTTGCCAAGCTGTAG
genome	CDS

Figure 17

1 TGGCTATCTATCACCCTCACTCCCACTCCGGACTCTGCTCTTCTCTCTCTCAACGTCGGCACTGTCTCTACTTCTTTACCACCCA
 101 CGCATCAGTCACAGCATGGTTGCTCTCCCACTCGTCGGACGAGCTGTCCAGCTGCATGTATGTGAGCTCAAGCTGGCACTTCTCTCGGATATGAAGT
 M V A L P L V A A A V P A A M Y V S S K L A L P R D M K L
 201 TGATTAGAGCTTGATCGGAGCCAAAGATGGCCTACAGTCCATGGAAAGAACGAGCCCTCAACCTGACACACTCCGCTTCGACGAGTGTACCGCAAGTA
 I K S L I G A K M A Y S A M E K N D A L N L T L R F D E C Y R K Y
 301 TCCTGACCGTGAAGCCCTGGTCTTTGAGGGCAATCCTATTCAATTCGCTGATATTGAGCTTCCTCCAACAGCTGGGCAACTGCTTGTGGCCAAAGGG
 P D R E A L V F E G K S Y S F R D I Q L A S N R C G N W L L A K G
 401 ATCAAGCGAGGAGATATCGTCTCGCTTTTCATGTTGAACAGCCGAGATTCATCTCTGTGGCTGGTCTCAACAAGATTGGAGCCACTGGTGCCTTCA
 I K R G D I V S L F M L N R P E F I F C W L G L N K I G A T G A F I
 501 TCAATACCAACCTTACGGGCAACCCCTGACACATTCCCTCCGACAGCCAGCTGCTCAATGTTGATCATGGACACGGAGTTGACAGACCGGATCCGCCAA
 N T N L T G K P L T H S L R T A T S S M L I M D T E L T D A I A N
 601 CTCCTGGATGAGATTGAGGATGGGCTATTCAATTTACTCTTACGACCCGAGCCGTGGACTTTGCTACCCCGATGGATATCTCGCAGGTCCAGAC
 S L D E I Q E M G Y S I Y S Y G P E A V D F A T P M D I S Q V P D
 701 ACCGATACACCCGAAACACCTCCGCGGAAACAGACCGGGATGACATTGGCATGCTCATCTACACCTCTGGAACCTACTGCTCTTCCCAAGCCCGGTGCTG
 T D T P E H L R R N T T A D D I A M L I Y T S G T T G L P K A G R V
 801 TCTCTATGCGCGTGCCTCTATGGGACCTCAGTTTGGAAACCGATTCTATCATTGAGAGCGAGAGGGTCTATCTGTCCCTTGCCTTGTACCAACAG
 S H A R A S M G P Q F W N R F Y H F S E S D R V Y L S L P L Y H S
 901 TGCTGGCGCATCTTGGGAGTGATTGCTTGTGGACCTCGGAGCAACCTTGATCTGCGCGCAACTTCTCCGCGACACATTTCTGGGAGGATTGCGCG
 A G A I L G V I A C W T S G A T L I L A R K F S A T H F W E D C R
 1001 GTGAACAACCGCAACTGTGATTCAATACATTGGAGAAATTTGCAGATATCTCTCAACAGCCGACAGATCAACCCCTGGACAGGCACACTCGATACGACTGG
 V N N A T V I Q V I G E I C R Y L L N T P E S P L D K A H S I R L A

Figure 17 (cont.)

1101 CACATGCTAATGGAATGGACCCGATGCTCTGCACTCGCTTCAGAGATCGGTTGGCATCCCGTTGATTTGGCAGCTGGTATGCATCGAGGGAACCTGG
 . H G N G M R P D V W T R F R D R F G I P L I G E W Y A S T E G T G .
 1201 AGCCTTGTCTGAATTATAACACAGGCCCGCCGCGCTGGAGGATTGGATACCGCGGTACGCTTGCACAGCATTGGATAAAGCACTCAGGATTGGGAGA
 . A L S N Y N T G P G G A G A I G Y R G T L A R A L D K G L R I A R
 1301 TTTGATGTCAGACAGAGGAGTTGGTTGGGACAAAAACGGTTATTGCATTGAGTCCAAACCTGGCAGACCCCGAGAAATTGCTGACCGCTTGTTCATGCTA
 F D V Q T E E L V R D K N G Y C I E C K P G E P G E L L T L V D A K .
 1401 AAGAGCCGACAAAGACTTCAAAGGATACCATCAAAACAGGAGCGACCAACAAAAAGATTGTCAAGATGCTTTCAAGCGCGGACATGTACTTCG
 . E P N K D F K G Y H Q N Q A A T N K K I V K D V F K A G D M Y F R .
 1501 TACCGGAGATATCCTTCGGCGCGATAGCGATCGGTACTTTTACTTTGGCGACCGTGTGGCGGATACATTCCCGTGGAACTCCGAGAAATGCTGTACGGCC
 . T G D I L R R D S D G Y F Y F G D R V G D T F R W K S E N V S T A
 1601 GAGGTGCTGAAGTCTCTCCGACTATCCGACTGTATCGAAGTCAATGTGTATGAGTTCCAGATCCAGGCGAGGACCGCCCGGTATGGCAGCGA
 E V S E V L S Q Y P D C I E V N V Y G V Q I P G Q D G R A G M A A I .
 1701 TTGTGTCCAAGAGACGATGGATTGGGAGAAATTTGGCGCGTATGCACCTCAAGAACCTGCGCGGTATTCTGTCCGATCTTTATCCGCAAGATGCCCGA
 . V S K S T M D W E K F A A Y A L K N L P R Y S V P I F I R K M P E .
 1801 GATGGAGATCAGGGACGTTCAAGCAGCGCAAAAGTCGAGTTGGTGAATCAGCGGAATCGACCCCAAGACGATTGCCAACGAGATGCTGTGGTTGGACGGA
 . M E I T G T F K Q R K V E L V N E G I D P K T I A N E M L W L D G
 1901 CACCACATATAGCGGTTCAAGGCGCGGAGCACCAGCGCTCATCAGCGGCAAGGCCAAGCTATAGTAGGGCGCGTGGCCCAATGCCAGTAGCAATACTAT
 H H Y K P F K A A E H Q R V I S G K A K L
 2001 TCCCCGCTTTGTCCATTAAAAAATAAAAAAAAAAAAAAAAAA

Figure 18A

genome	1	ATGGTTGGTGAGTAAACAGCGATCGCCCTGGGTCCAAATCGACTCATCTGCTAAATCTGATCTCACAGCTCCCTTATCAATTCACAAAGAAATAAAGAGA	100
CDS		ATGGTT	
genome	101	CAAGACAGAGAATTACTAACATTGGCTCTCTCCCTCGTGTGCGATGCGAGCTGCCACTGTCAGCAGGTGTCCACAGCTGCCATGTAATGTGAGCTCAAAG	200
CDS		CGTCTCCCACTCGTCCAGCAGCTGTCCACAGCTGTCCACAGCTGCCATGTAATGTGAGCTCAAAG	
genome	201	CTGGCACTTCCTGGGATATGAAGTTGATTAAAGAGCTTGATCGAGCAAGATGGCTACAGTGCATGGAAGAAGACGAGCCCTCAACCTGACACTCG	300
CDS		CTGGCACTTCCTGGGATATGAAGTTGATTAAAGAGCTTGATCGAGCAAGATGGCTACAGTGCATGGAAGAAGACGAGCCCTCAACCTGACACTCG	
genome	301	GCTTCGACGAGTGTACCGCAAGTATCCTGACCGTGAAGCCCTGGCTTTGAGGGCAATCCTATTTCATTTCCGTGATATTCAGCTTGTAAAGCCATTGTT	400
CDS		GCTTCGACGAGTGTACCGCAAGTATCCTGACCGTGAAGCCCTGGCTTTGAGGGCAATCCTATTTCATTTCCGTGATATTCAGCTTGTAAAGCCATTGTT	
genome	401	ACAGCGACTCAGCCACCGCTTCCTGCTTCAGAGCTCAGCACTGCTCGTGAACCTTCAATTTTGTATCGATCGATCAACGATCGAGCCACAT	500
CDS			
genome	501	TGCCTAGAGCTATGGCACACCGCCCTAAATGCATGCCTTCTTGTATGAAGCCTCCACAGGTGCGGCAACTGGTTGCTGGCCAAAGGGATCAAGCGAGGAG	600
CDS		CTCCACACAGGTGCGGCAACTGGTTGCTGGCCAAAGGGATCAAGCGAGGAG	
genome	601	ATATCGTCTCGCTTTTCAATGTGACAGCGCAGAGTTCATCTCTCTGGTGGTCTCAACAGATTGGAGCCACTGGTGCTTCATCAATACCAACCT	700
CDS		ATATCGTCTCGCTTTTCAATGTGACAGCGCAGAGTTCATCTCTCTGGTGGTCTCAACAGATTGGAGCCACTGGTGCTTCATCAATACCAACCT	
genome	701	TACGGCAACCCCTGACACATTCCCTCCGACAGCCACCTGGTCAATGTTGATATGACACCGAGTTGACAGCCGATGCGCAACTCCCTGGATGAG	800
CDS		TACGGCAACCCCTGACACATTCCCTCCGACAGCCACCTGGTCAATGTTGATATGACACCGAGTTGACAGCCGATGCGCAACTCCCTGGATGAG	

Figure 18A (cont.)

genome CDS	801 ATTCAGGAGATGGGCTATTCAATTTACTCTTTAAGGACCGAAGCGTGGACTTTGCTACCCGATGGATATCTCCAGGTCOCACACACACGATACACCCG ATTTCAGGAGATGGGCTATTCAATTTACTCTTTAAGGACCGAAGCGTGGACTTTGCTACCCGATGGATATCTCCAGGTCOCACACACACGATACACCCG 901 AACACCTGGCCGGGAACACGACCGCGGATGACATTTGGATGCTCATCTGGAAGTACTGGTCTTCCCAAGGCGGTCGTGTCTCTCATGGCGG AACACCTGGCCGGGAACACGACCGCGGATGACATTTGGATGCTCATCTGGAAGTACTGGTCTTCCCAAGGCGGTCGTGTCTCTCATGGCGG 1001 TGCCTCTAGTAAGTTGAGAGTCTTCAGCCTTTGACATACGTAATTTTGAAGGTGCTACTAACAGTCTCTGCTTGGCGTTATCTGCATATTTTCTAGTGGGA TGCCTCTA
genome CDS	1101 OCTCAGTTTGGACCGATTCTATCAGTTTCAGTGAGAGGAGGCTATCTGTGCTTGTACACAGTCTGCTGGCGCCATCTTTGGGAGTGAATTG OCTCAGTTTGGACCGATTCTATCAGTTTCAGTGAGAGGAGGCTATCTGTGCTTGTACACAGTCTGCTGGCGCCATCTTTGGGAGTGAATTG 1201 CTTGTGGACCTGGGAGCAACCTTGATCTGCTGCGCCGCAAGTTCTCGCGGACACATTTCTGGGAGGATTGGCGGTTGAACAAGGCAACTGTGTGATTCAATA CTTGTGGACCTGGGAGCAACCTTGATCTGCTGCGCCGCAAGTTCTCGCGGACACATTTCTGGGAGGATTGGCGGTTGAACAAGGCAACTGTGTGATTCAATA 1301 CATTTGGAGAAATTTGCAGATATCTGCTCAACACGCGCAGATACACCCCTGGACAGGACACACTGGATAGGACTGGGACATGGTAATGGAAATGGACACCGGAT CATTTGGAGAAATTTGCAGATATCTGCTCAACACGCGCAGATACACCCCTGGACAGGACACACTGGATAGGACTGGGACATGGTAATGGAAATGGACACCGGAT

