



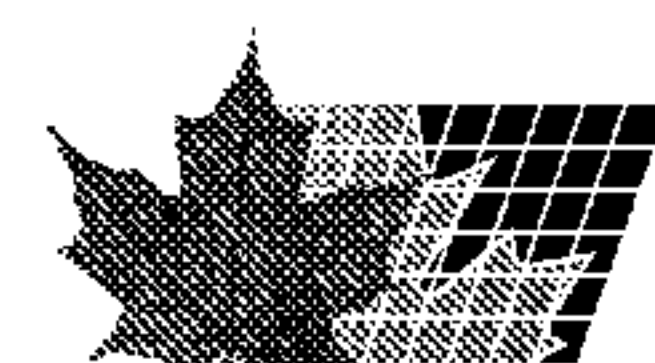
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(54) Titre : POLYNUCLEOTIDES ET POLYPEPTIDES DERIVES DE LACTOBACILLUS RHAMNOSUS HN001
(54) Title: POLYNUCLEOTIDES AND POLYPEPTIDES DERIVED FROM LACTOBACILLUS RHAMNOSUS HN001

(57) **Abrégé/Abstract:**

Novel polynucleotides isolated from *Lactobacillus rhamnosus*, as well as oligonucleotide probes and primers, genetic constructs comprising the polynucleotides, biological materials, including plants, microorganisms and multicellular organisms incorporating the polynucleotides, polypeptides expressed by the polynucleotides, and methods for using the polynucleotides and polypeptides are disclosed.



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(54) Title: POLYNUCLEOTIDES AND POLYPEPTIDES DERIVED FROM *LACTOBACILLUS RHAMNOSUS* HN001

(57) Abstract: Novel polynucleotides isolated from *Lactobacillus rhamnosus*, as well as oligonucleotide probes and primers, genetic constructs comprising the polynucleotides, biological materials, including plants, microorganisms and multicellular organisms incorporating the polynucleotides, polypeptides expressed by the polynucleotides, and methods for using the polynucleotides and polypeptides are disclosed.

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POLYNUCLEOTIDES AND POLYPEPTIDES DERIVED FROM *LACTOBACILLUS RHAMNOSUS* HN001

5 Technical Field of the Invention

This invention relates to polynucleotides isolated from lactic acid bacteria, together with probes and primers specific to the polynucleotides; genetic constructs comprising the polynucleotides; biological materials, including plants, microorganisms and multicellular organisms, incorporating the polynucleotides; polypeptides expressed by the polynucleotides;
10 and methods for using the polynucleotides and polypeptides.

Background of the Invention

The present invention relates to polynucleotides isolated from a specific strain of lactic acid bacteria, namely *Lactobacillus rhamnosus* HN001 (*L. rhamnosus* HN001). Lactic acid
15 bacteria, and their enzymes, are the major determinants of flavor and fermentation characteristics in fermented dairy products, such as cheese and yogurt. Flavors are produced through the action of bacteria and their enzymes on proteins, carbohydrates and lipids.

Lactobacillus rhamnosus strain HN001 are heterofermentative bacteria that are Gram positive, non-motile, non-spore forming, catalase negative, facultative anaerobic rods
20 exhibiting an optimal growth temperature of $37\pm 1^{\circ}\text{C}$ and an optimum pH of 6.0 – 6.5. Experimental studies have demonstrated that dietary supplementation with *Lactobacillus rhamnosus* strain HN001 induces a sustained enhancement in several aspects of both natural and acquired immunity (See PCT International Publication No. WO 99/10476). In addition, *L. rhamnosus* HN001, and certain other Gram-positive bacteria, can specifically and directly
25 modulate human and animal health (See, for example, Tannock *et al.*, *Applied Environ. Microbiol.* 66:2578-2588, 2000; Gill *et al.*, *Brit. J. Nutrition* 83:167-176; Quan Shu *et al.*, *Food and Chem. Toxicol.* 38:153-161, 2000; Quan Shu *et al.*, *Intl. J. Food Microbiol.* 56:87-96, 2000; Quan Shu *et al.*, *Intl. Dairy J.* 9:831-836, 1999; Prasad *et al.*, *Intl. Dairy J.* 8:993-1002, 1998; Sanders and Huis in't Veld, *Antonie van Leeuwenhoek* 76:293-315, 1999; Salminen *et al.*, 1998. *In: Lactic Acid Bacteria*, Salminen S and von Wright A (eds), Marcel Dekker Inc, New York, Basel, Hong Kong, pp. 211-253; Delcour *et al.*, *Antonie van Leeuwenhoek* 76:159-184, 1999; Blum *et al.*, *Antonie van Leeuwenhoek* 76:199-205, 1999; Yasui *et al.*, *Antonie van*
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Leeuwenhoek 76:383-389, 1999; Hirayama and Rafter, *Antonie van Leeuwenhoek* 76:391-394, 1999; Ouwehand, 1998. *In: Lactic Acid Bacteria*, Salminen S and von Wright A (eds), Marcel Dekker Inc, New York, Basel, Hong Kong, pp. 139-159; Isolauri *et al.*, S 1998. *In: Lactic Acid Bacteria*, Salminen S and von Wright A (eds), Marcel Dekker Inc, New York, Basel, Hong Kong, pp. 255-268; Lichtenstein and Goldin, 1998. *In: Lactic Acid Bacteria*, Salminen S and von Wright A (eds), Marcel Dekker Inc, New York, Basel, Hong Kong, pp. 269-277; El-Nezami and Ahokas, 1998. *In: Lactic Acid Bacteria*, Salminen S and von Wright A (eds), Marcel Dekker Inc, New York, Basel, Hong Kong, pp. 359-367; Nousianen *et al.*, 1998. *In: Lactic Acid Bacteria*, Salminen S and von Wright A (eds), Marcel Dekker Inc, New York, Basel, Hong Kong, pp. 437-473; Meisel and Bockelmann, *Antonie van Leeuwenhoek* 76:207-215, 1999; Christensen *et al.*, *Antonie van Leeuwenhoek* 76:217-246, 1999; Dunne *et al.*, *Antonie van Leeuwenhoek* 76:279-292, 1999).

Beneficial health effects attributed to these bacteria include the following:

15 **Increased resistance to enteric pathogens and anti-infection activity, including treatment of rotavirus infection and infantile diarrhea** – due to increases in antibody production caused by an adjuvant effect; increased resistance to pathogen colonization; alteration of intestinal conditions, such as pH; and the presence of specific antibacterial substances, such as bacteriocins and organic acids.

20

Aid in lactose digestion – due to lactose degradation by bacterial lactase enzymes (such as beta-galactosidase) that act in the small intestine.

25 **Anti-cancer (in particular anti-colon cancer) and anti-mutagenesis activities** – due to anti-mutagenic activity; alteration of procancerous enzymatic activity of colonic microbes; reduction of the carcinogenic enzymes azoreductase, beta-glucuronidase and nitroreductase in the gut and/or faeces; stimulation of immune function; positive influence on bile salt concentration; and antioxidant effects.

30 **Liver cancer reduction** – due to aflatoxin detoxification and inhibition of mould growth.

Reduction of small bowel bacterial overgrowth – due to antibacterial activity; and decrease in toxic metabolite production from overgrowth flora.

Immune system modulation and treatment of autoimmune disorders and allergies – due to enhancement of non-specific and antigen-specific defence against infection and tumors; enhanced mucosal immunity; adjuvant effect in antigen-specific immune responses; and
5 regulation of Th1/Th2 cells and production of cytokines.

Treatment of allergic responses to foods – due to prevention of antigen translocation into blood stream and modulation of allergenic factors in food.

10 **Reduction of blood lipids and prevention of heart disease** – due to assimilation of cholesterol by bacteria; hydrolysis of bile salts; and antioxidative effects.

Antihypertensive effect - bacterial protease or peptidase action on milk peptides produces antihypertensive peptides. Cell wall components act as ACE inhibitors

15

Prevention and treatment of urogenital infections – due to adhesion to urinary and vaginal tract cells resulting in competitive exclusion; and production of antibacterial substances (acids, hydrogen peroxide and biosurfactants).

20 **Treatment of inflammatory bowel disorder and irritable bowel syndrome** – due to immuno-modulation; increased resistance to pathogen colonization; alteration of intestinal conditions such as pH; production of specific antibacterial substances such as bacteriocins, organic acids, hydrogen peroxide and biosurfactants; and competitive exclusion.

25 **Modulation of infective endocarditis** – due to fibronectin receptor-mediated platelet aggregation associated with *Lactobacillus* sepsis.

Prevention and treatment of *Helicobacter pylori* infection – due to competitive colonization and antibacterial effect.

30

Prevention and treatment of hepatic encephalopathy – due to inhibition and/or exclusion of urease-producing gut flora.

Improved protein and carbohydrate utilization and conversion – due to production of beneficial products by bacterial action on proteins and carbohydrates.

Other beneficial health effects associated with *L. rhamnosus* include: improved
5 nutrition; regulation of colonocyte proliferation and differentiation; improved lignan and isoflavone metabolism; reduced mucosal permeability; detoxification of carcinogens and other harmful compounds; relief of constipation and diarrhea; and vitamin synthesis, in particular folate.

Peptidases are enzymes that break the peptide bonds linking the amino group of one
10 amino acid with the carboxy group (acid group) of an adjacent amino acid in a peptide chain. The bonds are broken in a hydrolytic reaction. There is a large family of peptidase enzymes that are defined by their specificity for the particular peptides bonds that they cleave (Barrett A J, Rawlings N D and Woessner J F (Eds.) 1998. *Handbook of proteolytic enzymes*. Academic Press, London, UK). The two main families are exopeptidases and endopeptidases.

15 Exopeptidases cleave amino acids from the N- or C- terminus of a peptide chain, releasing free amino acids or short (di- and tri-) peptides. Different types of exopeptidases include:

- Aminopeptidases - release a free amino acid from the N-terminus of a peptide chain;
- 20 • dipeptidyl-peptidases (also known as dipeptidyl-aminopeptidases) - release a dipeptide from the N-terminus of a peptide chain;
- tripeptidyl-peptidases (also known as tripeptidyl-aminopeptidases) - release a tripeptide from the N-terminus of a peptide chain);
- carboxypeptidases - release a free amino acid from the C-terminus of a peptide
25 chain;
- peptidyl-dipeptidase - release a dipeptide from the C-terminus of a peptide chain;
- dipeptidases - release two free amino acids from a dipeptide; and
- tripeptidases - release a free amino acid and a dipeptide from a tripeptide.

30 Peptidases are important enzymes in the process of cheese ripening and the development of cheese flavor. The hydrolysis of milk caseins in cheese results in textural changes and the development of cheese flavors. The raft of proteolytic enzymes that cause this

hydrolysis come from the lactic acid bacteria that are bound up in the cheese – either starter cultures that grow up during the manufacture of the cheese, or adventitious and adjunct non-starter lactic acid bacteria that grow in the cheese as it ripens (Law and Haandrikman, *Int. Dairy J.* 7:1-11, 1997).

- 5 Many other enzymes can also influence dairy product flavor, and functional and textural characteristics, as well as influencing the fermentation characteristics of the bacteria, such as speed of growth, acid production and survival (Urbach, *Int. Dairy J.* 5:877-890, 1995; Johnson and Somkuti, *Biotech. Appl. Biochem.* 13:196-204, 1991; El Soda and Pandian, *J. Dairy Sci.* 74:2317-2335, 1991; Fox *et al.*, In Cheese: chemistry, physics and microbiology. Volume 1, General aspects, 2nd edition, P Fox (ed) Chapman and Hall, London; Christensen *et al.*, *Antonie van Leeuwenhoek* 76:217-246, 1999; Stingle *et al.*, *J. Bacteriol.* 20:6354-6360, 10 1999; Stingle *et al.*, *Mol. Microbiol.* 32:1287-1295, 1999; Lemoine *et al.*, *Appl. Environ. Microbiol.* 63:1512-3518, 1997). Enzymes influencing specific characteristics and/or functions include the following:

15

- **Lysis of cells.** These enzymes are mostly cell wall hydrolases, including amidases; muramidases; lysozymes, including N-acetyl muramidase; muramidase; N-acetyl-glucosaminidase; and N-acetylmuramoyl-L-alanine amidase. DEAD-box helicase proteins also influence autolysis.

20

- **Carbohydrate utilization.** Lactose, citrate and diacetyl metabolism, and alcohol metabolism are particularly important. The enzymes involved include beta-galactosidase, lactate dehydrogenase, citrate lyase, citrate permease, 2,3 butanediol dehydrogenase (acetoin reductase), acetolactate decarboxylase, acetolactate synthase, pyruvate 25 decarboxylase, pyruvate formate lyase, diacetyl synthase, diacetyl reductase, alcohol decarboxylase, lactate dehydrogenase, pyruvate dehydrogenase, and aldehyde dehydrogenase.

- **Lipid degradation, modification or synthesis.** Enzymes involved include lipases, 30 esterases, phospholipases, serine hydrolases, desaturases, and linoleate isomerase.

- **Polysaccharide synthesis.** Polysaccharides are important not only for potential immune enhancement and adhesion activity but also for the texture of fermented dairy products.

The enzymes involved are a series of glucosyl transferases, including beta-(1-3) glucosyl transferase, alpha-N acetylgalactosaminyl transferase, phosphogalactosyl transferase, alpha-glycosyl transferase, UDP-N-acetylglucosamine C4 epimerase and UDP-N-acetylglucosamine transferase.

5

- **Amino acid degradation.** Enzymes include glutamate dehydrogenase, amino-transferases, amino acid decarboxylases, and enzymes involved in sulphur amino acid degradation including cystothione beta-lyase.

10 Sequencing of the genomes, or portions of the genomes, of numerous organisms, including humans, animals, microorganisms and various plant varieties, has been and is being carried out on a large scale. Polynucleotides identified using sequencing techniques may be partial or full-length genes, and may contain open reading frames, or portions of open reading frames, that encode polypeptides. Putative polypeptides may be identified based on
15 polynucleotide sequences and further characterized. The sequencing data relating to polynucleotides thus represents valuable and useful information.

Polynucleotides and polypeptides may be analyzed for varying degrees of novelty by comparing identified sequences to sequences published in various public domain databases, such as EMBL. Newly identified polynucleotides and corresponding polypeptides may also be
20 compared to polynucleotides and polypeptides contained in public domain information to ascertain homology to known polynucleotides and polypeptides. In this way, the degree of similarity, identity or homology of polynucleotides and polypeptides having an unknown function may be determined relative to polynucleotides and polypeptides having known functions.

25 Information relating to the sequences of isolated polynucleotides may be used in a variety of ways. Specified polynucleotides having a particular sequence may be isolated, or synthesized, for use in *in vivo* or *in vitro* experimentation as probes or primers. Alternatively, collections of sequences of isolated polynucleotides may be stored using magnetic or optical storage medium and analyzed or manipulated using computer hardware and software, as well as
30 other types of tools.

Summary of the Invention

The present invention provides isolated polynucleotides comprising a sequence selected from the group consisting of: (a) sequences identified in the attached Sequence Listing as SEQ ID NO: 1-121; (b) variants of those sequences; (c) extended sequences comprising the
5 sequences set out in SEQ ID NOS: 1-121, and their variants; and (d) sequences comprising at least a specified number of contiguous residues of a sequence of SEQ ID NO: 1-121 (*x*-mers). Oligonucleotide probes and primers corresponding to the sequences set out in SEQ ID NO: 1-121, and their variants are also provided. All of these polynucleotides and oligonucleotide probes and primers are collectively referred to herein, as “polynucleotides of the present
10 invention.”

The polynucleotide sequences identified as SEQ ID NO: 1-121 were derived from a microbial source, namely from fragmented genomic DNA of *Lactobacillus rhamnosus*, strain HN001, described in PCT International Publication No. WO 99/10476. *Lactobacillus rhamnosus* strain HN001 are heterofermentative bacteria that are Gram positive, non-motile,
15 non-spore forming, catalase negative, facultative anaerobic rods exhibiting an optimal growth temperature of $37\pm 1^{\circ}\text{C}$ and an optimum pH of 6.0 – 6.5. Experimental studies demonstrated that dietary supplementation with *Lactobacillus rhamnosus* strain HN001 induced a sustained enhancement in several aspects of both natural and acquired immunity. A biologically pure culture of *Lactobacillus rhamnosus* strain HN001 was deposited at the Australian Government
20 Analytical Laboratories (AGAL), The New South Wales Regional Laboratory, 1 Suakin Street, Pymble, NSW 2073, Australia, as Deposit No. NM97/09514, dated 18 August 1997.

Certain of the polynucleotide sequences disclosed herein are “partial” sequences in that they do not represent a full-length gene encoding a full-length polypeptide. Such partial sequences may be extended by analyzing and sequencing various DNA libraries using primers
25 and/or probes and well-known hybridization and/or PCR techniques. The partial sequences disclosed herein may thus be extended until an open reading frame encoding a polypeptide, a full-length polynucleotide and/or gene capable of expressing a polypeptide, or another useful portion of the genome is identified. Such extended sequences, including full-length polynucleotides and genes, are described as “corresponding to” a sequence identified as one of
30 the sequences of SEQ ID NO: 1-121 or a variant thereof, or a portion of one of the sequences of SEQ ID NO: 1-121 or a variant thereof, when the extended polynucleotide comprises an

identified sequence or its variant, or an identified contiguous portion (x-mer) of one of the sequences of SEQ ID NO: 1-121 or a variant thereof.

The polynucleotides identified as SEQ ID NO: 1-121 were isolated from *Lactobacillus rhamnosus* genomic DNA clones and represent sequences that are present in the cells from which the DNA was prepared. The sequence information may be used to identify and isolate, or synthesize, DNA molecules such as promoters, DNA-binding elements, open reading frames or full-length genes, that can then be used as expressible or otherwise functional DNA in transgenic organisms. Similarly, RNA sequences, reverse sequences, complementary sequences, antisense sequences and the like, corresponding to the polynucleotides of the present invention, may be routinely ascertained and obtained using the polynucleotides identified as SEQ ID NO: 1-121.

The present invention further provides isolated polypeptides encoded, or partially encoded, by the polynucleotides disclosed herein. In certain specific embodiments, the polypeptides of the present invention comprise a sequence selected from the group consisting of sequences identified as SEQ ID NO: 122-253, and variants thereof. Polypeptides encoded by the polynucleotides of the present invention may be expressed and used in various assays to determine their biological activity. Such polypeptides may be used to raise antibodies, to isolate corresponding interacting proteins or other compounds, and to quantitatively determine levels of interacting proteins or other compounds.

Genetic constructs comprising the inventive polynucleotides are also provided, together with transgenic host cells comprising such constructs and transgenic organisms, such as microbes, comprising such cells.

The present invention also contemplates methods for modulating the polynucleotide and/or polypeptide content and composition of an organism, such methods involving stably incorporating into the genome of the organism a genetic construct comprising a polynucleotide of the present invention. In one embodiment, the target organism is a microbe, preferably a microbe used in fermentation, more preferably a microbe of the genus *Lactobacillus*, and most preferably *Lactobacillus rhamnosus*, or other closely microbial related species used in the dairy industry. In a related aspect, methods for producing a microbe having an altered genotype and/or phenotype is provided, such methods comprising transforming a microbial cell with a genetic construct of the present invention to provide a transgenic cell, and cultivating the transgenic cell under conditions conducive to growth and multiplication. Organisms having an altered genotype or phenotype as a result of modulation of the level or content of a

polynucleotide or polypeptide of the present invention compared to a wild-type organism, as well as components and progeny of such organisms, are contemplated by and encompassed within the present invention.

The isolated polynucleotides of the present invention may be usefully employed for the
5 detection of lactic acid bacteria, preferably *L. rhamnosus*, in a sample material, using techniques well known in the art, such as polymerase chain reaction (PCR) and DNA hybridization, as detailed below.

The inventive polynucleotides and polypeptides may also be employed in methods for the selection and production of more effective probiotic bacteria; as "bioactive" (health-
10 promoting) ingredients and health supplements for immune function enhancement; for reduction of blood lipids such as cholesterol; for production of bioactive material from genetically modified bacteria; as adjuvants; for wound healing; in vaccine development, particularly mucosal vaccines; as animal probiotics for improved animal health and productivity; in selection and production of genetically modified rumen microorganisms for
15 improved animal nutrition and productivity, better flavor and improved milk composition; in methods for the selection and production of better natural food bacteria for improved flavor, faster flavor development, better fermentation characteristics, vitamin synthesis and improved textural characteristics; for the production of improved food bacteria through genetic modification; and for the identification of novel enzymes for the production of, for example,
20 flavors or aroma concentrates.

The isolated polynucleotides of the present invention also have utility in genome mapping, in physical mapping, and in positional cloning of genes of more or less related microbes. Additionally, the polynucleotide sequences identified as SEQ ID NO: 1-121, and their variants, may be used to design oligonucleotide probes and primers. Such oligonucleotide
25 probes and primers have sequences that are substantially complementary to the polynucleotide of interest over a certain portion of the polynucleotide. Oligonucleotide probes designed using the polynucleotides of the present invention may be used to detect the presence, and examine the expression patterns, of genes in any organism having sufficiently similar DNA and RNA sequences in their cells, using techniques that are well known in the art, such as slot blot DNA
30 hybridization techniques. Oligonucleotide primers designed using the polynucleotides of the present invention may be used for polymerase chain reaction (PCR) amplifications. Oligonucleotide probes and primers designed using the polynucleotides of the present invention

may also be used in connection with various microarray technologies, including the microarray technology of Affymetrix (Santa Clara, CA).

The polynucleotides of the present invention may also be used to tag or identify an organism or derived material or product therefrom. Such tagging may be accomplished, for example, by stably introducing a non-disruptive, non-functional, heterologous polynucleotide identifier into an organism, the polynucleotide comprising at least a portion of a polynucleotide of the present invention.

The polynucleotides of the present invention may also be used as promoters, gene regulators, origins of DNA replication, secretion signals, cell wall or membrane anchors for genetic tools (such as expression or integration vectors).

All references cited herein, including patent references and non-patent publications, are hereby incorporated by reference in their entireties.

Detailed Description

The polynucleotides disclosed herein were isolated by high throughput sequencing of DNA libraries from the lactic acid bacteria *Lactobacillus rhamnosus* as described below in Example 1. Cell wall, cell surface and secreted components of lactic acid bacteria are known to mediate immune modulation, cell adhesion and antibacterial activities, resulting in many beneficial effects including: resistance to enteric pathogens; modulation of cancer, including colon cancer; anti-mutagenesis effects; reduction of small bowel bacterial overgrowth; modulation of auto-immune disorders; reduction in allergic disorders; modulation of urogenital infections, inflammatory bowel disorder, irritable bowel syndrome, *Helicobacter pylori* infection and hepatic encephalopathy; reduction of infection with pathogens; regulation of colonocyte proliferation and differentiation; reduction of mucosal permeability; and relief of constipation and diarrhea. These cell components include, but are not limited to, peptidoglycans, teichoic acids, lipoteichoic acids, polysaccharides, adhesion proteins, secreted proteins, surface layer or S-layer proteins, collagen binding proteins and other cell surface proteins, and antibacterial substances such as bacteriocins and organic acids produced by these bacteria. Polynucleotides involved in the synthesis of these proteins and in the synthesis, modification, regulation, transport, synthesis and/or accumulation of precursor molecules for these proteins can be used to modulate the immune effects, antibacterial, cell adhesion and competitive exclusion effects of the bacteria or of components that might be produced by these bacteria.

In order to function effectively as probiotic bacteria, *L. rhamnosus* HN001 must survive environmental stress conditions in the gastrointestinal tract, as well as commercial and industrial processes. Modification of particular polynucleotides or regulatory processes has been shown to be effective against a number of stresses including oxidative stress, pH, osmotic stress, dehydration, carbon starvation, phosphate starvation, nitrogen starvation, amino acid starvation, heat or cold shock, and mutagenic stress. Polynucleotides involved in stress resistance often confer multistress resistance, i.e., when exposed to one stress, surviving cells are resistant to several non-related stresses. Bacterial genes and/or processes shown to be involved in multistress resistance include:

10

Intracellular phosphate pools - inorganic phosphate starvation leads to the induction of *pho* regulon genes, and is linked to the bacterial stringent response. Gene knockouts involving phosphate receptor genes appear to lead to multistress resistance.

15 **Intracellular guanosine pools** - purine biosynthesis and scavenger pathways involve the production of phosphate-guanosine compounds that act as signal molecules in the bacterial stringent response. Gene knockouts involving purine scavenger pathway genes appear to confer multistress resistance.

20 **Osmoregulatory molecules** - small choline-based molecules, such as glycine-betaine, and sugars, such as trehalose, are protective against osmotic shock and are rapidly imported and/or synthesized in response to increasing osmolarity.

Acid resistance - lactobacilli naturally acidify their environment through the excretion of lactic acid, mainly through the *cit* operon genes responsible for citrate uptake and utilization.

25

Stress response genes - a number of genes appear to be induced or repressed by heat shock, cold shock, and increasing salt through the action of specific promoters.

30 The isolated polynucleotides of the present invention, and genetic constructs comprising such polynucleotides, may be employed to produce bacteria having desired phenotypes, including increased resistance to stress and improved fermentation properties.

Many enzymes are known to influence dairy product flavor, functional and textural characteristics as well as general fermentation characteristics such as speed of growth, acid production and survival. These enzymes include those involved in the metabolism of lipids, polysaccharides, amino acids and carbohydrates as well as those involved in the lysis of the

5 bacterial cells.

The isolated polynucleotides and polypeptides of the present invention have demonstrated similarity to polynucleotides and/or polypeptides of known function. The identity and functions of the inventive polynucleotides based on such similarities are shown below in Table 1.

10

TABLE 1

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
1	122	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered viability in response to stress conditions. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes.	Homologue of purL, encoding a phosphoribosylformylglycinamide (FGAM) synthetase (EC 6.3.5.3). PurL catalyzes the fourth step in the biosynthesis of purines. It is involved in resistance environmental stress conditions and the stringent response through the control of intracellular phosphate levels. Purines also play essential roles in many other cellular functions, including DNA replication, transcription, intra- and extra-cellular signaling, energy metabolism, and as coenzymes for many biochemical reactions.
2	123	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations.	Homologue of 5'-Phosphoribosyl-5-aminoimidazole (AIR) carboxylase (EC 4.1.1.21). AIR carboxylase is responsible for CO ₂ fixation during purine biosynthesis. It catalyzes the carboxylation of AIR to 5'-phosphoribosyl-5-aminoimidazole-4-

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
		Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered viability in response to stress conditions. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes.	carboxylic acid, in the <i>de novo</i> biosynthesis of purine nucleotides. AIR carboxylase is composed of two nonidentical subunits, the catalytic subunit is encoded by the purE gene, while the CO₂-binding subunit is encoded by the purK gene. These two genes form an operon in which the termination codon of the purE gene overlapped the initiation codon of the purK gene. The purEK operon is regulated by the purR gene product, and a purR regulatory-protein-binding site related to the sequences found in other pur loci was identified in the purEK operon control region. It is involved in resistance environmental stress conditions and the stringent response through the control of intracellular phosphate levels. Purines also play essential roles in many other cellular functions, including DNA replication, transcription, intra- and extra-cellular signaling, energy metabolism, and as coenzymes for many biochemical reactions.
3	124	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered viability in response to stress conditions. Altered amino acid metabolism. Altered metabolic properties or	Homologue of amino acid antiporters gadC, Xasa and acsA. Amino acid antiporters are integral membrane proteins involved in the transport of amino acids into the cell and in extreme acid resistance. GadC is homologous to putative glutamate-gamma-aminobutyrate antiporters of <i>Escherichia coli</i> and <i>Shigella flexneri</i> and contains 12 putative membrane-spanning domains. It belongs to the amino acid-polyamine-organocation (APC) superfamily, and the Xasa family of transporters. It is involved in glutamate-dependent acid resistance and in antiport of glutamate and glutamate-gamma-aminobutyrate (GABA). The chloride-dependent expression is activated by

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
		regulation of metabolic pathways. Altered probiotic attributes.	gadR. GadC is involved in tolerance to environmental stress conditions such as high salt and low pH.
4	125, 126	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered phosphate metabolism. Altered viability in response to stress conditions. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes.	Homologue of the B-subunit of phosphate-specific transporter (PstB). PstB is an ATP binding cassette (ABC) protein. Phosphate-specific transporters (Pst) in bacteria are involved in phosphate transport. Pst is a multisubunit system and belongs to the ABC superfamily of transporters. (TC# 3.A.1.7.1) (Novak <i>et al.</i> , <i>J Bacteriol.</i> 181:1126-1133, 1999). Utility as a controlled expression vector and in the control of intracellular phosphate levels important for resistance to environmental stress conditions and induction of the stringent response.
5, 106	127, 230	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered phosphate metabolism. Altered viability in response to stress conditions. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes.	Homologue of PstA/PstC, which are the two hydrophobic subunits of a phosphate-specific transporter (PstB), an ATP binding cassette (ABC) protein. Phosphate specific transporter (Pst) in bacteria is involved in phosphate transport. Pst is a multisubunit system and belongs to the ABC superfamily of transporters. (TC# 3.A.1.7.1) (Novak <i>et al.</i> , <i>J Bacteriol.</i> 181:1126-1133, 1999). Utility as a controlled expression vector and in the control of intracellular phosphate levels important for resistance to environmental stress conditions and induction of the stringent response.

