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(71) Demandeur/Applicant:
BASF PLANT SCIENCE GMBH, DE

(72) Inventeurs/Inventors:
PUZIO, PIOTR, DE;
CHARDONNENS, AGNES, DE;
SHIRLEY, AMBER, US;
WANG, XI-QING, US;
SARRIA-MILLAN, RODRIGO, US;
...

(74) Agent: ROBIC

(54) Titre : SEQUENCE D'ACIDES NUCLEIQUES CODANT POUR DES PROTEINES ASSOCIEES A LA REPONSE DE STRESS ABIOTIQUE ET CELLULES VEGETALES ET PLANTES A TOLERANCE ACCRUE AU STRESS ENVIRONNEMENTAL

(54) Title: NUCLEIC ACID SEQUENCES ENCODING PROTEINS ASSOCIATED WITH ABIOTIC STRESS RESPONSE AND PLANT CELLS AND PLANTS WITH INCREASED TOLERANCE TO ENVIRONMENTAL STRESS

(57) Abrégé/Abstract:
This invention relates generally to nucleic acid sequences encoding proteins that are associated with abiotic stress responses and abiotic stress tolerance in plants.This invention further relates to transformed plant cells with altered metabolic activity compared to a corresponding non transformed wild type plant cell, wherein the metabolic activity is altered by transformation with a Stress-Related Protein (SRP) coding nucleic acid and results in increased tolerance and/or resistance to an environmental stress as compared to a corresponding non-transformed wild type plant cell.

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(72) Inventeurs(suite)/Inventors(continued): MCKERSIE, BRYAN, US; CHEN, RUOYING, US

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(71) Applicant *(for all designated States except US)*: **BASF PLANT SCIENCE GMBH** [DE/DE]; Carl-Bosch-Strasse 38, 67056 Ludwigshafen (DE).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **PUZIO, Piotr** [DE/DE]; Edeltraudweg 21, 13505 Berlin (DE). **CHARDONNENS, Agnes** [NL/DE]; Edelweisstr. 40, 13158 Berlin (DE). **SHIRLEY, Amber** [US/US]; 2832 Kimmon Way, Wake Forest, NC 27587 (US). **WANG, Xi-Qing** [CN/US]; 205 Laurens Way, Chapel Hill, NC 27516 (US). **SARRIA-MILLAN, Rodrigo** [CO/US]; 2324 Winter Walk Circle, Morrisville, NC 27560 (US). **MCKERSIE, Bryan** [CA/US]; 102 Parkarbor Lane, Cary, NC 27519 (US). **CHEN, Ruoying** [CN/US]; 105 Rustic Pine Court, Apex, NC 27502 (US).

(74) Agent: **REMENICK, James**; Morrison & Foerster, LLP, 1650 Tysons Boulevard, Suite 300, Mclean, VA 22102 (US).

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(54) **Title:** NUCLEIC ACID SEQUENCES ENCODING PROTEINS ASSOCIATED WITH ABIOTIC STRESS RESPONSE AND PLANT CELLS AND PLANTS WITH INCREASED TOLERANCE TO ENVIRONMENTAL STRESS

(57) **Abstract:** This invention relates generally to nucleic acid sequences encoding proteins that are associated with abiotic stress responses and abiotic stress tolerance in plants.This invention further relates to transformed plant cells with altered metabolic activity compared to a corresponding non transformed wild type plant cell, wherein the metabolic activity is altered by transformation with a Stress-Related Protein (SRP) coding nucleic acid and results in increased tolerance and/or resistance to an environmental stress as compared to a corresponding non-transformed wild type plant cell.

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NUCLEIC ACID SEQUENCES ENCODING PROTEINS ASSOCIATED WITH ABIOTIC STRESS RESPONSE AND PLANT CELLS AND PLANTS WITH INCREASED TOLERANCE TO ENVIRONMENTAL STRESS

0001.0.1 This invention relates generally to nucleic acid sequences encoding proteins that are associated with abiotic stress responses and abiotic stress tolerance in plants.

0002.0.1 This invention further relates to transformed plant cells with altered metabolic activity compared to a corresponding non transformed wild type plant cell, wherein the metabolic activity is altered by transformation with a Stress-Related Protein (SRP) coding nucleic acid and results in increased tolerance and/or resistance to an environmental stress as compared to a corresponding non-transformed wild type plant cell.

0003.0.1 In particular, this invention relates to nucleic acid sequences encoding proteins that confer drought, heat, cold, and/or salt tolerance and/or resistance to plants, especially by altering the metabolic activity leading to drought, heat, cold, and/or salt tolerance and/or resistance to plants. The invention also deals with methods of producing, screening for and breeding such plant cells or plants and method of detecting stress in plants cells or plants.

0004.0.1 Abiotic environmental stresses such as drought stress, salinity stress, heat stress and cold stress, are major limiting factors of plant growth and productivity (Boyer. 1982. *Science* 218, 443–448). Crop losses and crop yield losses of major crops such as rice, maize (corn) and wheat caused by these stresses represent a significant economic and political factor and contribute to food shortages in many underdeveloped countries.

0005.0.1 Plants are typically exposed during their life cycle to conditions of reduced environmental water content. Most plants have evolved strategies to protect themselves against these conditions of low water or desiccation (drought). However, if the severity and duration of the drought conditions are too great, the effects on plant development, growth and yield of most crop plants are profound. Continuous exposure to drought causes major alterations in the plant metabolism. These great changes in metabolism ultimately lead to cell death and consequently yield losses.

0006.0.1 Developing stress-tolerant plants is a strategy that has the potential to solve or mediate at least some of these problems (McKersie and Leshem, 1994. *Stress and Stress Coping in Cultivated Plants*, Kluwer Academic Publishers). However, traditional plant breeding strategies to develop new lines of plants that exhibit resistance (tolerance) to these types of stresses are relatively slow and require specific resistant lines for crossing with the desired line. Limited germplasm resources for

stress tolerance and incompatibility in crosses between distantly related plant species represent significant problems encountered in conventional breeding. Additionally, the cellular processes leading to drought, cold and salt tolerance are complex in nature and involve multiple mechanisms of cellular adaptation and numerous metabolic pathways (McKersie and Leshem, 1994. *Stress and Stress Coping in Cultivated Plants*, Kluwer Academic Publishers). This multi-component nature of stress tolerance has not only made breeding for tolerance largely unsuccessful, but has also limited the ability to genetically engineer stress tolerance plants using biotechnological methods.

0007.0.1 Drought, heat, cold and salt stresses have a common theme important for plant growth and that is water availability. Plants are exposed during their entire life cycle to conditions of reduced environmental water content. Most plants have evolved strategies to protect themselves against these conditions. However, if the severity and duration of the drought conditions are too great, the effects on plant development, growth and yield of most crop plants are profound. Since high salt content in some soils result in less available water for cell intake, its effect is similar to those observed under drought conditions. Additionally, under freezing temperatures, plant cells loose water as a result of ice formation that starts in the apoplast and withdraws water from the symplast (McKersie and Leshem, 1994. *Stress and Stress Coping in Cultivated Plants*, Kluwer Academic Publishers). Commonly, a plant's molecular response mechanisms to each of these stress conditions are similar.

0008.0.1 The results of current research indicate that drought tolerance is a complex quantitative trait and that no real diagnostic marker is available yet. High salt concentrations or dehydration may cause damage at the cellular level during drought stress but the precise injury is not entirely clear (Bray, 1997. *Trends Plant Sci.* 2, 48–54). This lack of a mechanistic understanding makes it difficult to design a transgenic approach to improve drought tolerance. However, an important consequence of damage may be the production of reactive oxygen radicals that cause cellular injury, such as lipid peroxidation or protein and nucleic acid modification. Details of oxygen free radical chemistry and their reaction with cellular components such as cell membranes have been described (McKersie and Leshem, 1994. *Stress and Stress Coping in Cultivated Plants*, Kluwer Academic Publishers).

0009.0.1 It is the object of this invention to identify new, unique genes capable of conferring stress tolerance to plants upon expression or over-expression.

0010.0.1 It is further object of this invention to identify, produce and breed new, unique stress tolerant and/or resistant plant cells or plants and methods of inducing and detecting stress tolerance and/or resistance in plants or plant cells. It is a further object to identify new methods to detect stress tolerance and/or

resistance in plants or plant cells. It is also the object of this invention to identify new, unique genes capable of conferring stress tolerance to plants upon expression or over-expression.

0011.0.1 The present invention provides a transformed plant cell with altered metabolic activity compared to a corresponding non transformed wild type plant cell, wherein the metabolic activity is altered by transformation with a Stress-Related Protein (SRP) coding nucleic acid and results in increased tolerance and/or resistance to an environmental stress as compared to a corresponding non-transformed wild type plant cell.

0012.0.2 The present invention provides a transgenic plant cell transformed by Stress-Related Protein (SRP) coding nucleic acid. selected from the group consisting of:

a) nucleic acid molecule encoding one of the polypeptides shown in Fig. 1a, 1b or 1c or a fragment thereof, which confers an an altered metabolic activity in an organism or a part thereof;

b) nucleic acid molecule comprising one of the nucleic acid molecule shown in Fig. 1a, 1b or 1c;

c) nucleic acid molecule whose sequence can be deduced from a polypeptide sequence encoded by a nucleic acid molecule of (a) or (b) as a result of the degeneracy of the genetic code and conferring an altered metabolic activity in an organism or a part thereof;

d) nucleic acid molecule which encodes a polypeptide which has at least 50% identity with the amino acid sequence of the polypeptide encoded by the nucleic acid molecule of (a) to (c) and conferring an altered metabolic activity in an organism or a part thereof;

e) nucleic acid molecule which hybidizes with a nucleic acid molecule of (a) to (c) under under stringent hybridisation conditions and conferring an altered metabolic activity in an organism or a part thereof;

f) nucleic acid molecule which encompasses a nucleic acid molecule which is obtained by amplifying nucleic acid molecules from a cDNA library or a genomic library using the primers as shown in table 2 and conferring an altered metabolic activity in an organism or a part thereof;

g) nucleic acid molecule encoding a polypeptide which is isolated with the aid of monoclonal antibodies against a polypeptide encoded by one of the nucleic acid molecules of (a) to (f) and conferring an altered metabolic activity in an organism or a part thereof;

h) nucleic acid molecule encoding a polypeptide comprising the consensus sequence shown in Fig. 2 and conferring an altered metabolic activity in an organism or a part thereof; and

i) nucleic acid molecule which is obtainable by screening a suitable nucleic acid library under stringent hybridization conditions with a probe comprising one of the sequences of the nucleic acid molecule of (a) to (k) or with a fragment thereof having at least 15 nt, preferably 20 nt, 30 nt, 50 nt, 100 nt, 200 nt or 500 nt of the nucleic acid molecule characterized in (a) to (k) and conferring an altered metabolic activity in an organism or a part thereof.

or comprising a sequence which is complementary thereto.

0013.0.1 As used herein, the term "metabolite" refers to intermediate substances, preferably such of low molecular weight, which occur during anabolism and catabolism in a cell or plant, in other words a substance produced or concumed by metabolism.

0014.0.1 The term "altered metabolic activity" refers to the change (increase oe decrease) of the amount, concentration or activity (meaning here the effective concentration for the purposes of chemical reactions and other mass action) of a metabolite in a specific volume relative to a corresponding volume (e.g. in an organism, a tissue, a cell or a cell compartment) of a control, reference or wild type, including the de novo creation of the activity or expression, measured for example by one of the methods described herein below, which is changed (increased or decreased) as compared to a corresponding non transformed wild type plant cell.

0015.0.2 The terms "increased", "rised", "extended", "enhanced", "improved" or "amplified" relate to a corresponding change of a property in an organism, a part of an organism such as a tissue, seed, root, leave, flower etc. or in a cell and are interchangeable. Preferrably, the overall activity in the volume is increased or enhanced in cases if the increase or enhancement is related to the increase or enhancement of an activity of a gene product, independent whether the amount of gene product or the specific activity of the gene product or both is increased or enhanced or whether the amount, stability or translation efficacy of the nucleic acid sequence or gene encoding for the gene product is increased or enhanced. The terms "reduction", "decrease" or "deletion" relate to a corresponding change of a property in an organism, a part of an organism such as a tissue, seed, root, leave, flower etc. or in a cell. Preferrably, the overall activity in the volume is reduced, decreased or deleted in cases if the reduction, decrease or deletion is related to the reduction, decrease or deletion of an activity of a gene product, independent whether the amount of gene product or the specific activity of the gene product or both is reduced, decreased or

deleted or whether the amount, stability or translation efficacy of the nucleic acid sequence or gene encoding for the gene product is reduced, decreased or deleted.

0016.0.2 The terms "increase" or "decrease" relate to a corresponding change of a property in an organism or in a part of an organism, such as a tissue, seed, root, leave, flower etc. or in a cell. Preferrably, the overall activity in the volume is increased in cases the increase relates to the increase of an activity of a gene product, independent whether the amount of gene product or the specific activity of the gene product or both is increased or generated or whether the amount, stability or translation efficacy of the nucleic acid sequence or gene encoding for the gene product is increased.

0017.0.2 Under "change of a property" it is understood that the activity, expression level or amount of a gene product or the metabolite content is changed in a specific volume relative to a corresponding volume of a control, reference or wild type, including the de novo creation of the activity or expression.