Figure 18B

genome	1401	GTCTGGACTCGCTTCAGAGATCGGTTTCGGCCATCCCGTTGATTTGGGAGTGGTATGTCATCGACTGAGGAACCTGGAGCCTTGTGGAATTATTAACACAGGCG	1500
CDS		GTCTGGACTCGCTTCAGAGATCGGTTTCGGCCATCCCGTTGATTTGGGAGTGGTATGTCATCGACTGAGGAACCTGGAGCCTTGTGGAATTATTAACACAGGCG	
genome	1501	CAGCGCGGCTCGAGCGATTGGATACCGCGGTACCCCTGCCAGAGCATTTGGATAAGGACTCAGGATTGGGAGATTTCATGTCACACAGAGGAGTTGGT	1600
CDS		CAGCGCGGCTCGAGCGATTGGATACCGCGGTACCCCTGCCAGAGCATTTGGATAAGGACTCAGGATTGGGAGATTTCATGTCACACAGAGGAGTTGGT	
genome	1601	TCGGGACAAAACGGTTATTGCCATTGAGGTAAACATAAGCGGCATTGTTGGAAGTCTAAATCATTTCAGATGCTTTGTTCCGGCATGCTTACCAAAACGCAC	1700
CDS		TCGGGACAAAACGGTTATTGCCATTGAG	
genome	1701	CGACCATCTTTTCACCTGCTGGGCATATAATAGTCGCAAAACCTGGGAGCCCGGAGAAATTGCTGAGCCTTGTGAGCCTAAAGAGCCGGAACAAGACTTCA	1800
CDS		TCGCAAACTCCCGAGCCCGGAGAAATTGCTGAGCCTTGTGAGCCTAAAGAGCCGGAACAAGACTTCA	
genome	1801	AAGGATACCATCAAAACCGAGCGGACCAACAAAAGATTGTCAAAGATGTTTTCAAAGCGGCGACATGCTACTTCGGTAACCGGAGATATCTCTGGGG	1900
CDS		AAGGATACCATCAAAACCGAGCGGACCAACAAAAGATTGTCAAAGATGTTTTCAAAGCGGCGACATGCTACTTCGGTAACCGGAGATATCTCTGGGG	
genome	1901	CGATAGCGATGGGTACTTTTACTTTGGGACGGTGTGGGCGATACATTCGGTGGAGTCCGAGATGTGCTACCGCCGAGGTGCTCTGAAGTCCCTCTCG	2000
CDS		CGATAGCGATGGGTACTTTTACTTTGGGACGGTGTGGGCGATACATTCGGTGGAGTCCGAGATGTGCTACCGCCGAGGTGCTCTGAAGTCCCTCTCG	
genome	2001	CAGTATCCGGACTGTATCGAAGTCAATGTGTATGGAGTTCAGATCCAGGCGAGGAGCGAGCGCGGTATGGCAGCGATTGTGTCACAGCAGCATGG	2100
CDS		CAGTATCCGGACTGTATCGAAGTCAATGTGTATGGAGTTCAGATCCAGGCGAGGAGCGAGCGCGGTATGGCAGCGATTGTGTCACAGCAGCATGG	
genome	2101	ATTGGGAGAAATTTCGGGGGTATGCACCTCAAGAACCTGCCCGGTATCTCTTCGATCTTTATTCGGCAGATGGCGAGATGGAGATCACAGGACGTT	2200
CDS		ATTGGGAGAAATTTCGGGGGTATGCACCTCAAGAACCTGCCCGGTATCTCTTCGATCTTTATTCGGCAGATGGCGAGATGGAGATCACAGGACGTT	

Figure 18B (cont.)

genome CDS	2201	CAAGCAGCGCAAGTGGAGTTGGTGAATGAGGGGAATGGACCCCAAGACGATTTGCCAACGAGATCGCTGTGGTTGGAOGGACACCACTATAAGCCGTTCAAG	2300
		CAAGCAGCGCAAGTGGAGTTGGTGAATGAGGGGAATGGACCCCAAGACGATTTGCCAACGAGATCGCTGTGGTTGGAOGGACACCACTATAAGCCGTTCAAG	
genome CDS	2301	GCGGCGAGCAACCAAGCGGTCTATCAGCGGCAAGGCCAAGCTATAG	2345
		GCGGCGAGCAACCAAGCGGTCTATCAGCGGCAAGGCCAAGCTATAG	

Figure 19A

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1  ATGGAACCTTGGTTAACGGAAGTATCGCGTCGAGTAGCAGAGGTGCGATCACAATCTATCGCAAGCTATGCTACAGCGGGCTCCTCGACAGGCTA
   M E T L V N G K Y A V E Y D E V D H I Y R N V M A T G G L L D R P M .
101 TGCCCTCCATACACAGCATCAAGCAGCGCAACCATGGCCCACTCTTGAGTATATGGCCAACACCTAGCAAGACAAGACGCCATGGGCTGGCGAGACAT
   . P P Y Y D I K E R T M A H L F E Y M A N T Y E D K D A M G W R D I .
201 TATCAAGGTCCACAAGGTGAGAGCAGGCTGCCAATCCTGGCGAGAGCCAAAGACCTGGATCACTTATGAGCTCTCGGACTACAACTGGATGTCTTAC
   . I K V H K V E K Q A A N P G E K P K T W I T Y E L S D Y N W M S Y
301 CGCCAAAGCCAAAGAACTATGCAGATCGAGTTGGCTTGGGCATCACAGGCTTGAGGTTGAGAGGGAGACCTTTGTCATGATCTTTGCTAGCAGATGTCCCG
   R Q A K N Y A D R V G L G I T R L G V E K G D F V M I F A S T C P E .
401 AATGGTTCTGACAGCGCATGGATGCTTCTCGGAGTCAGTGAATACTCGTGACAGCTAGGACTGGACGAGAACTGCTCCAGTTTATTGTTGACCA
   . W F L T A H G C F S Q S V T I V T A Y D S M D E K S I Q F I V D Q .
501 GTCCAGGCCAAGGCCATCTTTGCTGATGCGCACAGCTCCCTGTGTTGTCAAAACTATGCAGAAGGCAACAGTGGTGTCAAGGAGTCAATTACACA
   . S Q P K A I F A D A H T L P V V S K L M Q K G N S G V K A V I Y T
601 GGCCAAAGACTGGGAAGTGACCGATGCCAATCAAGAGATGCGAGCAAGTAGAAACCGCTCATTTGAGCTGTTTCATATCCAGCAACTCAAGAGACCAAGT
   G Q E W E V T D A I K K M E Q V E N R S F E L V H I D E L K K T K S .
701 CAGCATCTAACGGGGAACAGTCTGCCGGAAAGGGGAAGCAGAGATCATCTGAGGATGCCGAAGGCCCTCAGGAGCAGATCGAGGTCAATATACCCCTAAGGC
   . A S N G E Q S A G K G K Q R S S E D A E G A Q D E I E V I Y P K A .
801 GGATGATCTGGCCTGATTATGTATACCTCTGGGTGAGGGGTTCAGCCCAAGGGGGGCAATTGCACATGGAACCTTGATGCGGCCATTGGGAAGTGCT
   . D D L A C I M Y T S G S T G Q P K G A Q L T H G N L M A A I G S A
901 GCGGCATGGAGGGACAGCTGGACAAGGAACAGACATTGTTATTCATATCTGCAATTCGCCCATGCTCGAGTTTGCTCATTTCCACTTTGCTGG
   A A M E G D Q L D K E T D I V I S Y L P L A H V L E F V I S H F V V .
1001 TATCCATGGGCTCGCGTCTTGGATTTCGGAACGACGACCGCACTCTGATGGATGATGCGCTCCACCGCAGCAAGTGGCAGGTCCAGGGGCTTGGTGA
   . S M G C R L G F G R A R T L M D D A V A P T A G S G R S K G L G D .

```

Figure 19A (cont.)

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1101 TCTGAAGCGGCTCCAGCAACATGTGCGCTGCTGTGCCAAGCATCTGGAGCGTATCCGCAAGGCATCTCGCGAGGTCAACAAGCAATCCTTCCTT
    . L K A L Q P T L M A G V P T I W E R I R K G I L A E V N K Q S F P

1201 ATCCGTACACTCTCTTCTGCTGCACTCAACACCAAGTGGGCTATCGTCCAGGCTACCGGATCTGACAACCTTGTGCACCAAGCACTATGTACTGTGGTCT
    I R T L F A A L N T K W A I V Q A T G S E N F V T K T I D S L V F .

1301 TTAGTAAGGCTAAGGAGCTCGTTGGAGCCAAAGCTGGCCCTTACCTTGACTGGAGGGGCGGGAATCACTGATGAGACGCCACCGGTTCTTGAGCATGCTAAT
    . S K A K E L V G G K L R L T L T G G A G I S D E T H R F L S M V M .

1401 GTGCTACGTTATCTCGGATATGGTCTCACTCAAGTCTGTGCTGTGGCGCTGTCAACCTGCCACCTATGGGTCAACCGTCTCAGGACCGTTGGACCAACC
    . C Y V I S G Y G L T E V C G V A A V T L P R M G H R L R T V G P P

1501 GCGCCCACTCTTGAGCTCAAGTTGGTGAATGTGCCCAACACCGAGTACACAGGAGACAATGGATCGGGGGAATCTGGTTCCGTGACCTGCAGTGATGA
    A P S L E L K L V N V P D T E Y T G D N G S G E I W F R G P A V M K .

1601 AGCGATACCTCAAACTCCAGGAAGAGACCAAGGTGATGACCGGGAATGGTTGGTTCAAGACAGCGGACATTTGGCACCATGAACCCACAGCGGACACT
    . G Y F K L E E T K K V M T G D G W F K T G D I G T M N P D G T L .

1701 GTCAATCAAGGACAGGCTCAAGAATCTGGTCAAGCTCTCTCATGGAGAATATGTCCGCCCTGGAGAATGTCAAGCGGTTTATCGCGATTCCAAGGAGATC
    . S I K D R V K N L V K L S H G E Y V A L E K C E A V Y R D S K E I

1801 AAGAGCAATTGCATCGTTGGGACAATGGGTGCCCTGTGTGCTGGCGGTTGTGGAAACGACCGACGCGGCTGTGACAAGGAGATTTTGGATATCC
    K S I C I V A D N G C P V L L A V V E P S H A G A S D K E I L D I L .

```

Figure 19B

1901 TGAAGGCCAAGCCAGGGGGGGGCTCTCCAACTCCGAGACTGTGCAAGCGCTTATCATTTGATGATTCGGACTGGATGACGAATGGGTTTCATGACCTC
· K S Q A K A A G L S K S E T V Q G V I I D D S D W M T N G F M T S ·

2001 GAGCAGCAAGCTCAAGAGACCGAGGTCCGCAAGGCACACACAGGATATTGACGAGATGTGCAAGAAGTTCTAG
· S S K V K R R E V R K A H N K D I E E M W K K F *

Figure 20A

[illegible]

Figure 20A (cont.)

801	ATCACAGCATGATGAGATTCAACCGGGATTAGGTGACCGCTGTGATTGTGCAAAAGGGGGCCGGACAAATTTCAGACAGACTTGGGGAGGTGTTTCTCAT	900
genome CDS		
901	GACGACAAATCCAAGATTCAACAGAGACTGGTGCCAGGGAGAGTAGAGGGTGCCTCTCTTTGGCATATGAAAGTGGATTACGATATGGCTGACT	1000
genome CDS		
1001	TAGGAGTCTAATTTCATCCGGGAAAGAGTCCGGACTGAAGTCCCAAGTCCGGGACTGTAGAAAGTATTCCACTCTGCTGCTGGTCAATGAGGAGGACTG	1100
genome CDS		
1101	GGTTGGGCTTTGGAGTGCCGACGAGAAATCATGGAAATACGCTTCTCGGTCTTCAGTCCACTGATCCTCATGCGGCAATTGACTCTACAATAATAGGATG	1200
genome CDS		
1201	CTTCTCCAGTCAGTCACTATCGTGACAGCCTACGACTCGATGGACGAGAGTGGATCCAGTTTATTGTTCACAGTCCAGCCCAAGGCCATCTTTGCT	1300
genome CDS		
1301	GATGCCACACGCTCCCTGTGGTGTCCAAACTCATCCAGAGGGCAACAGTGGTGTCAAGCCAGTCATTACACAGGCCCAAGAGTGGGAAGTGAACGATG	1400
genome CDS		