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
6-10	128, 130-133	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered phosphate metabolism. Altered viability in response to stress conditions. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes.	Homologue of a response regulator belonging to the family of 2-component signal transduction proteins phosphorylated by a specific sensor kinase (phoR). PhoR activates/represses Pho regulon gene transcription in response to phosphate starvation. The gene is involved in cell cycle control, polysaccharide synthesis and intestinal adhesion, also multistress resistance. It is part of a phosphate (PHO) regulon which is regulated by extracellular phosphate and consists of 20 phosphate-regulated promoters, 10 regulatory genes and 2 phosphate transport systems. Under conditions of phosphate limitation, the response regulator PhoB is phosphorylated by the histidine kinase PhoR and binds to promoters that share a consensus PHO box. Under conditions of phosphate excess, PhoR, Pst, and PhoU downregulate the PHO regulon (Novak <i>et al.</i>, <i>J Bacteriol.</i> 181:1126-1133, 1999). Utility as a controlled expression vector and in the control of intracellular phosphate levels important for resistance to environmental stress conditions and induction of the stringent response.
6	129	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered phosphate metabolism.	Homologue of the response regulator PnpR. PnpR is part of a two-component regulatory system, PnpR-PnpS, and a downstream ABC transporter, similar to the Pst system in <i>E. coli</i>, including a gene encoding a PhoU protein. The <i>E. coli</i> Pst system belongs to the superfamily of ABC transporters. It is part of a phosphate (PHO) regulon which is regulated by extracellular phosphate and consists of 20 phosphate-regulated promoters, 10 regulatory genes and 2 phosphate transport systems. Under conditions of phosphate limitation, the response regulator PhoB

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
		Altered viability in response to stress conditions. Regulation of metabolic pathways. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes.	is phosphorylated by the histidine kinase PhoR and binds to promoters that share a consensus PHO box. Under conditions of phosphate excess, PhoR, Pst, and PhoU downregulate the PHO regulon (Novak <i>et al.</i> , <i>J Bacteriol.</i> 181:1126-1133, 1999). Utility in immune modulation, gut adhesion, cell wall synthesis and polysaccharide production, survival, controlled expression vector.
11	134	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered phosphate metabolism. Altered viability in response to stress conditions. Regulation of metabolic pathways. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes.	Homologue of the histidine kinase PhoR, which is involved in the <i>E. coli</i> Pst system. PhoR is part of a phosphate (PHO) regulon and phosphorylates under conditions of phosphate limitation the response regulator PhoB. Under conditions of phosphate excess, PhoR, Pst, and PhoU down regulate the PHO regulon (Novak <i>et al.</i> , <i>J Bacteriol.</i> 181:1126-1133, 1999) which consists of 20 phosphate-regulated promoters, 10 regulatory genes and 2 phosphate transport systems. Utility in immune modulation, gut adhesion, cell wall synthesis and polysaccharide production, survival, controlled expression vector.
12, 107	135, 231	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes,	Homologue of PnpS (which in turn is a homologue of PhoR), which is part of a two-component regulatory system, PnpR-PnpS, and a downstream ATP-binding cassette (ABC) transporter, similar to the Pst system in <i>E. coli</i> including a gene encoding a PhoU protein. The <i>E. coli</i> Pst system belongs to the superfamily of ABC transporters. It is part of a phosphate (PHO) regulon which is regulated by extracellular phosphate and consists of 20 phosphate-

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
		growth or storage in product formats, persistence in gut environment. Altered phosphate metabolism. Altered viability in response to stress conditions. Regulation of metabolic pathways. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes.	regulated promoters, 10 regulatory genes and 2 phosphate transport systems. Under conditions of phosphate limitation, the response regulator PhoB is phosphorylated by the histidine kinase PhoR and binds to promoters that share a consensus PHO box. Under conditions of phosphate excess, PhoR, Pst, and PhoU downregulate the PHO regulon. PnpS (Novak <i>et al.</i>, <i>J Bacteriol.</i> 181:1126-1133, 1999). Utility in immune modulation, gut adhesion, cell wall synthesis and polysaccharide production, survival, controlled expression vector.
13, 14	136, 137	Altered cell wall or cell surface characteristics, structures or functions. Improved antimicrobial properties Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved fermentation properties or other industrially useful processes.	Homologue of penicillin-binding protein 1B (Pbp1b) or murein polymerase. Penicillin-binding proteins (PBPs), targets of beta-lactam antibiotics, are membrane-bound enzymes essential for the biosynthesis of the bacterial cell wall. PBPs possess a penicillin-insensitive transglycosylase N-terminal domain (formation of linear glycan strands) and a penicillin-sensitive transpeptidase C-terminal domain (cross-linking of the peptide subunits) responsible for the final steps of the bacterial cell wall polymerization and cross-linking, respectively (Zhao <i>et al.</i>, <i>Protein Expr. Purif.</i> 16:331-339, 1999). Utility in immune modulation, gut adhesion, cell wall synthesis and polysaccharide production.
15, 42,	138, 167,	Altered cell wall or cell surface	Homologue of penicillin-binding protein

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
108	232	characteristics, structures or functions. Improved antimicrobial properties Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved fermentation properties or other industrially useful processes.	5 (Pbp5) also known as muramoylpentapeptide carboxypeptidase (EC 3.4.17.8, formerly EC 3.4.12.6). Pbp5 is a bacterial enzyme that requires a divalent cation for activity. Does not cleave the C-terminal D-alanine from the reaction product, UDP-N-acetyl-muramoyl-L-alanyl-D-glutamyl-6-carboxy-L-lysyl-D-alanine. Competitively inhibited by penicillins and cephalosporins. Penicillin-binding proteins (PBPs), targets of beta-lactam antibiotics, are membrane-bound enzymes essential for the biosynthesis of the bacterial cell wall. (Sifaoui <i>et al.</i>, <i>Antimicrob. Agents Chemother.</i> 45:2594-2597, 2001). Utility in immune modulation, gut adhesion, cell wall synthesis and polysaccharide production.
16, 109	139, 233	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment.	Homologue of the hydrophobic transmembrane protein psaC. PsaC is a member of the of ABC superfamily, involved in the transport of nutrients, translocation of signal molecules and chemotaxis (Janulczyk <i>et al.</i>, <i>Mol. Microbiol.</i> 34:596-606, 1999). May be employed in immune modulation, gut adhesion, cell wall synthesis, survival, and polysaccharide production.

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
		Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties.	
17	140	Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer gut health). Modified antibiotic resistance. Improved antimicrobial properties.	Homologue of plnH. PlnH is the accessory factor for ABC transporter plnG with strong similarities to the proposed transport proteins of several other bacteriocins and to proteins implicated in the signal-sequence-independent export of <i>E. coli</i> hemolysin (Huhne <i>et al.</i>, <i>Microbiol.</i> 142:1437-1448, 1996). LcnD is an accessory protein of <i>Lactococcus lactis</i> with similarities to other proteins involved in the secretion of various polypeptides. They operate in conjunction with a protein from the family of ABC1 transporters. The accessory proteins of Gram-negative bacteria are proposed to form a family of so-called membrane fusion proteins. It is hypothesized that they connect the inner and the outer membranes to facilitate the passage of substrates. CvaA, a member of the membrane fusion protein family, involved in the secretion of colicin V, has been shown to interact with both a cytoplasmic membrane protein (the ABC transporter) and a protein present in the outer membrane (Franke <i>et al.</i>, <i>J. Biol. Chem.</i> 274:8484-8490, 1999). May be employed as an antibacterial for control of infection and food preservation.
18, 121	141, 252		Homologue of Glyceraldehyde 3-phosphate dehydrogenase (GAPDH) (EC 1.2.1.12) is a tetrameric NAD-binding enzyme common to both the

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
			glycolytic and gluconeogenic pathways that catalyzes reversibly the oxidative phosphorylation of D-glyceraldehyde 3-phosphate (G3P) to form 1,3-diphosphoglycerate (1,3-dPG) in the presence of NAD and inorganic phosphate. This enzyme is useful in manipulating alcohol dehydrogenation <i>in vitro</i> or <i>in vivo</i>, e.g. in fermentation processes or with transgenic bacteria with deleted, added or modified alcohol dehydrogenase gene. It can also be useful as a controlled expression vector.
19	142	Removal of undesirable flavor characteristics. Production of desirable flavors. Modified flavor, aroma, or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Modified carbohydrate levels or functional properties. Altered metabolic properties. Modified carbohydrate metabolism. Altered probiotic attributes. Improved fermentation properties or other industrially useful processes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut health, lactose tolerance)	Homologue of the histidine-containing protein ptsH, also known as the phosphocarrier protein HPr. Hpr is a component of the phosphoenolpyruvate-dependent sugar phosphotransferase system (PTS), a major carbohydrate active-transport system. The phosphoryl group from phosphoenolpyruvate (PEP) is transferred to the phosphoryl carrier protein HPr by enzyme I. Phospho-HPr then transfers it to the permease (enzymes II/III). HPr is common to all PTS and belongs to the HPr family. The HPr family consists of bacterial proteins, all of which function as phosphoryl transfer proteins. They are energy-coupling constituents of the phosphotransferase system (PTS) (TC #4.A.1-4.A.6).which catalyzes sugar uptake via a group translocation mechanism. The <i>E. coli</i> genome encodes five HPr paralogues that function in PTS-related regulatory capacities. May be employed in survival and carbohydrate metabolism and as a controlled expression vector.
20	143	Removal of undesirable flavor characteristics. Production of desirable flavors.	Homologue of gamma (acyl carrier protein) subunit of citrate lyase. Citrate lyase (EC 4.1.3.6.) is part of the citrate

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
		Modified flavor, aroma, or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Modified carbohydrate levels or functional properties. Altered metabolic properties. Modified citrate metabolism. Altered probiotic attributes. Improved fermentation properties or other industrially useful processes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut health, lactose tolerance)	metabolism pathway and catalyzes the cleavage of citrate to oxaloacetate and acetate and is composed of three subunits (alpha, beta, and gamma). Lactobacillae contribute through the citrate metabolism actively to the flavor development of fermented dairy products (e.g., Dutch cheeses). It is also involved in citrate metabolism pathway that results in lactic acid production and acid tolerance (Magni <i>et al.</i>, <i>J. Bacteriol.</i> 181:1451-1457, 1999) and may be employed in survival and carbohydrate metabolism.
20	144	Removal of undesirable flavor characteristics. Production of desirable flavors. Modified flavor, aroma, or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Modified carbohydrate levels or functional properties. Altered metabolic properties. Modified citrate metabolism.	Homologue of beta (citryl-S-ACP lyase) subunit of citrate lyase. Citrate lyase (EC 4.1.3.6.) is part of the citrate metabolism and catalyzes the cleavage of citrate to oxaloacetate and acetate and is composed of three subunits (alpha, beta, and gamma). Lactobacillae contribute through the citrate metabolism actively to the flavor development of fermented dairy products (e.g., Dutch cheeses). It is also involved in citrate metabolism pathway that results in lactic acid production and acid tolerance (Magni <i>et al.</i>, <i>J. Bacteriol.</i> 181:1451-1457, 1999) and may be employed in survival and carbohydrate metabolism.

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
		Altered probiotic attributes. Improved fermentation properties or other industrially useful processes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut health, lactose tolerance).	
20	145	Removal of undesirable flavor characteristics. Production of desirable flavors. Modified flavor, aroma, or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Modified carbohydrate levels or functional properties. Altered metabolic properties. Modified citrate metabolism. Altered probiotic attributes. Improved fermentation properties or other industrially useful processes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut health, lactose tolerance).	Homologue of alpha subunit (citrate:acetyl-ACP transferase) of citrate lyase. Citrate lyase (EC 4.1.3.6.) is part of the citrate metabolism and catalyzes the cleavage of citrate to oxaloacetate and acetate and is composed of three subunits (alpha, beta, and gamma). Lactobacillae contribute through the citrate metabolism actively to the flavor development of fermented dairy products (e.g., Dutch cheeses). It is also involved in citrate metabolism pathway that results in lactic acid production and acid tolerance (Magni <i>et al.</i> , <i>J. Bacteriol.</i> 181:1451-1457, 1999) and may be employed in survival and carbohydrate metabolism.
21, 119	146, 243	Removal of undesirable flavor characteristics. Production of desirable flavors. Modified flavor, aroma, or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis	Homologue of malic enzyme (EC 1.1.1.39). Malic enzyme catalyzes L-malate oxidative decarboxylation and pyruvate reductive carboxylation and a malate transport protein (similar to citP) involved in membrane potential generation via malate/lactate exchange. Because lactobacilli appear not to have a functioning Krebs cycle, this enzyme

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
		amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Modified carbohydrate levels or functional properties. Altered metabolic properties. Modified carbohydrate metabolism. Altered probiotic attributes. Improved fermentation properties or other industrially useful processes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut health, lactose tolerance).	may be involved in carbohydrate metabolism, amino acid biosynthesis or L-malate utilization pathways.
22	147	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered viability in response to stress conditions. Increased resistance to high salt levels. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes.	Homologue of otsA, encoding trehalose-6-phosphate synthetase (UDP forming) (EC 2.4.1.15). OtsA combines two glucose molecules to trehalose. Trehalose plays a protective role in the ability of many organisms to tolerate adverse environmental conditions (Fernandes <i>et al.</i>, <i>Lett. Appl. Microbiol.</i> 32:42, 2001) and acts as an osmoprotectant as well as a carbon source (Rimmele and Boos, <i>J. Bacteriol.</i> 176:5654-5664, 1994). May be involved in carbohydrate and amino acid metabolism, survival and may have utility as a controlled expression vector.
23	148	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis	Homologue of trehalose-6-phosphate hydrolase (EC 3.2.1.93). Trehalose-6-phosphate hydrolase is the key enzyme of the phosphotransferase system and

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
		amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered viability in response to stress conditions. Increased resistance to high salt levels. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes.	hydrolyzes trehalose-6-phosphate to glucose and glucose 6-phosphate. The enzyme shows strong homology with those of oligo-1,6- glucosidases. Trehalose plays a protective role in the ability of many organisms to tolerate adverse environmental conditions (Fernandes <i>et al.</i>, <i>Lett. Appl. Microbiol.</i> 32:42, 2001) and acts as an osmoprotectant as well as a carbon source (Rimmele and Boos, <i>J. Bacteriol.</i> 176:5654-5664, 1994). May be involved in carbohydrate and amino acid metabolism, survival and may have utility as a controlled expression vector.
24	149	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered viability in response to stress conditions. Increased resistance to high salt levels. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes.	Homologue of proV. ProV is a glycine betaine/proline transporter that also transports proline betaine, carnitine, dimethyl proline, homobetaine, g-butyrobetaine and choline with low affinity (TC-Number: 3.A.1.12.1). ProV belongs to the ABC substrate binding protein-dependent transporter superfamily, May be involved in carbohydrate and amino acid metabolism, survival and may have utility as a controlled expression vector.
25	150	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors.	Homologue of rgg which positively regulates the expression of extracellular glucosyltransferase (GTF). rgg-like determinants make up a widely occurring gene family in pathogenic and

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
		Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties. Regulation of polysaccharide production, adhesion, immune modulation.	commensal bacterial species and appear to share positive regulatory functions (Vickerman and Minick, <i>Infect. Immun.</i> 70:1703-1714, 2002).
26	151	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including	Homologue of Cps14D. Cps gene products are involved in bacterial capsular polysaccharide (CP) biosynthesis. Bacterial CPs are generally composed of repeating oligosaccharides and are involved in resistance to opsonophagocytosis, avoidance of the immune system of the host and attachment. Cps genes are normally clustered on the bacterial chromosome and have a common genetic organization involving three functional regions. Cps14D codes for a protein involved in chain length determination and export of CP (Kolkman <i>et al.</i>, <i>J. Biol. Chem.</i> 272:19502-19508, 1997).

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
		immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties. Regulation of polysaccharide production, adhesion, immune modulation.	
27	152	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties. Regulation of polysaccharide production, adhesion, immune modulation.	Homologue of a Cps-like gene product. Cps-like gene products are involved in bacterial capsular polysaccharide (CP) biosynthesis. Bacterial CPs are generally composed of repeating oligosaccharides and are involved in resistance to opsonophagocytosis, avoidance of the immune system of the host and attachment. Cps genes are normally clustered on the bacterial chromosome and have a common genetic organization involving three functional regions (Kolkman <i>et al.</i> , <i>J. Biol. Chem.</i> 272:19502-19508, 1997). Cps14J encodes a beta-1,4-galactosyltransferase that requires beta-linked GlcNAc as an acceptor.
28	153	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for	Homologue of a Cps-like gene product. Cps-like gene products are involved in bacterial capsular polysaccharide (CP) biosynthesis. Bacterial CPs are generally composed of repeating oligosaccharides and are involved in resistance to opsonophagocytosis, avoidance of the immune system of the host and

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
		controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties. Regulation of polysaccharide production, adhesion, immune modulation.	attachment. Cps genes are normally clustered on the bacterial chromosome and have a common genetic organization involving three functional regions. (Kolkman <i>et al.</i>, <i>J. Biol. Chem.</i> 272:19502-19508, 1997). Cps14L encodes a transporter for the repeating unit of the polysaccharide (Kolkman <i>et al. J. Biochem.</i> 123:937-945, 1998).
29, 30	154, 155	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance.	Homologue of D-alanyl-D-alanine carboxypeptidase (EC 3.4.17.8, formerly EC 3.4.12.6). D-alanyl-D-alanine carboxypeptidase is a periplasmic membrane-attached protein involved in the construction and maintenance of the bacterial cell walls and also a penicillin binding protein involved in the late stages of murein synthesis. Peptidases are important in the process of cheese ripening and the development of cheese flavor. May have utility as a controlled expression vector.

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
		Improved antimicrobial properties. Regulation of polysaccharide production, adhesion, immune modulation.	
31	156	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	Homologue of aggregation protein aggH. Transgenic microbes with added, deleted or modified aggregation protein gene can have a modified aggregation response <i>in vitro</i> (useful in bioprocessing with bacteria, e.g. fermentation, flocculation) or <i>in vivo</i> (useful in enhancing/decreasing clumping of bacteria, e.g. in gastrointestinal tract, as desired). Aggregation protein gene can be used also for production of protein as antigen to vaccinate mammals. Gene can be used as vehicle for vaccination by fusing with an exogenous antigen with it, transforming a bacterium and treating the mammal to be immunized with killed or live bacteria for preventive or therapeutic vaccination (see patent WO9947657-A2; <i>Lactobacillus reuteri</i> bacterial aggregation protein). The aggregation protein is targeted for the bacterial surface, so this ensures efficient antigen presentation to the immune system as the <i>Lactobacillus</i> or other gastrointestinal bacteria adhere to epithelial cells. Finally, gene is useful for detecting <i>Lactobacillus</i> species using the DNA as detection probe.
32	157	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis	Homologue of exopolyphosphatase (PPX) (EC 3.6.1.11). Polyphosphate is made by polyphosphate kinase PPK (EC 2.7.4.1) and is broken down by PPX.

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
		amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	
33	158	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	Homologue of a peptidoglycan (mureins) bound protein with an LPXTG motif, similar to an adhesin. Adhesins mediate attachment of cells to collagen-containing substrata. Type I membrane protein. Collagen binding is important property in attachment and potential pathogenesis of various bacteria with mammalian hosts. The gene can be used to screen bacteria with DNA or protein probes/antibodies for the presence of collagen adhesion gene in various pathogenic and non-pathogenic bacteria, e.g. for selection of strains or for diagnostic purposes (see e.g. patent WO9207002). It is known that expression of a collagen adhesin is essential for the attachment of <i>Staphylococcus aureus</i> to cartilage, which contains collagen (Switalski <i>et al.</i>, <i>Mol. Microbiol.</i> 7:99-107, 1993). Deletion/addition or modification of the gene can alter collagen-binding properties of cells to the desired effect in bacteria-host interactions. Finally, protein can be used as an administered reagent in <i>in vitro</i> or <i>in vivo</i> collagen binding reactions.

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
34	159	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	Homologue of a bacterial hemolysin. Hemolysin is a bacterial toxin gene that can be used to develop vaccines against pathogenic bacteria carrying the gene/protein. Transgenic microbes with added, deleted or modified hemolysin protein gene can have a modified hemolytic activity <i>in vitro</i> (useful <i>e.g.</i> in bacteria-based assays) or <i>in vivo</i> (useful in enhancing/decreasing pathogenicity of bacteria, as desired (see <i>e.g.</i> <i>J. Biol. Chem.</i> 267:10902-10909, 1992)). Functional expression of the alpha-hemolysin gene of <i>Staphylococcus aureus</i> in intact <i>E. coli</i> and in cell lysates. Deletion of five C-terminal amino acids selectively impairs hemolytic activity. The peptide itself can be used as a reagent <i>e.g.</i> in <i>in vitro</i> assays of hemolytic activity. May be involved in scavenging iron from environment, and therefore is involved in cell survival and metabolism, as well as restricting growth of surrounding microbes.
35	160	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes,	Homologue of autoinducer 2 (AI-2). AI-2 participates in quorum sensing in bacteria. Autoinducer is secreted by bacteria and is used to communicate both the cell density and the metabolic potential of the environment. The gene can be used in DNA or protein assays to detect presence of the DNA or protein in microbes. The deletion, addition or modification of the gene can change the intercellular signaling of bacteria, affecting their growth mode, pathogenesis and survival. The peptide can be used as a reagent to modify the bacterial communication <i>in vitro</i> or <i>in vivo</i>.

SEQ ID NO: DNA	SEQ ID NO: PROT	Category	Description
		growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes. Regulation of cell numbers and growth.	
36	161	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes. Regulation of cell numbers and growth.	Homologue of autolysin. Autolysins control the lysis bacterial cells. It can be used for controlling lysis of food fermenting bacteria, e.g. in cheese production, as well as lysis of pathogenic organisms with in vivo or in vitro administration of the peptide or peptide-producing microorganisms. The deleted/added or modified gene in transgenic bacteria can be used to modify the lysis process as required. The DNA and peptide can be used in developing and using various screening assays to detect presence of hemolysin gene/protein and autolytic activity.

37-39	162-164	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes. Regulation of cell numbers and growth.	Homologue of a bacterial hemolysin. Hemolysin is a bacterial toxin gene that can be used to develop vaccines against pathogenic bacteria carrying the gene/protein. Transgenic microbes with added, deleted or modified hemolysin protein gene can have a modified hemolytic activity <i>in vitro</i> (useful <i>e.g.</i> in bacteria-based assays) or <i>in vivo</i> (useful in enhancing/decreasing pathogenicity of bacteria, as desired (see <i>e.g.</i> <i>J. Biol. Chem.</i> 267:10902-10909, 1992)). Functional expression of the alpha-hemolysin gene of <i>Staphylococcus aureus</i> in intact <i>E. coli</i> and in cell lysates. Deletion of five C-terminal amino acids selectively impairs hemolytic activity. The peptide itself can be used as a reagent <i>e.g.</i> in <i>in vitro</i> assays of hemolytic activity. May be involved in scavenging iron from environment, and therefore is involved in cell survival and metabolism, as well as restricting growth of surrounding microbes.
40, 41	165, 166	Altered cell wall or cell surface characteristics, structures or functions. Improved antimicrobial properties Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes,	Homologue of penicillin-binding proteins (PBPs). PBPs are enzymes involved in the final stages of peptidoglycan biosynthesis. The C-terminal module binds penicillin and catalyzes peptidoglycan cross-linking. The N-terminal domain can have transglycosylase activity (class A HMW PBPs). PBPs are the targets of beta-lactam antibiotics, which covalently bind to these proteins, inhibiting cell wall synthesis (Mariana <i>et al.</i>, <i>J. Bacteriol.</i> 182:1074-1079, 2000). Penicillin-binding protein gene can be used for modifications in transgenic bacteria, which can change their susceptibility to penicillin (see <i>e.g.</i>

		growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved fermentation properties or other industrially useful processes.	Smith and Klugman, <i>Antimicrob. Agents Chemother.</i> 42:1329-1333, 1998). Alterations in PBP 1A essential-for high-level penicillin resistance in <i>Streptococcus pneumoniae</i>. The DNA or protein can be used in various assays to detect the presence of the gene or protein in various biological samples, where penicillin binding is of interest.
42	167	Altered cell wall or cell surface characteristics, structures or functions. Improved antimicrobial properties Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved fermentation properties or other industrially useful processes.	Homologue of penicillin-binding protein 5 (Pbp5) also known as muramoylpentapeptide carboxypeptidase (EC 3.4.17.8, formerly EC 3.4.12.6). Pbp5 requires a divalent cation for activity. Penicillin-binding proteins (PBPs), targets of beta-lactam antibiotics, are membrane-bound enzymes essential for the biosynthesis of the bacterial cell wall (Sifaoui <i>et al.</i>, <i>Antimicrob. Agents Chemother.</i> 45:2594-2597, 2001). Penicillin-binding protein gene can be used for modifications in transgenic bacteria, which can change their susceptibility to penicillin (see <i>e.g.</i> Smith and Klugman, <i>Antimicrob. Agents Chemother.</i> 42:1329-1333, 1998). Alterations in PBP 1A essential-for high-level penicillin resistance in <i>Streptococcus pneumoniae</i>. The DNA or protein can be used in various assays to detect the presence of the gene or protein in various biological samples, where penicillin binding is of interest.
43	168	Altered cell wall or cell surface characteristics, structures or functions. Improved antimicrobial properties Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for	Homologue of penicillin-binding protein 1B (Pbp1b) or murein polymerase. Penicillin-binding proteins (PBPs), targets of beta-lactam antibiotics, are membrane-bound enzymes essential for the biosynthesis of the bacterial cell wall. PBPs possess a penicillin-insensitive transglycosylase n-terminal domain (formation of linear glycan

		controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved fermentation properties or other industrially useful processes.	strands) and a penicillin-sensitive transpeptidase c-terminal domain (cross-linking of the peptide subunits) responsible for the final steps of the bacterial cell wall polymerization and cross-linking, respectively (Zhao <i>et al.</i>, <i>Protein Expr. Purif.</i> 16:331-339, 1999). Penicillin-binding protein gene can be used for modifications in transgenic bacteria, which can change their susceptibility to penicillin (see <i>e.g.</i> Smith and Klugman, <i>Antimicrob. Agents Chemother.</i> 42:1329-1333, 1998). Alterations in PBP 1A essential for high-level penicillin resistance in <i>Streptococcus pneumoniae</i>. The DNA or protein can be used in various assays to detect the presence of the gene or protein in various biological samples, where penicillin binding is of interest.
44, 110	169, 234	Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified adhesion to human or animal cells or cell lines. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut health) Altered resistance to antibiotics. Improved antimicrobial properties.	Homologue of protein p60, encoded by the gene termed iap. p60 protein is a major extracellular product secreted by all isolates of <i>Listeria monocytogenes</i>. This protein has peptidoglycan hydrolase activity but also influences the uptake of <i>L. monocytogenes</i> by non-phagocytic cells. Proteins related to p60 are found in all other <i>Listeria</i> species. It has been shown that p60 protein is among the strongest antigens in listeriae for B- and T-cell responses. The protein p60 belongs to the <i>E. coli</i> nlpc / listeria p60 family. This gene can be useful as a probe to detect the presence of the gene/protein in various bacteria. Deletion, addition and modification of the gene in transgenic bacteria can alter their extracellular envelope structure, thereby altering their growth and pathogenicity characteristics. See <i>e.g.</i> Bubert <i>et al.</i>, <i>J. Bacteriol.</i> 174:8166-8171, 1992.
45	170	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or	Homologue of flotillin. Flotillins have been found in mammalian, insect and bacterial cells and behave as resident

		animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties.	integral membrane protein components of caveolae which are plasmalemmal microdomains that are involved in vesicular trafficking and signal transduction (Huang <i>et al.</i>, <i>Mol. Microbiol.</i> 31:361-371, 1999). Flotillins (also known as epidermal surface antigens (ESAs)) belong to the family of caveolae-associated integral membrane proteins and may act as a scaffolding protein within caveolar membranes. This gene is similar to an epidermal surface antigen of <i>Bacillus subtilis</i>. It is useful as a vaccine development target.
46	171	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance.	Homologue of fimbria associated protein. Fimbriae and pili are interchangeable terms used to designate short, hair-like structures on the surfaces of prokaryotic cells composed of protein. Fimbriae are most often involved in adherence of bacteria to surfaces, substrates and other cells in nature. This gene is similar to sortase, which is involved in covalent anchoring to the cell wall (see Cossart and Jonquieres, <i>Proc. Natl. Acad. Sci. USA</i> 97:5013-5015, 2000). The gene is useful as a target for antibiotic development as the gene performs a very important function in cell wall protein anchoring. The DNA and protein can be used <i>in vitro</i> and <i>in vivo</i> assays and treatments as a reagent. Transgenic bacteria with deleted, added or modified sortase gene can have modified protein anchoring at the cell surface layer.