0018.0.2 The terms "increase" or "decrease" include the change of said property in only parts of the subject of the present invention, for example, the modification can be found in compartment of a cell, like a organelle, or in a part of a plant, like tissue, seed, root, leave, flower etc. but is not detectable if the overall subject, i.e. complete cell or plant, is tested. Preferably, the increase or decrease is found cellular, thus the term "increase of an acitivity" or "increase of a metabolite content" relates to the cellular increase compared to the wild typ cell.

0019.0.2 Accordingly, the term "increase" or "decrease" means that the specific activity of an enzyme as well as the amount of a compound or metabolite, e.g. of a polypeptide, a nucleic acid molelcule or of the fine chemical of the invention or an encoding mRNA or DNA, can be increased or decreased in a volume.

0020.0.2 The terms "wild type", "control" or "reference" are exchangeable and can be a cell or a part of organisms such as an organelle or a tissue, or an organism, in particular a microorganism or a plant, which was not modified or treated according to the herein described process according to the invention. Accordingly, the cell or a part of organisms such as an organelle or a tissue, or an organism, in particular a microorganism or a plant used as wild typ, control or reference corresponds to the cell, organism or part thereof as much as possible and is in any other property but in the result of the process of the invention as identical to the subject matter of the invention as possible. Thus, the wild type, control or reference is treated identically or as identical as possible, saying that only conditions or properties might be different which do not influence the quality of the tested property.

0021.0.2 Preferably, any comparison is carried out under analogous conditions. The term "analogous conditions" means that all conditions such as, for example, culture or growing conditions, assay conditions (such as buffer composition, temperature, substrates, pathogen strain, concentrations and the like) are kept identical between the experiments to be compared.

0022.0.2 The "reference", "control", or "wild type" is preferably a subject, e.g. an organelle, a cell, a tissue, an organism, in particular a plant or a microorganism, which was not modified or treated according to the herein described process of the invention and is in any other property as similar to the subject matter of the invention as possible. The reference, control or wild type is in its genome, transcriptome, proteome or metabolome as similar as possible to the subject of the present invention. Preferably, the term "reference-" "control-" or "wild type-"-organelle, -cell, -tissue or –organism, in particular plant or microorganism, relates to an organelle, cell, tissue or organism, in particular plant or micororganism, which is nearly genetically identical to the organelle, cell, tissue or organism, in particular microorganism or plant, of the present invention or a part thereof preferably 95%, more peferred are 98%, even more preferred are 99,00%, in particular 99,10%, 99,30%, 99,50%, 99,70%, 99,90%, 99,99%, 99, 999% or more. Most preferable the "reference", "control", or "wild type" is a subject, e.g. an organelle, a cell, a tissue, an organism, which is genetically identical to the organism, cell or organelle used according to the process of the invention except that the responsible or acvitivity conferring nucleic acid molecules or the gene product encoded by them are amended, manipulated, exchanged or introduced according to the inventive process.

0023.0.2 Preferably, the reference, control or wild type differs form the subject of the present invention only in the cellular activity of the polypeptide of the invention, e.g. as result of an increase in the level of the nucleic acid molecule of the present invention or an increase of the specific activity of the polypeptide of the invention, e.g. by or in the expression level or activity of an protein having the activity of an Stress-Related Protein (SRP) or its homologs, its biochemical or genetical causes and the altered metabolic activity.

0024.0.2 In case, a control, reference or wild type differing from the subject of the present invention only by not being subject of the process of the invention can not be provided, a control, reference or wild type can be an organism in which the cause for the modulation of an activity conferring the altered metabolic activity or expression of the nucleic acid molecule of the invention as described herein has been switched back or off, e.g. by knocking out the expression of responsible gene product, e.g. by antisense inhibition, by inactivation of an activator or agonist, by activation of an

inhibitor or antagonist, by inhibition through adding inhibitory antibodies, by adding active compounds as e.g. hormones, by introducing negative dominant mutants, etc. A gene production can for example be knocked out by introducing inactivating point mutations, which lead to an enzymatic activity inhibition or a destabilization or an inhibition of the ability to bind to cofactors etc.

0025.0.2 Accordingly, preferred reference subject is the starting subject of the present process of the invention. Preferably, the reference and the subject matter of the invention are compared after standardization and normalization, e.g. to the amount of total RNA, DNA, or protein or activity or expression of reference genes, like housekeeping genes, such as ubiquitin, actin or ribosomal proteins.

0026.0.2 A series of mechanisms exists via which a modification of the a protein, e.g. the polypeptide of the invention can directly or indirectly affect the yield, production and/or production efficiency of the amino acid.

0027.0.2 For example, the molecule number or the specific activity of the polypeptide or the nucleic acid molecule may be increased. Larger amounts of the fine chemical can be produced if the polypeptide or the nucleic acid of the invention is expressed *de novo* in an organism lacking the activity of said protein. However, it is also possible to increase the expression of the gene which is naturally present in the organisms, for example by modifying the regulation of the gene, or by increasing the stability of the corresponding mRNA or of the corresponding gene product encoded by the nucleic acid molecule of the invention, or by introducing homologous genes from other organisms which are differently regulated, eg. not feedback sensitive.

0028.0.2 This also applies analogously to the combined increased expression of the nucleic acid molecule of the present invention or its gene product with that of further enzymes of the amino acid biosynthesis pathways, e.g. which are useful for the synthesis of the fine chemicals.

0029.0.2 The increase, decrease or modulation according to this invention can be constitutive, e.g. due to a stable permanent transgenic expression or to a stable mutation in the corresponding endogenous gene encoding the nucleic acid molecule of the invention or to a modulation of the expression or of the behaviour of a gene conferring the expression of the polypeptide of the invention, or transient, e.g. due to an transient transformation or temporary addition of a modulator such as a agonist or antagonist or inducible, e.g. after transformation with a inducible construct carrying the nucleic acid molecule of the invention under control of a induceable promoter and adding the inducer, e.g. tetracycline or as described herein below.

0030.0.2 The increase in activity of the polypeptide amounts in a cell, a tissue, a organelle, an organ or an organism or a part thereof preferably to at least 5%,

preferably to at least 20% or at to least 50%, especially preferably to at least 70%, 80%, 90% or more, very especially preferably are to at least 200%, most preferably are to at least 500% or more in comparison to the control, reference or wild type.

0031.0.2 The specific activity of a polypeptide encoded by a nucleic acid molecule of the present invention or of the polypeptide of the present invention can be tested as described in the examples. In particular, the expression of a protein in question in a cell, e.g. a plant cell or a microorganism and the detection of an increase the fine chemical level in comparison to a control is an easy test and can be performed as described in the state of the art.

0032.0.2 The term "increase" includes, that a compound or an activity is introduced into a cell *de novo* or that the compound or the activity has not been detectable before, in other words it is "generated".

0033.0.2 Accordingly, in the following, the term "increasing" also comprises the term "generating" or "stimulating". The increased activity manifests itself in an increase of the fine chemical.

0034.0.1 The transformed plant cells are compared to the corresponding non-transformed wild type of the same genus and species under otherwise identical conditions (such as, for example, culture conditions, age of the plants and the like). In this context, a change in metabolic activity of at least 10%, advantageously of at least 20%, preferably at least 30%, especially preferably of at least 40%, 50% or 60%, very especially preferably of at least 70%, 80%, 90%, 95% or even 100% or more, in comparison with the non-transformed organism is advantageous.

0035.0.1 Preferably the change in metabolite concentration of the transformed plant cells is the changed compared to the corresponding non-transformed wild type. Preferably the change in metabolite concentration is measured by HPLC and calculated by dividing the peak height or peak area of each analyte (metabolite) through the peak area of the respective internal standards. Data is normalised using the individual sample fresh weight. The resulting values are divided by the mean values found for wild type plants grown under control conditions and analysed in the same sequence, resulting in the so-called ratios, which represent values independent of the analytical sequence. These ratios indicate the behavior of the metabolite concentration of the transformed plants in comparison to the concentration in the wild type control plants.

0036.0.1 According to this method, the change in at least one metabolite concentration of the transformed plant cells compared to the corresponding non-transformed wild type is at least 10%, advantageously of at least 20%, preferably at

least 40%, 60% or 80%, especially preferably of at least 90%, 100% or 200%, very especially preferably of at least 700%, 800%, 900% 1000% or more.

0037.0.1 Data significance can be determinated by all statistical methods known by a person skilled in the art, preferably by a t-test, more preferablye by the student t-test.

0038.0.1 Altered metabolic activity also refers to metabolites that, compared to a corresponding non transformed wild type plant cell, are not produced after transformation or are only produced after transformation.

0039.0.1 Preferred metabolites of the invention are 2,3-dimethyl-5-phytylquinol or 2-hydroxy-palmitic acid or 3,4-dihydroxyphenylalanine (= dopa) or 3-hydroxy-palmitic acid or 5-oxoproline or alanine or alpha linolenic acid (c18:3 (c9, c12, c15)) or alpha-tocopherol or aminoadipic acid or anhydroglucose or arginine or aspartic acid or beta-apo-8' carotenal or beta-carotene or beta-sitosterol or beta-tocopherol or (delta-7-cis,10-cis)-hexadecadienic acid or hexadecatrienic acid or margaric acid or delta-15-cis-tetracosenic acid or ferulic acid or campesterol or cerotic acid (c26:0) or citrulline or cryptoxanthine or eicosenoic acid (20:1) or fructose or fumarate or galactose or gamma-aminobutyric acid or gamma-tocopherol or gluconic acid or glucose or glutamic acid or glutamine or glycerate or glycerinaldehyd or glycerol or glycerol-3-phosphate or glycine or homoserine or inositol or isoleucine or iso-maltose or isopentenyl pyrophosphate or leucine or lignoceric acid (c24:0) or linoleic acid (c18:2 (c9, c12)) or luteine or lycopene or malate or mannose or methionine or methylgalactofuranoside or methylgalactopyranoside or methylgalactopyranoside or palmitic acid (c16:0) or phenylalanine or phosphate or proline or putrescine or pyruvat or raffinose or ribonic acid or serine or shikimate or sinapine acid or stearic acid (c18:0) or succinate or sucrose or threonine or triacontanoic acid or tryptophane or tyrosine or ubichinone or udp-glucose or valine or zeaxanthine.

0040.0.1 Metabolic activity may also be altered concerning one or more derivates of one or more of the above metabolites.

0041.0.1 Preferably metabolic activity is altered concerning one or more metabolites selected from the group consisting of all of the above metabolites.

0042.0.1 Alternatively metabolic activity may be altered concerning one or more metabolites selected from the group consisting of mannose, inositol, phosphate, aspartic acid, isoleucine, leucine, gamma-aminobutyric acid, glycerinaldehyd, sucrose, campesterol, valine, beta-tocopherol,. ubichinone, palmitic acid (c16:0), 2-hydroxy-palmitic acid, 2,3-dimethyl-5-phytylquinol, beta-carotene, alpha-linolenic acid (c18:3 (c9, c12, c15)), lycopene.

0043.0.1 Alternatively metabolic activity may be altered concerning one or more metabolites selected from the group consisting of methylgalactofuranoside, beta-sitosterol, delta-15-cis-tetracosenic acid (c24:1 me), margaric acid (c17:0 me), stearic acid (c18:0), methylgalactopyranoside, gamma-tocopherol, linoleic acid (c18:2 (c9, c12)), hexadecatrienic acid (c16:3 me), shikimate, raffinose, glutamic acid, glutamine, udp-glucose, proline, threonine, isopentenyl pyrophosphate, 5-oxoproline, ferulic acid, sinapine acid.

0044.0.1 Alternatively metabolic activity may be altered concerning one or more metabolites selected from the group consisting of tryptophane, citrulline, serine, alanine, glycerate, arginine, 3-hydroxy-palmitic acid, putrescine, 3,4-dihydroxyphenylalanine (=dopa), alpha-tocopherol, aminoadipic acid, anhydroglucose, beta-apo-8' carotenal, delta-7-cis,10-cis-hexadecadienic acid (c16:2 me), cerotic acid (c26:0), cryptoxanthine, eicosenoic acid (20:1), fructose, fumarate.

0045.0.1 Alternatively metabolic activity may be altered concerning one or more metabolites selected from the group consisting of galactose, gluconic acid, glucose, glycerol, glycerol-3-phosphate, glycine, homoserine, iso-maltose, lignoceric acid (c24:0), luteine, malate, triacontanoic acid, methionine, phenylalanine, pyruvate, ribonic acid, succinate, tyrosine, zeaxanthine.

0046.0.1 The present invention provides a transgenic plant cell, wherein expression of said nucleic acid sequence in the plant cell results altered metabolic activity leading to increased tolerance and/or resistance to environmental stress as compared to a corresponding non-transformed wild type plant cell. One preferred wild type plant cell is a non-transformed Arabidopsis plant cell. An example here is the Arabidopsis wild type C24 (Nottingham Arabidopsis Stock Centre, UK; NASC Stock N906).

0047.0.1 Other preferred wild type plant cells are a non-transformed from plants selected from the group consisting of maize, wheat, rye, oat, triticale, rice, barley, soybean, peanut, cotton, rapeseed, canola, manihot, pepper, sunflower, flax, borage, safflower, linseed, primrose, rapeseed, turnip rape, tagetes, solanaceous plants, potato, tobacco, eggplant, tomato, Vicia species, pea, alfalfa, coffee, cacao, tea, Salix species, oil palm, coconut, perennial grass and forage crops.