Figure 20B

genome	1401	CAATCAAGACATGGAGCAAGTAGAAACCCCTCATTTGACCTGGTTCATATCGACCACTCAAGAGACCAAGTCAGCATCTACGGGCAACAGCTCTGG	1500
CDS		CAATCAAGACATGGAGCAAGTAGAAACCCCTCATTTGACCTGGTTCATATCGACCACTCAAGAGACCAAGTCAGCATCTAACGGCGAACAGCTCTGG	
genome	1501	CGGAAGGGGAAGCAGAGATCATCTGAGGATGCGAAGGGGCTCAGACAGATCGAGTCATATACCGCTAAGCGGATGATCTGGCCCTGTATTATGTAT	1600
CDS		CGGAAGGGGAAGCAGAGATCATCTGAGGATGCGAAGGGGCTCAGACAGATCGAGTCATATACCGCTAAGCGGATGATCTGGCCCTGTATTATGTAT	
genome	1601	ACCTCTGGGTGCAOGGGTCAOCCAGGGGCGGCAATTGACACATGGCAACTTGGATGGCGGCCATTGGAAGTGGCTGGCGCCATGGAGGGCGAACAGCTGG	1700
CDS		ACCTCTGGGTGCAOGGGTCAOCCAGGGGCGGCAATTGACACATGGCAACTTGGATGGCGGCCATTGGAAGTGGCTGGCGCCATGGAGGGCGAACAGCTGG	
genome	1701	ACAAGGAACAGACATGTATTTCATATCTGCCATTGGCCATGTCTCGAGTTTGICATTTCCCACTTTGTGGTATCCATGGTAAGTGAACATCCCT	1800
CDS		ACAAGGAACAGACATGTATTTCATATCTGCCATTGGCCATGTCTCGAGTTTGICATTTCCCACTTTGTGGTATCCATGG	
genome	1801	TTACATCTGCATCCCAAAATGGGGCTAAAGTCAAGTGTGTGAACCTGAACGTTTATATTCATCTTAGGGTGGCGCTTGGATTGGAGAGAGACGCCACTG	1900
CDS		CTGGCGGCTTTGGATTGGAGAGAGACGCCACTG	
genome	1901	TGATGGATGATGCAGTCCCTCCACCGCAGGAAGTGGCAGGTCCAGGGCTTGGTATCTGAAGGCGCTCCAGGCCAATTTGATGGGTATGATTGGCAT	2000
CDS		TGATGGATGATGCAGTCCCTCCACCGCAGGAAGTGGCAGGTCCAGGGCTTGGTATCTGAAGGCGCTCCAGGCCAATTTGATGG	
genome	2001	GAAGCCAGAGACTAATATGAGGTAGAGTGGCAAAACCTTATTTTGACGTATTGCATATTGTGTGGATTTTTCAAAACCATAGCTGGTGTGCCAACCAT	2100
CDS		CTGGTGTGCCAACCAT	
genome	2101	CTGGAGCGGTATCCGCAAGGGCATCTGGCGAGGTCAAGAGCAATCTTCCCTATTCGTACACTCTTCTTTGGTGCACCTCAACACCAAGTGGGCTATG	2200
CDS		CTGGAGCGGTATCCGCAAGGGCATCTGGCGAGGTCAAGAGCAATCTTCCCTATTCGTACACTCTTCTTTGGTGCACCTCAACACCAAGTGGGCTATG	

Figure 20B (cont.)

2201	genome	2300
CDS		
	GTCCAGGCTACCGGATCTGAGAACTTTTGTCAACAAGACTATTGACTCGTTGGTCTTTAGTAAGGCTAAGGAGCTGCTTGGAGGCAAGCTTGGCCCTTAACCT	
	GTCCAGGCTACCGGATCTGAGAACTTTTGTCAACAAGACTATTGACTCGTTGGTCTTTAGTAAGGCTAAGGAGCTGCTTGGAGGCAAGCTTGGCCCTTAACCT	
2301	genome	2400
CDS		
	TGACTGGAGGGGGCCGGAATCAGTGATGAGACGCAACCGGTTCTTGAGCATGGTAATGTGCTACGTTAATCTGGGATATGGTCTCACTGAAGTCTGTGGTGT	
	TGACTGGAGGGGGCCGGAATCAGTGATGAGACGCAACCGGTTCTTGAGCATGGTAATGTGCTACGTTAATCTGGGATATGGTCTCACTGAAGTCTGTGGTGT	
2401	genome	2500
CDS		
	TGCGGCTGTCAACCTGCCAAGTATGGGTCAACGTTCTCAGGACCGTTTGGACCAACCGGTAAGTCCGCTCGCATATCTTCTCGGATCTCTCAATATGGGAGCTG	
	TGCGGCTGTCAACCTGCCAAGTATGGGTCAACGTTCTCAGGACCGTTTGGACCAACCGGTAAGTCCGCTCGCATATCTTCTCGGATCTCTCAATATGGGAGCTG	
2501	genome	2600
CDS		
	TTTTTTTGTCTTCAAAAGCTAACACTTTGCTTTTTCGGACACACAGGGCCGACAGTCTTGAGCTGAAGTTGGTCAATGTGCCCCGACACCGAGTACACA	
	TTTTTTTGTCTTCAAAAGCTAACACTTTGCTTTTTCGGACACACAGGGCCGACAGTCTTGAGCTGAAGTTGGTCAATGTGCCCCGACACCGAGTACACA	
2601	genome	2700
CDS		
	GGAGACAATGGATCGGGGAAATCTGGTTCCGTGGACCTGCAAGTGAAGAGGATACCTTCAAACTGGAGGAGAGACCAAGCAAGGTGATGACCGGGGATG	
	GGAGACAATGGATCGGGGAAATCTGGTTCCGTGGACCTGCAAGTGAAGAGGATACCTTCAAACTGGAGGAGAGACCAAGCAAGGTGATGACCGGGGATG	
2701	genome	2800
CDS		
	GTGTGTTCAAGACAGGCGCACATTTGGCAGATGAACCCAGACGACACATGTCAATCAAGGACAGGTCAGAACTCTGGTCAAGCTGTCTCATGGAGAATA	
	GTGTGTTCAAGACAGGCGCACATTTGGCAGATGAACCCAGACGACACATGTCAATCAAGGACAGGTCAGAACTCTGGTCAAGCTGTCTCATGGAGAATA	
2801	genome	2900
CDS		
	TGTGGCCCTGGAGAAATGTGAAGCGTTTATCGCGATTCCAGGAGATCAAGAGCATTTGCAATGTTGGGACAAATGGGTGCCCCCTGTGTGCTGGCCGTT	
	TGTGGCCCTGGAGAAATGTGAAGCGTTTATCGCGATTCCAGGAGATCAAGAGCATTTGCAATGTTGGGACAAATGGGTGCCCCCTGTGTGCTGGCCGTT	

Figure 20C

genome	2901	GTGGAAOCAGCCACGCCAGGGGTGAGTGAGACGGCTTTGGCCCTGACAGGTCTCGTTCTTATGGGAATGTGGATCATTTACTCTATCACTAACGAGAGAGG	3000
CDS		GTGGAAOCAGCCACGCCAGGGG	
genome	3001	CTGTATTATCTACTTGGTAACGTGGCATAGGCGTCTGACACGGAGATTTTGGATATCCTGACAGGCCAAGCCAGCGCGCGCCCTCTCCAAAGTCCGA	3100
CDS		CGTCTGACACGGAGATTTTGGATATCCTGACAGGCCAAGCCAGCGCGCGCCCTCTCCAAAGTCCGA	
genome	3101	GACTGTGCAAGGGTTATCATTTGATGATTGGGACTGGATGACGAA TGGTTTCATGCACTCGACGCAAGGTCAAGACAGCGGAGGTCCGCAAGGCACAG	3200
CDS		GACTGTGCAAGGGTTATCATTTGATGATTGGGACTGGATGACGAA TGGTTTCATGCACTCGACGCAAGGTCAAGACAGCGGAGGTCCGCAAGGCACAG	
genome	3201	AACAAGGATATTGAGGAGATGTGGAAGAAGTTCTAG	3236
CDS		AACAAGGATATTGAGGAGATGTGGAAGAAGTTCTAG	

Figure 21A

1 CATGCCAAAGTGCTTTACCGTCAACGTCGGCCCCGAGGACGTCAAGGGCGAGACTCGCATCGCTCGCTCCATCCAGGCGCGTGCACAAACTCATGGACTCA
 M P K C F T V N V G P E D V K G E T R I R R S I Q A V D K L M D S

 101 CCCTCAAGCGCACATCAAGACCTTGTACGATGTATCCAGTACTCTGCCAAGTCCGCCCAACCTCAACGCCATCGGCTACGCCAAGATTGTCAAGATGA
 P S S D I K T L Y D V I Q Y S A K V R P N L N A I G Y R K I V K M I

 201 TCGAAGAGGAAAAGGAGATCACCAAGATGGTCAGCGGCGAGCCTGTCAAGGAGAGAAAAGCGTGGAAATACTTCAAGCTCTCCGGCTACCACTATCTGAC
 . E E E K E I T K M V S G E P V K E K K T W K Y F K L S G Y H Y L T

 301 CTACAAGGACACCAAGCGGTGTCGACAGCATTGGAAGTGGCTCGGCAAGTGGGTGTGAGCCCCAAGGAGGAGGATCACCGTCTTTGGTTCCACAAGT
 . Y K D T K A V I D S I G S G L R K W G V E P K E R I T V F G S T S

 401 GCCAACTGGTCTGCTGGTCCCTGCTCAGCGCAGTCCATGACCATCGTCACCGTGTATGACACTTTGGCGAGGAAGGATTGCTGCACTCGATCA
 A N W L L V A H G A F T Q S M T I V T V Y D T L G E E G L L H S M N

 501 ACGAGCGCGAGGTGGGAACGGCTACAGAACCGTGATTGTATCAAGACAATGACCAACGTTTCAGGACCGTCCCCACCCTCAAGAGGATCGTCTATGA
 . E A E V G T A Y T N A D L I K T M T N V S G R C P T L K R I V Y D

 601 CGGCGAAGCCAAACGACGACAGTGATCGCCCTTCAGACGGCCCATCCTCACTTCAGCTTATCACTCTGAGGAGCTGAAGCAGCTCGGTGTGGATCAC
 . G E A N A A D V I A L Q T A H P H L Q L I T L E E L K Q L G V D H

 701 CCTGTGGAGCCCACTCCTCCACCGCCGAGGATTGCTCCTGGCATCATGTACACTTCTGGATCGACCGGAAACCTAAGGAGTCACTCCTCACTCACGGAA
 P V E P T P P T A E D C S C I M Y T S G S T G N P K G V I L T H G N

 801 ACCTCATTTGCCGCCATTGGCGGAGTTAACAAGATGCTGGAAAAGTACATTCCCGAAGCGGATGTCTTGCCTTGCCTACCTTCCCTTGGCTCACGTTCTGGA
 . L I A A I G G V N K M L E K Y I R E G D V L L A Y L P L A H V L E

 901 ATTATGTTGAGAACCTCTGTCTCTTCTGGGGTGTAAACCTTGGATATGGTACTGTCCGACCGCTGACCGATGCCCTGTGTGCGTGAAGTCCAGGGTGAT
 . F M V E N L C L F W G V T L G Y G T V R T L T D A S V R E C Q G D

 1001 ATCAAGGAATTCCGGCCTACGCTTATGACCGCGGCTTCCAGCAGTGTGGAGACCATCCGCAAGGTGTTCTCGCCCAACTAACCAGGGTTACCTCTGG
 I K E L R P T L M T G V P A V W E T I R K G V L A Q V N Q G S P L V

Figure 21A (cont.)

1101 TTCAATCCGTCTTCAACGGCGGTCTGAACGCCAAGGCCTGGTGCAATGACCGCAAACTAGCGCTTTGACTGGAAATTTTCGACACTCTGGTGTCAACAA
 . Q S V F N A A L N A K A W C M D R K L G A L T G I F D T V V F N K .
 1201 GGTCGGCTCAGCAAACTGGAGGTGGTCTTTCGGCTACCGGCTCTCGGGCGGGCGGCTATCTCCAGGAGACCCAGCGCTTCTTGACCACAGCACTGTGGCCT
 . V R Q Q T G G R L R Y A L S G G A P I S Q E T Q R F L T T A L C P
 1301 ATCCTTCAAGCCTATGGCATGACTGAGTGGTGGGCAATGTGCTCGATCATGACTCCAGAGCGGTTCAACTACACCGGGTCGGTTCGCCCTGTTCCCTGCA
 I L Q A Y G M T E S C G M C S I M T P E A F N Y N R V G S P V P C T .
 1401 CAGAGGTCAAGCTCGTGGATGTGCCCGATGCAGGATACCTTTTCGACTGATTCGCCCGCGCCTCGTGGTGAGATTTGGATTCCGGACCGCTCCATCACTC
 . E V K L V D V P D A G Y F S T D S P R P R G E I W I R G P S I T S .
 1501 TGGATACTTCAACAAACGCTGAGGAGACCTCGGCAGGCCATCACAGAGGACCCGCTGGCTCAAGACTGGAGATATTGGAGAGTGGCATGCTGATGGCACACTC
 . G Y F K N A E E T S A A I T E D R W L K T G D I G E W H A D G T L
 1601 TCGGTCAATTGATCGCAAGAAGAACTTGGTCAAGTTGTCCGATGGCGAGTACATTGCTCTAGAGAAACTTGAGTGGTGCTACAAGAGCAGCGGCTTACTGCA
 S V I D R K K N L V K L S H G E Y I A L E K L E S V Y K S T A Y C N .
 1701 ACAACATCTGCGTTTATGCCGATTCCATGCCAAACAAAGCCTGTGGCGCTGATTGTCGAGTGAACCCCGCATCTCCAGCTGGCCAAGGCCAAGGGCCT
 . N I C V Y A D S M Q N K P V A L I V A S E P R I L E L A K A K G L .
 1801 GGAGAGCCGGACTTTGCAGTGTCTGCCACGATAAGGTGATCATCAAGGCTGTCTCGAGCGCCTGTCTCGGAGCTGCCAAAAGGCTGGCCTCAAGCCC
 . E S R D F A V L C H D K V I I K A V L D A C L A T A K K A G L K P