		Improved antimicrobial properties.	
47	172	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties.	Homologue of a collagen binding protein. Collagen binding is important property in attachment and potential pathogenesis of various bacteria with mammalian hosts. The gene can be used to screen bacteria with DNA or protein probes/antibodies for the presence of collagen adhesion gene in various pathogenic and non-pathogenic bacteria, e.g. for selection of strains or for diagnostic purposes (see e.g. patent WO9207002). It is known that expression of a collagen adhesin is essential for the attachment of <i>Staphylococcus aureus</i> to cartilage, which contains collagen (Switalski <i>et al.</i>, <i>Mol. Microbiol.</i> 7, 99-107, 1993). Deletion/addition or modification of the gene can alter collagen-binding properties of cells to the desired effect in bacteria-host interactions. Finally, protein can be used as an administered reagent in <i>in vitro</i> or <i>in vivo</i> collagen binding reactions.
48	173	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment.	Homologue of bacteriophage immunity repressor IMMREP. IMMREP is involved in the regulation of lysogeny in the temperate <i>Bacillus subtilis</i> phage phi 105, which can make <i>B. subtilis</i> immune to infection by phi 105 phage (see Cully and Garro, <i>Gene</i> 38:153-164, 1985). Can be used to manipulate bacteria as to their susceptibility to phage invasion and hence acquiring desired/undesired genetic element carried by the phage.

		Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antimicrobial properties.	
49	174	Altered cell wall or cell surface characteristics, structures or functions. Improved antimicrobial properties Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved fermentation properties or other industrially useful processes.	Homologue of N-acetylmuramoyl-L-alanine amidase (EC 3.5.1.28). N-acetylmuramoyl-L-alanine amidase hydrolyzes the link between N-acetylmuramoyl residues and L-amino acid residues in certain cell-wall glycopeptides. N-acetylmuramoyl-L-alanine amidases contain a COOH-terminal choline-binding domain and an NH₂-terminal catalytic domain. Useful for N-acetylmuramoyl-L-alanine amidase activity using the peptide <i>in vitro</i> or <i>in vivo</i>, or transgenic bacteria with the gene expressed to effect the enzyme activity. The DNA or protein can be used in assays to detect the presence of the gene or protein in various assays. This enterotoxin related gene is also a vaccine development target for pathogenic or other undesired bacteria, e.g. various <i>Lactobacillus</i> strains.
50	175	Removal of undesirable flavor characteristics. Production of desirable flavors. Modified flavor, aroma, or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics:	Homologue of hrdT. hrdT is a member of the multidrug resistance exporter (MDR) family (TC# 3.A.1.201) in the ATP-binding Cassette (ABC) Superfamily of transporters. ABC transporters translocate a wide variety of substrates, including amino acids, peptides, ions, sugars, toxins, lipids, and drugs

		survival of industrial processes, growth or storage in product formats, persistence in gut environment. Modified carbohydrate levels or functional properties. Altered metabolic properties. Altered probiotic attributes. Improved fermentation properties or other industrially useful processes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut health, lactose tolerance)	
51	176	Altered cell wall or cell surface characteristics, structures or functions. Improved antimicrobial properties Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved fermentation properties or other industrially useful processes.	Homologue of adhesin-involved-in-diffuse-adherence (AIDA) a fimbrial adhesin and virG (icsA) protein. VirG and AIDA are precursor virulence factors that transport themselves out of the bacterial cell and are then usually proteolytically digested to release a soluble protein that can promote virulence. They are members of the autotransporter (AT) family of outer membrane proteins and play an important role in virulence. The gene is useful as a target for vaccine development of bacteria having this kind of gene, as well as manipulation of virulence by deletion, addition or modification of the gene in transgenic bacteria.
52	177	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture	Homologue of cyclopropane fatty acid synthase (cfa). cfa is similar to the cyclopropane-fatty-acyl-phospholipid synthase of bacteria, and catalyzes a modification of the acyl chains of phospholipid bilayers. This gene is

		attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	useful in modifying the bacterial phospholipid bilayers by altered enzyme activity, e.g. by deleted, added or modified gene in transgenic bacteria (see e.g. US Patent 5,573,915: Determining the ability of a compound to inhibit the cyclopropanation of mycolic acids in pathogenic mycobacteria).
53	178	Removal of undesirable flavor characteristics. Production of desirable flavors. Modified flavor, aroma, or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Modified carbohydrate levels or functional properties. Altered metabolic properties. Modified carbohydrate metabolism. Altered probiotic attributes. Improved fermentation properties or other industrially useful processes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut	Homologue of adhE. adhE encodes a multifunctional dehydrogenase that catalyzes the conversion of acetyl-CoA into ethanol and has acetaldehyde dehydrogenase [acetylating] (EC 1.2.1.10) (ACDH) and alcohol dehydrogenase (ADH) (EC 1.1.1.1) activities (Arnau <i>et al.</i>, <i>J. Bacteriol.</i> 180:3049-3055, 1998). This enzyme is useful in manipulating alcohol dehydrogenation <i>in vitro</i> or <i>in vivo</i>, e.g. in fermentation processes or with transgenic bacteria with deleted, added or modified alcohol dehydrogenase gene.

		health, lactose tolerance).	
54	179	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	Homologue of biotin carboxylase (EC 6.3.4.14). Biotin carboxylase is one component of acetyl CoA carboxylase which, in turn, catalyzes the regulated step in long-chain fatty acid synthesis. This enzyme is useful in manipulating biotin carboxylation <i>in vitro</i> or <i>in vivo</i>, e.g. in transgenic plants with deleted, added or modified gene leading to altered biotin metabolism, thus affecting insect herbivores which require plant-derived biotin; may also have utility in manipulation of herbicide tolerance (see US Patent 5,910,626: Acetyl-CoA carboxylase compositions and methods of use).
55	180	Removal of undesirable flavor characteristics. Production of desirable flavors. Modified flavor, aroma, or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Modified carbohydrate levels or functional properties.	Homologue of the argE gene product of <i>E. coli</i>. argE is a N-acetyl-L-ornithine deacetylase that can remove the acetyl-group from N-acetylphosphinothricin giving the cytotoxic compound L-phosphinothricin (Pt, glufosinate). This gene is useful in related deacetylase reactions, <i>in vitro</i> or <i>in vivo</i> using the proteins as such, of bacteria engineered to produce the enzyme activity.

		Altered metabolic properties. Modified carbohydrate metabolism. Altered probiotic attributes. Improved fermentation properties or other industrially useful processes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut health, lactose tolerance).	
56	181	Production of bioactive or functional polypeptides. Removal of undesirable flavor characteristics. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut health). Altered resistance to antibiotics.	Homology to serine proteases, which break down milk proteins during the growth of the bacteria on milk. Contains the subtilase pattern of the subtilase family(G-T-S-x-[SA]-x-P-x(2)-[STAVC]-[AG]). Subtilases are an extensive family of serine proteases whose catalytic activity is provided by a charge relay system similar to that of the trypsin family of serine proteases but which evolved by independent convergent evolution. The sequence around the residues involved in the catalytic triad (aspartic acid, serine and histidine) are completely different from that of the analogous residues in the trypsin serine proteases and can be used as signatures specific to that category of proteases. This enzyme is similar to prochymosin, a protein used in cheese making. The gene is useful in protease utilization in protein processing (see e.g. NL8701378; <i>S. cremoris</i> proteinase).
57	182	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis	Homologue of GABA permeases. GABA permeases belong to the amino acid-polyamine-organocation (APC) superfamily. This superfamily of transport proteins includes members that function as solute:cation symporters and solute:solute antiporters. They occur in bacteria, archaea, yeast, fungi, unicellular eukaryotic protists, slime molds, plants and animals. This enzyme is similar to linoleate isomerase (see e.g.

		amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	WO9932604-A1). This gene is useful in enzyme reactions similar to lineolate isomerase, either as a purified protein, or in transgenic organisms containing the gene effecting the enzyme activity.
58	183	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	Homologue of iap. iap is a major extracellular protein in <i>Listeria</i>, and seems to be required for adherence to and invasion of 3T6 mouse fibroblasts. This gene can be useful as a probe to detect the presence of the gene/protein in various bacteria. Deletion, addition and modification of the gene in transgenic bacteria can alter their extracellular envelope structure, thereby altering their growth and pathogenicity characteristics. See e.g. Bubert <i>et al.</i>, <i>J. Bacteriol.</i> 174(24):8166-8171, 1992. Involved in the invasion of cells, could be necessary for the export of invasion related determinants. iap mediates adhesion to particular cell surfaces, therefore has utility in persistence in the gut environment, probiotic effects and pathogen exclusion.
59	184	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or	Homologue of preprotein translocase secY subunit. The sequence contains the protein secY signature 1 pattern

		animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	(SIFSMGVSPYITAQIVVQLL), the protein secY signature 2 pattern (WMGEQITDKGLGNGVSLLI) and C-5 cytosine-specific DNA methylases C-terminal signature pattern (KGLGNGVSLLIFSGIVARL). The eubacterial secY protein plays an important role in protein export. It interacts with the signal sequences of secretory proteins as well as with two other components of the protein translocation system: secA and secE. SecY is an integral plasma membrane protein of 419 to 492 amino acid residues that apparently contains ten transmembrane segments. Such a structure probably confers to secY a 'translocator' function, providing a channel for periplasmic and outer-membrane precursor proteins. This gene is useful for enhancing extracellular protein production by improved transport from cell (see <i>e.g.</i> JP5153979A2: Sec Y protein gene)
60	185	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered amino acid metabolism. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis).	Homologue of cationic amino acid transport protein ctrA. As a cell surface protein, ctrA has been shown to give a strong response as antigen and could be used as a prominent target for antibodies and diagnostic procedures or vaccine development (surface location enhances its exposure to the immune system). Amino acid metabolism plays a role not only in metabolism and growth, but also in the production of flavour and aroma compounds. Control over the import of amino acids will modulate the production of these compounds.

		Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	
61	186	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes. Vaccine development.	Homologue of lipoprotein plpB. Bacterial surface lipoproteins give strong responses as antigens and could be used as prominent targets for antibodies and diagnostic procedures. Thus, is useful in vaccine development (surface location enhances its exposure to the immune system). May also have a role in solute binding and adhesion to cell surfaces.
62	187	Altered cell wall or cell surface characteristics, structures or functions. Altered amino acid metabolism. Removal of undesirable flavor characteristics. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein	Homologue of dihydrodipicolinate synthase (EC 4.2.1.52). Dihydrodipicolinate synthase catalyzes the first step in the biosynthesis of diaminopimelate and lysine from aspartate semialdehyde; L-aspartate 4-semialdehyde and pyruvate to dihydrodipicolinate and water. It is feedback-inhibited by lysine and belongs to the dihydrodipicolinate synthetase (DHDPS) family. This gene is involved in bacterial wall synthesis, and is thus a target for antibiotic development, as its inhibition would affect growth of the

		manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance.	bacterium.
63	188	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered viability in response to stress conditions. Improved stress-response Altered probiotic attributes. Vaccine development.	Homologue of GroEL, a heat shock protein, which makes up the GroE chaperonin system in bacteria together with GroE. It is involved in the folding and assembly of newly synthesized polypeptide chains released from the translation machinery and the refolding of stress-denatured proteins. GroEL, a member of the hsp60 family is a highly conserved heat-shock chaperonin protein and is an oligomer of 14 subunits composed of two stacked rings of 7 subunits. This gene is similar to a gene used in mycobacterial vaccine development, and is thus a target for antibiotic development, as its inhibition would affect growth of the bacterium (see e.g. WO9932634-A2: Compositions derived from <i>Mycobacterium vaccae</i> and methods for their use). Also noted as having a role in resistance to environmental stress conditions.
64	189	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable texture. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein	Homologue of hyaluronan synthase. Hyaluronan (or hyaluronic acid or hyaluronate; HA) is a polysaccharide of the glycosaminoglycans class found in the extracellular matrix of vertebrate tissues and in the surface coating of certain <i>Streptococcus</i> and <i>Pasteurella</i> bacterial pathogens. It is a unique biopolymer found in all tissues and body fluids in every mammalian species as well as in microorganisms. HA synthases (HASs) are the enzymes that polymerize HA using uridine diphospho-

		manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	sugar precursors. In all known cases, HA is secreted out of the cell; therefore, HASs are normally found in the outer membranes of the organism. They were the first class of glycosyltransferases identified in which a single polypeptide species catalyzes the transfer of two different monosaccharides; this finding is in contrast to the usual 'single enzyme, single sugar' dogma of glycobiology. Derivatizing and complexing hyaluronan with other substances makes it possible to create bioactive (e.g. anti-thrombogenic, anti-bacterial) surfaces. This gene is involved in pathogenesis with cell-cell interactions, differentiation, tissue repair. The gene is also similar to an <i>Enterococcus</i> antigen that is useful in vaccine development (see e.g. WO9850554-A2; <i>Enterococcus faecalis</i> antigenic polypeptide fragment EF017).
65, 111	190, 235	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties.	Homologue of MurD. MurD encodes UDP-N-acetylmuramoylalanine--D-glutamate ligase (EC 6.3.2.9) also known as UDP-N-acetylmuramoyl-L-alanyl-D-glutamate synthetase or D-glutamic acid adding enzyme catalyzes the addition of D-glutamate to the nucleotide precursor UDP-N-acetylmuramoyl-l-alanine (UMA) and belongs to the cytoplasmic peptidoglycan synthetases involved in cell wall formation. Thus it is useful for antibiotic development to inhibit bacterial cell wall synthesis.

66	191	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable texture. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	Homologue of transmembrane glycoprotein involved in nephritis (inflammation of the kidney).
67	192	Altered amino acid metabolism. Removal of undesirable flavor characteristics. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes.	Homologue of glutamine transport ATP-binding protein glnQ (TC# 3.A.1.3.2). glnQ belongs to the polar amino acid uptake transporter (PAAT) family (TC# 3.A.1.3) of the ATP-binding Cassette (ABC) superfamily of transporters. The enzymatic degradation of amino acids in cheese plays a major role in cheese flavor development. Amino acid degradation products greatly contribute to flavor or to off-flavors (Rijnen <i>et al.</i>, <i>Appl. Environ. Microbiol.</i> 65:4873-4880, 1999).

		Modified health properties (including immunoregulatory, anticancer, gut health).	
68	193	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable texture. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	Homologue of fibronectin/fibrinogen-binding protein like FBP54. FBP54 is a surface protein that reacts with both fibronectin and fibrinogen and therefore may participate in the adhesion of bacteria to host cells. This gene is involved in bacterial entry into mammalian cells (see Joh <i>et al.</i>, <i>Matrix Biol.</i> 18:211-223, 1999). Thus this gene is useful in manipulation of the binding process to alter pathogenicity through drugs interfering with the gene product.
69	194	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics:	Homologue of virulence factor mviM. Bacteria that cause disease have special factors which are designated as virulence factors. These factors contribute to the virulence of the microorganisms and to their survival in the hostile environment within the body of their host. Various signals control the expression of the virulence factors. Oxygen, temperature, concentration of ions, and pH are some of the known signals that change the bacterial virulence. The action of virulence factors ranges from adhesion mediation to target cells to molecular mimicry and

		survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes. Vaccine development.	mobility to pH buffering. The gene is useful as a target for vaccine development of bacteria having this kind of gene, as well as manipulation of virulence by deletion, addition or modification of the gene in transgenic bacteria.
70	195	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Regulation of metabolic processes. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	Homologue of the response regulator cheY. Chemotactic receptors at the bacterial cell surface communicate with flagellar basal structures to elicit appropriate motor behavior in response to extracellular stimuli. Genetic and physiological studies indicate that the product of the cheY gene interacts directly with components of the flagellar motor to control swimming behavior. Response regulators are involved in production of virulence factors, motility, antibiotic resistance and cell replication. Inhibitors of these proteins would be useful in preventing bacterium from progressing to pathogenesis, thus useful in medical treatments against bacteria. May have utility as a controlled expression vector.
71, 112	196, 236	Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes.	Homologue of the mycobacterial RegX3 protein. RegX3 is a response regulator, which together with the histidine kinase SenX3 forms a two-component signal transduction system that is positively

		Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Regulation of metabolic processes. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	autoregulated (Himpens <i>et al.</i>, <i>Microbiol.</i> 146:3091-3098, 2000). Response regulators in bacteria are involved in the bacterium's ability to monitor its surroundings and adapt to changes in its environment. Several of these bacterial regulators are involved in virulence and bacterial pathogenesis within the host (see e.g. US Patent 5,910,572) The response regulators are involved in production of virulence factors, motility, antibiotic resistance and cell replication. Inhibitors of these proteins would be useful in preventing bacterium from progressing to pathogenesis, thus useful in medical treatments against bacteria. May have utility as a controlled expression vector.
72, 113	197, 237	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Regulation of metabolic processes. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	Homologue of spinosyn biosynthesis. Spinosyns are macrolides with a 21-carbon, tetracyclic lactone backbone to which the deoxysugars forosamine and tri-O-methylrhamnose are attached. Macrolides interfere with the peptidyltransfer function of the ribosome. The macrolide antibiotics, which include erythromycin, azithromycin, and the streptogramin family among others, work by binding the large ribosomal subunit. The molecular details of the binding site for macrolides are not well understood. The spinosyns, a novel family of insecticidal macrocyclic lactones, are active on a wide variety of insect pests, especially lepidopterans and dipterans (see WO9946387-A1: Biosynthetic genes for spinosyn insecticide production). This gene can be useful in a related compound biosynthesis utilization for bioactive compounds.

73	198	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable texture. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	Homologue of EpsK protein. EpsK is involved in exopolysaccharide biosynthesis. A broad variety of bacteria produce polysaccharides, which can either be excreted into the environment as exopolysaccharides (EPSs), form a capsule around the cell as capsular polysaccharides, or be attached to the cell membrane as the O antigens of lipopolysaccharides. The biosynthesis of polysaccharides that consist of repeating units includes their assembly on a lipid carrier by sequential transfer of monosaccharides from nucleotide sugars by glycosyltransferases (GTFs) and the subsequent polymerization and export of these repeating units. Secreted exopolysaccharides contribute to the cell protection against environmental influences, attachment to surfaces, nutrient gathering and to antigenicity. Due to the variation of monosaccharide sequences, condensation linkages and non-carbohydrate decorations, an infinite array of structures can be provided by these sugar polymers. Deletion, addition and modification of the gene in transgenic bacteria can alter their extracellular envelope structure, thereby altering their growth and pathogenicity characteristics.
74	199	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes,	Homologue of CpxA protein. CpxA is involved in several diverse cellular processes, such as the functioning of acetohydroxyacid synthetase I, in the biosynthesis of isoleucine and valine, the traJ protein activation activity for tra gene expression in F plasmid, and the synthesis, translocation, or stability of cell envelope proteins. It also activates CpxR by phosphorylation. The CpxA-CpxR two-component signal transduction system regulates gene expression in adaptation to adverse conditions. These include envelope protein distress, heat shock, oxidative stress, high pH, and entry into stationary

		growth or storage in product formats, persistence in gut environment. Regulation of metabolic processes. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	phase. This gene can be useful in manipulation the sensory apparatus related functions by deletion, addition or modification of the gene in transgenic bacteria, or as a drug target to interfere with bacterial signaling systems. May have utility as a controlled expression vector.
75	200	Altered cell wall or cell surface characteristics, structures or functions. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Regulation of metabolic processes. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	Homologue of 1,4-dihydroxy-2-naphthoate octaprenyltransferase. 1,4-dihydroxy-2-naphthoate octaprenyltransferase is a membrane-associated enzyme that converts the soluble bicyclic naphthalenoid compound 1,4-dihydroxy-2-naphthoic acid (DHNA) to membrane-bound demethylmenaquinone, a key step in the menaquinone biosynthesis.
76	201	Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations.	Homologue of the bifunctional bacterial gene HpcE coding for 2-hydroxyhepta-2,4-diene-1, 7-dioate isomerase and 5-carboxymethyl-2-oxo-hex-3-ene-1, 7-dioatedecarboxylase (EC 5.3.3.-). HpcE produces 2-hydroxyhepta-2,4-diene, 1,7-dioate from 5-carboxymethyl-2-oxo-hex-3-ene-1,5-dioate or 5-Carboxymethyl-2-hydroxymuconate.

		Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Regulation of metabolic processes. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	
77	202	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Regulation of metabolic processes. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	Homologue of UbiX. UbiX codes for 3-octaprenyl-4-hydroxybenzoate carboxylase (EC 4.1.1.-) and that catalyzes the third reaction in ubiquinone biosynthesis pathway, the conversion of 3-octaprenyl-4-hydroxybenzoate to 2-octaprenyl phenol, and normally functions in association with the cytoplasmic membrane.
78, 114	203, 238	Removal of undesirable flavor characteristics. Modified flavor, aroma, texture attributes. Construction of genetic vectors for controlled expression of RNA and/or	Homologue of lacG. LacG codes for the enzyme 6-phospho-beta-galactosidase (EC 3.2.1.85) that is part of the lactose metabolism and hydrolyzes phospholactose, the product of a phosphor-enolpyruvate-dependent

		protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: (survival of industrial processes, growth or storage in product formats, persistence in gut environment). Modified carbohydrate levels or functional properties. Altered metabolic properties. Modified lactose metabolism. Altered probiotic attributes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut health, lactose tolerance).	phosphotransferase system. It belongs to the glycosidase family 1 and contributes to bitter flavor.
79, 115	204, 239	Altered cell wall or cell surface characteristics, structures or functions. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Regulation of metabolic processes. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	Homologue of the <i>dnrH</i>, <i>dpsA</i>-<i>dpsF</i> genes, which encode daunorubicin (DNR)-doxorubicin (DXR) polyketide synthase (PKS). DNR and its C-14-hydroxylated derivative DXR are among the most important antitumor antibiotics in current use. Both antibiotics are produced by <i>Streptomyces peucetius</i> through a pathway involving a type II PKS, which executes the condensation of propionyl coenzyme A (CoA), as the starter unit, and nine malonyl-CoA extender units in the production of a 21-carbon decaketide (Bao <i>et al.</i>, <i>J. Bacteriol.</i> 181:4690-4695, 1999).
80	205	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production,	Homologue of decaprenyl diphosphate (decaprenyl-PP) synthase. Decaprenyl-PP synthase catalyzes the consecutive

		genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered phosphate metabolism. Altered viability in response to stress conditions. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	condensation of isopentenyl diphosphate with allylic diphosphates to produce decaprenyl-PP, which is used for the side chain of ubiquinone (Q)-10.
81, 116	206, 240	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered phosphate metabolism. Altered viability in response to stress conditions. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	Homologue of geranyltranstransferase (EC 2.5.1.10) also known as farnesyl-diphosphate synthase. Geranyltranstransferase catalyzes the basic chain-elongation reaction in the isoprene biosynthetic pathway, the condensation of isopentenyl pyrophosphate with dimethylallyl pyrophosphate to give geranyl pyrophosphate.
82	207	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production,	Homologue of heptaprenyl diphosphate synthase. Heptaprenyl diphosphate synthase catalyzes the condensation of

		genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered phosphate metabolism. Altered viability in response to stress conditions. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	four molecules of isopentenyl diphosphate with farnesyl diphosphate to give heptaprenyl diphosphate, which is involved in the biosynthesis of the side chain of menaquinone-7 (Zhang <i>et al.</i>, <i>J. Bacteriol.</i> 179:1417-1419, 1997)
83-85, 117	208-210, 241	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered phosphate metabolism. Altered viability in response to stress conditions. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	Homologue of the ispE (formerly designated ychB) gene. IspE encodes 4-(cytidine 5'-diphospho)-2-C-methyl-D-erythritol kinase also called 4-diphosphocytidyl-2-C-methyl-D-erythritol kinase (EC 2.7.1.148) that belongs to the non-mevalonate terpenoid biosynthesis pathway and catalyzes the phosphorylation of 4-diphosphocytidyl-2-C-methyl-D-erythritol yielding 4-diphosphocytidyl-2-C-methyl-D-erythritol 2-phosphate (Rohdich <i>et al.</i>, <i>Proc. Natl. Acad. Sci. USA</i> 97:8251-8256, 2000).
86, 88	211, 213	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production,	Homologue of MIAA that encodes tRNA delta(2)-isopentenylpyrophosphate transferase

		genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered phosphate metabolism. Altered viability in response to stress conditions. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	(EC 2.5.1.8), which catalyzes the first step in the biosynthesis of 2-methylthio-n6-(delta(2)-isopentenyl)-adenosine (ms[2]i[6]a) adjacent to the anticodon of several tRNA species.
87	212	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered phosphate metabolism. Altered viability in response to stress conditions. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	Homologue of mvaD coding for mevalonate pyrophosphate decarboxylase (EC 4.1.1.33). MvaD is part of the mevalonate pathway for the biosynthesis of the central isoprenoid precursor, isopentenyl diphosphate by catalyzing the reaction of mevalonate 5-diphosphate (MVADP) with ATP to produce isopentenyl diphosphate, ADP, CO₂, and inorganic phosphate.
89, 90	214, 215	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or	Homologue of mraY, coding for phospho-N-acetylmuramoyl-pentapeptide-transferase (EC 2.7.8.13)

		animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	also known as UDP-N-acetyl-muramoyl-L-alanyl-D-gamma-glutamyl-L-lysyl-D-alanyl-D-alanine:undecaprenoid-alcohol-phosphate-phospho-N-acetylmuramoyl-pentapeptide-transferase. mraY catalyzes the formation of undecaprenyl-pyrophosphoryl-N-acetylmuramoyl-pentapeptide from UDP-N-acetylmuramoyl-pentapeptide and undecaprenyl-phosphate, the first step in the lipid cycle reactions in biosynthesis of bacterial cell wall peptidoglycans. Phospho-N-acetylmuramoyl-pentapeptide-transferase is an integral membrane protein and belongs to the glycosyltransferase family 4 mraY subfamily.
91, 92	216, 217	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health).	Homologue of UPPS, encoding undecaprenyl pyrophosphate synthetase (EC 2.5.1.31). UPPS catalyzes the Z-oligomerization of isopentenyl units with farnesyl pyrophosphate as a priming substrate to give C50 and C55 prenyl pyrophosphates with Z,E mixed stereochemistry. Undecaprenyl pyrophosphate synthetase is required as a lipid carrier of glycosyl transfer in the biosynthesis of a variety of cell wall polysaccharide components in bacteria.

		Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	
93, 94	218, 219	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	Homologue of Cps-like gene products are involved in bacterial capsular polysaccharide (CP) biosynthesis. Bacterial CPs are generally composed of repeating oligosaccharides and are involved in resistance to opsonophagocytosis, avoidance of the immune system of the host and attachment. Cps genes are normally clustered on the bacterial chromosome and have a common genetic organization involving three functional regions. Cps14E codes for undecaprenyl-phosphate Glc-1-phosphate transferase that links glucose to an undecaprenylphosphate lipid carrier, the first step in the biosynthesis of enterobacterial common antigen as well as of many O-specific lipopolysaccharides (Kolkman <i>et al.</i>, <i>J. Biol. Chem.</i> 272:19502-19508, 1997).
95, 97	220, 221	Production of bioactive or functional polypeptides. Removal of undesirable flavor characteristics. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics:	Homologue of pepV, encoding Xaa-His dipeptidase (EC 3.4.13.3) (carnosinase). PepV is a metalloenzyme member of the metallopeptidase families M20A or M25, with activity against beta-alanyl-dipeptides. It hydrolyzes a broad range of dipeptides including carnosine (beta-alanyl-histidine) but no tri-, tetra-, or larger oligopeptides. PepV in related lactic acid bacteria act as intracellular dipeptidases (Hellendorn <i>et al.</i>, <i>J. Bacteriol.</i> 179:3410-3415) and are important in the final breakdown of casein. PepV mutants exhibit slower growth rates in milk and alter some

		survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut health). Altered resistance to antibiotics.	flavor characteristics. The proteolytic system of lactic acid bacteria is essential for bacterial growth in milk but also for the development of the organoleptic properties of dairy products. PepV is involved both in bacterial growth by supplying amino acids, and in the development of flavor in dairy products, by hydrolyzing peptides (including bitter peptides) and liberating aromatic amino acids which are important precursors of aroma compounds (Fernandez-Esplá and Rul, <i>Eur. J. Biochem.</i> 263:502-510, 1999).
98	222	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes. Vaccine production.	Homologue of a 19 kDa secreted immunogenic lipoprotein. The 19 kDa lipoprotein gives a strong response as antigen and could be used as a prominent target for antibodies and diagnostic procedures. It is a secreted lipoprotein isolated from <i>Mycobacterium tuberculosis</i> (Ashbridge <i>et al. Nucleic. Acids Res.</i> 17:1249-1253, 1989). It is immunogenic and stimulates TH1-type T cell responses (Mohaghehpour <i>et al.; J. Immunol.</i> 161:2400-2406, 1998).
99	223, 253	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines.	Homologue of LecLA2-20, a lectin-like protein LA2-20. Lectins are ubiquitous proteins, which exhibit a specific and reversible sugar-binding activity. They

		Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes. Vaccine production.	react with glycosylated macromolecules and cells and may coaggragate them and lead to their lysis or alterations (Gilboa-Garber and Garber, <i>FEMS Microbiol. Rev.</i> 5:211-221, 1989). May have a role in intestinal adhesion via mucin-binding capability (Matsumura <i>et al.</i>, <i>J. Dairy Sci.</i> 82:2523-2529, 1999).
100	224	Altered amino acid metabolism. Removal of undesirable flavor characteristics. Altered cell wall or cell surface characteristics, structures or functions. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut	Homologue of ilvB that encodes acetolactate synthase (EC 4.1.3.18). IlvB catalyzes the first step common to the biosynthesis of the branched-chain amino acids (valine, leucine and isoleucine). The enzyme catalyzes two parallel reactions: condensation of two molecules of pyruvate to give rise to acetolactate and condensation of pyruvate and alpha-ketobutyrate to yield acetohydroxybutyrate. The enzyme is inhibited by the end products of the pathway (Singh <i>et al.</i>, <i>Proc. Natl. Acad. Sci. USA</i> 88:4572-4576, 1991). Lactic acid bacteria are nutritionally demanding bacteria which need amino acids for optimal growth. Therefore the branched-chain amino acid (BCAA) biosynthesis pathway is an essential pathway for optimal growth of lactic acid bacteria in milk. Branch chain amino acids impact on cheese flavor (Yvon <i>et al.</i>, <i>Appl. Environ. Microbiol.</i>

		health). Improved fermentation properties or other industrially useful processes.	63:414-419, 1997).
101	225	Altered amino acid metabolism. Removal of undesirable flavor characteristics. Altered cell wall or cell surface characteristics, structures or functions. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health). Improved fermentation properties or other industrially useful processes.	Homologue of ilvG (an isoenzyme of ilvB) that encodes acetolactate synthase (EC 4.1.3.18). IlvG catalyzes the first step common to the biosynthesis of the branched-chain amino acids (valine, leucine and isoleucine). The enzyme catalyzes two parallel reactions: condensation of two molecules of pyruvate to give rise to acetolactate and condensation of pyruvate and alpha-ketobutyrate to yield acetohydroxybutyrate. The enzyme is inhibited by the end products of the pathway (Singh <i>et al.</i>, <i>Proc. Natl. Acad. Sci. USA</i> 88:4572-4576, 1991). Lactic acid bacteria are nutritionally demanding bacteria which need amino acids for optimal growth. Thus, the branched-chain amino acid (BCAA) biosynthesis pathway is an essential pathway for optimal growth of lactic acid bacteria in milk and impacts on cheese flavor (Yvon <i>et al.</i>, <i>Appl. Environ. Microbiol.</i> 63:414-419, 1997).
102	226	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats,	Homologue of basic surface protein BspA of <i>Lactobacillus fermentum</i>. BspA is involved in L-cysteine uptake. BspA is believed to belong to the family III of the bacterial solute-binding proteins and does not contain a lipoprotein consensus sequence (Turner <i>et al.</i>, <i>J. Bacteriol.</i> 179:3310-3316, 1997). Members of the family III solute binding proteins have been shown to bind polar amino acids and opines such as cystine, glutamine, arginine, histidine, lysine, octopine, and nopaline. Implicated in response to oxidative stress (Turner <i>et al.</i>, <i>J. Bacteriol.</i> 181:2192-2198, 1999).

		persistence in gut environment. Altered amino acid metabolism. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	
103, 118	227, 242	Altered cell wall or cell surface characteristics, structures or functions. Modified adhesion to human or animal cells or cell lines. Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered probiotic attributes. Modified health properties (including immunoregulatory, anticancer, gut health, apoptosis). Modified antibiotic resistance. Improved antimicrobial properties. Improved fermentation properties or other industrially useful processes.	Homologue of outer membrane lipoprotein gna1946, similar to HlpA of <i>H. influenzae</i>. HlpA belongs to the NlpA family of lipoproteins like the iap genes.
104	228	Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Production of desirable flavors. Modified flavor, aroma and/or texture attributes.	Homologue of cold shock protein cspB. CspB is involved in an adaptive process required for cell viability at low temperatures or may function as antifreeze protein. Several bacteria react to a sudden downshift in temperature by the production of a set of proteins, together forming the cold-shock stimulon, that includes small (7-kDa) cold-shock proteins (CSPs). In a variety

		Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered viability in response to stress conditions. Altered metabolic properties or regulation of metabolic pathways. Altered probiotic attributes. Improved fermentation properties or other industrially useful processes.	of bacteria, families of CSPs, consisting of three to nine members, have been described of which CspA in <i>E. coli</i> (CspAE) and CspB in <i>Bacillus subtilis</i> (CspBB) are the best characterized. CspAE and CspBB are capable of binding to single-stranded DNA and RNA, and based on these characteristics, several functions for CSPs have been suggested, such as transcriptional activators, RNA chaperones that facilitate the initiation of translation, and freeze-protective proteins. Recently it has been shown that CSPs might regulate the expression of cold-induced genes as antiterminators. Regulation of csp genes takes place at several levels, and for CspAE it was shown that cold-shock induction is achieved at the transcriptional level as well as at the level of mRNA and protein stability (Wouters <i>et al.</i>, <i>Appl. Environ. Microbiol.</i> 67:5171-5178, 2001).
105, 120	229, 244	Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Modified lipid, glycolipid or free fatty acid levels or functional properties. Modified production of short chain fatty acids. Altered lipid metabolism. Altered probiotic attributes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut	Homologue of fabF, beta-ketoacyl synthase (acyl carrier protein). FabF is part of the fatty acid biosynthesis (fab) gene cluster (fabD-fabH-acpP-fabF) involved in fatty acid biosynthesis. FabF is the condensing enzyme thought to be responsible for elongation of fatty acids. The fab genes are important in the production of butyric acid, with important flavor and health impacts. It also has antibiotic effects and may be protective against colon cancer (Mortensen and Clausen, <i>Scand. J. Gastroenterol. Suppl.</i> 216:132-148, 1996).

		health)	
120	245	Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Modified lipid, glycolipid or free fatty acid levels or functional properties. Modified production of short chain fatty acids. Altered lipid metabolism. Altered probiotic attributes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut health)	Homologue of accA, which encodes the acetyl-CoA carboxylase alpha subunit (EC 6.4.1.2). AccA is part of the acc operon. <i>E. coli</i> acetyl-CoA carboxylase catalyzes the first committed and rate-controlling step in fatty acid biosynthesis. Fatty acids in gram-positive bacteria act as signaling molecules that are important for cell differentiation (Marini <i>et al.</i>, <i>J. Bacteriol.</i> 177:7003-7006, 1995).
120	246	Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Modified lipid, glycolipid or free fatty acid levels or functional properties. Modified production of short chain fatty acids. Altered lipid metabolism.	Homologue of accB encoding biotin carboxyl carrier protein (BCCP), a part of the acc operon. <i>E. coli</i> acetyl-CoA carboxylase catalyzes the first committed and rate-controlling step in fatty acid biosynthesis. The overall reaction catalyzed by acetyl-CoA carboxylase proceeds via two half-reactions. To carry out this two-step reaction acetyl-CoA carboxylase requires three distinct components: biotin carboxylase, biotin carboxyl carrier protein, and carboxyltransferase. The biotin carboxylase component catalyzes the first half-reaction, which is an ATP-dependent carboxylation of the vitamin biotin. In vivo, biotin is covalently attached to the biotin carboxyl carrier protein designated as BCCP. (Janiyani <i>et al.</i>, <i>J. Biol. Chem.</i>

		Altered probiotic attributes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut health)	276:29864-29870, 2001). Indications are that fatty acids in gram-positive bacteria act as signaling molecules that are important for cell differentiation (Marini <i>et al.</i> , <i>J. Bacteriol.</i> 177:7003-7006, 1995).
120	247	Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Modified lipid, glycolipid or free fatty acid levels or functional properties. Modified production of short chain fatty acids. Altered lipid metabolism. Altered probiotic attributes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut health)	Homologue of accC encoding the biotin carboxylase (EC 6.3.4.14), a part of the acc operon. <i>E. coli</i> acetyl-CoA carboxylase catalyzes the first committed and rate-controlling step in fatty acid biosynthesis. The overall reaction catalyzed by acetyl-CoA carboxylase proceeds via two half-reactions. To carry out this two-step reaction acetyl-CoA carboxylase requires three distinct components: biotin carboxylase, biotin carboxyl carrier protein, and carboxyltransferase. The biotin carboxylase component catalyzes the first half-reaction, which is an ATP-dependent carboxylation of the vitamin biotin. <i>In vivo</i> , biotin is covalently attached to the biotin carboxyl carrier protein designated as BCCP. The second half-reaction, the transfer of the carboxyl group from carboxybiotin to acetyl-CoA to make malonyl-CoA, is catalyzed by the carboxyltransferase component. The chain length of newly synthesized fatty acids depends on the concentration of malonyl-CoA (Janiyani <i>et al.</i> , <i>J. Biol. Chem.</i> 276:29864-29870, 2001). Indications are that fatty acids in gram-positive bacteria act as signaling molecules that are important for cell differentiation (Marini <i>et al.</i> , <i>J. Bacteriol.</i> 177:7003-7006, 1995).
120	248	Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis	Homologue of accD encoding the acetyl-coA carboxylase carboxyl transferase subunit beta (EC 6.4.1.2), a part of the acc operon. <i>E. coli</i> acetyl-CoA carboxylase catalyzes the first committed and rate-controlling step in fatty acid biosynthesis. The overall

		amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Modified lipid, glycolipid or free fatty acid levels or functional properties. Modified production of short chain fatty acids. Altered lipid metabolism. Altered probiotic attributes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut health)	reaction catalyzed by acetyl-CoA carboxylase proceeds via two half-reactions. To carry out this two-step reaction acetyl-CoA carboxylase requires three distinct components: biotin carboxylase, biotin carboxyl carrier protein, and carboxyltransferase. The biotin carboxylase component catalyzes the first half-reaction, which is an ATP-dependent carboxylation of the vitamin biotin. <i>In vivo</i>, biotin is covalently attached to the biotin carboxyl carrier protein designated as BCCP. The second half-reaction, the transfer of the carboxyl group from carboxybiotin to acetyl-CoA to make malonyl-CoA, is catalyzed by the carboxyltransferase component. The chain length of newly synthesized fatty acids appears to depend on the concentration of malonyl-CoA (Janiyani <i>et al.</i>, <i>J. Biol. Chem.</i> 276:29864-29870, 2001). Indications are that fatty acids in gram-positive bacteria act as signaling molecules that are important for cell differentiation (Marini <i>et al.</i>, <i>J. Bacteriol.</i> 177:7003-7006, 1995).
120	249	Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Modified lipid, glycolipid or free fatty acid levels or functional properties. Modified production of short chain fatty acids. Altered lipid metabolism.	Homologue of fabD, malonyl coenzyme A-acyl carrier protein transacylase, which is part of the fatty acid biosynthesis (fab) gene cluster (fabD-fabH-acpP-fabF) involved in fatty acid biosynthesis. FabD overexpression leads to altered fatty acid composition in <i>E. coli</i>, with increased amounts of cis-vaccenate incorporated into membrane phospholipids. The fab genes are important in the production of butyric acid, with important flavor and health impacts. It also has antibiotic effects and may be protective against colon cancer (Mortensen and Clausen, <i>Scand. J. Gastroenterol. Suppl.</i> 216:132-148, 1996).

		Altered probiotic attributes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut health)	
120	250	Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Modified lipid, glycolipid or free fatty acid levels or functional properties. Modified production of short chain fatty acids. Altered lipid metabolism. Altered probiotic attributes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut health)	Homologue of fox2, encoding peroxisomal hydratase-dehydrogenase-epimerase (HDE) also known as multifunctional beta-oxidation protein (MFP). Fox2 is the second trifunctional enzyme acting on the beta-oxidation (cellular fatty acid degradation) pathway for fatty acids, possessing hydratase-dehydrogenase-epimerase activities. This enzyme converts trans-2-enoyl-CoA via d-3-hydroxyacyl-CoA to 3-ketoacyl-CoA.
120	251	Production of desirable flavors. Modified flavor, aroma and/or texture attributes. Construction of genetic vectors for controlled expression of RNA and/or protein, fusion protein production, genetic modification, mutagenesis amplification of genetic material or for other genetic or protein manipulations. Altered survival characteristics: survival of industrial processes, growth or storage in product formats, persistence in gut environment. Altered metabolic properties. Altered lipid metabolism.	Homologue of ncd2 gene, encoding 2-nitropropane dioxygenase (EC 1.13.11.32) also called nitroalkane oxidase. Ncd2 is a flavoprotein that catalyzes the oxidation of nitroalkanes to respective aldehydes or ketones with production of nitrite and water. Nitroalkanes are widely used as industrial solvents, chemical intermediates, explosives and fuels. Several nitroalkanes are toxic and/or carcinogenic. Thus, an enzymatic activity that converts nitroalkanes into less harmful species has significant potential for bioremediation.

		Altered probiotic attributes. Organisms or materials with improved health properties (including immunoregulatory, anticancer, gut health). Bioremediation of toxic, carcinogenic or otherwise harmful substances.	
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Isolated polynucleotides of the present invention include the polynucleotides identified herein as SEQ ID NO: 1-121; isolated polynucleotides comprising a polynucleotide sequence
 5 selected from the group consisting of SEQ ID NO: 1-121; isolated polynucleotides comprising at least a specified number of contiguous residues (*x*-mers) of any of the polynucleotides identified as SEQ ID NO: 1-121; isolated polynucleotides comprising a polynucleotide sequence that is complementary to any of the above polynucleotides; isolated polynucleotides comprising a polynucleotide sequence that is a reverse sequence or a reverse complement of
 10 any of the above polynucleotides; antisense sequences corresponding to any of the above polynucleotides; and variants of any of the above polynucleotides, as that term is described in this specification.

The word "polynucleotide(s)," as used herein, means a single or double stranded polymer of deoxyribonucleotide or ribonucleotide bases and includes DNA and corresponding
 15 RNA molecules, including mRNA molecules, both sense and antisense strands of DNA and RNA molecules, and comprehends cDNA, genomic DNA and recombinant DNA, as well as wholly or partially synthesized polynucleotides. A polynucleotide of the present invention may be an entire gene, or any portion thereof. A gene is a DNA sequence which codes for a functional protein or RNA molecule. Operable antisense polynucleotides may comprise a
 20 fragment of the corresponding polynucleotide, and the definition of "polynucleotide" therefore includes all operable antisense fragments. Antisense polynucleotides and techniques involving antisense polynucleotides are well known in the art and are described, for example, in Robinson-Benion, et al., "Antisense techniques," *Methods in Enzymol.* 254(23): 363-375, 1995; and Kawasaki, et al., *Artific. Organs* 20 (8): 836-848, 1996.

25 The definitions of the terms "complement," "reverse complement," and "reverse sequence," as used herein, are best illustrated by the following examples. For the sequence 5' AGGACC 3', the complement, reverse complement, and reverse sequences are as follows:

complement	3' TCCTGG 5'
reverse complement	3' GGTCCT 5'
reverse sequence	5' CCAGGA 3'

Preferably, sequences that are complements of a specifically recited polynucleotide
 5 sequence are complementary over the entire length of the specific polynucleotide sequence.

Identification of genomic DNA and heterologous species DNA can be accomplished by
 standard DNA/DNA hybridization techniques, under appropriately stringent conditions, using
 all or part of a DNA sequence as a probe to screen an appropriate library. Alternatively, PCR
 techniques using oligonucleotide primers that are designed based on known DNA and protein
 10 sequences can be used to amplify and identify other identical or similar DNA sequences.
 Synthetic DNA corresponding to the identified sequences or variants thereof may be produced
 by conventional synthesis methods. All of the polynucleotides described herein are isolated
 and purified, as those terms are commonly used in the art.

The polynucleotides identified as SEQ ID NO: 1-121 contain open reading frames
 15 ("ORFs"), or partial open reading frames, encoding polypeptides. Additionally,
 polynucleotides identified as SEQ ID NO: 1-121 may contain non-coding sequences such as
 promoters and terminators that may be useful as control elements. Open reading frames
 encoding polypeptides may also be identified in extended or full-length sequences
 corresponding to the sequences set out as SEQ ID NO: 1-121. Open reading frames may be
 20 identified using techniques that are well known in the art. These techniques include, for
 example, analysis for the location of known start and stop codons, most likely reading frame
 identification based on codon frequencies, similarity to known bacterial expressed genes, etc.
 Tools and software suitable for ORF analysis include GeneWise (The Sanger Center, Wellcome
 Trust Genome Campus, Hinxton, Cambridge CB10 1SA, United Kingdom), Diogenes
 25 (Computational Biology Centers, University of Minnesota, Academic Health Center, UMHG
 Box 43 Minneapolis MN 55455), and GRAIL (Informatics Group, Oak Ridge National
 Laboratories, Oak Ridge, Tennessee, TN). Open reading frames and portions of open reading
 frames may be identified in the polynucleotides of the present invention. Once a partial open
 reading frame is identified, the polynucleotide may be extended in the area of the partial open
 30 reading frame using techniques that are well known in the art until the polynucleotide for the
 full open reading frame is identified. Thus, polynucleotides and open reading frames encoding
 polypeptides may be identified using the polynucleotides of the present invention.

Once open reading frames are identified in the polynucleotides of the present invention, the open reading frames may be isolated and/or synthesized. Expressible genetic constructs comprising the open reading frames and suitable promoters, initiators, terminators, etc., which are well known in the art, may then be constructed. Such genetic constructs may be introduced
5 into a host cell to express the polypeptide encoded by the open reading frame. Suitable host cells may include various prokaryotic and eukaryotic cells. *In vitro* expression of polypeptides is also possible, as well known in the art.

As used herein, the term "oligonucleotide" refers to a relatively short segment of a polynucleotide sequence, generally comprising between 6 and 60 nucleotides, and
10 comprehends both probes for use in hybridization assays and primers for use in the amplification of DNA by polymerase chain reaction.

As used herein, the term "x-mer," with reference to a specific value of "x," refers to a polynucleotide comprising at least a specified number ("x") of contiguous residues of any of the polynucleotides identified as SEQ ID NO: 1-121. The value of x may be from about 20 to
15 about 600, depending upon the specific sequence.

In another aspect, the present invention provides isolated polypeptides encoded, or partially encoded, by the above polynucleotides. In specific embodiments, such polypeptides comprise a sequence selected from the group consisting of SEQ ID NO: 122-253, and variants thereof. As used herein, the term "polypeptide" encompasses amino acid chains of any length,
20 including full-length proteins, wherein the amino acid residues are linked by covalent peptide bonds. The term "polypeptide encoded by a polynucleotide" as used herein, includes polypeptides encoded by a polynucleotide which comprises an isolated polynucleotide sequence or variant provided herein. Polypeptides of the present invention may be naturally purified products, or may be produced partially or wholly using recombinant techniques. Such
25 polypeptides may be glycosylated with bacterial, fungal, mammalian or other eukaryotic carbohydrates or may be non-glycosylated.

Polypeptides of the present invention may be produced recombinantly by inserting a polynucleotide that encodes the polypeptide into an expression vector and expressing the polypeptide in an appropriate host. Any of a variety of expression vectors known to those of
30 ordinary skill in the art may be employed. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a polypeptide encoding a recombinant polypeptide. Suitable host cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are *Escherichia coli*, *Lactococcus lactis*,

Lactobacillus, insect, yeast or a mammalian cell line such as COS or CHO. The polynucleotide(s) expressed in this manner may encode naturally occurring polypeptides, portions of naturally occurring polypeptides, or other variants thereof.

In a related aspect, polypeptides are provided that comprise at least a functional portion
5 of a polypeptide having an amino acid sequence encoded by a polynucleotide of the present invention. As used herein, a "functional portion" of a polypeptide is that portion which contains the active site essential for affecting the function of the polypeptide, for example, the portion of the molecule that is capable of binding one or more reactants. The active site may be made up of separate portions present on one or more polypeptide chains and will generally
10 exhibit high binding affinity.

Functional portions of a polypeptide may be identified by first preparing fragments of the polypeptide by either chemical or enzymatic digestion of the polypeptide, or by mutation analysis of the polynucleotide that encodes the polypeptide and subsequent expression of the resulting mutant polypeptides. The polypeptide fragments or mutant polypeptides are then
15 tested to determine which portions retain biological activity, using, for example, the representative assays provided below.

Portions and other variants of the inventive polypeptides may be generated by synthetic or recombinant means. Synthetic polypeptides having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may be generated using techniques that are well
20 known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain (See Merrifield, *J. Am. Chem. Soc.* 85:2149-2154, 1963). Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin
25 Elmer/Applied Biosystems, Inc. (Foster City, CA), and may be operated according to the manufacturer's instructions. Variants of a native polypeptide may be prepared using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (Kunkel, *Proc. Natl. Acad. Sci. USA* 82:488-492, 1985). Sections of DNA sequences may also be removed using standard techniques to permit preparation of truncated polypeptides.

30 In general, the polypeptides and polynucleotides disclosed herein are provided in an isolated, substantially pure, form. Preferably, the polypeptides and polynucleotides are at least about 80% pure; more preferably at least about 90% pure; and most preferably at least about 99% pure.

As used herein, the term "variant" comprehends polynucleotide or polypeptide sequences different from the specifically identified sequences, wherein one or more nucleotides or amino acid residues is deleted, substituted, or added. Variants may be naturally occurring allelic variants, or non-naturally occurring variants. Variant polynucleotide and polypeptides
5 sequences preferably exhibit at least 60%, more preferably at least 75%, more preferably yet at least 90%, and most preferably at least 95% identity to a sequence of the present invention. The percentage identity is determined by aligning the two sequences to be compared as described below, determining the number of identical residues in the aligned portion, dividing that number by the total number of residues in the inventive (queried) sequence, and
10 multiplying the result by 100.

Polynucleotide and polypeptide sequences may be aligned, and the percentage of identical residues in a specified region may be determined against another polynucleotide or polypeptide, using computer algorithms that are publicly available. Two exemplary algorithms for aligning and identifying the similarity of polynucleotide sequences are the BLASTN and
15 FASTA algorithms. Polynucleotides may also be analyzed using the BLASTX algorithm, which compares the six-frame conceptual translation products of a nucleotide query sequence (both strands) against a protein sequence database. The percentage identity of polypeptide sequences may be examined using the BLASTP algorithm. The BLASTN, BLASTX and BLASTP programs are available on the NCBI anonymous FTP server and from the National
20 Center for Biotechnology Information (NCBI), National Library of Medicine, Building 38A, Room 8N805, Bethesda, MD 20894, USA. The BLASTN algorithm Version 2.0.4 [Feb-24-1998], Version 2.0.6 [Sept-16-1998] and Version 2.0.11 [Jan-20-2000], set to the parameters described below, is preferred for use in the determination of polynucleotide variants according to the present invention. The BLASTP algorithm, set to the parameters described below, is
25 preferred for use in the determination of polypeptide variants according to the present invention. The use of the BLAST family of algorithms, including BLASTN, BLASTP and BLASTX, is described in the publication of Altschul, *et al.*, *Nucleic Acids Res.* 25: 3389-3402, 1997.

The computer algorithm FASTA is available on the Internet and from the University of
30 Virginia by contacting David Hudson, Vice Provost for Research, University of Virginia, P.O. Box 9025, Charlottesville, VA 22906-9025, USA. FASTA Version 2.0u4 [February 1996], set to the default parameters described in the documentation and distributed with the algorithm, may be used in the determination of variants according to the present invention. The use of the

FASTA algorithm is described in Pearson and Lipman, *Proc. Natl. Acad. Sci. USA* 85:2444-2448, 1988; and Pearson, *Methods in Enzymol.* 183: 63-98, 1990.

The following running parameters are preferred for determination of alignments and similarities using BLASTN that contribute to the E values and percentage identity for polynucleotide sequences: Unix running command: blastall -p blastn -d embldb -e 10 -G 0 -E 0 -r 1 -v 30 -b 30 -i queryseq -o results; the parameters are: -p Program Name [String]; -d Database [String]; -e Expectation value (E) [Real]; -G Cost to open a gap (zero invokes default behavior) [Integer]; -E Cost to extend a gap (zero invokes default behavior) [Integer]; -r Reward for a nucleotide match (BLASTN only) [Integer]; -v Number of one-line descriptions (V) [Integer]; -b Number of alignments to show (B) [Integer]; -i Query File [File In]; and -o BLAST report Output File [File Out] Optional.

The following running parameters are preferred for determination of alignments and similarities using BLASTP that contribute to the E values and percentage identity of polypeptide sequences: blastall -p blastp -d swissprot -e 10 -G 0 -E 0 -v 30 -b 30 -i queryseq -o results; the parameters are: -p Program Name [String]; -d Database [String]; -e Expectation value (E) [Real]; -G Cost to open a gap (zero invokes default behavior) [Integer]; -E Cost to extend a gap (zero invokes default behavior) [Integer]; -v Number of one-line descriptions (v) [Integer]; -b Number of alignments to show (b) [Integer]; -I Query File [File In]; -o BLAST report Output File [File Out] Optional.

The "hits" to one or more database sequences by a queried sequence produced by BLASTN, FASTA, BLASTP or a similar algorithm, align and identify similar portions of sequences. The hits are arranged in order of the degree of similarity and the length of sequence overlap. Hits to a database sequence generally represent an overlap over only a fraction of the sequence length of the queried sequence.

The BLASTN, FASTA, and BLASTP algorithms also produce "Expect" values for alignments. The Expect value (E) indicates the number of hits one can "expect" to see over a certain number of contiguous sequences by chance when searching a database of a certain size. The Expect value is used as a significance threshold for determining whether the hit to a database, such as the preferred EMBL database, indicates true similarity. For example, an E value of 0.1 assigned to a polynucleotide hit is interpreted as meaning that in a database of the size of the EMBL database, one might expect to see 0.1 matches over the aligned portion of the sequence with a similar score simply by chance. By this criterion, the aligned and matched portions of the polynucleotide sequences then have a probability of 90% of being the same. For

sequences having an E value of 0.01 or less over aligned and matched portions, the probability of finding a match by chance in the EMBL database is 1% or less using the BLASTN or FASTA algorithm.

According to one embodiment, "variant" polynucleotides and polypeptides, with
5 reference to each of the polynucleotides and polypeptides of the present invention, preferably comprise sequences producing an E value of 0.01 or less when compared to the polynucleotide or polypeptide of the present invention. That is, a variant polynucleotide or polypeptide is any sequence that has at least a 99% probability of being the same as the polynucleotide or polypeptide of the present invention, measured as having an E value of 0.01 or less using the
10 BLASTN, FASTA, or BLASTP algorithms set at parameters described above. According to a preferred embodiment, a variant polynucleotide is a sequence having the same number or fewer nucleic acids than a polynucleotide of the present invention that has at least a 99% probability of being the same as the polynucleotide of the present invention, measured as having an E value of 0.01 or less using the BLASTN or FASTA algorithms set at parameters described above.
15 Similarly, according to a preferred embodiment, a variant polypeptide is a sequence having the same number or fewer amino acids than a polypeptide of the present invention that has at least a 99% probability of being the same as a polypeptide of the present invention, measured as having an E value of 0.01 or less using the BLASTP algorithm set at the parameters described above.

20 As noted above, the percentage identity is determined by aligning sequences using one of the BLASTN, FASTA, or BLASTP algorithms, set at the running parameters described above, and identifying the number of identical nucleic or amino acids over the aligned portions; dividing the number of identical nucleic or amino acids by the total number of nucleic or amino acids of the polynucleotide or polypeptide sequence of the present invention; and then
25 multiplying by 100 to determine the percentage identity. For example, a polynucleotide of the present invention having 220 nucleic acids has a hit to a polynucleotide sequence in the EMBL database having 520 nucleic acids over a stretch of 23 nucleotides in the alignment produced by the BLASTN algorithm using the parameters described above. The 23 nucleotide hit includes 21 identical nucleotides, one gap and one different nucleotide. The percentage identity of the
30 polynucleotide of the present invention to the hit in the EMBL library is thus $21/220$ times 100, or 9.5%. The polynucleotide sequence in the EMBL database is thus not a variant of a polynucleotide of the present invention.

In addition to having a specified percentage identity to an inventive polynucleotide or polypeptide sequence, variant polynucleotides and polypeptides preferably have additional structure and/or functional features in common with the inventive polynucleotide or polypeptide. Polypeptides having a specified degree of identity to a polypeptide of the present invention share a high degree of similarity in their primary structure and have substantially similar functional properties. In addition to sharing a high degree of similarity in their primary structure to polynucleotides of the present invention, polynucleotides having a specified degree of identity to, or capable of hybridizing to an inventive polynucleotide preferably have at least one of the following features: (i) they contain an open reading frame or partial open reading frame encoding a polypeptide having substantially the same functional properties as the polypeptide encoded by the inventive polynucleotide; or (ii) they contain identifiable domains in common.

Alternatively, variant polynucleotides of the present invention hybridize to the polynucleotide sequences recited in SEQ ID NO: 1-121, or complements, reverse sequences, or reverse complements of those sequences, under stringent conditions. As used herein, "stringent conditions" refers to prewashing in a solution of 6X SSC, 0.2% SDS; hybridizing at 65°C, 6X SSC, 0.2% SDS overnight; followed by two washes of 30 minutes each in 1X SSC, 0.1% SDS at 65°C and two washes of 30 minutes each in 0.2X SSC, 0.1% SDS at 65°C.

The present invention also encompasses polynucleotides that differ from the disclosed sequences but that, as a consequence of the discrepancy of the genetic code, encode a polypeptide having similar enzymatic activity to a polypeptide encoded by a polynucleotide of the present invention. Thus, polynucleotides comprising sequences that differ from the polynucleotide sequences recited in SEQ ID NO: 1-121, or complements, reverse sequences, or reverse complements of those sequences as a result of conservative substitutions are encompassed within the present invention. Additionally, polynucleotides comprising sequences that differ from the inventive polynucleotide sequences or complements, reverse complements, or reverse sequences as a result of deletions and/or insertions totaling less than 10% of the total sequence length are also contemplated by and encompassed within the present invention. Similarly, polypeptides comprising sequences that differ from the inventive polypeptide sequences as a result of amino acid substitutions, insertions, and/or deletions totaling less than 10% of the total sequence length are contemplated by and encompassed within the present invention, provided the variant polypeptide has similar activity to the inventive polypeptide.