0048.0.1 More preferred wild type plant cells are a non-transformed Linum plant cell, preferably Linum usitatissimum, more preferably the variety Brigitta, Golda, Gold Merchant, Helle, Juliel, Olpina, Livia, Marlin, Maedgold, Sporpion, Serenade, Linus, Taunus, Lifax or Liviola, a non-transformed Heliantus plant cell, preferably Heliantus annuus, more preferably the variety Aurasol, Capella, Flavia, Flores, Jazzy, Palulo, Pegasol, PIR64A54, Rigasol, Sariuca, Sideral, Sunny, Alenka, Candisol or Floyd, or a

non-transformed Brassica plant cell, preferably Brassica napus, more preferably the variety Dorothy, Evita, Heros, Hyola, Kimbar, Lambada, Licolly, Liconira, Licosmos, Lisonne, Mistral, Passat, Serator, Siapula, Sponsor, Star, Caviar, Hybridol, Baical, Olga, Lara, Doublol, Karola, Falcon, Spirit, Olymp, Zeus, Libero, Kyola, Licord, Lion, Lirajet, Lisbeth, Magnum, Maja, Mendel, Mica, Mohican, Olpop, Ontarion, Panthar, Prinoe, Pronio, Susanna, Talani, Titan, Transfer, Wiking, Woltan, Zeniah, Artus, Contact or Smart.

0049.0.1 The expression of said nucleic acid sequence in the plant cell may directly or indirectly influence the metabolic activity of the transformed plant cells. Preferably they influence the activity of the above metabolites.

0050.0.1 Preferably metabolic activity may be altered by transformation with one or more Stress-Related Protein (SRP) coding nucleic acid selected from the group comprising the nucleic acid of Fig. 1a, 1b or 1cb homologs of the afore mentioned sequences.

0051.0.1 It is within the scope of the invention to identify the genes encoded by a nucleic acid sequence selected from the group consisting of the nucleic acid of Fig. 1a, 1b or 1c and/or homologs thereof in target plants, especially crop plants, and then express the corresponding gene to achieve the altered metabolic activity resulting in increased tolerance and/or resistance to environmental stress. Consequently the invention is not limited to a specific plant.

0052.0.2 A protein having an activity conferring an altered metabolic activity preferably has the structure of the polypeptide described herein, in particular of the polypeptides comprising the consensus sequence shown in Fig. 2 or of the polypeptide as shown in Fig. 1a, 1b or 1c or the functional homologues thereof as described herein, or is encoded by the nucleic acid molecule characterized herein or the nucleic acid molecule according to the invention, for example by the nucleic acid molecule as shown in Fig. 1a, 1b or 1c or its herein described functional homologues and has the herein mentioned activity.

0053.0.1 It is further possible to detect environmental stress in plant cells or plants by screening the plant cells for altered metabolic activity as compared to non-stress conditions. This allows for monitoring of stress levels in plants, even when no symptoms are visible. Therefore counter action can be taken ealier and e.g. crop losses minimized by timely watering.

0054.0.1 It is also within the scope of the invention to screen plant cells or plants for increased tolerance and/or resistance to environmental stress by screening the plant cells under stress conditions for altered metabolic activity as compared to non-stress conditions. This allows selection of plants with increased tolerance and/or

resistance to environmental stress without the identification of genes or visual symptoms.

0055.0.1 With the invention it is further possible to breed plant cells or plants towards increased tolerance and/or resistance to environmental stress by screening the plant cells under stress conditions for altered metabolic activity as compared to non-stress conditions and selecting those with increased tolerance and/or resistance to environmental stress. The screening for metabolite activity is faster and easier than e.g. screening for genes.

0056.0.1 Screening is well known to those skilled in the art and generally refers to the search for a particular attribute or trait. In the invention this trait in a plant or plant cell is preferably the concentration of a metabolite, especially prefered the concentration of the above metabolites. The methods and devices for screening are familiar to those skilled in the art and include GC (gas chromatography), LC (liquid chromatography), HPLC (high performance (pressure) liquid chromatography), MS (mass spectrometry), NMR (nuclear magnetic resonance) spectroscopy, IR (infra red) spectroscopy, photometric methods etc and combinations of these methods.

0057.0.1 Breeding is also customary knowledge for those skilled in the art. It is understood as the directed and stable incorporation of a particular attribute or trait into a plant or plant cell.

0058.0.1 The various breeding steps are characterized by well-defined human intervention such as selecting the lines to be crossed, directing pollination of the parental lines, or selecting appropriate progeny plants. Different breeding measures can be taken, depending on the desired properties. All the techniques are well known by a person skilled in the art and include for example, but are not limited to hybridization, inbreeding, backcross breeding, multiline breeding, variety blend, interspecific hybridization, aneuploid techniques, etc. Hybridization techniques also can include the sterilization of plants to yield male or female sterile plants by mechanical, chemical, or biochemical means. Cross pollination of a male sterile plant with pollen of a different line assures that the genome of the male sterile but female fertile plant will uniformly obtain properties of both of the parental lines. The transgenic seeds and plants according to the invention can therefor be used for the breeding of improved plant lines, which can increase the effectiveness of conventional methods such as herbicide or pesticide treatment or which allow one to dispense with said methods due to their modified genetic properties. Alternatively new crops with improved stress tolerance, preferably drought and temperature, can be obtained, which, due to their optimized genetic "equipment", yield harvested product of better quality than products that were not able to tolerate comparable adverse developmental conditions.

0059.0.1 The invention provides that the environmental stress can be salinity, drought, temperature, metal, chemical, pathogenic and oxidative stresses, or combinations thereof, preferably drought and/or temperature.

0060.0.1 The object of the invention is a transgenic plant cell, wherein the SRP (=stress related protein) is selected preferably from yeast, preferably *Saccharomyces cerevisiae*, or *E. coli* or a plant, preferably *Brassica napus*, *Glycine max*, or *Oryza sativa*.

0061.0.1 Object of the invention is also a transgenic plant cell, wherein the SRP coding nucleic acid is at least about 50 % homologous to one of the nucleic acid of Fig. 1a, 1b or 1c.

0062.0.1 In the transgenic plant cell of the invention, the expression of said nucleic acid results in increased tolerance to an environmental stress, which is preferably achieved by altering metabolic activity, as compared to a corresponding non-transformed wild type plant cell. Herein, the environmental stress is selected from the group consisting of salinity, drought, temperature, metal, chemical, pathogenic and oxidative stresses, or combinations thereof, preferably drought and/or temperature.

0063.0.2 The term “expression” refers to the transcription and/or translation of a codogenic gene segment or gene. As a rule, the resulting product is an mRNA or a protein. However, expression products can also include functional RNAs such as, for example, antisense, nucleic acids, tRNAs, snRNAs, rRNAs, RNAi, siRNA, ribozymes etc. Expression may be systemic,local or temporal, for example limited to certain cell types, tissue, sorgans or time periods.

0064.0.2 Unless otherwise specified, the terms “polynucleotides”, “nucleic acid” and “nucleic acid molecule” are interchangeably in the present context. Unless otherwise specified, the terms “peptide”, “polypeptide” and “protein” are interchangeably in the present context. The term “sequence” may relate to polynucleotides, nucleic acids, nucleic acid molecules, peptides, polypeptides and proteins, depending on the context in which the term “sequence” is used. The terms ”gene(s)”, ”polynucleotide”, ”nucleic acid sequence”, ”nucleotide sequence”, or ”nucleic acid molecule(s)” as used herein refers to a polymeric form of nucleotides of any length, either ribonucleotides or deoxyribonucleotides. The terms refer only to the primary structure of the molecule.

0065.0.2 Thus, the terms ”gene(s)”, ”polynucleotide”, ”nucleic acid sequence”, ”nucleotide sequence”, or ”nucleic acid molecule(s)” as used herein include double- and single-stranded DNA and RNA. They also include known types of modifications, for example, methylation, ”caps”, substitutions of one or more of the naturally occurring

nucleotides with an analog. Preferably, the DNA or RNA sequence of the invention comprises a coding sequence encoding the herein defined polypeptide.

0066.0.2 A "coding sequence" is a nucleotide sequence, which is transcribed into mRNA and/or translated into a polypeptide when placed under the control of appropriate regulatory sequences. The boundaries of the coding sequence are determined by a translation start codon at the 5'-terminus and a translation stop codon at the 3'-terminus. A coding sequence can include, but is not limited to mRNA, cDNA, recombinant nucleotide sequences or genomic DNA, while introns may be present as well under certain circumstances.

0067.0.2 For the purposes of the invention, as a rule the plural is intended to encompass the singular and vice versa.

0068.0.1 Further, the transgenic plant cell is derived from a monocotyledonous plant. Alternativ, the transgenic plant cell is derived from a dicotyledonous plant. Preferably, the transgenic plant cell is selected from the group consisting of maize, wheat, rye, oat, triticale, rice, barley, soybean, peanut, cotton, rapeseed, canola, manihot, pepper, sunflower, flax, borage, sufflower, linseed, primrose, rapeseed, turnip rape, tagetes, solanaceous plants, potato, tabacco, eggplant, tomato, Vicia species, pea, alfalfa, coffee, cacao, tea, Salix species, oil palm, coconut, perennial grass, forage crops and Arabidopsis thaliana. Moreover, the transgenic plant cell of the present invention can be derived from a gymnosperm plant. Preferably, the plant is selected from the group of spruce, pine and fir.

0069.0.1 The invention further provides a seed produced by a transgenic plant transformed by a SRP coding nucleic acid, wherein the plant is true breeding for increased tolerance to environmental stress, which is preferably achieved by altering metabolic activity, as compared to a wild type plant cell. The transgenic plant might be a monocot, a dicot or a gymnosperm plant. The invention further provides a seed produced by a transgenic plant expressing an SRP wherein the plant is true breeding for increased tolerance to environmental stress, which is preferably achieved by altering metabolic activity, as compared to a wild type plant cell. The invention pertains to a seed produced by a transgenic plant, wherein the seed is genetically homozygous for a transgene conferring an increased tolerance to environmental stress, which is preferably achieved by altering metabolic activity, as compared to a wild type plant.

0070.0.1 The invention further provides an agricultural product produced by any of the below-described transgenic plants, plant parts such as leafs, petal, anther, roots, tubers, stems, buds, flowers or seeds. The invention further provides a isolated recombinant expression vector comprising a SRP encoding nucleic acid.

0071.0.1 The invention further provides a method of producing a transgenic plant with a SRP coding nucleic acid, wherein expression of the nucleic acid in the plant results in increased tolerance and/or resistance to an environmental stress, which is preferably achieved by altering metabolic activity, as compared to a corresponding non-transformed wild type plant cell, comprising

a) transforming a plant cell with an expression vector including a SRP encoding nucleic acid selected from the group comprising the nucleic acid of Fig. 1a, 1b or 1c and/or homologs or parts thereof and

b) generating from the plant cell a transgenic plant with an increased tolerance to environmental stress as compared to a corresponding non-transformed wild type plant.

0072.0.1 With regard to invention described here, "transformed or transgene" means all those plants or parts thereof which have been brought about by genetic manipulation methods and in which either

c) one or more genes, preferably encoded by one or more nucleic acid sequences as depicted in Fig. 1a, 1b or 1c and/or a homolog thereof, or

d) a genetic regulatory element, for example a promoter, which is functionally linked e.g. to the nucleic acid sequence as depicted in Fig. 1a, 1b or 1c and/or a homolog thereof, or

e) (a) and (b)

is/are not present in its/their natural genetic environment or has/have been modified by means of genetic manipulation methods, it being possible for the modification to be, by way of example, a substitution, addition, deletion, inversion or insertion of one or more nucleotide radicals.

0073.0.1 "Natural genetic environment" means the natural chromosomal locus in the organism of origin or the presence in a genomic library. In the case of a genomic library, the natural, genetic environment of the nucleic acid sequence is preferably at least partially still preserved. The environment flanks the nucleic acid sequence at least on one side and has a sequence length of at least 50 bp, preferably at least 500 bp, particularly preferably at least 1000 bp, very particularly preferably at least 5000 bp.

0074.0.1 In said method for producing a transgenic plant comprising an SRP, the SRP coding nucleic acid is selected from the group comprising the nucleic acid of Fig. 1a, 1b or 1c and/or homologs of the afore mentioned sequences. Further, the SRP coding nucleic acid used in the said method is at least about 50% homologous to one of the nucleic acid of Fig. 1a, 1b or 1c.

0075.0.1 A plant or plant cell is considered "true breeding" for a particular trait if it is genetically homozygous for that trait to the extent that, when the true-breeding plant is self-pollinated, a significant amount of independent segregation of the trait among the progeny is not observed. In the present invention, the trait arises from the transgenic expression of one or more DNA sequences introduced into a plant cell or plant.

0076.0.1 The present invention also provides methods of modifying stress tolerance of a plant comprising, modifying the level of expression of a SRP nucleic acid in the plant. The invention provides one method of producing a transgenic plant with a synthetic, novel or modified transcription factor that acts by increasing the transcription of a SRP gene. Theoretically it is also possible to obtain a decrease in expression of the gene.

0077.0.1 A method of detecting environmental stress in plant cells or plants comprising screening the plant cells for altered metabolic activity as compared to non-stress conditions is also in the scope of the invention.