Figure 21B

```
1901 GCCGAGTTGCTGCACGGGTGTGTACCTGGAGTCTGACGAGTGGACCGCTCAAGGCGGTTTGTGACTGCTCAGAAAATTCAAGCGCAAGGAAATCAACC  
    A E L L Q G V Y L E S E E W T A Q G G L L T A A Q K L K R K E I N Q  
2001 AGGCTTATGCTGACCAGATCAAGCAGATCTATGGCTCCAAGTAAAAATGAAC  
    . A Y A D Q I K Q I Y G S K
```

Figure 22A

genome	1	ATGCCAAAGTCTTTACCGTCAACGTGGGCGCCAGGAAGTCAAGGCGAGACTCCCATCCGTCCCTCCATCCAGGCCGTGGACAACTCATGCACTCAG	100
CDS		ATGCCAAAGTCTTTACCGTCAACGTGGGCGCCAGGAAGTCAAGGCGAGACTCCCATCCGTCCCTCCATCCAGGCCGTGGACAACTCATGCACTCAG	
genome	101	CCTCAAGCGAGATCAAGACCTTTGTACGATCTCATTCAGTACTCTGCCAAGGTCCGGCCCCAACCTCAACGCCATCGGCTACCGCAAGATTGTCAAGATGAT	200
CDS		CCTCAAGCGAGATCAAGACCTTTGTACGATCTCATTCAGTACTCTGCCAAGGTCCGGCCCCAACCTCAACGCCATCGGCTACCGCAAGATTGTCAAGATGAT	
genome	201	CCAAGAGGAAAGGAGATCACCAAGATGGTCAGCGCGAGGCTGTCAAGGAGAAAAGAGCTGGAAATACTTCAAGCTCTCCGGCTACCACTATCTGACC	300
CDS		CCAAGAGGAAAGGAGATCACCAAGATGGTCAGCGCGAGGCTGTCAAGGAGAAAAGAGCTGGAAATACTTCAAGCTCTCCGGCTACCACTATCTGACC	
genome	301	TACAAGGACACCAAGGCGGTTCATCGACAGCATTTGGAAGTGGCCCTGGCAAGTGGGTGTTGAGCCCAAGGAGAGGATCAACCGTCTTGGTTCCACAAGGT	400
CDS		TACAAGGACACCAAGGCGGTTCATCGACAGCATTTGGAAGTGGCCCTGGCAAGTGGGTGTTGAGCCCAAGGAGAGGATCAACCGTCTTGGTTCCACAAG	
genome	401	AATGTGTAGCGCCACCAAAATACGATCATTTTCAGCGTGAAGGCTGGGAGCAATTAGCGGGGAATGACATCGATAACAGGAACCGAAAAAATAAACA	500
CDS		AATGTGTAGCGCCACCAAAATACGATCATTTTCAGCGTGAAGGCTGGGAGCAATTAGCGGGGAATGACATCGATAACAGGAACCGAAAAAATAAACA	
genome	501	AGACGAAGTCGGAGATCCTCGCTATTGGCGTTTAAAGCACCGCCAGCGTCTCTTTTNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN	600
CDS		AGACGAAGTCGGAGATCCTCGCTATTGGCGTTTAAAGCACCGCCAGCGTCTCTTTTNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN	
genome	601	NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN	700
CDS		NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN	
genome	701	NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN	800
CDS		NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN	

Figure 22A (cont.)

801	genome	800
CCTTCACCTGACACGATACATGACCAACTGGCTGCTGGTCCGCTCATGGTGGCTTCACCGCAGTCGACGACCATGGTGCACCGGTGATGACACATTTGGGGGAGG	CDS	
901	genome	1000
AAGGATTGCTGCACCTCGATGAAACGAGGCGAGGTGGGAAACGGGCTACACGAAAGCTGATTTCAGACACATGACCAACGTTTCAGGACGCTGGCCACAC	CDS	
1001	genome	1100
CCTCAAGACGATGCTGCTATGAGGGGCAAGCCAAACGACGACAGCTGATCGCCCTTCAGAACGGGCGCCATCCTCACCCTTCAGCTTATCATCTTCGAGGAGCTG	CDS	
1101	genome	1200
AAGCAGCTCGGTGTGATCAACCTGTGGAGCCCACTCTCTCCACCGCGAGGATTTCTCTGTCATCATGTACACTTCGACATCTGATCGACCGGAAACCCCTAAGG	CDS	
1201	genome	1300
GAGTCATCTCACTCAGGAAACCTCATTTGGCGCAGTAGGTGTTTCTCTCACTCTCTTTAAACCCCTCTCTCTTCACTTCGAAATATGCTGGGAATCTCT	CDS	
1301	genome	1400
ACTTACCTGAATGTTACTGTTCTTCGGGTTATCAACCTAGTTGGCGGAGTTAACACAGATGCTTGGAAAGTACATTCGCGAAGCGGATGTCCTTCTTGGCTTGGCTT	CDS	

Figure 22B

genome	1401	1500
CDS	ACCCTCCCTTGGCTCAGGTTCTCGAATTTCATGTTGAGAACCTCTGTCTCTCTCTGGGGTGTAAOCTTGGATATGGTACTGTTCGCAOAGCTGACGGATGG ACCCTCCCTTGGCTCAGGTTCTCGAATTTCATGTTGAGAACCTCTGTCTCTCTCTGGGGTGTAAOCTTGGATATGGTACTGTTCGCAOAGCTGACGGATGG	
genome	1501	1600
CDS	CTCTGCGGTGAGTGCACGGGTGATCAAGGAATTTCGGGCTACGCTTATGAOOGGGTTTCACACAGTGTGGAGACCATTCGGCAAGGTGTCTCTGGC CTCTGCGGTGAGTGCACGGGTGATCAAGGAATTTCGGGCTACGCTTATGAOOGGGTTTCACACAGTGTGGAGACCATTCGGCAAGGTGTCTCTGGC	
genome	1601	1700
CDS	CAAGTAAACACAGGTTCAOCTCTGGTTCAATCCGTCTTCAACGGGCTCTCAACGGCAAGGCTGTGGATGGACGSCAAACTAGGGGCTTTGACTGGAA CAAGTAAACACAGGTTCAOCTCTGGTTCAATCCGTCTTCAACGGGCTCTCAACGGCAAGGCTGTGGATGGACGSCAAACTAGGGGCTTTGACTGGAA	
genome	1701	1800
CDS	TTTTCGACACTGTGGTGTTCACAAAGGTGGTTCACCAAACTGGAGTGGTCTTTCGCTACGGGCTCTTCGGGGGGGGGCTATCTCCAGGAGACCCAGCG TTTTCGACACTGTGGTGTTCACAAAGGTGGTTCACCAAACTGGAGTGGTCTTTCGCTACGGGCTCTTCGGGGGGGGGCTATCTCCAGGAGACCCAGCG	
genome	1801	1900
CDS	CTCTTGAOCACAGCACTGTGCOCTATCTTCAAGCTATGSCATGACTGAGTGTGGGATGTCTGCATCATCTCCAGAGGCGTTCAACTACAAQ CTCTTGAOCACAGCACTGTGCOCTATCTTCAAGCTATGSCATGACTGAGTGTGGGATGTCTGCATCATCTCCAGAGGCGTTCAACTACAAQ	
genome	1901	2000
CDS	CGCGTGGTTCCCTGTCACAGAGGTCAAGCTGGTGGATGTGGCGATGGAGGATACTTTTGGACTGATTGGCCCGGCTCTGGTGAGATT CGCGTGGTTCCCTGTCACAGAGGTCAAGCTGGTGGATGTGGCGATGGAGGATACTTTTGGACTGATTGGCCCGGCTCTGGTGAGATT	
genome	2001	2100
CDS	GGATTGGGGACCTCCATCAGCTCTGGATCTTCAAGAGCTGAGGAGACCTGGGAGCCATCAGAGGACCGCTGGCTCAAGACTGGAGATATTGG GGATTGGGGACCTCCATCAGCTCTGGATCTTCAAGAGCTGAGGAGACCTGGGAGCCATCAGAGGACCGCTGGCTCAAGACTGGAGATATTGG	
genome	2101	2200
CDS	AGAGTGGCATGCTGATGGACACTCTGGGTGATTGATGGCAGAGAACTTGGTCAAGTTGTGGCATGGGAGTACATTCTCTAGAGAACTTGGAGTGG AGAGTGGCATGCTGATGGACACTCTGGGTGATTGATGGCAGAGAACTTGGTCAAGTTGTGGCATGGGAGTACATTCTCTAGAGAACTTGGAGTGG	

Figure 22B (cont.)

genome	2201	2300
CDS	GTGTACAAGAGCAGCGCTTACTGCAACAACATCTGGGTTTATGCCGATTCCATGCAAAACAAGCCCTGTGGCGCTGATTGTTGGAGTGAACCCCGCATCC	GTGTACAAGAGCAGCGCTTACTGCAACAACATCTGGGTTTATGCCGATTCCATGCAAAACAAGCCCTGTGGCGCTGATTGTTGGAGTGAACCCCGCATCC
genome	2301	2400
CDS	TCCAGCTGGCCCAAGGCCAAGGGCTTGGAGAGCGCGGACTTTCCAGTGCCTCTGCCACGATTAAGGTGATCATCAAGGCTGTCTCGAGCCCTGTCTCGCGAG	TCCAGCTGGCCCAAGGCCAAGGGCTTGGAGAGCGCGGACTTTCCAGTGCCTCTGCCACGATTAAGGTGATCATCAAGGCTGTCTCGAGCCCTGTCTCGCGAG
genome	2401	2500
CDS	TGCCAAAAGGCTGGGCTCAAGCCCGGAGTTGCTCCAGGCTGTGTACCTGGAGTCTGAGCAGTGCACCCCTCAAGGCGGTTTGTGTGACTGTGCTCAG	TGCCAAAAGGCTGGGCTCAAGCCCGGAGTTGCTCCAGGCTGTGTACCTGGAGTCTGAGCAGTGCACCCCTCAAGGCGGTTTGTGTGACTGTGCTCAG
genome	2501	2569
CDS	AAATTGAAGCGCAAGGAAATCAACACAGGCTTATGCTGACACAGATCAAGCAGATCTATGGCTCCCAAGTAA	AAATTGAAGCGCAAGGAAATCAACACAGGCTTATGCTGACACAGATCAAGCAGATCTATGGCTCCCAAGTAA

Figure 23A

1 CCTTTATCCCGCCACCGGCATCTCTCTGGCGCGCCACCATCTCGCATTCGTTTCAATCCACACTCCCACTGTGCCCCCTGCTTTTTCAGTCCCGCTCTCATC
 101 CCGCCTTCTCCTTTTCATCAGCCCAATTCAACATGACAAAGTGCCTCACCTCGAAGTCGGACCCGCCAGCTCCAGGGCGAGACCCGCATCCGCGCTCC
 M T K C L T V E V G P A D V Q G E T R I R S
 201 GTCTCTCTGCCAAGCGCCTCATGTCTCGCCCTCGGATGACATCAAGACCTCTACGAGCTTTCACACCACTCCGTCAACCGTCCGCCGCCCAACCTCAACG
 V L S A K R L M S S P S D D I K T L Y D V F N H S V T V R P N L N A
 301 CGATCGGATACCGCAAGGTCGTCAAGATTGTGAGGAAGAAAGGAGGTGCTCAAGTTGTCAACGGCGAGGAAGTCAAGGAAAGACCTGGAGTT
 · I G Y R K V V K I V E E E K E V V K V V N G E E V K E K K T W K F
 401 CTTCAAGATGTCCGGCTACCACTGGCTCACCTACAAGGATGGAAGCAGGTGCTGACAGCATCCGATCGGGTCTTCGCAAGTTTGGCGTCCAGCCCAAG
 · F K M S G Y H W L T Y K D A K Q V V D S I G C G L R K F G V E P K
 501 GACAAGCTACCCGTTTTCGGTGCACAAAGTGCCAACTGCTCTGCTTGCACCGGTGCTTCAACCGAGTCCATCACCATTGTACCGCTAGCACACCC
 D K L T V F G A T S A N W L L L A H G A F T Q S I T I V T A Y D T L
 601 TGGGGAGGACGGTCTTTTGCACTCTATGAACGAGCGCGAGGTGGCCACCGCTTACACAAACCGCGACTTGCTCAACACTATCAAGAACGTTGGCGGCAA
 · G E D G L L H S M N E A E V A T A Y T N A D L L N T I K N V A G K
 701 ATGCCCCACCCCTGAAGAAGATCATCTACAGGGGATGCAAGCCCGCAGATGTCATTGCCCTCCAGAGGGCCCATCCTCACTCCAGCTCATCACCCCTC
 · C P T L K K I I Y D G D A K P A D V I A L Q E A H P H L Q L I T L
 801 GAGGAGCTGAAGCAGCTCGGAGTGGACAAACCTGTGCGCCCAACCCCTCTGCTGCCAAGGACTACTGCTGCATCATGTACACTTCGGGATCGACTGGCA
 E E L K Q L G V D N P V A P T P P A A K D Y C C I M Y T S G S T G N
 901 ACCCCAGGGAGTGTTCCTGACCCATGGAAACCTGCTTGCTGCCATCGGAGGTGTGAACAAGATGCTGACAAAGTACGTTACGAGGAGAGCTCTTGCT
 · P K G V L L T H G N L V A A I G G V N K M L T K Y V V H E G D V L L
 1001 CGGTACTTGCCCTTCTGCTACGTTCTCGAGTTCTGCTGGAACCGTCTGCTCTCTCTGCGGGTGTGACTCTTGCGTACGGTACCGTCCGGACACATTGACT
 · A Y L P L A H V L E F L V E N V C L F W G V T L G Y G T V R T L T

Figure 23A (cont.)