The polynucleotides of the present invention may be isolated from various libraries, or may be synthesized using techniques that are well known in the art. The polynucleotides may be synthesized, for example, using automated oligonucleotide synthesizers (*e.g.*, Beckman Oligo 1000M DNA Synthesizer) to obtain polynucleotide segments of up to 50 or more nucleic acids. A plurality of such polynucleotide segments may then be ligated using standard DNA manipulation techniques that are well known in the art of molecular biology. One conventional and exemplary polynucleotide synthesis technique involves synthesis of a single stranded polynucleotide segment having, for example, 80 nucleic acids, and hybridizing that segment to a synthesized complementary 85 nucleic acid segment to produce a 5-nucleotide overhang. The next segment may then be synthesized in a similar fashion, with a 5-nucleotide overhang on the opposite strand. The “sticky” ends ensure proper ligation when the two portions are hybridized. In this way, a complete polynucleotide of the present invention may be synthesized entirely *in vitro*.

Certain of the polynucleotides identified as SEQ ID NO: 1-121 are generally referred to as “partial” sequences, in that they may not represent the full coding portion of a gene encoding a naturally occurring polypeptide. The partial polynucleotide sequences disclosed herein may be employed to obtain the corresponding full-length genes for various species and organisms by, for example, screening DNA expression libraries using hybridization probes based on the polynucleotides of the present invention, or using PCR amplification with primers based upon the polynucleotides of the present invention. In this way one can, using methods well known in the art, extend a polynucleotide of the present invention upstream and downstream of the corresponding DNA, as well as identify the corresponding mRNA and genomic DNA, including the promoter and enhancer regions, of the complete gene. The present invention thus comprehends isolated polynucleotides comprising a sequence identified in SEQ ID NO: 1-121, or a variant of one of the specified sequences, that encode a functional polypeptide, including full-length genes. Such extended polynucleotides may have a length of from about 50 to about 4,000 nucleic acids or base pairs, and preferably have a length of less than about 4,000 nucleic acids or base pairs, more preferably yet a length of less than about 3,000 nucleic acids or base pairs, more preferably yet a length of less than about 2,000 nucleic acids or base pairs. Under some circumstances, extended polynucleotides of the present invention may have a length of less than about 1,800 nucleic acids or base pairs, preferably less than about 1,600 nucleic acids or base pairs, more preferably less than about 1,400 nucleic acids or base pairs, more preferably

yet less than about 1,200 nucleic acids or base pairs, and most preferably less than about 1,000 nucleic acids or base pairs.

Polynucleotides of the present invention comprehend polynucleotides comprising at least a specified number of contiguous residues (x-mers) of any of the polynucleotides identified as SEQ ID NO: 1-121 or their variants. According to preferred embodiments, the value of x is preferably at least 20, more preferably at least 40, more preferably yet at least 60, and most preferably at least 80. Thus, polynucleotides of the present invention include polynucleotides comprising a 20-mer, a 40-mer, a 60-mer, an 80-mer, a 100-mer, a 120-mer, a 150-mer, a 180-mer, a 220-mer, a 250-mer, a 300-mer, a 400-mer, a 500-mer or a 600-mer of a polynucleotide identified as SEQ ID NO: 1-121 or a variant of one of the polynucleotides identified as SEQ ID NO: 1-121.

Oligonucleotide probes and primers complementary to and/or corresponding to SEQ ID NO: 1-121, and variants of those sequences, are also comprehended by the present invention. Such oligonucleotide probes and primers are substantially complementary to the polynucleotide of interest. An oligonucleotide probe or primer is described as "corresponding to" a polynucleotide of the present invention, including one of the sequences set out as SEQ ID NO: 1-121 or a variant, if the oligonucleotide probe or primer, or its complement, is contained within one of the sequences set out as SEQ ID NO: 1-121 or a variant of one of the specified sequences.

Two single stranded sequences are said to be substantially complementary when the nucleotides of one strand, optimally aligned and compared, with the appropriate nucleotide insertions and/or deletions, pair with at least 80%, preferably at least 90% to 95%, and more preferably at least 98% to 100%, of the nucleotides of the other strand. Alternatively, substantial complementarity exists when a first DNA strand will selectively hybridize to a second DNA strand under stringent hybridization conditions. Stringent hybridization conditions for determining complementarity include salt conditions of less than about 1 M, more usually less than about 500 mM and preferably less than about 200 mM. Hybridization temperatures can be as low as 5°C, but are generally greater than about 22°C, more preferably greater than about 30°C and most preferably greater than about 37°C. Longer DNA fragments may require higher hybridization temperatures for specific hybridization. Since the stringency of hybridization may be affected by other factors such as probe composition, presence of organic solvents and extent of base mismatching, the combination of parameters is more important than the absolute measure of any one alone. DNA-DNA hybridization studies may

performed using either genomic DNA or DNA derived by preparing cDNA from the RNA present in a sample to be tested.

In addition to DNA-DNA hybridization, DNA-RNA or RNA-RNA hybridization assays are also possible. In the first case, the mRNA from expressed genes would then be detected
5 instead of genomic DNA or cDNA derived from mRNA of the sample. In the second case, RNA probes could be used. Artificial analogs of DNA hybridizing specifically to target sequences could also be used.

In specific embodiments, the oligonucleotide probes and/or primers comprise at least about 6 contiguous residues, more preferably at least about 10 contiguous residues, and most
10 preferably at least about 20 contiguous residues complementary to a polynucleotide sequence of the present invention. Probes and primers of the present invention may be from about 8 to 100 base pairs in length or, preferably from about 10 to 50 base pairs in length or, more preferably from about 15 to 40 base pairs in length. The primers and probes may be readily selected using procedures well known in the art, taking into account DNA-DNA hybridization
15 stringencies, annealing and melting temperatures, potential for formation of loops and other factors, which are well known in the art. Tools and software suitable for designing probes, and especially for designing PCR primers, are available from Premier Biosoft International, 3786 Corina Way, Palo Alto, CA 94303-4504. Preferred techniques for designing PCR primers are also disclosed in Dieffenbach and Dyksler, *PCR primer: a laboratory manual*, CSHL Press:
20 Cold Spring Harbor, NY, 1995.

A plurality of oligonucleotide probes or primers corresponding to a polynucleotide of the present invention may be provided in a kit form. Such kits generally comprise multiple DNA or oligonucleotide probes, each probe being specific for a polynucleotide sequence. Kits of the present invention may comprise one or more probes or primers corresponding to a
25 polynucleotide of the present invention, including a polynucleotide sequence identified in SEQ ID NO: 1-121.

In one embodiment useful for high-throughput assays, the oligonucleotide probe kits of the present invention comprise multiple probes in an array format, wherein each probe is immobilized in a predefined, spatially addressable location on the surface of a solid substrate.
30 Array formats which may be usefully employed in the present invention are disclosed, for example, in U.S. Patents No. 5,412,087, 5,545,531, and PCT Publication No. WO 95/00530, the disclosures of which are hereby incorporated by reference.

Oligonucleotide probes for use in the present invention may be constructed synthetically prior to immobilization on an array, using techniques well known in the art (*See*, for example, Gait, ed., *Oligonucleotide synthesis a practical approach*, IRL Press: Oxford, England, 1984). Automated equipment for the synthesis of oligonucleotides is available
5 commercially from such companies as Perkin Elmer/Applied Biosystems Division (Foster City, CA) and may be operated according to the manufacturer's instructions. Alternatively, the probes may be constructed directly on the surface of the array using techniques taught, for example, in PCT Publication No. WO 95/00530.

The solid substrate and the surface thereof preferably form a rigid support and are
10 generally formed from the same material. Examples of materials from which the solid substrate may be constructed include polymers, plastics, resins, membranes, polysaccharides, silica or silica-based materials, carbon, metals and inorganic glasses. Synthetically prepared probes may be immobilized on the surface of the solid substrate using techniques well known in the art, such as those disclosed in U.S. Patent No. 5,412,087.

15 In one such technique, compounds having protected functional groups, such as thiols protected with photochemically removable protecting groups, are attached to the surface of the substrate. Selected regions of the surface are then irradiated with a light source, preferably a laser, to provide reactive thiol groups. This irradiation step is generally performed using a mask having apertures at predefined locations using photolithographic techniques well known
20 in the art of semiconductors. The reactive thiol groups are then incubated with the oligonucleotide probe to be immobilized. The precise conditions for incubation, such as temperature, time and pH, depend on the specific probe and can be easily determined by one of skill in the art. The surface of the substrate is washed free of unbound probe and the irradiation step is repeated using a second mask having a different pattern of apertures. The surface is
25 subsequently incubated with a second, different, probe. Each oligonucleotide probe is typically immobilized in a discrete area of less than about 1 mm². Preferably each discrete area is less than about 10,000 mm², more preferably less than about 100 mm². In this manner, a multitude of oligonucleotide probes may be immobilized at predefined locations on the array.

The resulting array may be employed to screen for differences in organisms or samples
30 or products containing genetic material as follows. Genomic or cDNA libraries are prepared using techniques well known in the art. The resulting target DNA is then labeled with a suitable marker, such as a radiolabel, chromophore, fluorophore or chemiluminescent agent,

using protocols well known for those skilled in the art. A solution of the labeled target DNA is contacted with the surface of the array and incubated for a suitable period of time.

The surface of the array is then washed free of unbound target DNA and the probes to which the target DNA hybridized are determined by identifying those regions of the array to which the markers are attached. When the marker is a radiolabel, such as ^{32}P , autoradiography is employed as the detection method. In one embodiment, the marker is a fluorophore, such as fluorescein, and the location of bound target DNA is determined by means of fluorescence spectroscopy. Automated equipment for use in fluorescence scanning of oligonucleotide probe arrays is available from Affymetrix, Inc. (Santa Clara, CA) and may be operated according to the manufacturer's instructions. Such equipment may be employed to determine the intensity of fluorescence at each predefined location on the array, thereby providing a measure of the amount of target DNA bound at each location. Such an assay would be able to indicate not only the absence and presence of the marker probe in the target, but also the quantitative amount as well.

The significance of such high-throughput screening system is apparent for applications such as microbial selection and quality control operations in which there is a need to identify large numbers of samples or products for unwanted materials, to identify microbes, or samples or products containing microbial material, for quarantine purposes, etc., or to ascertain the true origin of samples or products containing microbes. Screening for the presence or absence of polynucleotides of the present invention used as identifiers for tagging microbes and microbial products can be valuable for later detecting the genetic composition of food, fermentation and industrial microbes or microbes in human or animal digestive system after consumption of probiotics, etc.

In this manner, oligonucleotide probe kits of the present invention may be employed to examine the presence/absence (or relative amounts in case of mixtures) of polynucleotides in different samples or products containing different materials rapidly and in a cost-effective manner. Examples of microbial species which may be examined using the present invention, include lactic acid bacteria, such as *Lactobacillus rhamnosus*, and other microbial species.

Another aspect of the present invention involves collections of a plurality of polynucleotides of the present invention. A collection of a plurality of the polynucleotides of the present invention, particularly the polynucleotides identified as SEQ ID NO: 1-121, may be recorded and/or stored on a storage medium and subsequently accessed for purposes of analysis, comparison, etc. Suitable storage media include magnetic media such as magnetic

diskettes, magnetic tapes, CD-ROM storage media, optical storage media, and the like. Suitable storage media and methods for recording and storing information, as well as accessing information such as polynucleotide sequences recorded on such media, are well known in the art. The polynucleotide information stored on the storage medium is preferably computer-
5 readable and may be used for analysis and comparison of the polynucleotide information.

Another aspect of the present invention thus involves storage medium on which are recorded a collection of the polynucleotides of the present invention, particularly a collection of the polynucleotides identified as SEQ ID NO: 1-121. According to one embodiment, the storage medium includes a collection of at least 20, preferably at least 50, more preferably at
10 least 100, and most preferably at least 200 of the polynucleotides of the present invention, preferably the polynucleotides identified as SEQ ID NO: 1-121, including variants of those polynucleotides.

Another aspect of the present invention involves a combination of polynucleotides, the combination containing at least 5, preferably at least 10, more preferably at least 20, and most
15 preferably at least 50 different polynucleotides of the present invention, including polynucleotides selected from SEQ ID NO: 1-121, and variants of these polynucleotides.

In another aspect, the present invention provides genetic constructs comprising, in the 5'-3' direction, a gene promoter sequence and an open reading frame coding for at least a functional portion of a polypeptide encoded by a polynucleotide of the present invention. In
20 certain embodiments, the genetic constructs of the present invention also comprise a gene termination sequence. The open reading frame may be oriented in either a sense or antisense direction. Genetic constructs comprising a non-coding region of a gene coding for a polypeptide encoded by an inventive polynucleotide or a nucleotide sequence complementary to a non-coding region, together with a gene promoter sequence, are also provided. A
25 terminator sequence may form part of this construct. Preferably, the gene promoter and termination sequences are functional in a host organism. More preferably, the gene promoter and termination sequences are common to those of the polynucleotide being introduced. The genetic construct may further include a marker for the identification of transformed cells.

Techniques for operatively linking the components of the genetic constructs are well
30 known in the art and include the use of synthetic linkers containing one or more restriction endonuclease sites as described, for example, by Sambrook *et al.*, in *Molecular cloning: a laboratory manual*, Cold Spring Harbor Laboratories Press: Cold Spring Harbor, NY, 1989. The genetic constructs of the present invention may be linked to a vector having at least one

replication system, for example, *E. coli*, whereby after each manipulation, the resulting construct can be cloned and sequenced and the correctness of the manipulation determined.

Transgenic microbial cells comprising the genetic constructs of the present invention are also provided by the present invention, together with microbes comprising such transgenic
 5 cells, products and progeny of such microbes, and materials including such microbes. Techniques for stably incorporating genetic constructs into the genome of target microbes, such as *Lactobacillus* species, *Lactococcus lactis* or *E. coli*, are well known in the art of bacterial transformation and are exemplified by the transformation of *E. coli* for sequencing described in Example 1.

10 Transgenic non-microbial cells comprising the genetic constructs of the present invention are also provided, together with organisms comprising such transgenic cells, and products and progeny of such organisms. Genetic constructs of the present invention may be stably incorporated into the genomes of non-microbial target organisms, such as fungi, using techniques well known in the art.

15 In preferred embodiments, the genetic constructs of the present invention are employed to transform microbes used in the production of food products, ingredients, processing aids, additives or supplements and for the production of microbial products for pharmaceutical uses, particularly for modulating immune system function and immunological effects, and in the production of chemoprotectants providing beneficial effects, probiotics and health supplements.

20 The inventive genetic constructs may also be employed to transform bacteria that are used to produce enzymes or substances such as polysaccharides, flavor compounds and bioactive substances, and to enhance resistance to industrial processes such as drying and to adverse stimuli in the human digestive system. The genes involved in antibiotic production, and phage uptake and resistance in *Lactobacillus rhamnosus* are considered to be especially useful. The
 25 target microbe to be used for transformation with one or more polynucleotides or genetic constructs of the present invention is preferably selected from the group consisting of bacterial genera *Lactococcus*, *Lactobacillus*, *Streptococcus*, *Oenococcus*, *Lactosphaera*, *Trichococcus*, *Pediococcus* and others potentially useful in various fermentation industries, and is most preferably selected from the group consisting of the following *Lactobacillus* species:
 30 *Lactobacillus acetotolerans*, *Lactobacillus acidophilus*, *Lactobacillus agilis*, *Lactobacillus alimentarius*, *Lactobacillus amylolyticus*, *Lactobacillus amylophilus*, *Lactobacillus amylovorus*, *Lactobacillus animalis*, *Lactobacillus arizonae*, *Lactobacillus aviarius*, *Lactobacillus bavaricus*, *Lactobacillus bif fermentans*, *Lactobacillus brevis*, *Lactobacillus*

buchneri, *Lactobacillus bulgaricus*, *Lactobacillus casei*, *Lactobacillus collinoides*,
Lactobacillus coryniformis, *Lactobacillus crispatus*, *Lactobacillus curvatus*, *Lactobacillus*
delbrueckii, *Lactobacillus delbrueckii* subsp. *bulgaricus*, *Lactobacillus delbrueckii* subsp.
lactis, *Lactobacillus farciminis*, *Lactobacillus fermentum*, *Lactobacillus fructivorans*,
5 *Lactobacillus gallinarum*, *Lactobacillus gasseri*, *Lactobacillus graminis*, *Lactobacillus*
hamsteri, *Lactobacillus helveticus*, *Lactobacillus helveticus* subsp. *jugurti*, *Lactobacillus*
hetero, *Lactobacillus hilgardii*, *Lactobacillus homohiochii*, *Lactobacillus japonicus*,
Lactobacillus johnsonii, *Lactobacillus kefir*, *Lactobacillus lactis*, *Lactobacillus leichmannii*,
Lactobacillus lindneri, *Lactobacillus mali*, *Lactobacillus maltaromicus*, *Lactobacillus*
10 *manihotivorans*, *Lactobacillus mucosae*, *Lactobacillus murinus*, *Lactobacillus oris*,
Lactobacillus panis, *Lactobacillus paracasei*, *Lactobacillus paracasei* subsp. *pseudoplanctarum*,
Lactobacillus paraplantarum, *Lactobacillus pentosus*, *Lactobacillus plantarum*, *Lactobacillus*
pontis, *Lactobacillus reuteri*, *Lactobacillus rhamnosus*, *Lactobacillus ruminis*, *Lactobacillus*
sake, *Lactobacillus salivarius*, *Lactobacillus salivarius* subsp. *salicinius*, *Lactobacillus*
15 *salivarius* subsp. *salivarius*, *Lactobacillus sanfranciscensis*, *Lactobacillus sharpeae*,
Lactobacillus thermophilus, *Lactobacillus vaginalis*, *Lactobacillus vermiforme*, and
Lactobacillus zeae.

In yet a further aspect, the present invention provides methods for modifying the
concentration, composition and/or activity of a polypeptide in a host organism, such as a
20 microbe, comprising stably incorporating a genetic construct of the present invention into the
genome of the host organism by transforming the host organism with such a genetic construct.
The genetic constructs of the present invention may be used to transform a variety of organisms
including plants, such as monocotyledonous angiosperms (e.g., grasses, corn, grains, oat, wheat
and barley); dicotyledonous angiosperms (e.g., *Arabidopsis*, tobacco, legumes, alfalfa, oaks,
25 eucalyptus, maple); gymnosperms, (e.g., Scots pine (Aronen, *Finnish Forest Res. Papers*, Vol.
595, 1996); white spruce (Ellis *et al.*, *Biotechnology* 11:84-89, 1993); larch (Huang *et al.*, *In*
Vitro Cell 27:201-207, 1991); and any kind of plant amenable to genetic engineering.

Thus, in yet another aspect, transgenic plant cells comprising the genetic constructs of
the present invention are provided, together with plants comprising such transgenic cells, and
30 fruits, seeds, products and progeny of such plants. Techniques for stably incorporating genetic
constructs into the genome of target organisms, such as plants, are well known in the art and
include *Agrobacterium tumefaciens* mediated introduction, electroporation, protoplast fusion,
injection into reproductive organs, injection into immature embryos, high velocity projectile

introduction and the like. The choice of technique will depend upon the target plant to be transformed. For example, dicotyledonous plants, and certain monocots and gymnosperms, may be transformed by *Agrobacterium* Ti plasmid technology, as described, for example by Bevan, *Nucleic Acids Res.* 12:8711-8721, 1984. Targets for the introduction of the genetic
5 constructs include tissues, such as leaf tissue, disseminated cells, protoplasts, seeds, embryos, meristematic regions, cotyledons, hypocotyls, and the like.

Once the cells are transformed, cells having the genetic construct incorporated in their genome are selected. Transgenic cells may then be cultured in an appropriate medium, using techniques well known in the art. In the case of protoplasts, the cell wall is allowed to reform
10 under appropriate osmotic conditions. In the case of seeds or embryos, an appropriate germination or callus initiation medium is employed. For explants, an appropriate regeneration medium is used. Regeneration of plants is well established for many species. For a review of regeneration of forest trees, see Dunstan *et al.*, "Somatic embryogenesis in woody plants," in Thorpe, T.A., ed., *In vitro embryogenesis of plants, (Current Plant Science and Biotechnology in Agriculture)*, 20(12):471-540, 1995. Specific protocols for the regeneration of spruce are
15 discussed by Roberts *et al.* ("Somatic embryogenesis of Spruce," in Redenbaugh K., ed., *Synseed: applications of synthetic seed to crop improvement*, CRC Press: Ch.23:427-449, 1993). The resulting transformed plants may be reproduced sexually or asexually, using methods well known in the art, to give successive generations of transgenic plants and
20 practically unlimited amounts of tagged plant-derived products.

The polynucleotides of the present invention may be further employed as non-disruptive tags for marking organisms, particularly microbes. Other organisms may, however, be tagged with the polynucleotides of the present invention, including commercially valuable plants, animals, fish, fungi and yeasts. Genetic constructs comprising polynucleotides of the
25 present invention may be stably introduced into an organism as heterologous, non-functional, non-disruptive tags. It is then possible to identify the origin or source of the organism at a later date by determining the presence or absence of the tag(s) in a sample of material. Detection of the tag(s) may be accomplished using a variety of conventional techniques, and will generally involve the use of nucleic acid probes. Sensitivity in assaying the presence of probe can be
30 usefully increased by using branched oligonucleotides, as described by Horn *et al.*, *Nucleic Acids Res.* 25(23):4842-4849, 1997, enabling detection of as few as 50 DNA molecules in the sample.

Polynucleotides of the present invention may also be used to specifically suppress gene expression by methods that operate post-transcriptionally to block the synthesis of products of targeted genes, such as RNA interference (RNAi), and quelling. Briefly, traditional methods of gene suppression, employing anti-sense RNA or DNA, operate by binding to the reverse
5 sequence of a gene of interest such that binding interferes with subsequent cellular processes and therefore blocks synthesis of the corresponding protein. RNAi also operates on a post-translational level and is sequence specific, but suppresses gene expression far more efficiently. Exemplary methods for controlling or modifying gene expression using RNAi are provided in WO 99/49029 and WO 99/53050. In these methods, post-transcriptional gene silencing is
10 brought about by a sequence-specific RNA degradation process which results in the rapid degradation of transcripts of sequence-related genes. Studies have shown that double-stranded RNA may act as a mediator of sequence-specific gene silencing (see, for example, Montgomery and Fire, *Trends in Genetics*, 14:255-258, 1998). Gene constructs that produce transcripts with self-complementary regions are particularly efficient at gene silencing. A unique feature of this
15 post-transcriptional gene silencing pathway is that silencing is not limited to the cells where it is initiated. The gene-silencing effects may be disseminated to other parts of an organism and even transmitted through the germ line to several generations.

The polynucleotides of the present invention may thus be employed to generate gene silencing constructs and/or gene-specific self-complementary RNA sequences that can be
20 delivered by conventional art-known methods to cells, such as microbial cells. Within genetic constructs, sense and antisense sequences can be placed in regions flanking an intron sequence in proper splicing orientation with donor and acceptor splicing sites, such that intron sequences are removed during processing of the transcript and sense and antisense sequences, as well as splice junction sequences, bind together to form double-stranded RNA. Alternatively, spacer
25 sequences of various lengths may be employed to separate self-complementary regions of sequence in the construct. During processing of the gene construct transcript, intron sequences are spliced-out, allowing sense and anti-sense sequences, as well as splice junction sequences, to bind forming double-stranded RNA. Select ribonucleases then bind to and cleave the double-stranded RNA, thereby initiating the cascade of events leading to degradation of
30 specific mRNA gene sequences, and silencing specific genes. Alternatively, rather than using a gene construct to express the self-complementary RNA sequences, the gene-specific double-stranded RNA segments are delivered to one or more targeted areas to be internalized into the cell cytoplasm to exert a gene silencing effect. The double-stranded RNA must have sufficient

homology to the targeted gene to mediate RNAi and is preferably at least 25 nucleotides in length. Preferably, the double-stranded RNA corresponds specifically to a polynucleotide of the present invention. Gene silencing RNA sequences comprising the polynucleotides of the present invention are useful for creating genetically modified organisms with desired
5 phenotypes as well as for characterizing genes (for example, in high-throughput screening of sequences), and studying their functions in intact organisms.

In another aspect, the present invention provides methods for using one or more of the inventive polypeptides or polynucleotides to treat disorders in a mammal, such as a human.

In this aspect, the polypeptide or polynucleotide is generally present within a
10 composition, such as a pharmaceutical or immunogenic composition. Pharmaceutical compositions may comprise one or more polypeptides, each of which may contain one or more of the above sequences (or variants thereof), and a physiologically acceptable carrier. Immunogenic compositions may comprise one or more of the above polypeptides and an immunostimulant, such as an adjuvant or a liposome, into which the polypeptide is
15 incorporated.

Alternatively, a composition of the present invention may contain DNA encoding one or more polypeptides described herein, such that the polypeptide is generated *in situ*. In such compositions, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, and bacterial and
20 viral expression systems. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminator signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus Calmette-Guerin*) that expresses an immunogenic portion of the polypeptide on its cell surface. In a preferred embodiment, the DNA may be introduced using a viral expression system (*e.g.*,
25 vaccinia or other poxvirus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic, or defective, replication competent virus. Techniques for incorporating DNA into such expression systems are well known in the art. The DNA may also be "naked," as described, for example, in Ulmer *et al.*, *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the
30 DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. For parenteral administration, such as subcutaneous injection, the

carrier preferably comprises water, saline, alcohol, a lipid, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (*e.g.*, polylactic galactide) may also
5 be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Any of a variety of adjuvants may be employed in the immunogenic compositions of the present invention to non-specifically enhance an immune response. Most adjuvants contain
10 a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a non-specific stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *M. tuberculosis*. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Freund's Complete Adjuvant (Difco Laboratories, Detroit, MI), and Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ). Other suitable
15 adjuvants include alum, biodegradable microspheres, monophosphoryl lipid A and Quil A.

Routes and frequency of administration, as well as dosage, vary from individual to individual. In general, the inventive compositions may be administered by injection (*e.g.*, intradermal, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. In general, the amount of polypeptide present in a dose (or produced *in situ* by the DNA
20 in a dose) ranges from about 1 pg to about 100 mg per kg of host, typically from about 10 pg to about 1 mg per kg of host, and preferably from about 100 pg to about 1 µg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 ml to about 2 ml.

25 The following examples are offered by way of illustration and not by way of limitation.

Example 1

ISOLATION AND CHARACTERIZATION OF DNA SEQUENCES FROM

LACTOBACILLUS RHAMNOSUS STRAIN HN001

30

Lactobacillus rhamnosus strain HN001 DNA libraries were constructed and screened as follows.

DNA was prepared in large scale by cultivating the bacteria in 2 x 100 ml cultures with 100 ml MRS broth (Difco Laboratories, Detroit MI) and 1 ml *Lactobacillus* glycerol stock as inoculum, placed into 500 ml culture flasks and incubated at 37 °C for approx. 16 hours with shaking (220 rpm).

5 The cultures were centrifuged at 3500 rpm for 10 min to pellet the cells. The supernatant was removed and the cell pellet resuspended in 40 ml fresh MRS broth and transferred to clean 500 ml culture flasks. Fresh MRS broth (60 ml) was added to bring the volume back to 100 ml and flasks were incubated for a further 2 hrs at 37°C with shaking (220 rpm). The cells were pelleted by centrifugation (3500 rpm for 10 min) and supernatant
10 removed. Cell pellets were washed twice in 20 ml buffer A (50 mM NaCl, 30 mM Tris pH 8.0, 0.5 mM EDTA).

Cells were resuspended in 2.5 ml buffer B (25% sucrose (w/v), 50 mM Tris pH 8.0, 1 mM EDTA, 20 mg/ml lysozyme, 20 µg/ml mutanolysin) and incubated at 37 °C for 45 min. Equal volumes of EDTA (0.25 M) was added to each tube and allowed to incubate at room
15 temperature for 5 min. 20% SDS (1 ml) solution was added, mixed and incubated at 65 °C for 90 min. 50 µl Proteinase K (Gibco BRL, Gaithersburg, MD) from a stock solution of 20 mg/ml was added and tubes incubated at 65 °C for 15 min.

DNA was extracted with equal volumes of phenol:chloroform:isoamylalcohol (25:24:1). Tubes were centrifuged at 3500 rpm for 40 min. The aqueous phase was removed to
20 clean sterile Oak Ridge centrifuge tubes (30 ml). Crude DNA was precipitated with an equal volume of cold isopropanol and incubated at -20°C overnight.

After resuspension in 500 µl TE buffer, DNase-free RNase was added to a final concentraion of 100 µg/ml and incubated at 37°C for 30 min. The incubation was extended for a further 30 min after adding 100 µl Proteinase K from a stock solution of 20 mg/ml. DNA was
25 precipitated with ethanol after a phenol:chloroform:isoamylalcohol (25:24:1) and a chloroform:isoamylalcohol (24:1) extraction and dissolved in 250 µl TE buffer.

DNA was digested with *Sau3AI* at a concentration of 0.004 U/µg in a total volume of 1480 µl, with 996 µl DNA, 138.75 µl 10X REACT 4 buffer and 252.75 µl H₂O. Following incubation for 1 hour at 37 °C, DNA was divided into two tubes. 31 µl 0.5 M EDTA was
30 added to stop the digestion and 17 µl samples were taken for agarose gel analysis. Samples were put into 15 ml Falcon tubes and diluted to 3 ml for loading onto sucrose gradient tubes.