0078.0.1 Further a method of screening plant cells or plants for increased tolerance and/or resistance to environmental stress comprising screening the plant cells under stress conditions for altered metabolic activity as compared to non-stress conditions is encompassed in the invention.

0079.0.1 The present invention also encloses a method of breeding plant cells or plants towards increased tolerance and/or resistance to environmental stress comprising screening the plant cells under stress conditions for altered metabolic activity as compared to non-stress conditions and selecting those with increased tolerance and/or resistance to environmental stress.

0080.0.1 In these methods metabolite activity is preferably altered concerning the above metabolites and groups of metabolites.

0081.0.1 The present invention also encompasses the use of altered metabolic activity and/or a SRP encoding nucleic acid selected from the group comprising the nucleic acid of Fig. 1a, 1b or 1c and/or homologs of the afore mentioned sequences or parts thereof as markers for selection of plants or plant cells with increased tolerance to environmental stress.

0082.0.1 The present invention further encompasses the use of altered metabolic activity and/or a SRP encoding nucleic acid selected from the group comprising the nucleic acid of Fig. 1a, 1b or 1c and/or homologs of the afore mentioned sequences or parts thereof as markers for detection of stress in plants or plant cells.

0083.0.1 The present invention also provides methods of modifying stress tolerance of a crop plant comprising utilizing a SRP coding nucleic acid sequence to

identify individual plants in populations segregating for either increased or decreased environmental stress tolerance (DNA marker).

0084.0.1 In the said method of modifying stress tolerance of a plant the SRP encoding nucleic acid may be selected from the group comprising the nucleic acid of Fig. 1a, 1b or 1c and/or homologs of the afore mentioned sequences. Further the SRP coding nucleic acid used therein may at least about 50% homologous to one of the nucleic acid of Fig. 1a, 1b or 1c. Also an expression vector as described in the present invention might be used in the said method.

0085.0.1 In a variant method of said method of modifying stress tolerance, the plant is transformed with an inducible promoter that directs expression of the SRP. For example, the promoter is tissue specific. In a variant method, the used promoter is developmentally regulated.

0086.0.2 In a further embodiment, the method of modifying stress tolerance comprises one or more of the following steps:

a) stabilizing a protein conferring the increased expression of a protein encoded by the nucleic acid molecule of the invention or of the polypeptid of the invention having the herein-mentioned activity of altering the metabolic activity;

b) stabilizing a mRNA conferring the increased expression of a protein encoded by the nucleic acid molecule of the invention or its homologs or of a mRNA encoding the polypeptide of the present invention having the herein-mentioned activity of altering the metabolic activity;

c) increasing the specific activity of a protein conferring the increasd expression of a protein encoded by the nucleic acid molecule of the invention or of the polypeptide of the present invention or decreasing the inhibitiory regulation of the polypeptide of the invention;

d) generating or increasing the expression of an endogenous or artificial transcription factor mediating the expression of a protein conferring the increased expression of a protein encoded by the nucleic acid molecule of the invention or of the polypeptide of the invention having the herein-mentioned activity of altering the metabolic activity;

e) stimulating activity of a protein conferring the increased expression of a protein encoded by the nucleic acid molecule of the present invention or a polypeptide of the present invention having the herein-mentioned activity of altering the metabolic activity by adding one or more exogenous inducing factors to the organismus or parts thereof;

f) expressing a transgenic gene encoding a protein conferring the increased expression of a polypeptide encoded by the nucleic acid molecule of the present invention or a polypeptide of the present invention, having the herein-mentioned activity of altering the metabolic activity; and/or

g) increasing the copy number of a gene conferring the increased expression of a nucleic acid molecule encoding a polypeptide encoded by the nucleic acid molecule of the invention or the polypeptide of the invention having the herein-mentioned activity of altering the metabolic activity;

h) increasing the expression of the endogenous gene encoding the polypeptide of the invention or its homologs by adding positive expression or removing negative expression elements, e.g. homologous recombination can be used to either introduce positive regulatory elements like for plants the 35S enhancer into the promoter or to remove repressor elements form regulatory regions. Further gene conversion methods can be used to disrupt repressor elements or to enhance to acitivty of positive elements-positive elements can be randomly introduced in plants by T-DNA or transposon mutagenesis and lines can be identified in which the positive elements have be integrated near to a gene of the invention, the expression of which is thereby enhanced; and/or

i) modulating growth conditions of the plant in such a manner, that the expression or activity of the gene encoding the protein of the invention or the protein itself is enhanced;

j) selecting of organisms with expecially high activity of the proteins of the invention from natural or from mutagenized resources and breeding them into the target organisms, eg the elite crops.

0087.0.2 Preferably, said mRNA is the nucleic acid molecule of the present invention and/or the protein conferring the increased expression of a protein encoded by the nucleic acid molecule of the present invention or the polypeptide having the herein mentioned activity is the polypeptide of the present invention, e.g. conferring increased tolerance to environmental stress by altering the metabolic activity.

0088.0.2 In general, the amount of mRNA, polynucleotide or nucleic acid molecule in a cell or a compartment of an organism correlates with the amount of encoded protein and thus with the overall activity of the encoded protein in said volume. Said correlation is not always linear, the activity in the volume is dependent on the stability of the molecules, the degradation of the molecules or the presence of

activating or inhibiting co-factors. Further, product and educt inhibitions of enzymes are well known, e.g. Zinser et al. "Enzyminhibitoren / Enzyme inhibitors".

0089.0.2 The activity of the abovementioned proteins and/or poylpeptide encoded by the nucleic acid molecule of the present invention can be increased in various ways. For example, the activity in an organism or in a part thereof, like a cell, is increased via increasing the gene product number, e.g. by increasing the expression rate, like introducing a stronger promoter, or by increasing the stability of the mRNA expressed, thus increasing the translation rate, and/or increasing the stability of the gene product, thus reducing the proteins decayed. Further, the activity or turnover of enzymes can be influenced in such a way that a reduction or increase of the reaction rate or a modification (reduction or increase) of the affinity to the substrate results, is reached. A mutation in the catalytic centre of an polypeptide of the invention, e.g. as enzyme, can modulate the turn over rate of the enzyme, e.g. a knock out of an essential amino acid can lead to a reduced or completely knock out activity of the enzyme, or the deletion or mutation of regulator binding sites can reduce a negative regulation like a feedback inhibition (or a substrate inhibition, if the substrate level is also increased). The specific activity of an enzyme of the present invention can be increased such that the turn over rate is increased or the binding of a co-factor is improved. Improving the stability of the encoding mRNA or the protein can also increase the activity of a gene product. The stimulation of the activity is also under the scope of the term "increased activity".

0090.0.2 Moreover, the regulation of the abovementioned nucleic acid sequences may be modified so that gene expression is increased. This can be achieved advantageously by means of heterologous regulatory sequences or by modifying, for example mutating, the natural regulatory sequences which are present. The advantageous methods may also be combined with each other.

0091.0.2 In general, an activity of a gene product in an organism or part thereof, in particular in a plant cell, a plant, or a plant tissue or a part thereof or in a microorganism can be increased by increasing the amount of the specific encoding mRNA or the corresponding protein in said organism or part thereof. "Amount of protein or mRNA" is understood as meaning the molecule number of polypeptides or mRNA molecules in an organism, a tissue, a cell or a cell compartment. "Increase" in the amount of a protein means the quantitative increase of the molecule number of said protein in an organism, a tissue, a cell or a cell compartment or part thereof - for example by one of the methods described herein below - in comparison to a wild type, control or reference.

0092.0.2 The increase in molecule number amounts preferably to at least 1%, preferably to more than 10%, more preferably to 30% or more, especially preferably to

50%, 70% or more, very especially preferably to 100%, most preferably to 500% or more. However, a de novo expression is also regarded as subject of the present invention.

0093.0.2 A modification, i.e. an increase or decrease, can be caused by endogenous or exogenous factors. For example, an increase in activity in an organism or a part thereof can be caused by adding a gene product or a precursor or an activator or an agonist to the media or nutrition or can be caused by introducing said subjects into a organism, transient or stable.

0094.0.2 In one embodiment the increase or decrease in metabolic activity in the plant or a part thereof, e.g. in a cell, a tissue, a organ, an organelle etc., is achieved by increasing the endogenous level of the polypeptide of the invention. Accordingly, in an embodiment of the present invention, the present invention relates to a process wherein the gene copy number of a gene encoding the polynucleotide or nucleic acid molecule of the invention is increased. Further, the endogenous level of the polypeptide of the invention can for example be increased by modifiying the transcriptional or translational regulation of the polypeptide.

0095.0.2 In one embodiment the metabolic activity in the plant or part thereof can be altered by targeted or random mutagenesis of the endogenous genes of the invention. For example homologous recombination can be used to either introduce positive regulatory elements like for plants the 35S enhancer into the promoter or to remove repressor elements form regulatory regions. In addition gene conversion like methods described by Kochevenko and Willmitzer (Plant Physiol. 2003 May;132(1):174-84) and citations therein can be used to disrupt repressor elements or to enhance to acitivty of positive regulatory elements. Furthermore positive elements can be randomly introduced in (plant) genomes by T-DNA or transposon mutagenesis and lines can be screened for, in which the positive elements has be integrated near to a gene of the invention, the expression of which is thereby enhanced. The activation of plant genes by random integrations of enhancer elements has been described by Hayashi et al., 1992 (Science 258:1350-1353) or Weigel et al., 2000 (Plant Physiol. 122, 1003-1013) and others citated therein.

0096.0.2 Reverse genetic strategies to identify insertions (which eventually carrying the activation elements) near in genes of interest have been described for various cases eg. Krysan et al., 1999 (Plant Cell 1999, 11, 2283-2290); Sessions et al., 2002 (Plant Cell 2002, 14, 2985-2994); Young et al., 2001, (Plant Physiol. 2001, 125, 513-518); Koprek et al., 2000 (Plant J. 2000, 24, 253-263) ; Jeon et al., 2000 (Plant J. 2000, 22, 561-570) ; Tissier et al., 1999 (Plant Cell 1999, 11, 1841-1852); Speulmann et al., 1999 (Plant Cell 1999 ,11 , 1853-1866). Briefly material from all plants of a large

T-DNA or transposon mutagenized plant population is harvested and genomic DNA prepared. Then the genomic DNA is pooled following specific architectures as described for example in Krysan et al., 1999 (Plant Cell 1999, 11, 2283-2290). Pools of genomics DNAs are then screened by specific multiplex PCR reactions detecting the combination of the insertional mutagen (eg T-DNA or Transposon) and the gene of interest. Therefore PCR reactions are run on the DNA pools with specific combinations of T-DNA or transposon border primers and gene specific primers. General rules for primer design can again be taken from Krysan et al., 1999 (Plant Cell 1999, 11, 2283-2290) Rescreening of lower levels DNA pools lead to the identifcation of individual plants in which the gene of interest is activated by the insertional mutagen.

0097.0.2 The enhancement of positive regulatory elements or the disruption or weaking of negative regulatory elements can also be achieved through common mutagenesis techniques: The production of chemically or radiation mutated populations is a common technique and known to the skilled worker. Methods for plants are described by Koorneef et al. 1982 and the citations therein and by Lightner and Caspar in "Methods in Molecular Biology" Vol 82. These techniques usually induce pointmutations that can be identified in any known gene using methods such as TILLING (Colbert et al. 2001).

0098.0.2 Accordingly, the expression level can be increased if the endogenous genes encoding a polypeptide conferring an increased expression of the polypeptide of the present invention, in particular genes comprising the nucleic acid molecule of the present invention, are modified via homologous recombination, Tilling approaches or gene conversion

0099.0.2 Regulatory sequences can be operatively linked to the coding region of an endogenous protein and control its transcription and translation or the stability or decay of the encoding mRNA or the expressed protein. In order to modify and control the expression, promoter, UTRs, splicing sites, processing signals, polyadenylation sites, terminators, enhancers, repressors, post transcriptional or posttranslational modification sites can be changed, added or amended For example, the activation of plant genes by random integrations of enhancer elements has been described by Hayashi et al., 1992 (Science 258:1350-1353) or Weigel et al., 2000 (Plant Physiol. 122, 1003-1013) and others citated therein. For example, the expression level of the endogenous protein can be modulated by replacing the endogenous promoter with a stronger transgenic promoter or by replacing the endogenous 3'UTR with a 3'UTR, which provides more stablitiy without amending the coding region. Further, the transcriptional regulation can be modulated by introduction of a artifical transcription

factor as described in the examples. Alternative promoters, terminators and UTRs are described below.

0100.0.2 The activation of an endogenous polypeptide having above-mentioned activity, e.g. conferring an increased tolerance to environmental stress after altering the metabolic activity can also be increased by introducing a synthetic transcription factor, which binds close to the coding region of the protein of the invention encoding gene and activates its transcription. A chimeric zinc finger protein can be construed, which comprises a specific DNA-binding domain and an activation domain as e.g. the VP16 domain of Herpes Simplex virus. The specific binding domain can bind to the regulatory region of the protein coding region. The expression of the chimeric transcription factor in a plant leads to a specific expression of the protein of the invention, see e.g. in WO01/52620, Oriz, Proc. Natl. Acad. Sci. USA, 2002, Vol. 99, 13290 or Guan, Proc. Natl. Acad. Sci. USA, 2002, Vol. 99, 13296.