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1101 GATGCCTCAGTCCTGAGTCCAGGTCATATCAAGGAGTTGGGCCCTACATTGATCAGCGGTGTTCTGCTGTGTGGAGACGATTGTTAAGGAGTGT
    D A S V R E C Q G D I K E L R P T L M T G V P A V W E T I R K G V L
1201 TGGCTCAGGTTTCCAGGGCTCAGCTCTTGTTCAAAAGATCTTCCATGCTGCTTTGAAGCCCAAGGCTGTGCTGACCCCAAGTTGGTGGCTTGAC
    A Q V S Q G S P L V Q K I F H A A L N A K A W C L D R K L G A L T
1301 TCGAATCTTGGATAGTGTGCTTCAACAAGTCAACGAGCAGACAGGAGGCTCTTGGCTTGGCCCTTTGGGAGGTGACACCCATCTCTCAGGAGACC
    G I F D T V V F N K V K Q Q T G G R L R F A L S G G A P I S Q E T
1401 CAGCGCTTCTTGACGACAGCTTTGTGCCCTATCCTCCAGGGCTACGGTATGACAGAGTCTTGGCGCATGTGGGCCATTTTGACCCCGATGTCTTCAACT
    Q R F L T T A L C P I L Q G Y G M T E S C G M C A I L T P D V F N Y
1501 ACAGCCGTGTGGATCCCGAGTTCCTTCCACGGAGTCAAGTTGGTCGATGTGCCCGATGCAAGGATACCACTCAACGGACTTGCCTCTCCGCCGTGGTGA
    S R V G S P V P C T E V K L V D V P D A G Y H S T D L P L P R G E
1601 GGCTGCAATTGGACCCCTCCATCACTGCTGGATCTTCAAGAACCCCGAGGAGACCTCCGCCACATTGACTGCTGATTCGCTGCTCAAGACTCGAGAT
    V C I R G P S I T A G Y F K N P E E T S A T L T A D R W L K T G D
1701 ATCCGAGAGTGGACCCCGACGGCACTATCTCGATCATTGACCCGCAAGAACTTGGTCAAGCTGTCAACGGAGAGTACATTGCTTTGGAGAAAGCTTG
    I G E W H P D G T I S I I D R K K N L V K L S H G E Y I A L E K L E
1801 AGTCTGTCTACAGAGCAGGCTACTGCAACACATTGTGCTGTATGCCGACTCGATGCAAGAACGCCGTTGGCAATTATTTGTCACAGCAACCCCG
    S V Y K S T A Y C N N I C V Y A D S M Q N K P V A I I V A S E P R
1901 CATCCTCGAGTTGGCCAAAGGCCAAGGCATTGAGAGCGCGGACTTGTGCTCTCTGCCACGACAGGTTATCATCAAGGCTGTCCACGATGCCCTGCCCTC
    I L E L A K A K A K G I E S R D F A A L C H D K V I I K A V H D A C L

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Figure 23B

```
2001  GCCACTGCCAAGCGTGTGGACTCAAGCGCGCTGAGATGCTTCAGGGAGTGTACTTGGAGTCAGACGAATGACGGGCCAGGCTGGCATGTTGACTGCCG  
    A T A K R A G L K P A E M L Q G V Y L E S E E W T A Q A G M L T A A  
2101  CTCAGAGCTCAAGCGCAAGGAGATCAACCGGCTATGTCTCACAGATCAAGCAGCTTTATGGAACGGCCTAAGTCGCTGAAGGTGTGCTTTGTGCG  
    . Q K L K R K E I N Q A Y V S Q I K Q L Y G T A  
2201  TCTCTTCAAGCCACACAGTCTCTATGTATATGACCGCGCGGCTCCTTTAATCCTATACCCACCCCTTTTACACGTTAAGACGCCACATTTTGTGT  
2301  TCTTTTTTTTCTCTCGGCACACACTACACACTCCCCATCCATTCCCTCCAAACAGGATGTTGTCTCGCAATATAATTGACGAATTTTCTCTTGAAAAAAA  
2401  AAAAAAAAAAAAAA
```

Figure 24A

1	ATGACAAAGTGCCTCAGCGTGGAGTGGACCGGAGCGTCCAGGGGAGACCGGCAATCGGCGCTCGTCTCTGCAAGCGGCTCATGTCTCTCGG	100
genome		
CDS		
101	ATGACAAAGTGCCTCAGCGTGGAGTGGACCGGAGCGTCCAGGGGAGACCGGCAATCGGCGCTCGTCTCTGCAAGCGGCTCATGTCTCTCGG	200
genome		
CDS		
201	OCTCGGATGACATCAAGACCGTCTACGACGCTTTCACCCACTCCGTCACCGTCCGCGCCCAACCTCAACGGGATGGGATACGGCAAGGTGTCAGATTGCT	300
genome		
CDS		
301	CGAGGAAGAAAGGAGGTCGTCACAGGTTGTCAACGGCGAGGAGTCAAGGAAAGAGAGACCTGGAGTTCTTCAAGATGTGCGGCTACCACTGGCTCAGC	400
genome		
CDS		
401	ITACAAGGATGCGAAGCAGGTGCTCCACAGCATGGATGGCGTCTTGGCAAGTTTGGCGTCGAGCCCAAGGACAAGCTGACCGTTTTCGGTGGCCACAAGGT	500
genome		
CDS		
501	TAGTGGGTGACCATGCTTGGTATCCAAATGCTGGGAGACAGAGCGGACCGCAATATGGCTCTGCTCTGCGGGGATGGAGTGGCCCAAGTGTGGGATAC	600
genome		
CDS		
601	ATATCCTCGCGGTGGGTGTCCGGGTGGCGGCTTGAATCTTGTGAAGCATGATATGTGAATGTGGACCGCAATCAACGCTCAGATTATGGGTAGCAAGC	700
genome		
CDS		
701	GTGTGTGCTAGTCTACATCATGCTCACAGGTATTACATTATTACATTTCACCTCTATCTGGCTCTTAGTGGCAACTGGCTCTGGCTTGGCCACAGGTGCTT	800
genome		
CDS		

Figure 24A (cont.)

genome	801	900
CDS	TCACCCAGTCCATCAACATTGTTACCGCTTAGACACCCCTGGCGGAGGAGGTCTTTGGACTCTATGAGGAGGCGGAGGTGGCCACCGCTTACACAAA TCACCCAGTCCATCAACATTGTTACCGCTTAGACACCCCTGGCGGAGGAGGTCTTTGGACTCTATGAGGAGGCGGAGGTGGCCACCGCTTACACAAA	901
genome	901	1000
CDS	CGCCGACCTTGCTCAACACTATCAAGAAAGTTGCGGCAAAATGCCCAACCCCTGAAGAGATCATCTACGAGGGGATGCCAAGCGCGCAGATGTGATTGGC CGCCGACCTTGCTCAACACTATCAAGAAAGTTGCGGCAAAATGCCCAACCCCTGAAGAGATCATCTACGAGGGGATGCCAAGCGCGCAGATGTGATTGGC	1001
genome	1001	1100
CDS	CTCCAGGAGGCGCAATGGTCAAGTCCAGCTCATCAACCTCGAGGAGGTGAAGCAGGTGGAGTGGACAAACCTGTGGCCCAACCCCTCTCTGCTGCCAAGG CTCCAGGAGGCGCAATGGTCAAGTCCAGCTCATCAACCTCGAGGAGGTGAAGCAGGTGGAGTGGACAAACCTGTGGCCCAACCCCTCTCTGCTGCCAAGG	1101
genome	1101	1200
CDS	ACTACTGCTGCATCATGTACACTTCGGGATCGACTGGCAACCCCAAGGAGTGTGCTCAACCCATGGAACCTCGTTGCTGCCAAGTACGTATCTTTCTCG ACTACTGCTGCATCATGTACACTTCGGGATCGACTGGCAACCCCAAGGAGTGTGCTCAACCCATGGAACCTCGTTGCTGCCAAGTACGTATCTTTCTCG	1201
genome	1201	1300
CDS	TCATGATCGTCTCCCGCATTTCCACTGGGCTTGTACCATTTCATGGGAATGTATTTAACCCGAACACACATTTTCTTTCTTCACACTTGGCCAC	1301
genome	1301	1400
CDS	GTCACTAGTCCGAGGTGTGAACAAGATGCTGACAAAGTACGTTCAACAGGAGAGACCTCTTGGCTGGGTACTTGGCTCTTGGCTGACGTTCTCGAGTTCTCG GTCACTAGTCCGAGGTGTGAACAAGATGCTGACAAAGTACGTTCAACAGGAGAGACCTCTTGGCTGGGTACTTGGCTCTTGGCTGACGTTCTCGAGTTCTCG	1401

Figure 24B

genome	1401	1500
CDS	GTGAAACGCTCTCTCTCTGCGGGGTGAGCTCTTGGCTACGGTACGGTACGCTAGTCTGAGTGGAGGCTGATATCAAGG GTGAAACGCTCTCTCTCTGCGGGGTGAGCTCTTGGCTACGGTACGGTACGCTAGTCTGAGTGGAGGCTGATATCAAGG	
genome	1501	1600
CDS	AGTTGGCCCTACATTGATGACCGGTGTTCTGCTCTGTGCGGAGACGATTGCTAGGAGTGTGGCTCAGGTTTCCAGGGCTCAOCTCTTGTTCAAA AGTTGGCCCTACATTGATGACCGGTGTTCTGCTCTGTGCGGAGACGATTGCTAGGAGTGTGGCTCAGGTTTCCAGGGCTCAOCTCTTGTTCAAA	
genome	1601	1700
CDS	GATCTTCCATGCTGCTTTGAACGCCAAGGCGTGGTCCCTGGACGGCAAGTTGGGTGGTTGACTGGAACTCTTGATACTGTGCTTCAACAAGGTCAAG GATCTTCCATGCTGCTTTGAACGCCAAGGCGTGGTCCCTGGACGGCAAGTTGGGTGGTTGACTGGAACTCTTGATACTGTGCTTCAACAAGGTCAAG	
genome	1701	1800
CDS	CAGCAGACAGGAGGAGCTCTTGGCTTGGCCCTTTCGGGAGGTGACCCATCTCTCAGGAGACCCAGCGGTTCTTGACGACAGCTTTGTGGCCCTATCTCTCC CAGCAGACAGGAGGAGCTCTTGGCTTGGCCCTTTCGGGAGGTGACCCATCTCTCAGGAGACCCAGCGGTTCTTGACGACAGCTTTGTGGCCCTATCTCTCC	
genome	1801	1900
CDS	AGGGCTAAGGTATGACAGAGTCTTGGCGCATGTGGCCATTTTGACCCCGCATGCTTCAACTAGAGCGGTGTGGATCCCGAGTTCCTTGCACGGAGGT AGGGCTAAGGTATGACAGAGTCTTGGCGCATGTGGCCATTTTGACCCCGCATGCTTCAACTAGAGCGGTGTGGATCCCGAGTTCCTTGCACGGAGGT	
genome	1901	2000
CDS	CAAGTTGGTGGATGTGCGCGATGACAGATACCACTCAACGGACTTGGCTCTCCCGGTGGTGGAGTGTGCAATTCGTGGAGCCCTCCATCAGTCTGGATAC CAAGTTGGTGGATGTGCGCGATGACAGATACCACTCAACGGACTTGGCTCTCCCGGTGGTGGAGTGTGCAATTCGTGGAGCCCTCCATCAGTCTGGATAC	
genome	2001	2100
CDS	TTCAAGAACCCGAGGAGACCTCCGCCACATTTGACTGCTGTGCTGGCTCAAGACTGGAGATATCGGAGGTGGACCCCGAGCGCACTATCTCGATCA TTCAAGAACCCGAGGAGACCTCCGCCACATTTGACTGCTGTGCTGGCTCAAGACTGGAGATATCGGAGGTGGACCCCGAGCGCACTATCTCGATCA	
genome	2101	2200
CDS	TTGACCCGCAAGAGAACTTGGTCAAGCTGTCAACCGGAGATACATTTGCTTTGGAGAAGCTTGAGTCTGTCTACAGAGCAGCAGCTACTTGCACAACAT TTGACCCGCAAGAGAACTTGGTCAAGCTGTCAACCGGAGATACATTTGCTTTGGAGAAGCTTGAGTCTGTCTACAGAGCAGCAGCTACTTGCACAACAT	