Sucrose gradient size fractionation was conducted as follows. 100 ml of 50% sucrose (w/v) was made in TEN buffer (1M NaCl, 20 mM Tris pH 8.0, 5 mM EDTA) and sterile

filtered. Dilutions of 5, 10, 15, 20, 25, 30, 35 and 40% sucrose were prepared and overlaid carefully in Beckman Polyallomer tubes, and kept overnight at 4°C. TEN buffer (4 ml) was loaded onto the gradient, with 3 ml of DNA solution on top. The gradients were centrifuged at 26K for 18 hours at 4°C in a Centricon T-2060 centrifuge using a Kontron TST 28-38 rotor.

5 After deceleration without braking (approx. 1 hour), the gradients were removed and fractions collected using an auto Densi-Flow (Haake-Buchler Instruments). Agarose gel was used to analyze the fractions. The best two pairs of fractions were pooled and diluted to contain less than 10% sucrose. TEN buffer (4 ml) was added and DNA precipitated with 2 volumes of 100% ice cold ethanol and an overnight incubation at -20°C.

10 DNA pellets were resuspended in 300 µl TE buffer and re-precipitated for approx. 6 hours at -20°C after adding 1/10 volume 3 M NaOAC pH 5.2 and 2 volumes of ethanol. DNA was pelleted at top speed in a microcentrifuge for 15 min, washed with 70% ethanol and pelleted again, dried and resuspended in 10 µl TE buffer.

DNA was ligated into dephosphorylated *Bam*HI-digested pBluescript SK II⁺ and
15 dephosphorylated *Bam*HI-digested lambda ZAP Express using standard protocols. Packaging of the DNA was done using Gigapack III Gold packaging extract (Stratagene, La Jolla, CA) following the manufacturer's protocols. Packaged libraries were stored at 4 °C.

Mass excision from the primary packaged phage library was done using XL1-Blue MRF' cells and ExAssist Helper Phage (Stratagene). The excised phagemids were diluted with
20 NZY broth (Gibco BRL, Gaithersburg, MD) and plated out onto LB-kanamycin agar plates containing 5-bromo-4-chloro-3-indolyl-β-D-galactoside (X-gal) and isopropylthio-beta-galactoside (IPTG). After incubation, single colonies were picked for PCR size determination before the most suitable libraries were selected for sequencing.

Of the colonies picked for DNA minipreps and subsequent sequencing, the large
25 majority contained an insert suitable for sequencing. Positive colonies were cultured in LB broth with kanamycin or ampicillin depending on the vector used, and DNA was purified by means of rapid alkaline lysis minipreps (solutions: Qiagen, Venlo, The Netherlands; clearing plates, Millipore, Bedford, MA). Agarose gels at 1% were used to screen sequencing templates for chromosomal contamination and concentration. Dye terminator sequencing reactions were
30 prepared using a Biomek 2000 robot (Beckman Coulter, Inc., Fullerton, CA) and Hydra 96 (Robbins Scientific, Sunnyvale, CA) for liquid handling. DNA amplification was done in a

9700 PCR machine (Perkin Elmer/Applied Biosystems, Foster City, CA) according to the manufacturer's protocol.

The sequence of the genomic DNA fragments were determined using a Perkin Elmer/Applied Biosystems Division Prism 377 sequencer. The DNA clones were sequenced
5 from the 5' and/or 3' end, and are identified as SEQ ID NO: 1-121 disclosed herein.

This example not only shows how the sequences were obtained, but also that a bacterium (*E. coli*) can be stably transformed with any desired DNA fragment of the present invention for permanent marking for stable inheritance.

The determined DNA sequences were compared to and aligned with known sequences
10 in the public databases. Specifically, the polynucleotides identified in SEQ ID NO: 1-121 were compared to polynucleotides in the EMBL database as of August 12, 2002, using BLASTN algorithm Version 2.0.11 [Jan-20-2000], set to the following running parameters: Unix running command: blastall -p blastn -d embldb -e 10 -G 0 -E 0 -r 1 -v 30 -b 30 -i queryseq -o results. Multiple alignments of redundant sequences were used to build up reliable consensus
15 sequences. The polypeptides identified in SEQ ID NO: 122-253 were compared to polypeptides in the SwissPROT-TrEMBL database as of August 12, 2002, using BLASTP algorithm Version 2.0.11 [Jan-20-2000], set to the following running parameters: Unix running command: blastall -p blastp -d swissprotrembledb -e 10 -G 0 -E 0 -v 30 -b 30 -i queryseq -o results.

20

BLASTN Polynucleotide Analysis

The sequences of SEQ ID NO: 1-18, 20-50, 52-62, 64-69, 71-83, 85-93 and 95-122 were determined to have less than 50% identity, determined as described above, to sequences in the EMBL database using the computer algorithm BLASTN, as described above. The sequence
25 of SEQ ID NO: 94 was determined to have less than 75% identity, determined as described above, to sequences in the EMBL database using the computer algorithm BLASTN, as described above. Finally, the sequence of SEQ ID NO: 19 was determined to have less than 98% identity, determined as described above, to sequences in the EMBL database using the computer algorithm BLASTN, as described above.

30

BLASTP Amino Acid Analysis

The amino acid sequences of SEQ ID NO: 124, 133, 134, 137-139, 141, 148, 150-156, 159, 162, 164-168, 170-172, 174, 175, 178, 184, 187, 188, 190, 194, 195, 198-200, 202, 203,

205-208, 212-214, 216, 221-224, 227, 229, 234, 235, 237, 240, 242-245, 249 and 252 were determined to have less than 50% identity, determined as described above, to sequences in the SWISSPROT-TrEMBL database using the BLASTP computer algorithm as described above. The amino acid sequences of SEQ ID NO: 123, 125-129, 131, 144, 149, 158, 160, 161, 163, 5 169, 173, 176, 179-181, 183, 185, 186, 191-193, 197, 201, 209, 211, 215, 217, 218, 225, 226, 228, 230-233, 238, 239, 247, 248, 250, 251, 253, 254 and 256 were determined to have less than 75% identity, determined as described above, to sequences in the SWISSPROT-TrEMBL database using the computer algorithm BLASTP, as described above. The amino acid sequences of SEQ ID NO: 132, 135, 142, 145-147, 157, 182, 204, 219, 241, 246 and 255 were 10 determined to have less than 90% identity, determined as described above, to sequences in the SWISSPROT-TrEMBL database using the computer algorithm BLASTP, as described above. The amino acid sequences of SEQ ID NOS: 140 and 236 were determined to have less than 98% identity, determined as described above, to sequences in the SWISSPROT-TrEMBL database using the computer algorithm BLASTP, as described above.

15

BLASTX Polynucleotide Analysis

The cDNA sequences of SEQ ID NO: 1-10, 12-18, 20-30, 32-42, 44-50, 52, 53, 55, 58, 59, 61, 62, 64, 66-69, 71-77, 79-83, 85-88, 90, 92, 95-105, 107-109, 111-114, 116-119, 121 and 122 were determined to have less than 50% identity, determined as described above, to 20 sequences in the SWISSPROT-TrEMBL database using the computer algorithm BLASTX, as described above. The cDNA sequences of SEQ ID NO: 11, 19, 43, 54, 57, 60, 65, 70, 78, 89, 91, 93, 106, 110, 115 and 120 were determined to have less than 75% identity, determined as described above, to sequences in the SWISSPROT-TrEMBL database using BLASTX, as described above. The cDNA sequences of SEQ ID NO: 31, 51, 56 and 63 were determined to 25 have less than 90% identity, determined as described above, to sequences in the SWISSPROT-TrEMBL database using BLASTN, as described above. The cDNA sequence of SEQ ID NO: 94 was determined to have less than 98% identity, determined as described above, to sequences in the SWISSPROT-TrEMBL database using BLASTX, as described above.

30 Based on similarity to known sequences, the isolated polynucleotides of the present invention identified as SEQ ID NO: 1-121 were putatively identified as encoding polypeptides having similarity to the polypeptides shown above in Table 1. The amino acid sequences

encoded by the DNA sequences of SEQ ID NO: 1-121 are provided in SEQ ID NO: 122-253, respectively.

Several of the sequences provided in SEQ ID NO: 1-121 were found to be full-length and to contain open reading frames (ORFs). These full-length sequences, the location of ORFs
5 (by nucleotide position) contained within these sequences, and the corresponding amino acid sequences are provided in Table 2 below.

TABLE 2

Polynucleotide SEQ ID NO:	ORF	Polypeptide SEQ ID NO:
1	4828-5511	122
2	370-1485	123
3	617-2071	124
4	344-1162	125
4	1172-1936	126
6	513-1217	128
7	543-1352	130
8	599-1265	131
9	449-1189	132
10	1530-2306	133
11	164-1432	134
13	340-2367	136
14	92-2407	137
17	505-1884	140
19	5-271	142
20	6159-6464	143
20	5293-6171	144
20	3761-5293	145
22	282-1235	147
23	1938-3620	148
24	1965-2924	149
25	2978-3901	150
26	1212-1991	151
27	10894-11889	152
28	3687-5126	153
29	250-1275	154
30	464-2593	155
34	92-397	159
36	460-1098	161

Polynucleotide SEQ ID NO:	ORF	Polypeptide SEQ ID NO:
37	651-1481	162
40	92-2407	165
45	713-2266	170
47	237-1049	172
50	30-1469	175
52	40-1221	177
55	196-1347	180
59	505-1827	184
69	1192-2109	194
70	118-822	195
73	25-1419	198
77	63-638	202
97	424-1743	221
98	1008-1571	222
100	4987-6948	224
101	90-1090	225
102	1702-2514	226
106	5-915	230
107	925-2592	231
108	167-2155	232
109	131-1024	233
110	57-923	234
111	611-1962	235
112	53-748	236
113	348-1301	237
114	235-1659	238
115	634-1458	239
116	2339-3190	240
117	649-1527	241
118	94-924	242
119	1-1221	243
120	4011-5249	244
120	8691-9464	245
120	5246-5701	246
120	6229-7578	247
120	7594-8409	248
120	2357-3280	249
120	3461-4006	250
120	1347-2327	251

Polynucleotide SEQ ID NO:	ORF	Polypeptide SEQ ID NO:
121	146-1168	252

SEQ ID NO: 106, 107, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118 and 119 are full-length sequences of SEQ ID NO: 5, 12, 16, 44, 65, 71, 72, 78, 79, 81, 83, 103 and 21, respectively, with SEQ ID NO: 108 being a full-length sequence of SEQ ID NO: 15 and 42. SEQ ID NO: 253 is the full-length sequence of SEQ ID NO: 99.

SEQ ID NO: 1-253 are set out in the attached Sequence Listing. The codes for nucleotide sequences used in the attached Sequence Listing, including the symbol "n," conform to WIPO Standard ST.25 (1998), Appendix 2, Table 1.

10 All references cited herein, including patent references and non-patent publications, are hereby incorporated by reference in their entireties.

While in the foregoing specification this invention has been described in relation to certain preferred embodiments, and many details have been set forth for purposes of illustration, it will be apparent to those skilled in the art that the invention is susceptible to additional embodiments and that certain of the details described herein may be varied considerably without departing from the basic principles of the invention.

SEQUENCE LISTING

<110> Glenn, Matthew
 Havukkala, Ilkka J
 Lubbers, Mark William
 Dekker, James

<120> Polynucleotides, materials incorporating
 them, and methods for using them.

<130> JC220405-142

<160> 253

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 5739

<212> DNA

<213> Lactobacillus rhamnosus

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<213> Lactobacillus rhamnosus

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<213> Lactobacillus rhamnosus

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<211> 4159

<212> DNA

<213> Lactobacillus rhamnosus

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<210> 31

<211> 196

<212> DNA

<213> Lactobacillus rhamnosus

<400> 31

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aggatgtttt	cgctgcaagt	aaaggcgtga	ccgcccaca	cttaacaacg	aacaccaagg	180
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<210> 32

<211> 1449

<212> DNA

<213> Lactobacillus rhamnosus

<400> 32

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<210> 33

<211> 1349

<212> DNA

<213> Lactobacillllus rhamnosus

<400> 33

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cccgacaacg	cctaaggaac	ctcaagttcc	taataatggg	aataaggtaa	caccaaagga	1260
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<210> 34

<211> 412

<212> DNA

<213> Lactobacillllus rhamnosus

<400> 34

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gggctaccag	cgattttatt	ccccgttatt	tccgcccag	tgctgggtatt	atccgacttg	180
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gattgctcgg	atthttacgat	gcaaccctt	tgttaaagg	gggctagatc	cggtgccagc	300
ttatthttacg	ttgcggcgta	atccgcatcc	cgaaaatgat	ttggatctta	gtgacattca	360
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<210> 35

<211> 1836

<212> DNA

<213> Lactobacillllus rhamnosus

<400> 35

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aatcaaacat	tagccatccc	tccgtcgtta	tctcttccta	tcaccaatat	agcaagcatc	180
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<210> 36

<211> 1412

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 36

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<210> 37

<211> 1914

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 37

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<210> 38

<211> 1469

<212> DNA

<213> Lactobacillus rhamnosus

<400> 38

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<210> 39

<211> 681

<212> DNA

<213> Lactobacillus rhamnosus

<400> 39

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<211> 3279

<212> DNA

<213> Lactobacillus rhamnosus

<400> 40

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<213> Lactobacillus rhamnosus

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<212> DNA

<213> Lactobacillus rhamnosus

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<210> 44
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<210> 46

<211> 1601

<212> DNA

<213> Lactobacillus rhamnosus

<400> 46

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gacctgtacc	ccgtatatga	tcaactccca	ccgcttgcta	gtgaccggca	aacgggtacc	1560
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<210> 47

<211> 1681
 <212> DNA
 <213> Lactobacillllus rhamnosus

<400> 47
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 aatgccaatg cacaaaccac gcaattataa tccgccattt tgaaaggaag aaagctatgt 240
 taaagaaaaa gttgtggttc ctggttgccgc ttgtggcctt ggtaaccttc acgctcaccg 300
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<210> 48
 <211> 754
 <212> DNA
 <213> Lactobacillllus rhamnosus

<400> 48
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 acaggaaaag gtcgccaaaa gaatccacga attagactc agcaaatcca tgaccagga 180
 acaactagcc gaaaaagcca acatggacgt ttccatgcta gccagaatcg aacgcggaag 240
 ccgcggcgac atcagaatga gcacactaga acgcacgtt tccggattag acgtcagtta 300
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 gaggttttta tgtgcgataa ctaaaagagt gaaagttgaa tgtccggaga aagtcocgag 660
 aagacgggac ttttggtggt aggcacaatg ccgtctgggt ttaggttagg cacaacttta 720
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<210> 49
 <211> 1535

<212> DNA

<213> *Lactobacillus rhamnosus*

<400> 49

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cctgtggtgc	tgcattgagg	ccgtccacat	taaagtagat	cgttttaaca	tcagcgttga	1500
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<210> 50

<211> 2174

<212> DNA

<213> *Lactobacillus rhamnosus*

<400> 50

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<210> 51

<211> 1337

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 51

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gtcctcgata	ttacaggagg	caaccacact	tttgctgtca	gcaccataat	agcaaaagat	180
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<210> 52

<211> 1370

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 52

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gaagaaacat	atggaacagg	cgagccgacg	atcacgatta	aaatgaaaaa	agcgatocca	180

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<210> 53

<211> 344

<212> DNA

<213> Lactobacillus rhamnosus

<400> 53

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<210> 54

<211> 1511

<212> DNA

<213> Lactobacillus rhamnosus

<400> 54

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<210> 55

<211> 1721

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 55

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gtgattaaaa	aagtcaacga	tcaaaccgaa	gctaagacag	tgctgcttga	tgaactcaga	180
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<210> 56

<211> 802

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 56

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cattgttaat	aatgatggca	catcacacacc	tttgacttgc	atttctctaa	cggtactttt	360
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tcctaatgac	agtctgggog	taaaaattgc	cttggcattg	ttgccaatc	aaaattataa	480
agcagatcgg	atgtcaagtt	tcacttcata	tggccctgta	tctgatcttt	cctttaagcc	540
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agcgctaaat	aataaagaca	atgagttcta	tgccgattac	aagcaactta	aaggcacagc	720
attaaccgat	tttctcaaaa	cagttgaaat	gaatactgca	aagccgatta	atgatattaa	780
ctatgataat	gtcatogtct	ct				802

<210> 57

<211> 805

<212> DNA

<213> Lactobacillus rhamnosus

<400> 57

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gcatgtcaga	gatgattgac	attgggtgaat	acttcaaatt	ttgggtggcc	gagctgccgg	180
catggctgcc	tggcctgggt	gcgatcacct	tccttggttt	ggcaaactct	atttcgggtg	240
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ttgccctgtc	cattgtgctt	ggttcttacc	aaggcggtga	gttactcggc	atcacagctg	480
gggaagcgga	aaacccgcaa	ccaacaattg	ttaaagcggt	caaagacacc	atcggacgaa	540
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<210> 58

<211> 890

<212> DNA

<213> Lactobacillus rhamnosus

<400> 58

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<210> 59

<211> 2278

<212> DNA

<213> Lactobacillus rhamnosus

<400> 59

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gagtatgcaa	ttgcacgaat	taaagccgag	tgtcggctcc	cgtcatgccc	gcaagcgtct	120
gggccgtggt	acttctagcg	gtcaaggtaa	gacagctggt	aaagggacaa	aaggtcaatt	180
ggcaocgacaa	ggcggcaaga	cacgtcttgg	cttcgaagg	ggccagatgc	cattattccg	240
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cgggattggt	aagaacgaaa	agaacgggtg	taagttgctg	gcagacggta	aacttgagaa	420
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gcattaggtta	aggaagcaaa	gggctttatt	gataaagggtc	aactgggtacc	cgactcgggt	2160
accaatggca	ttgtcaagga	acgccttgct	gagtcgcgata	ccgatgcggg	ctacatgctt	2220
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<210> 60

<211> 522

<212> DNA

<213> Lactobacillus rhamnosus

<400> 60

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gaatcgggct	ttggcggtgc	tcacacttat	tgccgttatt	atcgggtcgt	tctttccatt	360
tgccgtttctt	gccagctga	tttcgcgggg	gactctgac	gcattcatgt	ttgtcacact	420
tggcattttac	cggctgcgtc	cgcgtgaggg	gcaggacatt	gccaagccac	gtttttcggat	480
gccatttttac	ccagtgttgc	cagcgggttc	ctttctcgga	tc		522

<210> 61
 <211> 670
 <212> DNA
 <213> Lactobacillllus rhamnosus

<400> 61
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 ggtactaaaa 670

<210> 62
 <211> 341
 <212> DNA
 <213> Lactobacillllus rhamnosus

<400> 62
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 gaaccaaagt actggttaga acaggtttga acggaacagc ggaaaccatt cgcttcagtc 180
 aaaaggtagc gtcttttaaaa ccagacgcaa ttaccttagt tgctccttca tttgttgctc 240
 cctcgcaaca ggaacttggt gatcacggct gggaagaaag caaccagtac gttgggtgtg 300
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<210> 63
 <211> 732
 <212> DNA
 <213> Lactobacillllus rhamnosus

<400> 63
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 ctcttgcaag aaatcgtgca acaaggtaag gcactgttga tcattgctga cgatgttgcc 180
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 caattaggcc gtgcaggtaa agttacgggt accaaggacg acaccaccat tgttgatggc 420
 gctggttcca aggatgctat tgctgaacgg gttaacatca tcaagaagca gattgctgat 480
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 cagactggga tc 732

<210> 64
 <211> 1589
 <212> DNA
 <213> Lactobacillllus rhamnosus

<400> 64

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aacgaaagcc	gtttccgctc	atcatctgcg	gaaacggcct	tttatagtgc	gctaacttca	1560
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<210> 65

<211> 425

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 65

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cggcgtcaat	gcagcgcgct	tactacataa	attaggggct	ttggtaaccg	tcaacgataa	180
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gaatg						425

<210> 66

<211> 803

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 66

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atctgoccca	agcggtgacg	gttttttggca	ttgccttttt	tgctttgatg	acggcagtgga	180
gtgaaatgaa	tgcaccacag	ttgctgacgc	ggacctttga	tcgtaattac	atcgtcaaat	240
atctcgggtt	ggcgcctttt	acaattttacg	atgcagctaa	aacggcacaa	aacaatcagg	300
tacgggctca	ggcagacagt	gcaaattctcg	atccggttct	acaatacacg	cgttcgcatt	360
atgccgctcc	taacgctagc	tattacggag	ccgctaaagg	caagaacgtg	atcatcattc	420

accttgaaag	cttccagcaa	tttctgatcg	gtcaaaaaat	cgatgggtcag	gaagtaacgc	480
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aagtcggact	cggcaaaacc	agtgaacgcg	aaaatatgct	ggaaaccagc	acgttcggga	600
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cgatttttaa	tcaacgcgct	ggctatacca	gtgctgtctt	ccatggcggc	tccgcttcat	720
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<210> 67

<211> 1115

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 67

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cggcgagatc	ttgattgacg	gtgaagacat	tgcgcataaa	ggaacgaata	tcaataaagt	180
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ggatattatg	ctattogatg	agccgaccag	tgccttggtg	ccggaaatgg	ttggcgatgt	480
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gtcacgccga	tatcgagttc	gcggtcgcca	tacaaagcgg	ctggatcaat	taacgcgggc	1080
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<210> 68

<211> 425

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 68

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actcgactac	cttgaaggca	tcatggcgca	gattgatgta	gctagtccga	aagatttagt	180
cgatattcga	ttggaattac	agcaacaagg	ctatctacgt	aaacagaaat	ccggaaaaaa	240
aggcaataaa	cgccaaaaag	tctccaaacc	agatcaattc	tatgctagt	acggcactaa	300
aatctgggtc	ggaaaaaaca	acttacataa	tgatcagttg	accctacaca	ccgcgaaaaa	360
aaccgacatt	tggctgcacg	tcaaagatat	ccggggatca	cacgtgatta	tcgatagcag	420
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<210> 69

<211> 2271

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 69

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cttgggatcg	cgttctttaa	acgggtaacg	tgccacatcg	accgggaaat	tgataatgtc	180
aatcggactg	ttagttttgc	aatgtgtcgt	aatcatatgt	gcgcaccaag	gccctagtga	240
aaccatgtgc	agtccgaggc	tataagtacg	gcgcgccatc	tggtaacgat	caccgtatgg	300
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ctcccattgg	caaacaagtt	cctttatagc	ctggatagtt	aaattcggcg	ttttgaatca	480
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aacaactaga	cagggtacta	acccaaaatg	cttttgaaga	tcgataaaat	gaaatctgcc	2160
agcttgaaca	tgagtgtcgg	accagcagat	aaggaagggg	acaagtgtca	tgtatcaaaa	2220
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<210> 70

<211> 1030

<212> DNA

<213> Lactobacillus rhamnosus

<400> 70

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cacattgcag	tcattgatga	tcaagcagcg	actagagaag	caacgggtcaa	gctcattcgg	180
cagtttagcg	aaccgtcaca	gccattgcag	gtggcggtctt	attcaaatgc	cgagcagttc	240
ctgtttgcag	aaaaatcagc	cgatctgctg	ttgcttgata	ttaagttggg	atctggcatg	300
gacggcatgg	cgcttgccaa	aaaaattcgc	caacatgatc	ccgaaaccgc	catcgctttt	360
gtcagtaact	acgacgaatt	cgtgttcgat	ggttacgatg	tgaacgcgat	tgactacatc	420
ctcaagccgc	ttacgggtggc	aaaactcaaa	cacctaatg	aaaaggtagc	tagccagacg	480
cagccaaaac	tcttggcatt	gcaaaccgct	gccgggtctag	tacgcgtgcc	aatgtatgac	540
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taccgctcca	tcgtcattaa	cctgaatttc	ctctcgcagc	tgataaaacg	aaccgttgtg	720
atggcagatg	gcaccactta	tcccgtttcc	cgccagcagg	caccgctagt	taaacaggca	780
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ctttggggttg	ctagtagtag	gttgatatgtg	gcagttatgg	tggatttttc	ggcgccagca	900
aaactggccg	gtgcgctgg	taaacctcat	cattgccatc	gtatcgttga	gcagttgggtg	960
gttatggccg	cttccggttg	tccgcggctt	gctttttacc	atcactgtgt	tagcaggcag	1020
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<210> 71

<211> 791

<212> DNA

<213> *Lactobacillus rhamnosus*

<400> 71

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atattatgct	gccggagctg	aatgggtttg	atttgcttaa	acagttgcga	gctaagcaag	180
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gtccgtttga	agtccaccta	aaccggcacg	aagtcttaat	tcaogacaaa	ccagtagcgt	420
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cgaaggatca	gattttttgat	cggttgtggg	gatttgattc	ggatacggcc	gtcagtgctg	540
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agataaaggc	attaagcgac	aacagcgacg	tttattttatc	ggtcaactac	tgagcttcgc	720
cggacttttt	ctagtgtctg	gggtcattgt	ttttttcctt	tatgaacggt	cgatttatca	780
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<210> 72

<211> 623

<212> DNA

<213> *Lactobacillus rhamnosus*

<400> 72

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ccggcaagca	tgtgattgtt	gaaaagccct	tggttgcaac	cgctatggaa	tttgaaaaac	180
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atgagcacia	ttttcaggtt	gtcgatcaat	ttacccatca	tcatccgatt	gacggggcta	300
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agagtgggtg	ggatggcgat	ggggttgcgc	gcttggatta	tgatcaattc	gccgtgacac	540
tgattacggg	aaaaacaacc	aatagtttcc	tgccatccga	aattttattcc	ggtaagcaaa	600
cgttgactat	ggacaatgct	gct				623

<210> 73

<211> 1420

<212> DNA

<213> *Lactobacillus rhamnosus*

<400> 73

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acgaattcga	ttgttcagta	ttttgttcta	tttgggacat	tggggctaac	aatgtatgga	180
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gtaccatatt	taaaaaaata	cgttggttg	cgcattgg	atgatttgaa	agtcattgat	600
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gtcaacaaga	caatgctggg	agcccttg	ggggttcagg	catcaggctt	ctatgataac	720
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<210> 74

<211> 679

<212> DNA

<213> Lactobacillus rhamnosus

<400> 74

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aaacttggttc	cggctaccaa	aacgggttact	tggaagggtcg	agaaccagat	gacaacaaac	180
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acgcaattat	gcgcggcgca	tcgggggtcat	tttacaattg	ccaatcaacc	agatacccaa	480
ggcgtcagca	ccattgccga	atgttggtttt	ttaacgcctg	cctccagctc	gactgattga	540
tcaagtttga	aattttttgct	tgggttaatta	atggcgaata	ttttgggatgt	aagctgattc	600
ctgagacagc	ttcttagcgg	tcatttgaac	gctaagtaca	gaagtggctt	ttagttttata	660
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<210> 75

<211> 487

<212> DNA

<213> Lactobacillus rhamnosus

<400> 75

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tttgtttgca	gtgacttatt	ttcacgcctt	tgattggctc	aatacgcttt	tatttttttac	180
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gttgggtcgtg	cggacggatt	ggctgttgct	gttaatgggg	atggcttggt	ttgccattgg	420
tattttgtat	acttgggggc	cattaccgct	ttctcgtttg	ccgcttggtg	aaattttttc	480
cgggatc						487

<210> 76

<211> 1136

<212> DNA

<213> Lactobacillus rhamnosus

<400> 76

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tggttaatgg	ctcatctgaa	aggaagcatt	tatttttgaaa	attgocaaat	taaacaacca	180
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gacagcttta	acccaccgcg	acaccttaac	attcgggttct	gaaattaact	ttaaaccgga	300
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tgatcattcg	caagagattc	acatcaagtt	accogaagtt	ccgagcgtct	tcactaaatt	420
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<210> 77

<211> 746

<212> DNA

<213> Lactobacillus rhamnosus

<400> 77

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acctgctcca	gcattttacat	cgctgcctg	atgtcgaagt	tcatttggtg	atgagtgttt	180
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cggattatgt	ttatcctgtt	caaaaccaag	gggcaacat	tgcaagcggc	agttttttta	300
ccgatgcaat	ggtcattgtc	ccagcaagta	tgaaaacat	tgccgggcatt	gcgatgggct	360
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cccacattgg	cgttcaaata	attccgcta	ttccggcttt	ctatcagcat	cccaaacca	540
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aaaccgctag	tcgctggaat	ggagcgtcgt	taagatgaaa	aaagttctca	ataaacagag	660
tatcgggttt	ctcatcgga	ttgcgggtgg	cctcattgtt	tacctggccc	cactgagcgg	720
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<210> 78

<211> 1442

<212> DNA

<213> Lactobacillus rhamnosus

<400> 78

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ctgacaaaca	acgggtgatat	ggcactggat	tttggttgagt	ccaatcttta	ggtgttcaac	180
aacttagaca	gactcgtctg	catactttat	aggaggaagt	taaaacatgc	gtaaacaatt	240
acccaaggac	tttgtaatcg	gtggcgcaac	tgctgcttac	caagttgaag	gggcaaccaa	300
agaagacgga	aaaggtcgag	ttctttggga	tgattttctg	gaaaaacaag	ggcgggtttag	360
tcctgacccc	gccgctgatt	tttatcatcg	ctatgatgag	gatttgccgt	tagcagaagc	420
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cggggcggtg	gaatctcgtg	gcgttgcttt	ctatcatcgg	ctctttgctg	cctgtgcca	540

gcatcatctt	atcccgtttg	taacgttgca	tcattttgat	acaccagaac	ggttacacga	600
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tccgttagta	ccagccatct	atgtcaccga	aaacgggtatt	ggattgaaag	aatccttacc	1380
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<210> 79