0101.0.2 In one further embodiment of the method according to the invention, plants are used in which one of the abovementioned genes, or one of the abovementioned nucleic acids, is mutated in a way that the activity of the encoded gene products is less influenced by cellular factors, , or not at all, in comparison with the unmutated proteins. For example, well known regulation mechanism of enzymic activity are substrate inhibition or feed back regulation mechanisms. Ways and techniques for the introduction of substitutions, deletions and additions of one or more bases, nucleotides or amino acids of a corresponding sequence are described herein below in the corresponding paragraphs and the references listed there, e.g. in Sambrook et al., Molecular Cloning, Cold Spring Habour, NY, 1989. The person skilled in the art will be able to identify regulation domains and binding sites of regulators by comparing the sequence of the nucleic acid molecule of the present invention or the expression product thereof with the state of the art by computer software means which comprise algorithms for the identifying of binding sites and regulation domains or by introducing into a nucleic acid molecule or in a protein systematically mutations and assaying for those mutations which will lead to an increased specifiy activity or an increased activity per volume, in particular per cell.

0102.0.2 It is therefore adavantageously to express in a plant a nucleic acid molecule of the invention or a polypeptide of the invention derived from a evolutionary distantly related organism, as e.g. using a prokaryotic gene in a eukaryotic host, as in these cases the regulation mechanism of the host cell may not weaken the activity (cellular or specific) of the gene or its expression product

0103.0.2 The mutation is introduced in such a way that the production of the amino acids is not adversely affected..

0104.0.2 Less influence on the regulation of a gene or its gene product is understood as meaning a reduced regulation of the enzymatic activity leading to an increased specific or cellular activity of the gene or its product. An increase of the enzymatic activity is understood as meaning an enzymatic activity, which is increased by at least 10%, advantageously at least 20, 30 or 40%, especially advantageously by at least 50, 60 or 70% in comparison with the starting organism.

0105.0.1 The invention provides that the above methods can be performed such that the stress tolerance is increased. It is also possible to obtain a decrease in stress tolerance.

0106.0.1 The invention is not limited to specific nucleic acids, specific polypeptides, specific cell types, specific host cells, specific conditions or specific methods etc. as such, but may vary and numerous modifications and variations therein will be apparent to those skilled in the art. It is also to be understood that the terminology used herein is for the purpose of describing specific embodiments only and is not intended to be limiting.

0107.0.1 The present invention also relates to isolated Stress Related Proteins (SRP) which are selected from the group comprising the proteins of Fig. 1a, 1b or 1c and/or homologs thereof. Preferably, the isolated Stress Related Proteins (SRP) of the present invention are selected from yeast or E. coli. Further, the present invention is related to isolated Stress Related Protein (SRP) encoding nucleic acids selected from the group comprising the nucleic acid of Fig. 1a, 1b or 1c and/or homologs thereof. Here, preferably, an isolated Stress Related Protein (SRP) encoding nucleic acid encodes an SRP which is selected from yeast or E. coli.

0108.0.1 The present invention provides stress related gene sequences selected from the group consisting of the the nucleic acid of Fig. 1a, 1b or 1c of yeast, preferably from *Saccharomyces cerevisiae* or *E. coli.*

0109.0.1 Homologs of the aforementioned sequences can be isolated advantageously from yeast, fungi, viruses, algae, bacteria, such as Acetobacter (subgen. Acetobacter) aceti; Acidithiobacillus ferrooxidans; Acinetobacter sp.; Actinobacillus sp; Aeromonas salmonicida; Agrobacterium tumefaciens; Aquifex aeolicus; Arcanobacterium pyogenes; Aster yellows phytoplasma; Bacillus sp.; Bifidobacterium sp.; Borrelia burgdorferi; Brevibacterium linens; Brucella melitensis; Buchnera sp.; Butyrivibrio fibrisolvens; Campylobacter jejuni; Caulobacter crescentus; Chlamydia sp.; Chlamydophila sp.; Chlorobium limicola; Citrobacter rodentium; Clostridium sp.; Comamonas testosteroni; Corynebacterium sp.; Coxiella burnetii; Deinococcus radiodurans; Dichelobacter nodosus; Edwardsiella ictaluri; Enterobacter sp.; Erysipelothrix rhusiopathiae; Escherichia coli; Flavobacterium sp.; Francisella

tularensis; Frankia sp. CpI1; Fusobacterium nucleatum; Geobacillus stearothermophilus; Gluconobacter oxydans; Haemophilus sp.; Helicobacter pylori; Klebsiella pneumoniae; Lactobacillus sp.; Lactococcus lactis; Listeria sp.; Mannheimia haemolytica; Mesorhizobium loti; Methylophaga thalassica; Microcystis aeruginosa; Microscilla sp. PRE1; Moraxella sp. TA144; Mycobacterium sp.; Mycoplasma sp.; Neisseria sp.; Nitrosomonas sp.; Nostoc sp. PCC 7120; Novosphingobium aromaticivorans; Oenococcus oeni; Pantoea citrea; Pasteurella multocida; Pediococcus pentosaceus; Phormidium foveolarum; Phytoplasma sp.; Plectonema boryanum; Prevotella ruminicola; Propionibacterium sp.; Proteus vulgaris; Pseudomonas sp.; Ralstonia sp.; Rhizobium sp.; Rhodococcus equi; Rhodothermus marinus; Rickettsia sp.; Riemerella anatipestifer; Ruminococcus flavefaciens; Salmonella sp.; Selenomonas ruminantium; Serratia entomophila; Shigella sp.; Sinorhizobium meliloti; Staphylococcus sp.; Streptococcus sp.; Streptomyces sp.; Synechococcus sp.; Synechocystis sp. PCC 6803; Thermotoga maritima; Treponema sp.; Ureaplasma urealyticum; Vibrio cholerae; Vibrio parahaemolyticus; Xylella fastidiosa; Yersinia sp.; Zymomonas mobilis, preferably Salmonella sp. or Escherichia coli or plants, preferably from yeasts such as from the genera Saccharomyces, Pichia, Candida, Hansenula, Torulopsis or Schizosaccharomyces or plants such as Arabidopsis thaliana, maize, wheat, rye, oat, triticale, rice, barley, soybean, peanut, cotton, borage, sufflower, linseed, primrose, rapeseed, canola and turnip rape, manihot, pepper, sunflower, tagetes, solanaceous plant such as potato, tobacco, eggplant and tomato, Vicia species, pea, alfalfa, bushy plants such as coffee, cacao, tea, Salix species, trees such as oil palm, coconut, perennial grass, such as ryegrass and fescue, and forage crops, such as alfalfa and clover and from spruce, pine or fir for example. More preferably homologs of aforementioned sequences can be isolated from *Saccharomyces cerevisiae, E. coli* or plants, preferably *Brassica napus*, *Glycine max*, or *Oryza sativa*.

0110.0.1 The stress related proteins of the present invention are preferably produced by recombinant DNA techniques. For example, a nucleic acid molecule encoding the protein is cloned into an expression vector, for example in to a binary vector, the expression vector is introduced into a host cell, for example the Arabidopsis thaliana wild type NASC N906 or any other plant cell as described in the examples see below, and the stress related protein is expressed in said host cell. Examples for binary vectors are pBIN19, pBI101, pBinAR, pGPTV, pCAMBIA, pBIB-HYG, pBecks, pGreen or pPZP (Hajukiewicz, P. et al., 1994, Plant Mol. Biol., 25: 989-994 and Hellens et al, Trends in Plant Science (2000) 5, 446–451.).

0111.0.1 Advantageously, the nucleic acid sequences according to the invention or the gene construct together with at least one reporter gene are cloned into an expression cassette, which is introduced into the organism via a vector or directly into the genome. This reporter gene should allow easy detection via a growth, fluorescence, chemical, bioluminescence or resistance assay or via a photometric measurement. Examples of reporter genes which may be mentioned are antibiotic- or herbicide-resistance genes, hydrolase genes, fluorescence protein genes, bioluminescence genes, sugar or nucleotide metabolic genes or biosynthesis genes such as the Ura3 gene, the Ilv2 gene, the luciferase gene, the β-galactosidase gene, the gfp gene, the 2–desoxyglucose–6–phosphate phosphatase gene, the β-glucuronidase gene, β-lactamase gene, the neomycin phosphotransferase gene, the hygromycin phosphotransferase gene or the BASTA (= gluphosinate-resistance) gene. These genes permit easy measurement and quantification of the transcription activity and hence of the expression of the genes. In this way genome positions may be identified which exhibit differing productivity.

0112.0.1 In a preferred embodiment a nucleic acid contruct, for example an expression cassette, comprises upstream, i.e. at the 5' end of the encoding sequence, a promoter and downstream, i.e. at the 3' end, a polyadenylation signal and optionally other regulatory elements which are operably linked to the intervening encoding sequence with the nucleic acid of Fig. 1a, 1b or 1c. By an operable linkage is meant the sequential arrangement of promoter, encoding sequence, terminator and optionally other regulatory elements in such a way that each of the regulatory elements can fulfill its function in the expression of the encoding sequence in due manner. The sequences preferred for operable linkage are targeting sequences for ensuring subcellular localization in plastids. However, targeting sequences for ensuring subcellular localization in the mitochondrium, in the endoplasmic reticulum (= ER), in the nucleus, in oil corpuscles or other compartments may also be employed as well as translation promoters such as the 5' lead sequence in tobacco mosaic virus (Gallie et al., Nucl. Acids Res. 15 (1987), 8693 -8711).

0113.0.1 A nucleic acid construct, for example an expression cassette may, for example, contain a constitutive promoter or a tissue-specific promoter (preferably the USP or napin promoter) the gene to be expressed and the ER retention signal. For the ER retention signal the KDEL amino acid sequence (lysine, aspartic acid, glutamic acid, leucine) or the KKX amino acid sequence (lysine-lysine-X-stop, wherein X means every other known amino acid) is preferably employed.

0114.0.1 For expression in a prokaryotic or eukaryotic host organism, for example a microorganism such as a fungus or a plant the expression cassette is

advantageously inserted into a vector such as by way of example a plasmid, a phage or other DNA which allows optimum expression of the genes in the host organism. Examples of suitable plasmids are: in E. coli pLG338, pACYC184, pBR series such as e.g. pBR322, pUC series such as pUC18 or pUC19, M113mp series, pKC30, pRep4, pHS1, pHS2, pPLc236, pMBL24, pLG200, pUR290, pIN-III^{113}-B1, λgt11 or pBdCI; in Streptomyces pIJ101, pIJ364, pIJ702 or pIJ361; in Bacillus pUB110, pC194 or pBD214; in Corynebacterium pSA77 or pAJ667; in fungi pALS1, pIL2 or pBB116; other advantageous fungal vectors are described by Romanos, M.A. et al., [(1992) „Foreign gene expression in yeast: a review", *Yeast* 8: 423-488] and by van den Hondel, C.A.M.J.J. et al. [(1991) „Heterologous gene expression in filamentous fungi" as well as in More Gene Manipulations in Fungi [J.W. Bennet & L.L. Lasure, eds., pp. 396-428: Academic Press: San Diego] and in „Gene transfer systems and vector development for filamentous fungi" [van den Hondel, C.A.M.J.J. & Punt, P.J. (1991) in: Applied Molecular Genetics of Fungi, Peberdy, J.F. et al., eds., pp. 1-28, Cambridge University Press: Cambridge]. Examples of advantageous yeast promoters are 2µM, pAG-1, YEp6, YEp13 or pEMBLYe23. Examples of algal or plant promoters are pLGV23, pGHlac^{+}, pBIN19, pAK2004, pVKH or pDH51 (see Schmidt, R. and Willmitzer, L., 1988). The vectors identified above or derivatives of the vectors identified above are a small selection of the possible plasmids. Further plasmids are well known to those skilled in the art and may be found, for example, in the book Cloning Vectors (Eds. Pouwels P.H. et al. Elsevier, Amsterdam-New York-Oxford, 1985 , ISBN 0 444 904018). Suitable plant vectors are described inter alia in „Methods in Plant Molecular Biology and Biotechnology" (CRC Press), Ch. 6/7, pp. 71-119. Advantageous vectors are known as shuttle vectors or binary vectors which replicate in E. coli and Agrobacterium.

0115.0.1 By vectors is meant with the exception of plasmids all other vectors known to those skilled in the art such as by way of example phages, viruses such as SV40, CMV, baculovirus, adenovirus, transposons, IS elements, phasmids, phagemids, cosmids, linear or circular DNA. These vectors can be replicated autonomously in the host organism or be chromosomally replicated, chromosomal replication being preferred.

0116.0.1 In a further embodiment of the vector the expression cassette according to the invention may also advantageously be introduced into the organisms in the form of a linear DNA and be integrated into the genome of the host organism by way of heterologous or homologous recombination. This linear DNA may be composed of a linearized plasmid or only of the expression cassette as vector or the nucleic acid sequences according to the invention.

0117.0.1 In a further advantageous embodiment the nucleic acid sequence according to the invention can also be introduced into an organism on its own.

0118.0.1 If in addition to the nucleic acid sequence according to the invention further genes are to be introduced into the organism, all together with a reporter gene in a single vector or each single gene with a reporter gene in a vector in each case can be introduced into the organism, whereby the different vectors can be introduced simultaneously or successively.

0119.0.1 The vector advantageously contains at least one copy of the nucleic acid sequences according to the invention and/or the expression cassette (= gene construct) according to the invention.