Figure 24B (cont.)

genome CDS	2201	TTGGGTGATGCGGACTGCTGATGTCAGAAACAAGCCGGTTGCCATTATTGTTCGACGGAACCCCGCATCTCTCGAGTTGGCCAAAGGCCAATTCAGAGC	2300
		TTGGGTGATGCGGACTGCTGATGTCAGAAACAAGCCGGTTGCCATTATTGTTCGACGGAACCCCGCATCTCTCGAGTTGGCCAAAGGCCAATTCAGAGC	
genome CDS	2301	CCGGACTTTGCTGCTCTCTGCGACGACAAAGGTTATCATCAAGGCTGTCCACGATGCTGCTGCTGCGCAAGCGTGTCTGGACTCAAGCCCGCTGAGA	2400
		CCGGACTTTGCTGCTCTCTGCGACGACAAAGGTTATCATCAAGGCTGTCCACGATGCTGCTGCTGCGCAAGCGTGTCTGGACTCAAGCCCGCTGAGA	
genome CDS	2401	TGCTTCAGGGAGTGTACTTGGAGTCAGAGAAATGGACGGCCACGGCTGGCATGTTGACTGCGCGCTCAGAGCTCAAGCGCAAGGAGATCAACCAGGCTTA	2500
		TGCTTCAGGGAGTGTACTTGGAGTCAGAGAAATGGACGGCCACGGCTGGCATGTTGACTGCGCGCTCAGAGCTCAAGCGCAAGGAGATCAACCAGGCTTA	
genome CDS	2501	TGTTCTCAGATCAACGAGCTTTATGGAACGGGCTAA	2537
		TGTTCTCAGATCAACGAGCTTTATGGAACGGGCTAA	

Figure 25A

1

MaACS-3 METDALTTIALTAIVLALVKFNEKPDHLPLTLCQQSSVT---PIRNE

MaACS-4 MSLDQAQSVLPGR-QPGQTCIYRRKGFENALLAVPPSRP---HIKNI

MaACS-5 MTTQLYSIEVACSPETPGCKPRRSVLSPDKLVQSYQSFNGDGSITTL

MaACS-6 MATQMSYVWVPNSPDIPGCKPRRSVLCPDKILLENYPSVKAGSTLTTU

MaACS-8 MPSPFKKYNLDQKQSVETPGR-KPGASGHYRHAAYGDALVTNIREAP---HIETU

MaACS-10 METLVNGKYAVEYDEVVDHIYRNVMATGGLIDRPMPPYVDIKERTM

MaACS-11 MPKCFTHAVGPEDVKGETRIRRS---IQAVDKLMDSP---SSDIKTI

MaACS-12 MTKCLTVEVGPADVQGETRIRRS---VLSAKRLMSSP---SDDIKTI

ScFAA1 MVAQYTNVPYKKAANEHETAPRNN---YQCREKPLVRPPNTKCSIV

ScFAA2 MAAPDYALTDLIESDPRFESKTRLGAYTKGSDEVIEELYSQPLPITSYPYKTFLLKQAVASINPDNEAGESSIYRS---SLSENLVSCVDKNLRTA

ScFAA3 MSEQHSMAVCKKAANEHETAPRNN---VRVKRPLIRPLINSSASTU

ScFAA4 MTEQYSMAVGEAANEHETAPRNN---IRVKDQPLIRPINSSASTU

100

101

MaACS-3	GESVITHRSKTVPHGTLTKRPSEKIKTLHDVWQGTGAAVNPAGRSLMFMLQNQFAFIEATVEQVNRRIIGGRFTAEVFKATGLKPKTDTPVVGTEMPYS
MaACS-4	NDAPQHGLKLPNGAALGSVYDPVDTDFGGVWQTYAQVNDRIITRFSGLVKTHKDVHGLATVQGKWSLGIWAINR
MaACS-5	VENPLEGIQRSEGGEFLGHEDIVDNAOPVEWLSVTRVQGERVANFETALITOLGLKVDSNFGIFRSINR
MaACS-6	VENVEQGLVLRSGAHLGHLPDIVNGQPQAKVQSGVWVDSKRVTHFETALAHGLGSPKQNFGLIESINR
MaACS-8	NMMWQNSVTKYGGNDFLGHLPDNTVAOTYGGVSWETVRQINQVNAFSGIMHLNEVILGNRQLNRWALGLWHSGR
MaACS-10	AHLEEYMANTYEDKDAMGVEDILKVKHKVERQAANPGEKPTWITTYELSDVNMSSVQAQNVADRVLTITRLGVKEGDFWMTFASFC
MaACS-11	MDVLOYSAKVRPNLNAIGYEDKIVMTBEEKELTKMWSGEPVKEKKTWKYFKLSGVHYLTAKDKAIDSISSGLRWGVPEPKE
MaACS-12	MDVENHSHVTRPNLNAIGYEDKIVKVEEEKVVKVNGEEVKEKKTWKFKFMSGVHWTADAKQVDSISGLRWGVPEPKD
ScFAA1	VEFVLECFQAKNNSNANGCHDYKEIHEESKSMWKKVDGKETSVEKQWVYELSHYHVSFDQLTDMHETETAEVKGICLKPNDIDKLHLVYATS
ScFAA2	MDHWMFSARRVQRDCLGSPEDKATGTVVEETFRPESVSTVSKPCNHSILSLVNTKRKRPLEANDFVVAULSHNN
ScFAA3	VEFALCEFNKGGKRGDMAWDQVIEIHTKKTIVKRVGDKDKSEKTKTLVYEMSPYKMTYQELIIVWHDGCEIAKIGIKPNGEHKHFIFASTS
ScFAA4	VEFALCEFTKGGKRGDMAWDQIIDIHETKKTIVKRVGDKDKPIEKTWLYVELTPYMTNTYEEMICVMHDIQSLIKIGVKNGENKHFIFASTS

Figure 25A (cont.)

301
 QESVAAQAFVRYSFVAVPIHDLRNNDLVEVVDQTKLKADIVSOKVLPILQLSLKE-CPTIKITIMAGIYISQEQLE-----M-----AAQHG
 PEWTIASEACSAYNLVSGLYDTLGPFAVTVYGINHAECISIVTISVDHIATILNESSK-MPLGKUIISMDDLDGTGRAGPG-----LA-----PTGTILRTVYADQKG
 PEWTMSELJAGVMYFITSPLDYDTLQVSAIEYVNOCTEMETITIASADKASILLNMKST-LPTLKNIVVMGSLLEDALVVE-----GREMD
 PEWTMSELJAGVMYFITSPLDYDTLGVAAIEYVNOCTEMETITIASADKASILLNMKSA-LPTVQVTHVMGFTDALVAE-----GKELN
 PEWFITEMSONCYNLISVALYDTLGEDAVEYIVNHAIEIYVSSANHIASLLENAEK-LEKIKMIVSMDALHDTVPVPG-----AT-SAAQVLRAWGAQKG
 PEWFLTAIGFOSQSVNITVITAYDSMDKSI OFIVDSQPKAFIADAHTLPVSKLMOKGNSGVKAWIYTGQEWETDAIKKMEQVENRISFELVHIDELKKT
 ANWILLVAHGAFITSMILVITVDTLGBEGLIHSWNEAEVGTATINADLIKTMTNVSGR-CPTLKNIVYDGEANAAD-----VIALQTAHPH
 ANWILLAHGAFITSMILVITVDTLGEDGLIHSWNEAEVATATINADLIINTIKNVACK-CPTLKKLIVYDGDAPAD-----VIALQEAHPH
 HKWMKMFJGAOSQGIPIWYATVDTLGEKGLIHSLVQIGSKAFTIDNSLPSLIKPVQA-AQDVKYVLIHFDSISSDDRQSGKIQS-AHDAINRIKEVRPD
 PEWILTDLJACQVSLNTALNETLGPNTSEYILNLEAPILIFAKSNMTHVKMVPD-MKFVNTLVCMDELTHDELMLN-----ESLLPVKNSLNEK
 HKWMKIFLGOISQGIPIWYATVDTLGEKGLIHSWNETESAFTIDNQLAKMIVPLOS-AKDIKFLHNHNEPDPNDRRQNGKLYKA-AKDAINKITREVRPD
 HKWMKFTLGOISQGIPIWYATVDTLGEKGLIHSWNETESVAFITIDNQLSKLAVPLKT-AKNVKEVTHNEPDPNDRRQNGKLYKA-AKDAVAVDKIKEVRPD

301
 VKLLKFAAVDVEB-----SSTLMPEVQIPEDVAVDIAVNTKSSSLSGKAMLTAEALIAAMTAFTESLPAK---KRPSSKDRLLSHESNGDVLVSFVM
 VLLYDWSEVEAV-----IQHGRKHTPPSSDAYTLCYTSQITGLP---CAILTCGLIALASSDVA-----TPVLADDCUJSISELPLPHVFGCRM
 ITHIVAWSOVERD-----FNNPAPANPPDPDVATLCYTSQITGTP---CAILTCGLIFVAGLASFHMMAKHQKFFIPSSVDTHISVPLAHVFERLS
 INIVSWTDMKS-----LERPVEAVHPDAEDIALCYTSQITGTP---CAILTCGLIFVATIASFHMMAKHGFFIPSPADTHSVPLAHVEERLC
 IKVYDFNEIESL-----AEFRKHLPEBADEVASLCYTSQITGTP---CAMLTFRFVATVGTNREG-----MLLTEDDVLTSELPLAHTGSRVI
 KSASNGEQSAGKQKORSSEDAEGAQDELEVIVKADDLACIAYTSQITGTP---CAOLTICGLMAATGSAAMEG---DQLDKETDIVLSVPLAHVLEFVI
 LQLITLEELKQL-----VDHPVEPTPBAEDCSQIAYTSQITGTP---CEWILTICGLIJAFATGGVKNMLEK-----YIREGDVLLAYPLAHVLEFVW
 LQLITLEELKQL-----VDNPVAPTPAAKYCCQIAYTSQITGTP---CEMLTICGLIJAFATGGVKNMILT---YVHEGDVLLAYPLAHVLEFLV
 IKTFSFDDILKLEKE-----SCNEIDVHPGKDDLCQIAYTSQITGTP---CEWLKESVWAGVGCASLNVLK---FVGNTRDVTGFLPLAHVLEFLV
 IITFSLEQVEQV-----CFNKIPAIPDPDSLYTISFTSQITGLP---CEWMSRNIASQIAFAFSTFRIP-PDKRQQLYDMCFPLPLAHVFERMV
 IKIYSFEERWKLEKK-----SKDEVKLHPPEPKOLACIAYTSQISAP---CEWLTICGLIJNSGIAVGHNVRG---WIGSTDVLSFPLPLAHVLEFLV
 IKIYSFDEIIELEKK-----AKDEVELHFPEDPACIAYTSQITGTP---CEWLTICGLIJNSGIAVGHNVRG---WIGSTDVLSFPLPLAHVLEFLV