<211> 793

<212> DNA

<213> Lactobacillus rhamnosus

<400> 79

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tttcgcatga	agaatcgact	cgatgatatt	acagatttaa	tggcacttgg	tcogactccg	180
gatgcccgtg	acattcagcg	acgtcaaacc	gcccaccgaa	tcgcaattgc	agacgcttgg	240
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gtttttggcag	atcaagtggg	tcccagcggg	catgtcaccg	ggatcgacat	tgcttcgcgc	360
gattacgggtg	caccgctcac	actcggacaa	gcatgggatc	atctgtttaa	cggaccgtta	420
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gggttacttt	atgcgattgc	gccaagtgat	gttgccaaca	ttcgcacttt	aatcacgcct	720
gataccttag	cgcagattgc	ccatgataac	acatggctct	acactgctgg	caagctaata	780
gaatgtccgg	atc					793

<210> 80

<211> 156

<212> DNA

<213> Lactobacillus rhamnosus

<400> 80

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atattggccg	cagctcggca	tgccctttca	aatgattgat	gatttacttg	attataccca	120
aactgccaaa	acattgaata	aaccggcgct	tgagga			156

<210> 81

<211> 847

<212> DNA

<213> Lactobacillus rhamnosus

<400> 81

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cggccggtgc	tgattattgag	cggtgtgtgc	atgtacgatg	gtgtgggtgc	cgaggcatta	180

ccggctgcag	ctgcacttga	atttgtacat	acctattcct	tgattcatga	cgatttgcct	240
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gcttttggtc	tgggttttca	aatcaaagat	gatatcaatg	atgtgactaa	aaccaccgcg	660
gaattaggta	agactgccga	taaggatgtg	gccgaacaca	aaaatacatt	tcccgaactg	720
ctgggattag	ccggtgccaa	acaagcattg	gcgaccaggt	ttcagctagc	cactgctgcg	780
ttaaacagcc	tgaccgttga	tgcaaccgac	ttaaaatcga	ttttggcggt	gttacaagca	840
tgacaaa						847

<210> 82

<211> 340

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 82

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ctagcgcggt	ttggcgaacc	tgtcaacgct	gagcttgtga	cggctgggtg	tgcgattgaa	180
gcactacacc	tagccacact	ggttcaogat	gatgtgctgg	atcatgccga	tattcgctcg	240
ggcatgacca	cggtttctgc	cgagtcogga	aatcgtgaag	ccatctatgc	cggtgatttc	300
ctgtatgcaa	tctattttca	attgcttagc	gaacaggatc			340

<210> 83

<211> 300

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 83

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gtgcgcggat	tcatattgaa	aaacacattc	ccgtcgctgc	aggtttgggc	ggtggttcga	120
gtgatgcagc	tgccgttttg	cggggcttaa	attcactatt	gcagttagggt	tatagtcgct	180
cgcagctggc	tcgcatcggc	ttacagggtg	atagcgatgt	gccttactgc	gtttactcgg	240
agacggcctt	ggttaccgga	cgcggcgatg	tggtcacgcc	attgggaagt	ttaccgaact	300

<210> 84

<211> 121

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 84

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taaagatcct	gaactcccgc	gcaatacgcc	aaaaagggtca	atagaaacgt	tgctaaaatg	120
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<210> 85

<211> 941

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 85

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cgttcgagcg	tgtctcttat	agttacgcgg	atcttctgac	taagtcaatc	aagatcacct	120
tcgaaggcga	agaaaaagcg	tcataatttc	agatactaac	cgacgattaa	atcgtttatt	180

ttgagcaggc	ctogatgtca	ttggcatcga	ggcctttttgc	tatcttcttg	aaagactgat	240
ctgtacaagg	tgacgaattt	ttgacacgcg	gcaatgaaaa	tcgggacgca	aaacagtata	300
ctgaaaataa	cgatacggcg	gatgcatgca	tcgtcgtttg	cagtgtgagc	tctocctgta	360
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agatatcttg	aagaaaatgt	ttggaagaaa	tggcccaaag	ttttaatgga	tgcacaaaag	900
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<210> 86

<211> 326

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 86

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tgcgagggcg	ctgcaggcaa	ttggctacaa	agaattgatc	ccgtactttc	gcgggcaagc	180
tgatttagca	acctgtgtgg	ccttgattaa	acagcattca	cgtcattttg	ccaagcgcca	240
actgacctat	tttcgcaacc	agatgccaac	acattgggtt	gacttggttg	cccatccaga	300
agaaaagact	gctgtccggt	gctttg				326

<210> 87

<211> 363

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 87

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atgattgccc	ttgccgccc	ggaccaggca	cggcaatta	tccaggcact	aaaggtagcc	180
aatgccgtta	aagtctggga	ataccacttt	gaaacgaaat	gaggctgcta	tgacaactta	240
tgcaogcgcg	cacactaaca	ttgcattgat	caaataattg	ggcaaagcaa	ataagcaatt	300
gatgctgccg	gcaaccagca	gtatttgcgt	tactctaaat	gactttttaca	cggacacggc	360
ggt						363

<210> 88

<211> 493

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 88

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tcagcagtcg	gcgccacctg	cgatTTTTag	ttggcggcac	cggctttttac	cttaacagtt	120
tgcgccctgaa	tttaccgctg	ggtggcaagg	cacgcgcgac	tgagtcocgt	cagcgttggc	180
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cagtggcagc	taaccaaatt	gaatcggcaa	atacgcgcgc	ggtgattcgg	gccttagaag	300
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cgttggtgat	cggtttgacg	acagcacgcc	ctgtttttgta	cgaccggatt	aatgcgcgcg	420
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ccccggatgc	gca					493

<210> 89
 <211> 322
 <212> DNA
 <213> Lactobacilllus rhamnosus

<400> 89
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 tggttgccgg tcagacaacc atttcatttg caacgtatgc agtgattgcg gttcgtgaag 180
 gccgcgttga cgtgttgatt atttgtctgg tgactgtcgg cgcgatgctt ggatttttga 240
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 ggatgctggc agttgctgcc at 322

<210> 90
 <211> 716
 <212> DNA
 <213> Lactobacilllus rhamnosus

<400> 90
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 gagcgcattgc catgacgttc cggccatcca tattgcgtat gcgcggtaat cgcgccgca 540
 ccaccggaac cacagaagct aatgcccata tcggcttttt ctttatccat cacctgaccc 600
 aaacgcatat ccgccccat accaggcacc acaacggcag taccaccagc ggcttcaacc 660
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<210> 91
 <211> 465
 <212> DNA
 <213> Lactobacilllus rhamnosus

<400> 91
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 ccaaggcagc aagtcgtctc ggggttaaag ttttgacttt gtatgctttt tcaactgaaa 180
 attggaagcg ccccggttct gaggtgaatt acctcatgcg cttaccggtt gactttttta 240
 acgattttat gcctgattta atcaaagaaa atgttaaagt tgaagttagt ggtgagttaa 300
 ccgacttacc tgagccgaca cgcaaggcga gtgaaaaagc tatggcggat acggccaaca 360
 acaccggcat gattcttaac tttgcgctga attatggtgg tcgtgacgaa ctgggttcacg 420
 ctgcccgga actggcaagc gcggtgcgtg atggtcaatt agatc 465

<210> 92
 <211> 402
 <212> DNA
 <213> Lactobacilllus rhamnosus

<400> 92
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 gaggcggcga tcgcaactta ccaggctaga gaccggcgtt ttggcggttt aaaaaataa 120
 tcaactaaat aaatgggtgat ggaggatttg ttatcatgaa acaacgggtc ataacggctg 180
 tcgttgcttt ggcaattttt attccaattc taattgccgg tggcggttgg atcgatacag 240

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<210> 93

<211> 921

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 93

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<210> 94

<211> 258

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 94

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<210> 95

<211> 2499

<212> DNA

<213> Lactobacilllus rhamnosus

<400> 95

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2587

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<210> 102

<211> 2665

<212> DNA

<213> Lactobacillus rhamnosus

<400> 102

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<211> 2634

<212> DNA

<213> Lactobacillllus rhamnosus

<400> 103

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<210> 104

<211> 3269

<212> DNA

<213> Lactobacillllus rhamnosus

<400> 104

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<210> 105

<211> 10303

<212> DNA

<213> Lactobacillus rhamnosus

<400> 105

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<211> 2222

<212> DNA

<213> Lactobacillus rhamnosus

<400> 108

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<211> 1207

<212> DNA

<213> Lactobacillus rhamnosus

<400> 109

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<211> 960

<212> DNA

<213> Lactobacillus rhamnosus

<400> 110

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<210> 111

<211> 2322

<212> DNA

<213> Lactobacillus rhamnosus

<400> 111

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<210> 112

<211> 1123

<212> DNA

<213> Lactobacillllus rhamnosus

<400> 112

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<210> 113

<211> 1591

<212> DNA

<213> Lactobacillllus rhamnosus

<400> 113

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 <211> 2196
 <212> DNA
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<400> 114
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cacgatcacc	gcgataatgg	cagttcagca	gacgctcacc	cggctcaatc	agatgcgtga	10020
taagcgggtg	agtattctct	acagacatgt	ttacggttta	tcactcgacg	aaagggaagg	10080
tgcactgggt	ttgggttcagc	ggccgcagca	ggttatacca	ccggttctgc	ggggtttctg	10140
gattctgtcc	ggaaactgac	ctgcgttggc	agagtagggc	tacgcctcat	gccgttaata	10200
tctttacacc	gggtatgggtg	gtgcctatcg	tgctttttaga	cgatgcacaa	gacgtttatac	10260
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<210> 121

<211> 1716

<212> DNA

<213> Lactobacilllus rhamnosus

<220>

<221> misc_feature

<222> (1)...(1716)

<223> n = A,T,C or G

<400> 121

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accagacgtc	ggttccacaa	actcgatttt	aactggggca	acccgttaga	ataaaccttt	120
atttcctaaa	ggaggaaatt	ttagcatgac	tgtaaagatt	ggtattaatg	gttttggcgg	180
tatcggtcgt	ttggcattcc	gtcgtattta	cgaattgggt	gcaaagagca	atgacattca	240
ggttgttgcg	atcaacgatt	tgaccagccc	aaccatgctg	gctcacttgc	tgaagtatga	300
ttcaaccac	ggtaactttcc	ctgggtgaagt	tagtgcaacc	gataacggta	ttgtcgttga	360
cggtaaagaa	taccgtgtct	acgcagaacc	gcaagcccag	aacattcctt	gggttaagaa	420
cgacggcgtt	gactacgttc	ttgaatgcac	aggcttctat	acttctgctg	aaaagtcaca	480
agctcacttg	gatgcaggcg	caaagcgtgt	tctgatttct	gccccagctg	gcaagattaa	540
gactatcgtt	tataacgtta	atgatgacac	cttgaatgca	gacgacaaga	tcgtttctgc	600
aggttcttgc	acgaccaact	gcttggcacc	aatggcttac	ttcctgaacc	aggaattcgg	660
cattgaagtt	ggtaccatga	ccaccgttca	tgccacacac	tcaactcaga	tggttgcttga	720
cggcccagtt	cgtggcggca	acctgcgtgc	tgacagttca	gctgctgcta	acacgattcc	780
tcacagcact	ggtgctgcta	aggctatcgg	tttggttata	ccagaattga	acggcaagtt	840
acagggtcac	gcacagcgtg	tttctgttgt	tgacggttcc	ttgactgaat	tggtttccat	900
cttgaagacc	aagaacgtta	cggctgacca	agtcaacgaa	gctatcaaga	agcacaccga	960
aaacaaccct	agctttggct	ggaacgaaga	cgaaatcgta	tcttcogatg	ttatcggtac	1020
gacatacggc	tcaatcttcg	atcctactca	gaccgaagtt	acaactgccg	gtgactatca	1080
attagtttaag	acggttgctt	ggtacgataa	cgaatatggc	tttacttgcc	agatgatccg	1140
taccttgctg	aaatttgcta	ctctctaata	cggagtaacg	cttttctaac	cgcaacatcc	1200
gaagcggagg	gagctttact	ccctccgctt	tttttggaat	gaccattaaa	aggtgctttt	1260
atcagtgtcg	ctttggcctt	tgtaaacgag	atggtgatgg	taagcttaat	tgaaacatca	1320
tctttaggaa	aatgaaggag	gtcatatctt	ttggctaaat	taatcgtttc	agatttagac	1380
gttaaagaca	aaaaagtctt	gattcgcgtt	gacttcaacg	tgccgatcaa	agacggcgtt	1440
atcgggtgatg	acaatcggat	cgtggcagca	ttgccaaacca	tccaatatgt	cattgatcac	1500
ggcgggcaag	gcaattctgc	tgtcttacc	ttggccgggt	taaaaccgaa	gaagataagg	1560
gcaaagctga	cccttgaagc	cctgtttgca	gaaacgcctt	ttagagggaat	ttgcctggaa	1620
aaaagcccca	nttaccttnt	tggttacccg	acttaccocg	cgggttaaaa	gaaatttggg	1680
aaagaacccc	gcacccggca	aagtttaaaa	aggacg			1716

<210> 122

<211> 227

<212> PRT

<213> Lactobacillus rhamnosus

<400> 122

Met	Ser	Thr	His	Ile	Asp	Ala	Pro	Lys	Gly	Ala	Ile	Ala	Asp	Val	Val
1				5					10					15	
Leu	Leu	Pro	Gly	Asp	Pro	Leu	Arg	Ala	Gln	Tyr	Ile	Ala	Glu	His	Phe
			20					25					30		
Leu	Glu	Lys	Ala	Val	Arg	Tyr	Asn	Thr	Val	Arg	Asn	Ala	Phe	Gly	Tyr
		35					40					45			
Thr	Gly	Thr	Phe	Glu	Gly	Arg	Arg	Ile	Ser	Val	Gln	Ala	Thr	Gly	Met
	50					55					60				
Gly	Ile	Pro	Ser	Ile	Ser	Ile	Tyr	Val	Asn	Glu	Leu	Ile	Gln	Asp	Tyr
65					70				75					80	
Gly	Val	Lys	Thr	Leu	Ile	Arg	Val	Gly	Thr	Ala	Gly	Gly	Met	Gly	Ser
			85					90						95	

Asp Val Lys Val Arg Asp Val Ile Leu Val Gln Gly Ser Ser Thr Asp
 100 105 110
 Ser Ser Ile Val Leu Asn Thr Phe Gly Ala Gly Met Tyr Phe Ala Pro
 115 120 125
 Ile Ala Asp Phe Gln Leu Leu Arg Glu Ala Ala Asn Leu Ala Asp Ala
 130 135 140
 Gly Ala Leu Arg Tyr His Val Gly Asn Val Leu Gly Glu Asp Arg Phe
 145 150 155 160
 Tyr Asn Asp Glu Met Asp Arg Gln Lys Leu Ile Asp Tyr Gly Val Leu
 165 170 175
 Ala Thr Glu Met Glu Thr Pro Ala Leu Tyr Leu Leu Ala Ala Lys Phe
 180 185 190
 His Ala Gln Ala Leu Ser Ile Leu Thr Val Ser Asn His Leu Ile Thr
 195 200 205
 Gly Glu Glu Thr Thr Ala Gln Glu Arg Gln Thr Ser Phe Asn Asp Met
 210 215 220
 Ile Leu Lys
 225

<210> 123

<211> 371

<212> PRT

<213> Lactobacillus rhamnosus

<400> 123

Met Ile Asp Val Val Thr Ser Pro Ala Thr Ile Gly Ile Ile Gly Gly
 1 5 10 15
 Gly Gln Leu Gly Arg Met Leu Thr Gln Ser Ala Lys Thr Met Gly Tyr
 20 25 30
 Arg Val Gly Ile Leu Glu Pro Thr Pro Asn Ser Pro Ala Gly Gln Val
 35 40 45
 Ala Asp Phe Gln Ile Thr Ala Pro Tyr Asp Asp Gln Ala Ala Leu Thr
 50 55 60
 Lys Leu Ala Lys Glu Ser Asp Val Leu Thr Tyr Glu Phe Glu Asn Val
 65 70 75 80
 Asp Leu Ala Ala Leu Glu Ala Val Arg Asp Leu Thr Arg Ile Pro Gln
 85 90 95
 Gly Thr Ala Ile Leu Ala Thr Thr Arg Asp Arg Ile Lys Glu Lys Thr
 100 105 110
 Phe Leu Gln Thr His Gly Val Pro Val Thr Pro Phe Ala Ala Val Asp
 115 120 125
 Arg Pro Glu Ala Leu Thr Ala Ala Ile Glu Lys Ile Gly Leu Pro Ser
 130 135 140
 Ile Leu Lys Thr Thr Thr Gly Gly Tyr Asp Gly His Gly Gln Gln Asp
 145 150 155 160
 Ile Asn Thr Met Ala Asp Val Pro Ala Ala Glu Gln Leu Leu Ala His
 165 170 175
 Gly Pro Cys Ile Leu Glu Lys Arg Gln Gln Phe Asp Arg Glu Ala Ser
 180 185 190
 Val Met Ile Thr Arg Asp Gly Arg Asp Gln Val Arg Val Phe Pro Ile
 195 200 205
 Val Glu Asn Arg His Lys Asn His Val Leu His Leu Thr Leu Ala Pro
 210 215 220
 Ala Pro Asn Ile Ser Pro Val Leu Ala Glu Lys Ile Asp Asp Leu Ala
 225 230 235 240
 Thr Lys Ile Thr Leu Gly Leu Asp Leu Arg Gly Val Leu Gly Val Glu
 245 250 255

Leu	Phe	Leu	Glu	Gly	Asp	Asn	Val	Val	Ala	Asn	Glu	Leu	Ala	Pro	Arg
			260					265					270		
Pro	His	Asn	Ser	Gly	His	Tyr	Ser	Ile	Glu	Ala	Cys	Asn	Phe	Ser	Gln
		275					280					285			
Phe	Asp	Ala	His	Ile	Leu	Ser	Ile	Cys	Gly	Leu	Pro	Ile	Pro	Gln	Ile
	290					295					300				
Thr	Leu	Lys	Gln	Pro	Ala	Val	Met	Arg	Asn	Leu	Leu	Gly	Asp	Asp	Leu
305					310					315					320
Thr	Gln	Ala	Lys	Ala	Lys	Trp	Pro	Gln	His	Pro	Glu	Trp	His	Met	His
				325					330					335	
Asp	Tyr	Gly	Lys	Ala	Glu	Ile	Arg	Pro	Gly	Arg	Lys	Met	Gly	His	Ile
		340						345					350		
Thr	Val	Thr	Asp	Ala	Arg	Asp	Val	Met	Asp	Ile	Leu	Lys	Gln	Met	Glu
		355					360					365			
Ala	Ala	Trp													
		370													

<210> 124

<211> 484

<212> PRT

<213> Lactobacillus rhamnosus

<400> 124

Met	Phe	Val	Ala	Asp	Thr	Lys	Lys	Gln	Leu	Arg	Trp	Tyr	Asn	Val	Ala
1				5					10					15	
Leu	Ile	Ala	Phe	Val	Ser	Val	Trp	Gly	Leu	Gly	Asn	Val	Phe	Asn	Asn
		20						25					30		
Tyr	Ala	Gln	Gln	Gly	Leu	Ser	Val	Val	Thr	Ser	Trp	Ile	Leu	Ile	Met
	35					40					45				
Leu	Ile	Tyr	Phe	Val	Pro	Tyr	Ala	Leu	Ile	Val	Gly	Gln	Leu	Gly	Ser
	50					55					60				
Thr	Phe	Lys	Asp	Gln	Ala	Gly	Gly	Val	Ser	Ser	Trp	Ile	Lys	Glu	Thr
65					70					75					80
Gly	Ser	Val	Arg	Leu	Ala	Tyr	Tyr	Ala	Ala	Trp	Thr	Tyr	Trp	Val	Val
			85					90						95	
His	Ile	Pro	Tyr	Leu	Ala	Gln	Lys	Pro	Gln	Ala	Ile	Leu	Ile	Ala	Leu
		100						105					110		
Ser	Trp	Leu	Phe	Lys	Gly	Asn	Gly	Asp	Phe	Val	Asn	Thr	Val	Ser	Ser
		115					120					125			
Met	Thr	Val	Ser	Leu	Ile	Cys	Leu	Ala	Leu	Phe	Leu	Leu	Phe	Leu	Trp
	130					135					140				
Leu	Ser	Ser	Arg	Gly	Leu	Thr	Thr	Leu	Asn	Arg	Ile	Gly	Ser	Met	Ala
145					150					155					160
Gly	Thr	Ala	Met	Phe	Leu	Met	Ser	Ile	Leu	Phe	Ile	Ile	Leu	Ala	Val
			165						170					175	
Thr	Ala	Pro	Leu	Met	Val	Lys	Gly	Val	His	Val	Ala	Thr	Pro	Asn	Met
			180					185						190	
Gly	Asp	Ile	His	Thr	Tyr	Leu	Pro	Lys	Phe	Asp	Leu	Asn	Tyr	Phe	Thr
	195					200						205			
Thr	Ile	Ser	Met	Leu	Val	Phe	Ala	Val	Gly	Gly	Ala	Glu	Lys	Ile	Ser
	210					215					220				
Pro	Tyr	Val	Asn	Asn	Thr	Lys	His	Ala	Ser	Lys	Glu	Phe	Pro	Leu	Gly
225					230					235					240
Met	Leu	Val	Leu	Ala	Gly	Met	Val	Ala	Phe	Cys	Ala	Leu	Leu	Gly	Ser
			245						250					255	
Phe	Gly	Met	Gly	Met	Leu	Phe	Asn	Ser	His	His	Ile	Pro	Thr	Asp	Leu
			260					265					270		

Met	Ala	Asn	Gly	Pro	Tyr	Thr	Ala	Phe	Ala	Met	Leu	Gly	Lys	Tyr	Tyr
		275					280					285			
His	Val	Gly	Gly	Leu	Phe	Val	Ile	Leu	Tyr	Ser	Ile	Ala	Asn	Ala	Leu
	290					295					300				
Ala	Ser	Ile	Ser	Ala	Leu	Ala	Phe	Ser	Ile	Asp	Ala	Pro	Leu	Lys	Ile
305					310					315					320
Leu	Leu	Ser	Asp	Ala	Asp	Pro	His	Phe	Ile	Pro	Lys	Lys	Leu	Arg	Arg
			325						330					335	
Ile	Asn	Arg	Lys	Gly	Thr	Pro	Ile	Asn	Gly	Tyr	Trp	Met	Thr	Gly	Ile
		340						345					350		
Leu	Val	Ser	Leu	Leu	Ile	Ile	Ile	Pro	Ala	Phe	Gly	Ile	Gly	Asn	Met
	355						360					365			
Asn	Glu	Leu	Tyr	Lys	Trp	Leu	Leu	Asn	Leu	Asn	Ser	Val	Val	Met	Pro
	370					375					380				
Leu	Arg	Tyr	Leu	Trp	Val	Phe	Leu	Ala	Tyr	Tyr	Leu	Leu	Asn	Gln	His
385					390					395					400
Leu	Glu	Lys	Phe	Gln	Ala	Asp	Tyr	Met	Leu	Val	Lys	Asn	Lys	Arg	Leu
			405						410					415	
Gly	Met	Leu	Val	Gly	Arg	Trp	Cys	Phe	Phe	Phe	Thr	Ala	Phe	Ala	Cys
		420						425					430		
Leu	Leu	Gly	Met	Leu	Pro	Lys	Ile	Ser	Tyr	Leu	Asn	Asp	Pro	Gly	Thr
	435					440						445			
Trp	Trp	Phe	Gln	Met	Gly	Leu	Asn	Ile	Ile	Thr	Pro	Val	Ile	Leu	Leu
	450					455					460				
Ala	Leu	Gly	Leu	Ile	Leu	Pro	Val	Ile	Ala	Arg	Leu	His	Glu	Asn	Asp
465					470					475					480
Leu	Asp	Ala	Gln												

<210> 125

<211> 272

<212> PRT

<213> Lactobacillus rhamnosus

<400> 125

Met	Gln	Glu	Leu	Glu	Lys	Tyr	Ser	Leu	Asp	Asp	Thr	Tyr	Ile	Arg	Pro
1				5					10					15	
Phe	Asp	Arg	Glu	Lys	Gln	Glu	Ile	Ala	Leu	Glu	Thr	Lys	Asp	Leu	His
		20						25					30		
Val	Phe	Tyr	Gly	Asp	Asn	Glu	Ala	Ile	His	Gly	Val	Ser	Leu	Pro	Phe
	35					40					45				
Glu	Arg	Tyr	Lys	Ile	Thr	Ala	Leu	Ile	Gly	Ser	Ser	Gly	Ser	Gly	Lys
	50					55					60				
Ser	Thr	Tyr	Leu	Arg	Ser	Leu	Asn	Arg	Met	Asn	Asp	Asn	Ile	Glu	Ser
65					70					75					80
Ala	Arg	Val	Thr	Gly	Lys	Ile	Met	Tyr	Arg	Asn	Ile	Asp	Ile	Asn	Ser
			85						90					95	
Asp	Ala	Val	Asp	Val	Tyr	Glu	Met	Arg	Lys	His	Ile	Gly	Met	Val	Phe
		100						105					110		
Gln	Arg	Pro	Asn	Pro	Phe	Ala	Lys	Ser	Ile	Tyr	Asp	Asn	Ile	Ala	Phe
	115						120					125			
Ala	Leu	Arg	Arg	Phe	Gly	Ile	Lys	Glu	Lys	Lys	Lys	Leu	Asp	Glu	Ile
	130					135						140			
Val	Glu	Thr	Ser	Leu	Lys	Gln	Ala	Ala	Leu	Trp	Asp	Gln	Val	Lys	Asp
145					150					155					160
Asp	Leu	Asn	Gln	Ser	Gly	Met	Ser	Leu	Ser	Gly	Gly	Gln	Ala	Gln	Arg
			165						170					175	

Leu Cys Ile Ala Arg Ala Ile Ala Met Lys Pro Asp Ile Leu Leu Leu
 180 185 190
 Asp Glu Pro Ala Ser Ala Leu Asp Pro Ile Ser Thr Ser Ala Val Glu
 195 200 205
 Asp Thr Leu Leu Ser Leu Lys Asp Lys Tyr Thr Ile Ile Ile Val Thr
 210 215 220
 His Asn Met Gln Gln Ala Ala Arg Ile Ser Asp Tyr Thr Ala Phe Phe
 225 230 235 240
 Tyr Ser Gly Ala Ala Leu Glu Tyr Asp Glu Thr Arg Lys Ile Phe Thr
 245 250 255
 Arg Pro Lys Ile Lys Ala Thr Asn Asp Tyr Val Ser Gly His Phe Gly
 260 265 270

<210> 126

<211> 254

<212> PRT

<213> Lactobacillus rhamnosus

<400> 126

Met Ala Glu Ala Gln Lys Ile Ile Thr Ser Ser Asp Val His Leu Phe
 1 5 10 15
 Tyr Gly Lys Phe Glu Ala Leu Lys Gly Ile Asn Leu Asp Phe Asn Glu
 20 25 30
 His Glu Ile Thr Ala Leu Ile Gly Pro Ser Gly Cys Gly Lys Ser Thr
 35 40 45
 Tyr Leu Arg Thr Leu Asn Arg Met Asn Asp Leu Ile Pro Gly Val Thr
 50 55 60
 Ile Thr Gly Thr Ile Ser Leu Arg Gly Gln Asn Ile Tyr Ala Pro Ser
 65 70 75 80
 Glu Asp Val Val Gln Leu Arg Lys Gln Val Gly Met Val Phe Gln Gln
 85 90 95
 Pro Asn Pro Phe Pro Phe Ser Ile Tyr Glu Asn Val Ile Tyr Gly Leu
 100 105 110
 Arg Leu Ala Gly Val Lys Asp Lys Ser Ile Leu Asp Glu Ala Val Glu
 115 120 125
 Thr Ser Leu Lys Gln Ala Ala Ile Trp Asp Glu Val Lys Asp His Leu
 130 135 140
 His Asp Ser Ala Leu Ser Leu Ser Gly Gly Gln Gln Gln Arg Val Cys
 145 150 155 160
 Ile Ala Arg Val Leu Ala Val Lys Pro Asp Val Val Leu Leu Asp Glu
 165 170 175
 Pro Thr Ser Ala Leu Asp Pro Ile Ser Ser Thr Gln Ile Glu Asn Met
 180 185 190
 Leu Leu Glu Leu Arg Asp Gln Tyr Thr Ile Ile Leu Val Thr His Ser
 195 200 205
 Met His Gln Ala Ser Arg Ile Ser Asp Lys Thr Ala Phe Phe Leu Thr
 210 215 220
 Gly Asn Leu Ile Glu Phe Ala Asp Thr Lys Gln Met Phe Leu Asn Pro
 225 230 235 240
 Lys Glu Lys Glu Thr Glu Asp Tyr Ile Thr Gly Arg Phe Gly
 245 250