0120.0.3 The invention further provides an isolated recombinant expression vector comprising a SRP nucleic acid as described above, wherein expression of the vector in a host cell results in increased tolerance to environmental stress as compared to a wild type variety of the host cell. As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid," which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (e.g., bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (e.g., non-episomal mammalian vectors) are integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they are operatively linked. Such vectors are referred to herein as "expression vectors." In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. In the present specification, "plasmid" and "vector" can be used interchangeably as the plasmid is the most commonly used form of vector. However, the invention is intended to include such other forms of expression vectors, such as viral vectors (e.g., replication defective retroviruses, adenoviruses, and adeno-associated viruses), which serve equivalent functions.

0121.0.3 The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell, which means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis of the host cells to be used for expression, which is operatively linked to the nucleic acid sequence to be expressed. As used herein with respect to a recombinant expression vector, "operatively linked" is intended to mean

that the nucleotide sequence of interest is linked to the regulatory sequence(s) in a manner which allows for expression of the nucleotide sequence (e.g., in an *in vitro* transcription/translation system or in a host cell when the vector is introduced into the host cell). The term "regulatory sequence" is intended to include promoters, enhancers, and other expression control elements (e.g., polyadenylation signals). Such regulatory sequences are described, for example, in Goeddel, Gene Expression Technology: Methods in Enzymology 185, Academic Press, San Diego, CA (1990) and Gruber and Crosby, in: Methods in Plant Molecular Biology and Biotechnology, eds. Glick and Thompson, Chapter 7, 89-108, CRC Press: Boca Raton, Florida, including the references therein. Regulatory sequences include those that direct constitutive expression of a nucleotide sequence in many types of host cells and those that direct expression of the nucleotide sequence only in certain host cells or under certain conditions. It will be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of polypeptide desired, etc. The expression vectors of the invention can be introduced into host cells to thereby produce polypeptides or peptides, including fusion polypeptides or peptides, encoded by nucleic acids as described herein (e.g., SRPs, mutant forms of SRPs, fusion polypeptides, etc.).

0122.0.3 The recombinant expression vectors of the invention can be designed for expression of SRPs in prokaryotic or eukaryotic cells. For example, SRP genes can be expressed in bacterial cells such as *C. glutamicum*, insect cells (using baculovirus expression vectors), yeast and other fungal cells (See Romanos, M.A. et al., 1992, Foreign gene expression in yeast: a review, Yeast 8:423-488; van den Hondel, C.A.M.J.J. et al., 1991, Heterologous gene expression in filamentous fungi, in: More Gene Manipulations in Fungi, J.W. Bennet & L.L. Lasure, eds., p. 396-428: Academic Press: San Diego; and van den Hondel, C.A.M.J.J. & Punt, P.J., 1991, Gene transfer systems and vector development for filamentous fungi, in: Applied Molecular Genetics of Fungi, Peberdy, J.F. et al., eds., p. 1-28, Cambridge University Press: Cambridge), algae (Falciatore et al., 1999, Marine Biotechnology 1(3):239-251), ciliates of the types: Holotrichia, Peritrichia, Spirotrichia, Suctoria, Tetrahymena, Paramecium, Colpidium, Glaucoma, Platyophrya, Potomacus, Pseudocohnilembus, Euplotes, Engelmaniella, and Stylonychia, especially of the genus Stylonychia lemnae with vectors following a transformation method as described in PCT Application No. WO 98/01572, and multicellular plant cells (See Schmidt, R. and Willmitzer, L., 1988, High efficiency *Agrobacterium tumefaciens*-mediated transformation of *Arabidopsis thaliana* leaf and cotyledon explants, Plant Cell Rep. 583-586; Plant Molecular Biology and

Biotechnology, C Press, Boca Raton, Florida, chapter 6/7, S.71-119 (1993); F.F. White, B. Jenes et al., Techniques for Gene Transfer, in: Transgenic Plants, Vol. 1, Engineering and Utilization, eds. Kung und R. Wu, 128-43, Academic Press: 1993; Potrykus, 1991, Annu. Rev. Plant Physiol. Plant Molec. Biol. 42:205-225 and references cited therein) or mammalian cells. Suitable host cells are discussed further in Goeddel, Gene Expression Technology: Methods in Enzymology 185, Academic Press: San Diego, CA (1990). Alternatively, the recombinant expression vector can be transcribed and translated *in vitro*, for example using T7 promoter regulatory sequences and T7 polymerase.

0123.0.3 Expression of polypeptides in prokaryotes is most often carried out with vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion polypeptides. Fusion vectors add a number of amino acids to a polypeptide encoded therein, usually to the amino terminus of the recombinant polypeptide but also to the C-terminus or fused within suitable regions in the polypeptides. Such fusion vectors typically serve three purposes: 1) to increase expression of a recombinant polypeptide; 2) to increase the solubility of a recombinant polypeptide; and 3) to aid in the purification of a recombinant polypeptide by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the recombinant polypeptide to enable separation of the recombinant polypeptide from the fusion moiety subsequent to purification of the fusion polypeptide. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin, and enterokinase.

0124.0.1 By way of example the plant expression cassette can be installed in the pRT transformation vector ((a) Toepfer et al., 1993, Methods Enzymol., 217: 66-78; (b) Toepfer et al. 1987, Nucl. Acids. Res. 15: 5890 ff.).

0125.0.1 Alternatively, a recombinant vector (= expression vector) can also be transcribed and translated in vitro, e.g. by using the T7 promoter and the T7 RNA polymerase.

0126.0.1 Expression vectors employed in prokaryotes frequently make use of inducible systems with and without fusion proteins or fusion oligopeptides, wherein these fusions can ensue in both N-terminal and C-terminal manner or in other useful domains of a protein. Such fusion vectors usually have the following purposes: i.) to increase the RNA expression rate; ii.) to increase the achievable protein synthesis rate; iii.) to increase the solubility of the protein; iv.) or to simplify purification by means of a binding sequence usable for affinity chromatography. Proteolytic cleavage points are also frequently introduced via fusion proteins, which allow cleavage of a portion of the

fusion protein and purification. Such recognition sequences for proteases are recognized, e.g. factor Xa, thrombin and enterokinase.

0127.0.1 Typical advantageous fusion and expression vectors are pGEX [Pharmacia Biotech Inc; Smith, D.B. and Johnson, K.S. (1988) *Gene* 67: 31-40], pMAL (New England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ) which contains glutathione S-transferase (GST), maltose binding protein or protein A.

0128.0.3 In one embodiment, the coding sequence of the SRP is cloned into a pGEX expression vector to create a vector encoding a fusion polypeptide comprising, from the N-terminus to the C-terminus, GST-thrombin cleavage site-X polypeptide. The fusion polypeptide can be purified by affinity chromatography using glutathione-agarose resin. Recombinant PKSRP unfused to GST can be recovered by cleavage of the fusion polypeptide with thrombin.

0129.0.1 Other examples of E. coli expression vectors are pTrc [Amann et al., (1988) *Gene* 69:301-315] and pET vectors [Studier et al., Gene Expression Technology: Methods in Enzymology 185, Academic Press, San Diego, California (1990) 60-89; Stratagene, Amsterdam, The Netherlands].

0130.0.3 Target gene expression from the pTrc vector relies on host RNA polymerase transcription from a hybrid trp-lac fusion promoter. Target gene expression from the pET 11d vector relies on transcription from a T7 gn10-lac fusion promoter mediated by a co-expressed viral RNA polymerase (T7 gn1). This viral polymerase is supplied by host strains BL21(DE3) or HMS174(DE3) from a resident λ prophage harboring a T7 gn1 gene under the transcriptional control of the lacUV 5 promoter.

0131.0.3 One strategy to maximize recombinant polypeptide expression is to express the polypeptide in a host bacteria with an impaired capacity to proteolytically cleave the recombinant polypeptide (Gottesman, S., Gene Expression Technology: Methods in Enzymology 185, Academic Press, San Diego, California (1990) 119-128). Another strategy is to alter the sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in the bacterium chosen for expression, such as C. glutamicum (Wada et al., 1992, Nucleic Acids Res. 20:2111-2118). Such alteration of nucleic acid sequences of the invention can be carried out by standard DNA synthesis techniques.

0132.0.1 Other advantageous vectors for use in yeast are pYepSec1 (Baldari, et al., (1987) *Embo J.* 6:229-234), pMFa (Kurjan and Herskowitz, (1982) *Cell* 30:933-943), pJRY88 (Schultz et al., (1987) *Gene* 54:113-123), and pYES derivatives (Invitrogen Corporation, San Diego, CA). Vectors for use in filamentous fungi are described in: van den Hondel, C.A.M.J.J. & Punt, P.J. (1991) „Gene transfer systems

and vector development for filamentous fungi", in: Applied Molecular Genetics of Fungi, J.F. Peberdy, et al., eds., pp. 1-28, Cambridge University Press: Cambridge.

0133.0.1 Alternatively, insect cell expression vectors can also be advantageously utilized, e.g. for expression in Sf 9 cells. These are e.g. the vectors of the pAc series (Smith et al. (1983) *Mol. Cell Biol.* 3:2156-2165) and the pVL series (Lucklow and Summers (1989) *Virology* 170:31-39).

0134.0.1 Furthermore, plant cells or algal cells can advantageously be used for gene expression. Examples of plant expression vectors may be found in Becker, D., et al. (1992) „New plant binary vectors with selectable markers located proximal to the left border", *Plant Mol. Biol.* 20: 1195-1197 or in Bevan, M.W. (1984) „Binary *Agrobacterium* vectors for plant transformation", *Nucl. Acid. Res.* 12: 8711-8721.

0135.0.1 Furthermore, the nucleic acid sequences may also be expressed in mammalian cells, advantageously in nonhuman mammalian cells. Examples of corresponding expression vectors are pCDM8 and pMT2PC referred to in: Seed, B. (1987) *Nature* 329:840 or Kaufman et al. (1987) *EMBO J.* 6: 187-195). At the same time promoters preferred for use are of viral origin, such as by way of example promoters of polyoma, adenovirus 2, cytomegalovirus or simian virus 40. Other prokaryotic and eukaryotic expression systems are referred to in chapters 16 and 17 of Sambrook et al., *Molecular Cloning: A Laboratory Manual. 2nd, ed., Cold Spring Harbor Laboratory,* Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989.

0136.0.3 In a preferred embodiment of the present invention, the SRPs are expressed in plants and plants cells such as unicellular plant cells (e.g. algae) (See Falciatore et al., 1999, Marine Biotechnology 1(3):239-251 and references therein) and plant cells from higher plants (e.g., the spermatophytes, such as crop plants). A SRP may be "introduced" into a plant cell by any means, including transfection, transformation or transduction, electroporation, particle bombardment, agroinfection, and the like. One transformation method known to those of skill in the art is the dipping of a flowering plant into an *Agrobacteria* solution, wherein the *Agrobacteria* contains the SRP nucleic acid, followed by breeding of the transformed gametes.

0137.0.3 Other suitable methods for transforming or transfecting host cells including plant cells can be found in Sambrook, et al., Molecular Cloning: A Laboratory Manual. 2nd, ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989, and other laboratory manuals such as Methods in Molecular Biology, 1995, Vol. 44, *Agrobacterium* protocols, ed: Gartland and Davey, Humana Press, Totowa, New Jersey. As biotic and abiotic stress tolerance is a general trait wished to be inherited into a wide variety of plants like maize, wheat, rye,

oat, triticale, rice, barley, soybean, peanut, cotton, rapeseed and canola, manihot, pepper, sunflower and tagetes, solanaceous plants like potato, tobacco, eggplant, and tomato, Vicia species, pea, alfalfa, bushy plants (coffee, cacao, tea), Salix species, trees (oil palm, coconut), perennial grasses, and forage crops, these crop plants are also preferred target plants for a genetic engineering as one further embodiment of the present invention. Forage crops include, but are not limited to, Wheatgrass, Canarygrass, Bromegrass, Wildrye Grass, Bluegrass, Orchardgrass, Alfalfa, Salfoin, Birdsfoot Trefoil, Alsike Clover, Red Clover, and Sweet Clover.

0138.0.3 In one embodiment of the present invention, transfection of a SRP into a plant is achieved by *Agrobacterium* mediated gene transfer. *Agrobacterium* mediated plant transformation can be performed using for example the GV3101(pMP90) (Koncz and Schell, 1986, Mol. Gen. Genet. 204:383-396) or LBA4404 (Clontech) *Agrobacterium tumefaciens* strain. Transformation can be performed by standard transformation and regeneration techniques (Deblaere et al., 1994, Nucl. Acids Res. 13:4777-4788; Gelvin, Stanton B. and Schilperoort, Robert A, Plant Molecular Biology Manual, 2nd Ed. - Dordrecht : Kluwer Academic Publ., 1995. - in Sect., Ringbuc Zentrale Signatur: BT11-P ISBN 0-7923-2731-4; Glick, Bernard R.; Thompson, John E., Methods in Plant Molecular Biology and Biotechnology, Boca Raton : CRC Press, 1993 360 S., ISBN 0-8493-5164-2). For example, rapeseed can be transformed via cotyledon or hypocotyl transformation (Moloney et al., 1989, Plant cell Report 8:238-242; De Block et al., 1989, Plant Physiol. 91:694-701). Use of antibiotics for *Agrobacterium* and plant selection depends on the binary vector and the *Agrobacterium* strain used for transformation. Rapeseed selection is normally performed using kanamycin as selectable plant marker. ,*Agrobacterium* mediated gene transfer to flax can be performed using, for example, a technique described by Mlynarova et al., 1994, Plant Cell Report 13:282-285. Additionally, transformation of soybean can be performed using for example a technique described in European Patent No. 0424 047, U.S. Patent No. 5,322,783, European Patent No. 0397 687, U.S. Patent No. 5,376,543, or U.S. Patent No. 5,169,770. Transformation of maize can be achieved by particle bombardment, polyethylene glycol mediated DNA uptake or via the silicon carbide fiber technique. (See, for example, Freeling and Walbot "The maize handbook" Springer Verlag: New York (1993) ISBN 3-540-97826-7). A specific example of maize transformation is found in U.S. Patent No. 5,990,387, and a specific example of wheat transformation can be found in PCT Application No. WO 93/07256.