301
 MaACS-3
 MaACS-4
 MaACS-5
 MaACS-6
 MaACS-8
 MaACS-10
 MaACS-11
 MaACS-12
 ScFAA1
 ScFAA2
 ScFAA3
 ScFAA4

400
 MaACS-3
 MaACS-4
 MaACS-5
 MaACS-6
 MaACS-8
 MaACS-10
 MaACS-11
 MaACS-12
 ScFAA1
 ScFAA2
 ScFAA3
 ScFAA4

Figure 25B

401	SSAIIIMGGSLVFPSPGLMKN	VLHISQASAEITIPASTPIILEKIEHEALQLTYGQG	SMRRGRFAA	500	ITTT		
MaACS-3	ELFAMAAGGKIGYSTGDPJR	LLBNVSHKLSIFPAPRLLNRYVAKVYAA TVCAPGJTGALARRGLATL	NIREGK	GFFH			
MaACS-4	QAVMISGAARIGYVQGDITJK	LLDNVAIIQITIFVSPRLLNRYDKVLGKAKGGLAAFLFNRAFET	KVANLRK	ILEH			
MaACS-5	QAVMISGAARIGYVQGDITJK	LLDNVAVLRHTIFASVPRLNRYDKVLGKAKGGLAAFLFNRAVNS	KVANLRK	VLEH			
MaACS-6	DTCSMYSGGKIGYFRGDIIL	LLBNVAELRHTIFEPAPRLLNRYAKLVASTIEAPGLVGAARGVAA	MANLAAGK	GVNH			
MaACS-8	SHFVVMGCRLEGRARTLMDDAVAPTAGSRSKGLGLKALQ	TLMAGVPTTIFERIRKGLAEVNKQSPFIRTLFFAALNT	WAIIVQATGS	ENFVT			
MaACS-10	ENCLFWGVTLGYGTVRTLTDASVR	ECQGIKELRITLMTGVPVAVETIRKGVLAQVNQGSPLVQSVFNAALNA	AWCMRDKL	GALT			
MaACS-11	ENVCLFWGVTLGYGTVRTLTDASVR	ECQGIKELRITLMTGVPVAVETIRKGVLAQVSQGSPLVQKIFHAALNA	AWCLDRKL	GALT			
MaACS-12	ELLSFYWGACIGVATVKTLTSSSVR	NCQGLQBEKPTIMVGVAAVVETVRKGLINQIDNLPFLTKIFNTAYNT	LNMR-LH	IPGG			
ScFAA1	IAYDLATGFGIGFLHKPDBT	VLVEILKILKAYALDVPRIILTRFEAGIKNALDKS-TVQRNVANTILDS	SARFTARGGPKSIMNF				
ScFAA2	EFEAFYWGILGYGSVKTLTNTSTR	NCKGHLVEFKPTIMIGVAAVVETVRKATLEKISDLTPVLQKIFNSAYSME	KS	VPCT			
ScFAA3	EFEAFYWGILGVANVKTLTPTSTR	NCQGLMEFKPTIMVGVAAVVETVRKGLAKINELPQWSQTLFWTYAL	EE	RN			
501	SLWDLIGLGEVRSKLGG	KVRMVVTH	PIKPEITLDYIRAMGIIHITTT	QRIH	TSGIVTARNMLDYANAPHL	PPVGCNEVK	VDDVAAGFTSADEPNP
MaACS-3	PLWDRILFSKVAQALGG	NVRLMLTASAPISAEILLERVRVAFCCWEALGG	QGGGAATNTVI	GETEAGHV	PPACCEIK	VDVPELNFATDKPFP	
MaACS-4	AIWDRLVFGAIRARLGG	KVKHIVSGSAPIAPDVMDFLRICFSADWYEG	QIIP	QWAGLCMSYR	GDLTSCQV	PPQLQVEVR	RDVPMHMTSQDKPRP
MaACS-5	PLWDRLVFGAIRARLGG	KVKHIVSGSAPISPDVMDFLRICFSADWYEG	QIIP	QWAGLCMSYR	GDLTSCQV	PPQLQTEVR	KDTPSMNYSADKPPF
MaACS-6	ALWDRLLFNKVMALGG	RVDVILLTGSAPIAKEVLSFLIRAGGVWLEG	SL	GMATATITMA	DEYTPGHI	CPRAGCEIK	VDVPAMNVLSTDQVP
MaACS-8	KTIDSLVFSMAKELVGG	KLRLTITGGAGISDETHRFISWMV	QVNLSG	LVCGVAAVTLPRMGHRLTIV	PPAPSLEIK	VNVPDTEVTGDN	
MaACS-10	GIFDTWVFNKVRQOTGG	RLRYALSAGAPISQETQREITTL	CPILQAG	SCGKCSIMTP	EAFNNRV	SRVPCTEVR	VDVPDAGVSTDSRP
MaACS-11	GIFDTWVFNKVRQOTGG	RLRPAISGAPISQETQREITTL	CPILQAG	SCGMCALITP	DVENYSRV	SRVPCTEVR	VDVPDAGVSTDLPLP
MaACS-12	GALGNLVEKKIRIATGG	QLRVILNGGSPISRDQOERLNL	CPMLIG	LETCNSTITLDP	ANFELGVAG	DLTGOVTWR	VDVEELGYFAKNN
ScFAA1	LVYHRVLDKIRDSL	QLSNHSPIITGSAPISKDITLPLRSALDIGRQGG	LE	TFAGVCLSEP	FEKDVGSQA	AGISAECR	KSVPEMGYHADKO-L
ScFAA2	GFLSNVFNKVRQATGG	HLKVTMNGGSAISIDAKPESIVL	CPMLIG	LE	TVANACVLEP	DHFEYGLVAG	DLVGSVTAK
ScFAA3	GLLSGLIFKRIREATGG	NLRFTLNGGSAISIDAKPESLNL	CPMLIG	LE	GVANACVLEP	EHEFDYGLAG	DLVGTITAK
ScFAA4							VDVEDLGYFAKNN

Figure 25B (cont.)

601
 MaACS-3 RGEILIRGPNVMAKGVYKPKGALSTAIIDEECDEHSHS ELGTFFHSNGLDVLGKKKTKSAVGSPTS
 MaACS-4 RGEICVRGPGMIPGVLDEAKPKETIDEEGHLHS DJATMSCKGTYNIDRKANVFKLSOGEYIAENIEGRFLSKVPFIQOVLVHGDSTESCLVAILIP
 MaACS-5 RGEIMLRGHSVFKGVYKPKQHEETLDAGCBASTDVGWDERGRINVIDRVKNIFKLAOGEYIAPKIBAVLAKHY-LMAOVFVYGDSTFQATLVGWVVP
 MaACS-6 RGEIMLRGHSVFKGVYKPKQHEETLDADQSSSTDVGQWDAORIVVIDRVKNIFKLAOGEYIAPKIBAVLAKHF-LMAOIFVYGHSLQATTIVANVVP
 MaACS-8 RGEIMLRGHSVFKGVYKPKQHEETLDADQSSSTDVGQWDAORIVVIDRVKNIFKLAOGEYIAPKIBAVLAKHF-LMAOIFVYGHSLQATTIVANVVP
 MaACS-10 RGEIMLRGHSVFKGVYKPKQHEETLDADQSSSTDVGQWDAORIVVIDRVKNIFKLAOGEYIAPKIBAVLAKHF-LMAOIFVYGHSLQATTIVANVVP
 MaACS-11 RGEIMLRGHSVFKGVYKPKQHEETLDADQSSSTDVGQWDAORIVVIDRVKNIFKLAOGEYIAPKIBAVLAKHF-LMAOIFVYGHSLQATTIVANVVP
 MaACS-12 RGEIMLRGHSVFKGVYKPKQHEETLDADQSSSTDVGQWDAORIVVIDRVKNIFKLAOGEYIAPKIBAVLAKHF-LMAOIFVYGHSLQATTIVANVVP
 ScFAA1 RGEIMLRGHSVFKGVYKPKQHEETLDADQSSSTDVGQWDAORIVVIDRVKNIFKLAOGEYIAPKIBAVLAKHF-LMAOIFVYGHSLQATTIVANVVP
 ScFAA2 RGEIMLRGHSVFKGVYKPKQHEETLDADQSSSTDVGQWDAORIVVIDRVKNIFKLAOGEYIAPKIBAVLAKHF-LMAOIFVYGHSLQATTIVANVVP
 ScFAA3 RGEIMLRGHSVFKGVYKPKQHEETLDADQSSSTDVGQWDAORIVVIDRVKNIFKLAOGEYIAPKIBAVLAKHF-LMAOIFVYGHSLQATTIVANVVP
 ScFAA4 RGEIMLRGHSVFKGVYKPKQHEETLDADQSSSTDVGQWDAORIVVIDRVKNIFKLAOGEYIAPKIBAVLAKHF-LMAOIFVYGHSLQATTIVANVVP

701
 MaACS-3 EPEAFIPFYKYNVLNVLPQGLAAYRKIVNNPKLRQAVLKELIKACKDAGLKGFBIPKAILLESEAFVENDKMTPTFKIKRHPVVOYREQLTALYNB
 MaACS-4 DAETLKPWADHGL-----GKSYBELCAHPAYKETLLKELKEFGRENDLKGFBIILKNHVTABQFSFENDLLPTFKLKRHTAKEKYIABIELMYNG
 MaACS-5 DAETLKLWAKENKL-----GKSYBELCALPOLRTTLQKELATFGKESDLKGFBIIPKNEHVISEQFSFENDLLPTFKLKRHTAKEKYIABIELMYNG
 MaACS-6 EPETFLPPANA IAG-ASV TAGDVEGLNKLQDPKVKTA VVKELERKAGAGAMRGFEFVKRVHLTTDAFSVDNGMMPTFKVRRPOVAEHFREQITAMYKE
 MaACS-8 S-----HAGASDKFEILDILKSQAAGLKSSETVQGVIIIDSDMMT-NGFMSSSKVKRREVRKAHNDTEEMWKK
 MaACS-10 SEPRILELAKAKGLESR-----DFAVLCHDKVILKAVLDACLATKAKAGLKPABELIQQVYLESEHWTAGCGLLPAQKLKRKEINQAVADQTKQVGS
 MaACS-11 SEPRILELAKAKGLESR-----DFAVLCHDKVILKAVLDACLATKAKAGLKPABELIQQVYLESEHWTAGCGLLPAQKLKRKEINQAVADQTKQVGS
 MaACS-12 NHAPLTKLAKKLGIMEQKOS--SINIENYLEDAKILKAWSDILKTKDQGLNGIELLAGIVFFDGEWTPONGFVTSACLKRKDILNAVKKVDVAVSS
 ScFAA1 DVDAAOPTILAAKHIPEVKTW-KEVLVENLRNKKLRKFFLNKINKCT--DGLQGFEKLHNKVGLEPIJLEDDVPTFKIKRASKFEKFDLQDLVAB
 ScFAA2 NPGPLSKFAPVKLRIMKKGE-----DIENYTHDKALRNVAIFKEMATAKSGQLNGIELLAGIVFFDGEWTPONGFVTSACLKRKDILNAVKKVDVAVSS
 ScFAA3 NLGHLKSLAIELGLMVPGE-----DVESYTHEKLDQAYCKDMLSTAKSGQLNGIELLAGIVFFDGEWTPONGFVTSACLKRKDILNAVKKVDVAVSS
 ScFAA4

Figure 25C

MaACS-3	801	---
MaACS-4	IHQESKL	---
MaACS-5	IH	---
MaACS-6	IA	---
MaACS-8	INASTPVAKL	---
MaACS-10	F	---
MaACS-11	K	---
MaACS-12	A	---
ScFAA1	S	---
ScFAA2	GSLVKTEKL	---
ScFAA3	NS	---
ScFAA4	NT	---