<210> 127

<211> 300

<212> PRT

<213> Lactobacillus rhamnosus

<400> 127

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Met Leu Lys Lys Ser Arg Ser Ser Lys Leu Glu Arg Arg Gly Lys Thr
 1           5           10           15
Ile Ser Leu Ile Cys Ile Ser Leu Ile Val Leu Val Val Val Ala Ile
          20           25           30
Phe Phe Phe Val Ala Ser Lys Gly Leu Ala Thr Phe Phe Gln Asn Lys
          35           40           45
Ile Asn Leu Trp Ser Phe Leu Ser Lys Ser Val Trp Asn Pro Ser Ile
          50           55           60
Lys Asp Ala His Gly Asn Pro Glu Val Gly Ala Leu Pro Met Ile Val
65           70           75           80
Gly Ser Phe Gly Val Thr Phe Leu Ser Ala Ile Val Ala Thr Pro Phe
          85           90           95
Ala Val Gly Ala Gly Ile Phe Met Thr Glu Ile Ser His Lys Trp Gly
          100          105          110
Gln Lys Val Leu Gln Pro Val Ile Glu Leu Leu Val Gly Ile Pro Ser
          115          120          125
Val Val Tyr Gly Phe Ile Gly Leu Ser Val Ile Val Pro Phe Ile Arg
          130          135          140
His Ile Phe Gly Gly Thr Gly Phe Gly Ile Leu Ala Gly Thr Phe Val
145          150          155          160
Leu Phe Val Met Ile Leu Pro Thr Val Thr Ser Met Thr Val Asp Ala
          165          170          175
Leu Lys Ala Val Pro Arg His Tyr Arg Glu Ala Ser Leu Ala Leu Gly
          180          185          190
Ala Thr Arg Trp Gln Thr Thr Tyr Arg Val Val Leu Arg Ala Ala Ile
          195          200          205
Pro Gly Ile Leu Thr Gly Ile Val Phe Gly Met Ala Arg Ala Phe Gly
          210          215          220
Glu Ala Leu Ala Val Gln Met Val Ile Gly Asn Ala Ala Leu Leu Pro
225          230          235          240
Lys Asn Leu Val Ser Pro Ala Ser Thr Leu Thr Ser Val Leu Thr Ser
          245          250          255
Gly Ile Gly Asn Thr Val Met Gly Ser Leu Glu Asn Asn Ala Leu Trp
          260          265          270
Ser Leu Ala Leu Leu Leu Leu Leu Met Ser Leu Ala Phe Asn Leu Leu
          275          280          285
Ile Arg Trp Ile Gly Lys Lys Gly Glu Leu Asn Lys
          290          295          300

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<210> 128

<211> 234

<212> PRT

<213> Lactobacillus rhamnosus

<400> 128

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Met Lys Lys Ile Leu Ile Val Asp Asp Glu Pro Ala Ile Leu Thr Leu
 1           5           10           15
Leu Gln Tyr Asn Leu Glu Ala Glu His Tyr Gln Val Glu Thr Ala Thr
          20           25           30
Asp Gly Gln Glu Ala Leu Asp Lys Val Arg Ser Glu Pro Phe Asp Phe
          35           40           45
Ile Ile Leu Asp Leu Met Leu Pro Ser Leu Ser Gly Leu Asp Val Thr
          50           55           60
Cys Lys Ile Arg Glu Glu Lys Ile Gln Thr Pro Ile Met Ile Leu Thr
65           70           75           80
Ala Lys Asp Asn Glu Thr Asp Lys Ile Val Gly Leu Glu Leu Gly Ala

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				85					90					95			
Asp	Asp	Tyr	Val	Thr	Lys	Pro	Phe	Ser	Pro	Arg	Glu	Ile	Ile	Ala	Arg		
			100					105					110				
Ile	Lys	Ala	Ile	Glu	Arg	Arg	Ser	Gln	Ser	Gln	Pro	Gln	Ala	Pro	Leu		
		115					120					125					
Ser	Arg	Asn	Ala	Asn	Gln	Ile	Thr	Val	Gly	Gln	Ile	Thr	Ile	Asp	Pro		
	130					135					140						
Glu	Asn	Tyr	Lys	Ala	Ser	Lys	Ala	Gly	His	Arg	Leu	Gln	Leu	Thr	Pro		
145					150					155					160		
Lys	Glu	Phe	Glu	Leu	Leu	Val	Tyr	Phe	Ala	Gln	Arg	Val	Gly	Lys	Thr		
			165						170					175			
Leu	Ser	Arg	Asp	Ala	Leu	Leu	Asn	Gly	Val	Trp	Gly	Phe	Asp	Tyr	Pro		
			180					185					190				
Ala	Glu	Thr	Arg	Met	Val	Asp	Ile	Gln	Val	Ser	His	Leu	Arg	Asp	Lys		
		195					200					205					
Ile	Glu	Thr	Asp	Pro	Lys	His	Pro	Asp	Tyr	Leu	Lys	Thr	Val	Arg	Gly		
	210					215					220						
Phe	Gly	Tyr	Gln	Met	Glu	Ala	Pro	His	Glu								
225					230												

<210> 129

<211> 250

<212> PRT

<213> Lactobacillus rhamnosus

<220>

<221> VARIANT

<222> (1)...(250)

<223> Xaa = Any Amino Acid

<400> 129

Met	Leu	Leu	Ser	Gly	Phe	Leu	Val	Lys	Met	Ala	Leu	Leu	Thr	Asn	Ser		
1				5				10						15			
Trp	Asn	Leu	Ser	Glu	Leu	Val	His	Asn	Ser	Cys	Xaa	Ile	Leu	Asn	Leu		
		20						25					30				
Leu	Asp	Tyr	His	Leu	Ser	Lys	Glu	Gly	Phe	Ser	Thr	Gln	Leu	Val	Thr		
	35					40						45					
Asn	Gly	Arg	Lys	Ala	Leu	Ala	Leu	Ala	Glu	Thr	Glu	Pro	Phe	Asp	Phe		
	50					55					60						
Ile	Leu	Leu	Asp	Ile	Met	Leu	Pro	Gln	Leu	Asp	Gly	Met	Glu	Val	Cys		
65				70						75					80		
Lys	Arg	Leu	Arg	Ala	Lys	Gly	Val	Lys	Thr	Pro	Ile	Met	Met	Val	Ser		
			85					90						95			
Ala	Lys	Ser	Asp	Glu	Phe	Asp	Lys	Val	Leu	Ala	Leu	Glu	Leu	Gly	Ala		
		100						105						110			
Asp	Asp	Tyr	Leu	Thr	Lys	Pro	Phe	Ser	Pro	Arg	Glu	Leu	Leu	Ala	Arg		
	115						120					125					
Val	Lys	Ala	Val	Leu	Arg	Arg	Thr	Lys	Gly	Glu	Gln	Glu	Gly	Asp	Asp		
	130					135						140					
Ser	Asp	Asn	Ile	Ala	Asp	Asp	Ser	Trp	Leu	Phe	Gly	Thr	Leu	Lys	Val		
145					150					155					160		
Tyr	Pro	Glu	Arg	His	Glu	Val	Tyr	Lys	Ala	Asn	Lys	Leu	Leu	Ser	Leu		
			165					170						175			
Thr	Pro	Lys	Glu	Phe	Glu	Leu	Leu	Leu	Tyr	Leu	Met	Lys	His	Pro	Asn		
		180						185					190				
Met	Thr	Leu	Thr	Arg	Glu	Arg	Leu	Leu	Glu	Arg	Ile	Trp	Gly	Tyr	Asp		
	195						200					205					

Phe Gly Gln Glu Thr Arg Leu Val Asp Val His Ile Gly Lys Leu Arg
 210 215 220
 Glu Lys Ile Glu Asp Asn Pro Lys Ala Pro Gln Phe Ile Arg Thr Ile
 225 230 235 240
 Arg Gly Tyr Gly Tyr Lys Phe Lys Glu Leu
 245 250

<210> 130
 <211> 269
 <212> PRT
 <213> Lactobacillus rhamnosus

<400> 130
 Met Gln Ser Thr Tyr Gly Thr Arg Phe Leu Arg Val Phe Val Lys Asn
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 35 40 45
 Asp Asp Lys Glu Ile Val Glu Leu Leu Ser Ile Tyr Val Lys Asn Glu
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 Gly Tyr Glu Pro Ile Gln Ala Tyr Ser Gly Lys Glu Ala Ile Thr Lys
 65 70 75 80
 Leu Val Thr Asn Pro Asp Ile Ala Leu Met Ile Leu Asp Ile Met Met
 85 90 95
 Pro Asn Met Ser Gly Met Asp Val Val Lys Glu Val Arg Lys Asp Ser
 100 105 110
 Gln Ile Pro Ile Ile Ile Val Ser Ala Lys Thr Ala Asp Met Asp Lys
 115 120 125
 Ile Gln Gly Leu Ile Thr Gly Ala Asp Asp Tyr Val Thr Lys Pro Phe
 130 135 140
 Asn Pro Leu Glu Val Met Ala Arg Val Lys Ser Leu Leu Arg Arg Ser
 145 150 155 160
 Gln Asn Glu Val Thr Asn Ser Glu Pro Asp Val Leu Glu Val Gly Pro
 165 170 175
 Leu Thr Ile Lys Lys Asp Ser His Glu Val Thr Thr Leu Thr Gly Lys
 180 185 190
 Gln Ile Gln Leu Thr Ala Leu Glu Phe Gly Ile Leu Tyr Leu Leu Ala
 195 200 205
 Ser His Pro Asn Arg Val Phe Ser Ala Asp Glu Ile Phe Glu Arg Val
 210 215 220
 Trp Gln Gln Glu Ser Ile Val Ser Ala Lys Thr Val Met Val His Val
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 <212> PRT
 <213> Lactobacillus rhamnosus

<400> 131
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Gln	Lys	Ile	Arg	Glu	Val	Ser	Lys	Val	Pro	Val	Ile	Phe	Ile	Ser	Ser		
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Arg	Asn	Thr	Asn	Met	Asp	Met	Val	Met	Ala	Met	Asn	Met	Gly	Ala	Asp		
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Asp	Phe	Leu	Asn	Lys	Pro	Phe	Ala	Met	Glu	Val	Leu	Ile	Ala	Lys	Ile		
		100					105						110				
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	115					120						125					
Val	Leu	Glu	His	Asn	Gly	Leu	Met	Leu	Asn	Leu	Lys	Asn	Gly	Met	Ala		
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Gln	Ile	Gly	Glu	Lys	Glu	Ile	Asn	Leu	Ser	Lys	Asn	Glu	Tyr	Lys	Leu		
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			165						170					175			
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		180						185					190				
Leu	Thr	Val	Asn	Val	Asn	Arg	Leu	Arg	Lys	Lys	Ile	Glu	Glu	Ala	Gly		
	195					200						205					
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<210> 132

<211> 246

<212> PRT

<213> Lactobacillus rhamnosus

<400> 132

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Ala	Ile	Leu	Ala	Met	Leu	Lys	Arg	Tyr	Phe	Ala	Trp	Arg	Leu	Pro	Glu		
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Ala	Gln	Gln	Pro	Asp	Leu	Ile	Leu	Leu	Asp	Val	Asn	Leu	Pro	Asp	Ile		
65					70					75					80		
Asp	Gly	Phe	Thr	Leu	Thr	Ser	Arg	Ile	Arg	Ala	Ile	Thr	Ser	Val	Pro		
			85						90					95			
Ile	Ile	Phe	Leu	Thr	Ala	Arg	Ile	Thr	Asp	Gln	Asp	Lys	Val	Gln	Gly		
		100						105					110				
Leu	Gly	Ala	Gly	Gly	Asp	Asp	Tyr	Val	Thr	Lys	Pro	Phe	Ser	Leu	Thr		
	115					120						125					
Glu	Leu	Gly	Ala	Arg	Ile	Lys	Ala	His	Val	Arg	Arg	Ala	His	Gln	Pro		
	130					135					140						
Asp	Lys	Gln	Ala	Gln	Ile	Ala	Val	Phe	Gly	Arg	Ile	Met	Ile	Asp	Tyr		
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His	Ala	His	Gln	Val	Ser	Val	Asp	Thr	Thr	Cys	Leu	Lys	Leu	Glu	Asn		
			165						170					175			
Lys	Gln	Tyr	Gln	Leu	Ile	Glu	Trp	Leu	Ser	Leu	Asn	Pro	Gly	Gln	Val		
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Phe	Ser	Arg	Glu	Gln	Leu	Tyr	Glu	Lys	Ile	Trp	Gly	Tyr	Asp	Ala	Gln		

	195		200		205										
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	210					215					220				
Phe	Asp	Ala	Cys	Gln	Val	Thr	Ser	Pro	Ile	Val	Thr	Val	Trp	Gly	Val
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Gly	Tyr	Lys	Trp	Gln	Asn										
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<210> 133
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 <213> Lactobacillus rhamnosus

<400> 133

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		20						25					30		
Leu	Thr	Leu	Val	Lys	Ile	Leu	Val	Val	Glu	Asp	Asp	Arg	Asn	Phe	Asn
	35					40					45				
Asp	Leu	Ile	Ala	Thr	Ile	Leu	Arg	Gln	Asn	Gly	Tyr	Thr	Val	Gln	Gly
50					55					60					
Ala	Glu	Asn	Pro	Pro	Ala	Ala	Tyr	Asp	Leu	Leu	Gln	Ser	Glu	Gln	Phe
65				70					75						80
Asp	Leu	Val	Leu	Ser	Asp	Ile	Met	Met	Pro	Gln	Val	Asp	Gly	Tyr	Gln
			85				90							95	
Phe	Ala	Gln	Glu	Leu	Arg	Arg	Thr	Asp	Pro	Ser	Ile	Pro	Ile	Leu	Phe
		100					105						110		
Ile	Thr	Ala	Arg	Asp	Asp	Ile	Ala	Ser	Lys	Glu	Lys	Gly	Phe	Asn	Ser
	115					120						125			
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Leu	Leu	Ile	Val	Gly	Asn	Leu	Thr	Leu	Asn	Asn	Glu	Ala	Ile	Thr	Ala
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	180					185						190			
Leu	Tyr	Lys	Leu	Leu	Ser	Tyr	Pro	Asp	His	Ala	Phe	Ser	Arg	Ala	Glu
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Gly	Phe	Thr	Ile	Lys	Thr	Ile	His	Gly	Leu	Gly	Tyr	Lys	Ala	Val	Leu
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 Ile Ala Thr Asp Arg Arg Gly Asn Val Ile Ile Ile Asn Gln Thr Ala
 65 70 75 80
 Leu Ser Phe Leu Asn Thr Lys Asn Glu Asp Val Ile Gly Val Ser Ile
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 Leu Lys Leu Leu Asn Ile Ala Lys Asp Tyr Thr Leu Arg Asp Leu Leu
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 Glu His Gln Thr Glu Leu Leu Leu Asp Phe Ser Glu Gln Leu Asp His
 115 120 125
 Asp Leu Ile Leu Arg Val Asp Phe Ser Leu Ile Gln Arg Glu Thr Gly
 130 135 140
 Phe Ile Ser Gly Leu Val Ala Val Leu His Asp Val Thr Glu Gln Gln
 145 150 155 160
 Lys Ile Asp Arg Asp Arg Lys Glu Phe Val Ser Asn Val Ser His Glu
 165 170 175
 Leu Arg Thr Pro Leu Thr Ser Val Arg Ser Tyr Ile Glu Ala Leu Ser
 180 185 190
 Asp Gly Ala Trp Lys Asp Ser Lys Leu Ala Pro Gln Phe Leu Asn Val
 195 200 205
 Thr Gln Glu Glu Thr Asp Arg Met Ile Arg Met Ile Asn Asp Leu Leu
 210 215 220
 Ser Leu Ser Arg Leu Asp Ser Gly Thr Ser Lys Phe Asn Leu Glu Thr
 225 230 235 240
 Val Asn Leu Asn Glu Phe Phe Asn Tyr Val Leu Asp Arg Phe Asp Met
 245 250 255
 Met Leu Lys Thr Asp Asn Glu His Thr Gly Glu Ala Arg Thr Ala Gln
 260 265 270
 Pro Leu Pro Gln Pro Asp Gly Gln Lys Lys Arg Tyr Ser Ile Lys Arg
 275 280 285
 Glu Ile Thr His Glu Asp Leu Trp Val Glu Ile Asp Thr Asp Lys Phe
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 Asp Gly Gly Val Ile Thr Ala Arg Leu Phe Gln Met His Asp His Val
 325 330 335
 Ile Leu Ser Ile Ser Asp Gln Gly Leu Gly Ile Pro Arg Gln Asp Leu
 340 345 350
 Gly Lys Ile Phe Asp Arg Phe Tyr Arg Val Asp Lys Ala Arg Ser Arg
 355 360 365
 Lys Gln Gly Gly Thr Gly Leu Gly Leu Ala Ile Ser Lys Glu Val Val
 370 375 380
 Glu Ala Leu His Gly Arg Ile Trp Val Asp Ser Gln Glu Gly Arg Gly
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<211> 422

<212> PRT

<213> Lactobacillus rhamnosus

<400> 135

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			20					25					30		
Glu	Val	Ala	Phe	Glu	Thr	Leu	His	Gln	Pro	Leu	Leu	Thr	Ser	Ser	Glu
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			180					185					190		
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225					230					235					240
Tyr	Lys	Glu	Ser	Leu	Arg	Leu	Glu	His	Ile	Val	Glu	His	Leu	Leu	Thr
				245					250					255	
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			260					265					270		
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Val	Ser	Asp	Ser	Gln	Leu	Leu	Ser	Gln	Ile	Leu	Leu	Asn	Leu	Leu	Ser
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				325					330					335	
Gln	Lys	Val	Asn	Glu	Gly	Ile	Lys	Ile	Ser	Val	Ser	Asp	Thr	Gly	Ile
			340					345					350		
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		355					360					365			
Val	Asn	Lys	Gly	Arg	Ser	Arg	Gln	Thr	Gly	Gly	Thr	Gly	Leu	Gly	Leu
		370				375					380				
Ala	Ile	Val	Lys	Glu	Leu	Ser	Gln	Leu	Leu	Gly	Gly	Gln	Val	Thr	Val
385					390					395					400
Thr	Ser	Gln	Leu	Gly	Arg	Gly	Ser	Cys	Phe	Thr	Ile	Phe	Leu	Pro	Asn
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<210> 136
 <211> 675
 <212> PRT
 <213> Lactobacillus rhamnosus

<400> 136

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			20					25					30		
Leu	Ile	Phe	Ser	Ala	Trp	Phe	Thr	Tyr	Lys	Ala	Lys	Thr	Ala	Asp	Val
		35					40					45			
Gln	Asn	Ile	Lys	Ser	Thr	Leu	Gln	Thr	Lys	Thr	Val	Ile	Tyr	Asp	Ala
	50					55					60				
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65					70					75					80
Glu	Leu	Ser	Ala	Ile	Ser	Pro	Gln	Val	Gln	Asn	Ala	Val	Ile	Ser	Thr
				85					90					95	
Glu	Asp	Arg	Thr	Phe	Tyr	Ser	Asn	Gly	Gly	Phe	Ser	Ile	Lys	Gly	Ile
			100					105					110		
Leu	Arg	Ser	Ala	Leu	Asn	Tyr	Val	Ile	His	His	Gly	Gln	Ile	Met	Gly
		115					120					125			
Gly	Gly	Ser	Thr	Ile	Thr	Gln	Gln	Leu	Ala	Lys	Asn	Thr	Leu	Leu	Thr
	130					135						140			
Gln	Lys	Gln	Thr	Met	Leu	Arg	Lys	Ala	Gln	Glu	Leu	Phe	Met	Ala	Ile
145					150					155					160
Gln	Leu	Asn	Lys	Val	Tyr	Ser	Lys	Gln	Asp	Ile	Leu	Ala	Met	Tyr	Leu
				165					170					175	
Asn	Asn	Ala	Tyr	Phe	Gly	Asn	Gly	Val	Trp	Gly	Val	Gln	Asp	Ala	Ala
			180					185					190		
Lys	Arg	Tyr	Phe	Gly	Lys	Asn	Ala	Ser	Gln	Leu	Asp	Ala	Ser	Glu	Gly
		195					200					205			
Ala	Ile	Leu	Ala	Gly	Met	Leu	Arg	Asn	Pro	Ser	Tyr	Tyr	Asn	Pro	Ala
	210					215						220			
Asp	His	Lys	Asp	Asn	Ala	Ile	Ser	Arg	Arg	Asn	Val	Val	Leu	Gln	Leu
225					230					235					240
Met	Val	Asp	Asn	His	Lys	Leu	Thr	Gln	Ala	Gln	Ala	Asn	Ala	Ala	Lys
				245					250					255	
Ala	Gln	Ser	Val	Gln	Val	Val	Asp	Ala	Phe	Ser	Asn	Ala	Asn	Ala	Gln
			260					265					270		
Lys	Tyr	Pro	Ser	Tyr	Phe	Asp	Ser	Val	Ile	Glu	Glu	Ala	Arg	Ser	Glu
		275					280					285			
Gly	Ile	Ser	Val	Asp	Asp	Ile	Leu	Asn	Lys	Gly	Tyr	Lys	Ile	Tyr	Thr
	290					295						300			
Asn	Leu	Asp	Gln	Thr	Tyr	Gln	Gln	Asn	Leu	Gln	Thr	Ser	Phe	Glu	Gln
305					310					315					320
Asp	Trp	Ala	Phe	Pro	Ala	Asn	Ala	Ala	Asp	Gly	Lys	Gln	Val	Gln	Gly
				325					330					335	
Ala	Ser	Ile	Ile	Leu	Asp	Pro	Lys	Thr	Gly	Gly	Val	Arg	Ala	Val	Val
			340					345					350		
Gly	Asn	Arg	Gly	Glu	His	Thr	Phe	Leu	Gly	Phe	Asn	Tyr	Ala	Thr	Gln
		355					360					365			
Leu	Arg	Asn	Ser	Pro	Gly	Ser	Thr	Ile	Lys	Pro	Leu	Met	Val	Tyr	Thr
	370					375						380			
Pro	Ala	Leu	Glu	Asn	Gly	Tyr	His	Tyr	Asp	Ser	Ile	Leu	Lys	Asp	Glu
385					390					395					400
Lys	Leu	Ser	Tyr	Gly	Lys	Asn	Asn	Tyr	Thr	Pro	Thr	Asn	Ala	Thr	Gly

DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 2
CONTENANT LES PAGES 1 À 207

NOTE : Pour les tomes additionels, veuillez contacter le Bureau canadien des brevets

JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

THIS IS VOLUME 1 OF 2
CONTAINING PAGES 1 TO 207

NOTE: For additional volumes, please contact the Canadian Patent Office

NOM DU FICHER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

Claims

1. An isolated polynucleotide comprising a sequence selected from the group consisting of: SEQ ID NO: 84-121.
2. An isolated polynucleotide comprising a sequence selected from the group consisting of:
 - (a) complements of SEQ ID NO: 84-121;
 - (b) reverse complements of SEQ ID NO: 84-121; and
 - (c) reverse sequences of SEQ ID NO: 84-121.
3. An isolated polynucleotide comprising a sequence selected from the group consisting of:
 - (a) sequences having at least 75% identity to a sequence of SEQ ID NO: 84-121;
 - (b) sequences having at least 90% identity to a sequence of SEQ ID NO: 84-121; and
 - (c) sequences having at least 95% identity to a sequence of SEQ ID NO: 84-121.
4. An isolated polynucleotide comprising a sequence selected from the group consisting of:
 - (a) nucleotide sequences that are 200-mers of a sequence recited in SEQ ID NO: 84-121;
 - (b) nucleotide sequences that are 100-mers of a sequence recited in SEQ ID NO: 84-121;
 - (c) nucleotide sequences that are 40-mers of a sequence recited in SEQ ID NO: 84-121; and

- (d) nucleotide sequences that are 20-mers of a sequence recited in SEQ ID NO: 84-121.
5. An isolated oligonucleotide probe or primer comprising at least 10 contiguous residues complementary to 10 contiguous residues of a nucleotide sequence recited in any one of claims 1-3.
6. A kit comprising a plurality of oligonucleotide probes or primers of claim 5.
7. A genetic construct comprising a polynucleotide of any one of claims 1-3.
8. A transgenic host cell comprising a genetic construct according to claim 7.
9. An isolated polynucleotide comprising a nucleotide sequence that differs from a nucleotide sequence recited in SEQ ID NO: 84-121 as a result of deletions and/or insertions totaling less than 10% of the total sequence length.
10. An isolated polynucleotide comprising a nucleotide sequence that differs from a nucleotide sequence recited in SEQ ID NO: 84-121 as a result of substitutions, insertions, and/or deletions totaling less than 15% of the total sequence length.
11. A genetic construct comprising, in the 5'-3' direction:
- (a) a gene promoter sequence; and
 - (b) a polynucleotide sequence comprising at least one of the following: (1) a polynucleotide coding for an amino acid sequence selected from the group consisting of: (i) SEQ ID NO: 122-253, and (ii) sequences having at least 75% identity to a sequence of SEQ ID NO: 122-253; and (2) a polynucleotide comprising a non-coding region of a polynucleotide of any one of claims 1-3.

12. The genetic construct of claim 11, wherein the polynucleotide is in a sense orientation.
13. The genetic construct of claim 11, wherein the polynucleotide is in an anti-sense orientation.
14. The genetic construct of claim 11, wherein the gene promoter sequence is functional in a prokaryote or eukaryote.
15. A transgenic host cell comprising a construct of claim 11.
16. A transgenic organism comprising a transgenic host cell according to claim 15, or progeny thereof.
17. The transgenic organism of claim 16, wherein the organism is selected from the group consisting of *Lactobacillus* species.
18. A method for modulating the activity of a polypeptide in an organism, comprising stably incorporating into the genome of the organism a polynucleotide of any one of claims 1-3.
19. The method of claim 18, wherein the organism is a microbe.
20. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of: sequences recited in SEQ ID NO: 122-253.
21. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:
 - (a) sequences having at least 75% identity to a sequence of SEQ ID NO: 122-253;

- (b) sequences having at least 90% identity to a sequence of SEQ ID NO: 122-253; and
 - (c) sequences having at least 95% identity to a sequence of SEQ ID NO: 122-253.
22. An isolated polynucleotide that encodes a polypeptide of any one of claims 20 and 21.
23. A fusion protein comprising at least one polypeptide according to any one of claims 20 and 21.
24. An isolated polypeptide encoded by a polynucleotide of any one of claims 1-3.
25. A composition comprising a polypeptide according to any one of claims 20 and 21 and at least one component selected from the group consisting of: physiologically acceptable carriers; and immunostimulants.
26. A composition comprising a polynucleotide according to any one of claims 1-3 and at least one component selected from the group consisting of: physiologically acceptable carriers and immunostimulants.
27. A method for treating a disorder in a mammal, comprising administering a composition according to claim 25.
28. A method for treating a disorder in a mammal, comprising administering a composition according to claim 26.
29. A method of identifying an organism, or reproductive material or an extract therefrom, as having a specific origin, comprising detecting in the genetic complement of the organism, material or extract the presence or absence of a polynucleotide identifier

representative of said origin, wherein the polynucleotide identifier comprises a sequence recited in SEQ ID NO: 84-121.

30. A method for improving the properties of microbes used in the manufacture of milk-derived products, food products, food additives, nutritional supplements, bioactive substances or probiotic supplements, comprising modulating the polynucleotide content or composition of the microbes by transforming the microbes with a polynucleotide of any one of claims 1-4.
31. A method for modifying the flavor, aroma, texture and/or nutritional, immune system modulating, and health benefits of a milk-derived, food, food additive, nutritional supplement, bioactive or probiotic supplement product comprising adding one or more polypeptides of any one of claims 20 and 21 to the milk or other material from which the product is derived.
32. A composition comprising one or more species of probiotic microbes, or extracts thereof, that are non-pathogenic to mammalian organisms, said microbes comprising at least one isolated polynucleotide according to any one of claims 1-4.
33. The composition of claim 32, wherein said microbes are selected from the group consisting of: *Bacillus*, *Lactobacillus*, *Sporolactobacillus* and *Bifidiobacterium* species.
34. A transgenic microbial population for use in cheese ripening, flavor development and bioactive peptide production, wherein the transgenic microbial population comprises a polynucleotide of SEQ ID NO: 84-92, 95, 97, 100, 101, 105, 114, 117, 119 or 120.
35. A transgenic microbial population with modified survivability in manufacturing processes, storage in product formats or in intestinal or other environments, wherein the transgenic microbial population comprises a polypeptide selected from the group consisting of SEQ ID NO: 84-92, 95, 97, 100, 101, 105, 114, 117, 119 or 120.

36. A transgenic *Lactobacillus rhamnosus* HN001 strain comprising a genetic construct that leads to the insertional mutagenesis and/or targeted disruption of polynucleotides selected from the group consisting of SEQ ID NO: 84-121, wherein the transgenic *Lactobacillus rhamnosus* HN001 strain possesses modified properties of flavor, aroma, texture, nutrition, immune system modulation, bioactive compound production, probiotic or health-related benefits, adhesion, or survival of industrial processes, in storage or in the environment.

37. A method for identifying microorganisms having a trait associated with a polynucleotide of SEQ ID NO: 84-121, the method comprising detecting in the genetic complement of the microorganism, the presence or absence of a polynucleotide of SEQ ID NO: 1-84.