0139.0.3 According to the present invention, the introduced SRP may be maintained in the plant cell stably if it is incorporated into a non-chromosomal autonomous replicon or integrated into the plant chromosomes. Alternatively, the

introduced SRP may be present on an extra-chromosomal non-replicating vector and be transiently expressed or transiently active.

0140.0.3 In one embodiment, a homologous recombinant microorganism can be created wherein the SRP is integrated into a chromosome, a vector is prepared which contains at least a portion of a SRP gene into which a deletion, addition, or substitution has been introduced to thereby alter, e.g., functionally disrupt, the SRP gene. Preferably, the SRP gene is a yeast, E.coli, *Brassica napus*, *Glycine max*, or *Oryza sativa* SRP gene, but it can be a homolog from a related plant or even from a mammalian or insect source. In one embodiment, the vector is designed such that, upon homologous recombination, the endogenous SRP gene is functionally disrupted (i.e., no longer encodes a functional polypeptide; also referred to as a knock-out vector). Alternatively, the vector can be designed such that, upon homologous recombination, the endogenous SRP gene is mutated or otherwise altered but still encodes a functional polypeptide (e.g., the upstream regulatory region can be altered to thereby alter the expression of the endogenous SRP). To create a point mutation via homologous recombination, DNA-RNA hybrids can be used in a technique known as chimeraplasty (Cole-Strauss et al., 1999, Nucleic Acids Research 27(5):1323-1330 and Kmiec, 1999 Gene therapy American Scientist. 87(3):240-247). Homologous recombination procedures in *Physcomitrella patens* are also well known in the art and are contemplated for use herein.

0141.0.3 Whereas in the homologous recombination vector, the altered portion of the SRP gene is flanked at its 5' and 3' ends by an additional nucleic acid molecule of the SRP gene to allow for homologous recombination to occur between the exogenous SRP gene carried by the vector and an endogenous SRP gene, in a microorganism or plant. The additional flanking SRP nucleic acid molecule is of sufficient length for successful homologous recombination with the endogenous gene. Typically, several hundreds of base pairs up to kilobases of flanking DNA (both at the 5' and 3' ends) are included in the vector. See, e.g., Thomas, K.R., and Capecchi, M.R., 1987, Cell 51:503 for a description of homologous recombination vectors or Strepp et al., 1998, PNAS, 95 (8):4368-4373 for cDNA based recombination in *Physcomitrella patens*). The vector is introduced into a microorganism or plant cell (e.g., via polyethylene glycol mediated DNA), and cells in which the introduced PKSRP gene has homologously recombined with the endogenous PKSRP gene are selected using art-known techniques.

0142.0.3 In another embodiment, recombinant microorganisms can be produced that contain selected systems which allow for regulated expression of the introduced gene. For example, inclusion of a SRP gene on a vector placing it under control of the

lac operon permits expression of the SRP gene only in the presence of IPTG. Such regulatory systems are well known in the art.

0143.0.3 Whether present in an extra-chromosomal non-replicating vector or a vector that is integrated into a chromosome, the SRP polynucleotide preferably resides in a plant expression cassette. A plant expression cassette preferably contains regulatory sequences capable of driving gene expression in plant cells that are operatively linked so that each sequence can fulfill its function, for example, termination of transcription by polyadenylation signals. Preferred polyadenylation signals are those originating from *Agrobacterium tumefaciens* t-DNA such as the gene 3 known as octopine synthase of the Ti-plasmid pTiACH5 (Gielen et al., 1984, EMBO J. 3:835) or functional equivalents thereof but also all other terminators functionally active in plants are suitable. As plant gene expression is very often not limited on transcriptional levels, a plant expression cassette preferably contains other operatively linked sequences like translational enhancers such as the overdrive-sequence containing the 5´-untranslated leader sequence from tobacco mosaic virus enhancing the polypeptide per RNA ratio (Gallie et al., 1987, Nucl. Acids Research 15:8693-8711). Examples of plant expression vectors include those detailed in: Becker, D. et al., 1992, New plant binary vectors with selectable markers located proximal to the left border, Plant Mol. Biol. 20: 1195-1197; and Bevan, M.W., 1984, Binary *Agrobacterium* vectors for plant transformation, Nucl. Acid. Res. 12:8711-8721; and Vectors for Gene Transfer in Higher Plants; in: Transgenic Plants, Vol. 1, Engineering and Utilization, eds.: Kung and R. Wu, Academic Press, 1993, S. 15-38.

0144.0.1 "Transformation" is defined herein as a process for introducing heterologous DNA into a plant cell, plant tissue, or plant. It may occur under natural or artificial conditions using various methods well known in the art. Transformation may rely on any known method for the insertion of foreign nucleic acid sequences into aprokaryotic or eukaryotic host cell. The method is selected based on the host cell being transformed and may include, but is not limited to, viral infection, electroporation, lipofection, and particle bombardment. Such "transformed" cells include stably transformed cells in which the inserted DNA is capable of replication either as an autonomously replicating plasmid or as part of the host chromosome. They also include cells which transiently express the inserted DNA or RNA for limited periods of time. Transformed plant cells, plant tissue, or plants are understood to encompass not only the end product of a transformation process, but also transgenic progeny thereof.

0145.0.1 The terms "transformed," "transgenic," and "recombinant" refer to a host organism such as a bacterium or a plant into which a heterologous nucleic acid molecule has been introduced. The nucleic acid molecule can be stably integrated into

the genome of the host or the nucleic acid molecule can also be present as an extrachromosomal molecule. Such an extrachromosomal molecule can be auto-replicating. Transformed cells, tissues, or plants are understood to encompass not only the end product of a transformation process, but also transgenic progeny thereof. A "non-transformed," "non-transgenic," or "non-recombinant" host refers to a wild-type organism, e.g., a bacterium or plant, which does not contain the heterologous nucleic acid molecule.

0146.0.1 A "transgenic plant", as used herein, refers to a plant which contains a foreign nucleotide sequence inserted into either its nuclear genome or organellar genome. It encompasses further the offspring generations i.e. the T1-, T2- and consecutively generations or BC1-, BC2- and consecutively generation as well as crossbreeds thereof with non-transgenic or other transgenic plants.

0147.0.1 The host organism (= transgenic organism) advantageously contains at least one copy of the nucleic acid according to the invention and/or of the nucleic acid construct according to the invention.

0148.0.2 In principle all plants can be used as host organism. Preferred transgenic plants are, for example, selected from the families Aceraceae, Anacardiaceae, Apiaceae, Asteraceae, Brassicaceae, Cactaceae, Cucurbitaceae, Euphorbiaceae, Fabaceae, Malvaceae, Nymphaeaceae, Papaveraceae, Rosaceae, Salicaceae, Solanaceae, Arecaceae, Bromeliaceae, Cyperaceae, Iridaceae, Liliaceae, Orchidaceae, Gentianaceae, Labiaceae, Magnoliaceae, Ranunculaceae, Carifolaceae, Rubiaceae, Scrophulariaceae, Caryophyllaceae, Ericaceae, Polygonaceae, Violaceae, Juncaceae or Poaceae and preferably from a plant selected from the group of the families Apiaceae, Asteraceae, Brassicaceae, Cucurbitaceae, Fabaceae, Papaveraceae, Rosaceae, Solanaceae, Liliaceae or Poaceae. Preferred are crop plants such as plants advantageously selected from the group of the genus peanut, oilseed rape, canola, sunflower, safflower, olive, sesame, hazelnut, almond, avocado, bay, pumpkin/squash, linseed, soya, pistachio, borage, maize, wheat, rye, oats, sorghum and millet, triticale, rice, barley, cassava, potato, sugarbeet, egg plant, alfalfa, and perennial grasses and forage plants, oil palm, vegetables (brassicas, root vegetables, tuber vegetables, pod vegetables, fruiting vegetables, onion vegetables, leafy vegetables and stem vegetables), buckwheat, Jerusalem artichoke, broad bean, vetches, lentil, dwarf bean, lupin, clover and Lucerne for mentioning only some of them.

0149.0.2 In one prefered embodiment, the host plant is selected from the families Aceraceae, Anacardiaceae, Apiaceae, Asteraceae, Brassicaceae, Cactaceae, Cucurbitaceae, Euphorbiaceae, Fabaceae, Malvaceae, Nymphaeaceae, Papaveraceae, Rosaceae, Salicaceae, Solanaceae, Arecaceae, Bromeliaceae,

Cyperaceae, Iridaceae, Liliaceae, Orchidaceae, Gentianaceae, Labiaceae, Magnoliaceae, Ranunculaceae, Carifolaceae, Rubiaceae, Scrophulariaceae, Caryophyllaceae, Ericaceae, Polygonaceae, Violaceae, Juncaceae or Poaceae and preferably from a plant selected from the group of the families Apiaceae, Asteraceae, Brassicaceae, Cucurbitaceae, Fabaceae, Papaveraceae, Rosaceae, Solanaceae, Liliaceae or Poaceae. Preferred are crop plants and in particular plants mentioned herein above as host plants such as the families and genera mentioned above for example preferred the species *Anacardium occidentale, Calendula officinalis, Carthamus tinctorius, Cichorium intybus, Cynara scolymus, Helianthus annus, Tagetes lucida, Tagetes erecta, Tagetes tenuifolia*; *Daucus carota*; *Corylus avellana, Corylus colurna, Borago officinalis*; *Brassica napus, Brassica rapa* ssp., *Sinapis arvensis Brassica juncea, Brassica juncea var. juncea, Brassica juncea var. crispifolia, Brassica juncea var. foliosa, Brassica nigra, Brassica sinapioides, Melanosinapis communis, Brassica oleracea*, Arabidopsis thaliana, *Anana comosus, Ananas ananas, Bromelia comosa, Carica papaya, Cannabis sative, Ipomoea batatus, Ipomoea pandurata, Convolvulus batatas, Convolvulus tiliaceus, Ipomoea fastigiata, Ipomoea tiliacea, Ipomoea triloba, Convolvulus panduratus, Beta vulgaris, Beta vulgaris var. altissima, Beta vulgaris var. vulgaris, Beta maritima, Beta vulgaris var. perennis, Beta vulgaris var. conditiva, Beta vulgaris var. esculenta, Cucurbita maxima, Cucurbita mixta, Cucurbita pepo, Cucurbita moschata, Olea europaea, Manihot utilissima, Janipha manihot,, Jatropha manihot., Manihot aipil, Manihot dulcis, Manihot manihot, Manihot melanobasis, Manihot esculenta, Ricinus communis, Pisum sativum, Pisum arvense, Pisum humile, Medicago sativa, Medicago falcata, Medicago varia, Glycine max Dolichos soja, Glycine gracilis, Glycine hispida, Phaseolus max, Soja hispida, Soja max, Cocos nucifera, Pelargonium grossularioides, Oleum cocoas, Laurus nobilis, Persea americana, Arachis hypogaea, Linum usitatissimum, Linum humile, Linum austriacum, Linum bienne, Linum angustifolium, Linum catharticum, Linum flavum, Linum grandiflorum, Adenolinum grandiflorum, Linum lewisii, Linum narbonense, Linum perenne, Linum perenne var. lewisii, Linum pratense, Linum trigynum, Punica granatum, Gossypium hirsutum, Gossypium arboreum, Gossypium barbadense, Gossypium herbaceum, Gossypium thurberi, Musa nana, Musa acuminata, Musa paradisiaca, Musa* spp., *Elaeis guineensis, Papaver orientale, Papaver rhoeas, Papaver dubium, Sesamum indicum, Piper aduncum, Piper amalago, Piper angustifolium, Piper auritum, Piper betel, Piper cubeba, Piper longum, Piper nigrum, Piper retrofractum, Artanthe adunca, Artanthe elongata, Peperomia elongata, Piper elongatum, Steffensia elongata, , Hordeum vulgare, Hordeum jubatum, Hordeum murinum, Hordeum secalinum, Hordeum distichon Hordeum aegiceras, Hordeum*

hexastichon., Hordeum hexastichum, Hordeum irregulare, Hordeum sativum, Hordeum secalinum, Avena sativa, Avena fatua, Avena byzantina, Avena fatua var. sativa, Avena hybrida, Sorghum bicolor, Sorghum halepense, Sorghum saccharatum, Sorghum vulgare, Andropogon drummondii, Holcus bicolor, Holcus sorghum, Sorghum aethiopicum, Sorghum arundinaceum, Sorghum caffrorum, Sorghum cernuum, Sorghum dochna, Sorghum drummondii, Sorghum durra, Sorghum guineense, Sorghum lanceolatum, Sorghum nervosum, Sorghum saccharatum, Sorghum subglabrescens, Sorghum verticilliflorum, Sorghum vulgare, Holcus halepensis, Sorghum miliaceum millet, Panicum militaceum, Zea mays, Triticum aestivum, Triticum durum, Triticum turgidum, Triticum hybernum, Triticum macha, Triticum sativum or *Triticum vulgare, Cofea spp., Coffea arabica, Coffea canephora, Coffea liberica, Capsicum annuum, Capsicum annuum var. glabriusculum, Capsicum frutescens, Capsicum annuum, Nicotiana tabacum, Solanum tuberosum, Solanum melongena, Lycopersicon esculentum, Lycopersicon lycopersicum., Lycopersicon pyriforme, Solanum integrifolium, Solanum lycopersicum Theobroma cacao* or *Camellia sinensis.*