Figure 26A

1	MaACS-1	MDAVPAVAAAAIPAAMVVGSKLATPRDVKLAKGLVSAKLQPSYEKNDISINISYRFEETCKKHPHREALVFEKG	100
	MaACS-2	MASTKSLRTWRLEFALVSMHAKDLRPWSRIGTAVFTGSRNNAKSGLSLLPLFLRLTRLTGCTWISWRPT	
	MaACS-9	MVALPIVAAAVPAAMVYSSKALPRDMKLKSLIGAKMAVSAMEKNDALNLTREDECYRKYPDREALVFEKG	
	MaACS-7	MHIINATRPFSRLSPTVRRPWLGCGQTRPYAIAQTEASPRLSVWRCGTTVGTQLCEDPIGAYWDRVVRNKHGRLGLVVKHE	
	ScFAT1	MSPIQVVVFALSRIFLLPRLIKLIITPIQKSLGYLFGNVFDELDRKRYRKEDWYIIIPYELKSVFCQIIDVRRHRFQNWYLFIKQVQQNGDHLAISIYTRP	
	ScFAT2	MTSAATVTASFNDFTSVSDNVAVIVPEJDTQVTVRDLSHMWGH	
101	MaACS-1	LSKGVKRGELVSLFMQKPERLEFWLGLNKGATGARLNTNLSGKPLTHSRRTAFASIIIMDAELPTPIY-	200
	MaACS-2	KKKERVAMMHNSPLFIITWILMLKIMVVPATFNQIAGPVIHVSUKVADAKFLFDYELAPVIQ-	
	MaACS-9	LAKGIKRGDIVSLFMLRPERIFCVLGLNKGATGARLNTNLTGKPLTHSRRTATSSMIMDTLTDAIA-	
	MaACS-7	LYESGLRKGRJAVWMPNSAWATLQVATAKSGITLVTLNPAVRRQELLOTSLVECKSLVYVPSLKTSNYS	
	ScFAT1	MAEKGEFQLETFITYIETYNIVLRSLHILHFDYVYQAGDVAIDCTKPLFVFLWLSLWNIGAIAPAFISVNTKGTPLVHSEKISNITQVFIQVDPDASNPJR-	
	ScFAT2	FQTMFTNPNSP-LYGAMFRQDTVAISMRNGLEFIVAFLGATMDAKIGAPLSPNYKKEKERNFYINDLKSKAICVPRKGTTKLQSS	
201	MaACS-1	SVLDDEVLEMGVQIYSYG	300
	MaACS-2	KSLNEIKDMGVNLYTVTPKDQVLGQLYANLPEAARQVLDPAFSPFCYVEWQNLSTEGSNESRQ	
	MaACS-9	NSLDEIDEMGYSIYSYG	
	MaACS-7	EMLLDLLPELQYQSPNQLLTEKLPSLRQVIVFDNGSQVPETAKLGLTKYQDLLKNPSTANDGALEKERLAIDNRDITNLQFISGTHGLPAGVSLSHDN	
	ScFAT1	ESEEEIKNALPDVKLNY	
	ScFAT2	FILKSASTFGCFIVELAFDTRFR-VEYDIYSPEDNYKRVYRSLNNAKFNVTNPVKFPG-FARSSDVALIILHESSEIESTENTVPLIHLN	

Figure 26A (cont.)

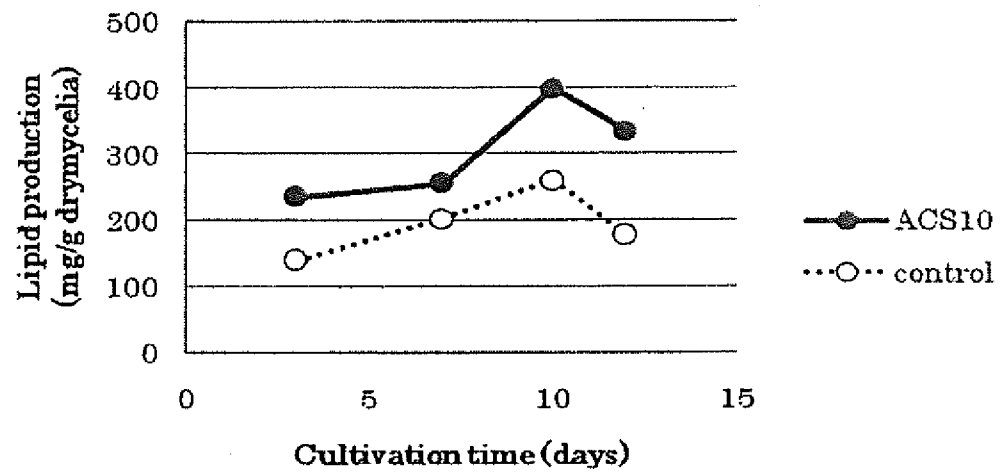
	301	ANVAALFWTSFVHFSEKDRVIALPIVTSAGAVLGCVAWVTGATWVLAR-KESTTSFDECRANKVTVIQYIGECRYLLNA--PSPDKTHTIRMAH	400
MaACS-1		CNLASISVGTLCGKPKENKVYITLPIVTSAGAILGLGQSFFSGCTINLAR-KTSVTHFWRDCEVNDVTHFQYVIGELCRYLLNA--ESPLDKRHKVRMAF	
MaACS-2		ASMGPPQFVNRFRVHFSESDRVYLSLPIVTSAGAILGVIACTSCATLILAR-KESATHFWEDGRVANNATVQYIGECRYLLNT--ESPLDKRAHSIRLAH	
MaACS-9		ILNNGIHLGDMRLTEKDLCCPVPIFCFGLVIASLAAHTGAGI IYPSQS-DAEATLRVSEECATALHGVPTMLEEMNH--NFAKYNLSTLRTGIAA	
MaACS-7		SSVGCQVFGVHLHMTNESNFTAMPPIFSTANLGCACAILSHGGCLALSH-KESATFWKQVYL TGA THIQYVGEVCRYLLHT--ISKYEKMHKKVAV	
ScFAT1		IVRSTLNIANIYKLTPLDQSYVVMPIFIVHGLIGVLLSTFRTCQSVWVPD-GHPKLFWDQFVKVNCNWFSCVPTISMILNME--KPNPFPHIRFIRSC	
ScFAT2			
	401	GNGMRPDVWNRFRDRFGTPIIGEMVASTGTGTLTNVNTGPNCGAIGYRSLAR-TYDKGLKIAKFDIQTEELTRDKN--GRGIECVADEPCELLTMIDS	500
MaACS-1		GNGMRPDVWAKFOERFNIPHIVYVYAMS-GTSSILNVARNKRDGCAVGFRPPVWR-ALTPPVQLVKVDFDTEELTRDKKTGLCVLCQPCGEI--ELVITLADN	
MaACS-2		GNGMRPDVWTRFRDRFGTPIIGEMVASTGTGALSNVNTGPGGACAGYRSLAR-ALDKGLRIARFDVQTEELVRDKN--GYGIECKPGEI--ELLTLVDA	
MaACS-9		GSPVPIEVMKNVQTKMLKELTIOGMITSPVSEMTLITDELDRDCETVRIMP--HLEAKVVPETG----ETLPVNSS--ELQTRGYA	
MaACS-7		CNGLRPDIWQDFRKRFTNIEVIGERFMAITAPFATITFQKGFQGTGACRNVTILIQWFLSFQQLVRMDPNDDSVTVRNSKGFCEVAPVGEI--MLMRIF	
ScFAT1		SSALAPATFHKLEKEFNAPVL-BAMANTASHQMTSNLPPG--KRKPPITVQV--PQGVTVVTLDDN--DNVLPQGV--EAVSIRGEN	
ScFAT2			
	501	SD-FTRAEQ--HKNAGANSKAWQDAPSVGDQYERTGILIRDDADGYFTFGDVGDTFRWKS--NVSTAEVSEVLSAYPD--CIEVAVYVQVPGHDGRAG	600
MaACS-1		KT-TGARYA--FNQPEVSKARLVQNVVVDKDIYERTELLDY-SKQVWYFADAGDTFRWKG--NVSTAEIADTIGRVEGV--ASCTVY--VSVPGMDGRAG	
MaACS-2		KE-PNKDEK--HQNAATNKKIYKQVFEKAGDMYERTGILIRDSGDFYFEGDVGDTFRWKS--NVSTAEVSEVLSQVPCD--IEVNVYVQVPGQDGRAG	
MaACS-9		VMEG----WRSQEQI--DAWYDK-DGMHTSTAVLDDKGFCDRIKDMVIRGGKIHPIV--VENCLEFMDGV--KNVSMIVPDKRYGEQVC	
MaACS-7		PKKPETSFG--LGNAKETKSWVRDVFRRGDWVRG--ELLKADVGLWYFLDMGDTFRWKS--NVSTAEVSEVLSQVPCD--IEVNVYVQVPGQDGRAG	
ScFAT1		VT-----LEMANNPKAN--K--ENFTKR--ENYFKTGRQGYFDPGEFLVLTGRIKELINRGGKISPIELDGLMLSHPKI--DEAVAF--VPDDWYGVVQV	
ScFAT2			

Figure 26B

601	MaACS-1	MAAIVSKSDTMNWD	FAKFAKNLPKYSV	IFIRKMP	EMEITGTFKQKQELVNEGMDPSKIDEMLWLDG-HSYRPF	700
	MaACS-2	MAALVLKNSIVQMACGSQAKPHVDEAALNAFLRDLSDVVKLPAYAI	RFRLIAEQ	ELETTGTFANKKEELKKEGFDLCKVKERLYMTPKGEYAPF		
	MaACS-9	MAAIVSKSDMDWEK	FAAYALKNLPKYSV	IFIRKMP	EMEITGTFKQKQELVNEGIDPKTIANEMLWLDG-HHYKPF	
	MaACS-7	AWISTKDGKTVSLPAVQK	FCEGKIAH	YKQVPRVWVWESNEFPTIPSGKITQKNEMRELTKAKLQLP		
	ScFAT1	FVIFKLTJDNSLDITAKTKLLN	DSLRLNLPSSAM	LFVKFVDE	IKMTDNHKILKQYREQKLPKGLDGDNDTIFHLKNYKRYEVL	
	ScFAT2	AAIVLKKGEKMTYEELVN	FLKKHLAS	FKIPTKJVFVDK	LPKTATGKIQRRILAEITFAKSSRNKSKL	
701	MaACS-1	KEAEHTRVWSGKARL	RIKLRFVR			
	MaACS-2	GVAENEQILAGARL				
	MaACS-9	KAAEHQRVISGKARL				
	MaACS-7	TAADWEAIDAQTIKL				
	ScFAT1					
	ScFAT2					
726						

Figure 27

A



B

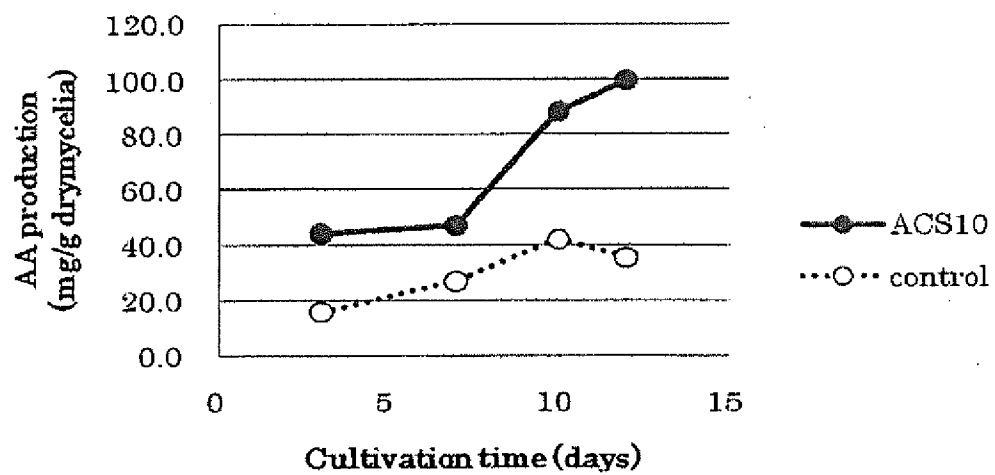
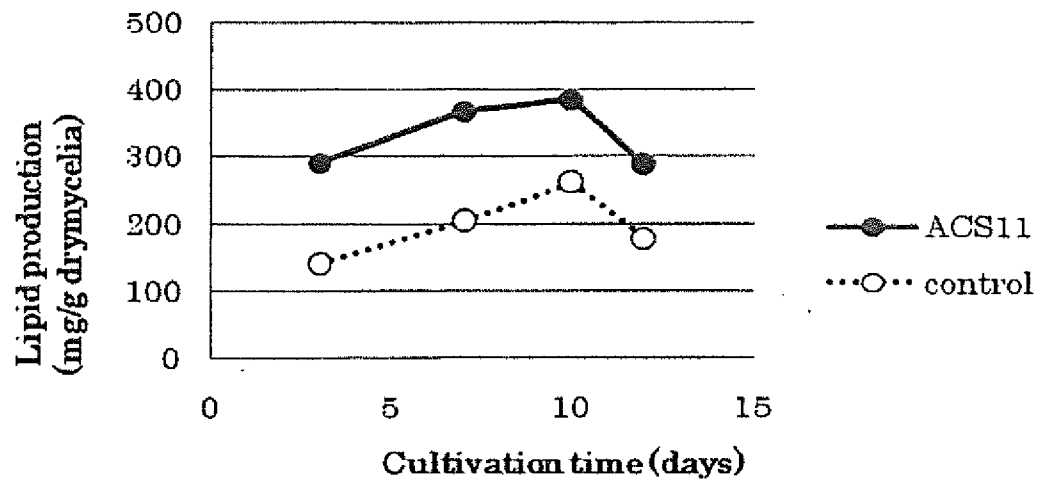


Figure 28

A



B