0150.0.2 Anacardiaceae such as the genera Pistacia, Mangifera, Anacardium e.g. the species *Pistacia vera* [pistachios, Pistazie], *Mangifer indica* [Mango] or *Anacardium occidentale* [Cashew]; Asteraceae such as the genera Calendula, Carthamus, Centaurea, Cichorium, Cynara, Helianthus, Lactuca, Locusta, Tagetes, Valeriana e.g. the species *Calendula officinalis* [Marigold], *Carthamus tinctorius* [safflower], *Centaurea cyanus* [cornflower], *Cichorium intybus* [blue daisy], *Cynara scolymus* [Artichoke], *Helianthus annus* [sunflower], Lactuca sativa, *Lactuca crispa, Lactuca esculenta, Lactuca scariola L. ssp. sativa, Lactuca scariola L. var. integrata, Lactuca scariola L. var. integrifolia, Lactuca sativa subsp. romana, Locusta communis, Valeriana locusta* [lettuce], *Tagetes lucida, Tagetes erecta or Tagetes tenuifolia* [Marigold]; Apiaceae such as the genera Daucus e.g. the species *Daucus carota* [carrot]; Betulaceae such as the genera Corylus e.g. the species *Corylus avellana* or *Corylus colurna* [hazelnut]; Boraginaceae such as the genera Borago e.g. the species *Borago officinalis* [borage]; Brassicaceae such as the genera Brassica, Melanosinapis, Sinapis, Arabadopsis e.g. the species *Brassica napus, Brassica rapa* ssp. [canola, oilseed rape, turnip rape], *Sinapis arvensis Brassica juncea, Brassica juncea var. juncea, Brassica juncea var. crispifolia, Brassica juncea var. foliosa, Brassica nigra, Brassica sinapioides, Melanosinapis communis* [mustard], *Brassica oleracea* [fodder beet] or Arabidopsis thaliana; Bromeliaceae such as the genera Anana, Bromelia e.g. the species *Anana comosus, Ananas ananas* or *Bromelia comosa* [pineapple]; Caricaceae such as the genera Carica e.g. the species *Carica papaya* [papaya]; Cannabaceae such as the genera Cannabis e.g. the species *Cannabis*

sative [hemp], Convolvulaceae such as the genera Ipomea, Convolvulus e.g. the species *Ipomoea batatus, Ipomoea pandurata, Convolvulus batatas, Convolvulus tiliaceus, Ipomoea fastigiata, Ipomoea tiliacea, Ipomoea triloba* or *Convolvulus panduratus* [sweet potato, Man of the Earth, wild potato], Chenopodiaceae such as the genera Beta, i.e. the species *Beta vulgaris, Beta vulgaris var. altissima, Beta vulgaris var. Vulgaris, Beta maritima, Beta vulgaris var. perennis, Beta vulgaris var. conditiva* or *Beta vulgaris var. esculenta* [sugar beet]; Cucurbitaceae such as the genera Cucubita e.g. the species *Cucurbita maxima, Cucurbita mixta, Cucurbita pepo* or *Cucurbita moschata* [pumpkin, squash]; Elaeagnaceae such as the genera Elaeagnus e.g. the species *Olea europaea* [olive]; Ericaceae such as the genera Kalmia e.g. the species *Kalmia latifolia, Kalmia angustifolia, Kalmia microphylla, Kalmia polifolia, Kalmia occidentalis, Cistus chamaerhodendros* or *Kalmia lucida* [American laurel, broad-leafed laurel, calico bush, spoon wood, sheep laurel, alpine laurel, bog laurel, western bog-laurel, swamp-laurel]; Euphorbiaceae such as the genera Manihot, Janipha, Jatropha, Ricinus e.g. the species *Manihot utilissima, Janipha manihot,, Jatropha manihot., Manihot aipil, Manihot dulcis, Manihot manihot, Manihot melanobasis, Manihot esculenta* [manihot, arrowroot, tapioca, cassava] or *Ricinus communis* [castor bean, Castor Oil Bush, Castor Oil Plant, Palma Christi, Wonder Tree]; Fabaceae such as the genera Pisum, Albizia, Cathormion, Feuillea, Inga, Pithecolobium, Acacia, Mimosa, Medicajo, Glycine, Dolichos, Phaseolus, Soja e.g. the species *Pisum sativum, Pisum arvense, Pisum humile* [pea], *Albizia berteriana, Albizia julibrissin, Albizia lebbeck, Acacia berteriana, Acacia littoralis, Albizia berteriana, Albizzia berteriana, Cathormion berteriana, Feuillea berteriana, Inga fragrans, Pithecellobium berterianum, Pithecellobium fragrans, Pithecolobium berterianum, Pseudalbizzia berteriana, Acacia julibrissin, Acacia nemu, Albizia nemu, Feuilleea julibrissin, Mimosa julibrissin, Mimosa speciosa, Sericanrda julibrissin, Acacia lebbeck, Acacia macrophylla, Albizia lebbek, Feuilleea lebbeck, Mimosa lebbeck, Mimosa speciosa* [bastard logwood, silk tree, East Indian Walnut], *Medicago sativa, Medicago falcata, Medicago varia* [alfalfa] *Glycine max Dolichos soja, Glycine gracilis, Glycine hispida, Phaseolus max, Soja hispida* or *Soja max* [soybean]; Geraniaceae such as the genera Pelargonium, Cocos, Oleum e.g. the species *Cocos nucifera, Pelargonium grossularioides* or *Oleum cocois* [coconut]; Gramineae such as the genera Saccharum e.g. the species *Saccharum officinarum;* Juglandaceae such as the genera Juglans, Wallia e.g. the species *Juglans regia, Juglans ailanthifolia, Juglans sieboldiana, Juglans cinerea, Wallia cinerea, Juglans bixbyi, Juglans californica, Juglans hindsii, Juglans intermedia, Juglans jamaicensis, Juglans major,*

Juglans microcarpa, Juglans nigra or *Wallia nigra* [walnut, black walnut, common walnut, persian walnut, white walnut, butternut, black walnut]; Lauraceae such as the genera Persea, Laurus e.g. the species laurel *Laurus nobilis* [bay, laurel, bay laurel, sweet bay], *Persea americana Persea americana, Persea gratissima* or *Persea persea* [avocado]; Leguminosae such as the genera Arachis e.g. the species *Arachis hypogaea* [peanut]; Linaceae such as the genera Linum, Adenolinum e.g. the species *Linum usitatissimum, Linum humile, Linum austriacum, Linum bienne, Linum angustifolium, Linum catharticum, Linum flavum, Linum grandiflorum, Adenolinum grandiflorum, Linum lewisii, Linum narbonense, Linum perenne, Linum perenne var. lewisii, Linum pratense* or *Linum trigynum* [flax, linseed]; Lythrarieae such as the genera Punica e.g. the species *Punica granatum* [pomegranate]; Malvaceae such as the genera Gossypium e.g. the species *Gossypium hirsutum, Gossypium arboreum, Gossypium barbadense, Gossypium herbaceum* or *Gossypium thurberi* [cotton]; Musaceae such as the genera Musa e.g. the species *Musa nana, Musa acuminata, Musa paradisiaca, Musa* spp. [banana]; Onagraceae such as the genera Camissonia, Oenothera e.g. the species *Oenothera biennis* or *Camissonia brevipes* [primrose, evening primrose]; Palmae such as the genera Elacis e.g. the species *Elaeis guineensis* [oil plam]; Papaveraceae such as the genera Papaver e.g. the species *Papaver orientale, Papaver rhoeas, Papaver dubium* [poppy, oriental poppy, corn poppy, field poppy, shirley poppies, field poppy, long-headed poppy, long-pod poppy]; Pedaliaceae such as the genera Sesamum e.g. the species *Sesamum indicum* [sesame]; Piperaceae such as the genera Piper, Artanthe, Peperomia, Steffensia e.g. the species *Piper aduncum, Piper amalago, Piper angustifolium, Piper auritum, Piper betel, Piper cubeba, Piper longum, Piper nigrum, Piper retrofractum, Artanthe adunca, Artanthe elongata, Peperomia elongata, Piper elongatum, Steffensia elongata.* [Cayenne pepper, wild pepper]; Poaceae such as the genera Hordeum, Secale, Avena, Sorghum, Andropogon, Holcus, Panicum, Oryza, Zea, Triticum e.g. the species *Hordeum vulgare, Hordeum jubatum, Hordeum murinum, Hordeum secalinum, Hordeum distichon Hordeum aegiceras, Hordeum hexastichon., Hordeum hexastichum, Hordeum irregulare, Hordeum sativum, Hordeum secalinum* [barley, pearl barley, foxtail barley, wall barley, meadow barley], *Secale cereale* [rye], Avena sativa, *Avena fatua, Avena byzantina, Avena fatua var. sativa, Avena hybrida* [oat], *Sorghum bicolor, Sorghum halepense, Sorghum saccharatum, Sorghum vulgare, Andropogon drummondii, Holcus bicolor, Holcus sorghum, Sorghum aethiopicum, Sorghum arundinaceum, Sorghum caffrorum, Sorghum cernuum, Sorghum dochna, Sorghum drummondii, Sorghum durra, Sorghum guineense, Sorghum lanceolatum,*

Sorghum nervosum, Sorghum saccharatum, Sorghum subglabrescens, Sorghum verticilliflorum, Sorghum vulgare, Holcus halepensis, Sorghum miliaceum millet, *Panicum militaceum [Sorghum, millet], Oryza sativa, Oryza latifolia* [rice], *Zea mays* [corn, maize] *Triticum aestivum, Triticum durum, Triticum turgidum, Triticum hybernum, Triticum macha, Triticum sativum* or *Triticum vulgare* [wheat, bread wheat, common wheat], Proteaceae such as the genera Macadamia e.g. the species *Macadamia intergrifolia* [macadamia]; Rubiaceae such as the genera Coffea e.g. the species Cofea spp., *Coffea arabica, Coffea canephora* or *Coffea liberica* [coffee]; Scrophulariaceae such as the genera Verbascum e.g. the species *Verbascum blattaria, Verbascum chaixii, Verbascum densiflorum, Verbascum lagurus, Verbascum longifolium, Verbascum lychnitis, Verbascum nigrum, Verbascum olympicum, Verbascum phlomoides, Verbascum phoenicum, Verbascum pulverulentum* or *Verbascum thapsus* [mullein, white moth mullein, nettle-leaved mullein, dense-flowered mullein, silver mullein, long-leaved mullein, white mullein, dark mullein, greek mullein, orange mullein, purple mullein, hoary mullein, great mullein]; Solanaceae such as the genera Capsicum, Nicotiana, Solanum, Lycopersicon e.g. the species *Capsicum annuum, Capsicum annuum var. glabriusculum, Capsicum frutescens* [pepper], *Capsicum annuum* [paprika], *Nicotiana tabacum, Nicotiana alata, Nicotiana attenuata, Nicotiana glauca, Nicotiana langsdorffii, Nicotiana obtusifolia, Nicotiana quadrivalvis, Nicotiana repanda, Nicotiana rustica, Nicotiana sylvestris* [tobacco], *Solanum tuberosum* [potato], *Solanum melongena* [egg-plant] (*Lycopersicon esculentum, Lycopersicon lycopersicum., Lycopersicon pyriforme, Solanum integrifolium* or *Solanum lycopersicum* [*tomato*]; Sterculiaceae such as the genera Theobroma e.g. the species *Theobroma cacao* [cacao]; Theaceae such as the genera Camellia e.g. the species *Camellia sinensis*) [tea].

0151.0.1 The introduction of the nucleic acids according to the invention, the expression cassette or the vector into organisms, plants for example, can in principle be done by all of the methods known to those skilled in the art. The introduction of the nucleic acid sequences gives rise to recombinant or transgenic organisms.

0152.0.1 In the case of microorganisms, those skilled in the art can find appropriate methods in the textbooks by Sambrook, J. et al. (1989) Molecular cloning: A laboratory manual, Cold Spring Harbor Laboratory Press, by F.M. Ausubel et al. (1994) Current protocols in molecular biology, John Wiley and Sons, by D.M. Glover et al., DNA Cloning Vol.1, (1995), IRL Press (ISBN 019-963476-9), by Kaiser et al. (1994) Methods in Yeast Genetics, Cold Spring Harbor Laboratory Press or Guthrie et al.

Guide to Yeast Genetics and Molecular Biology, Methods in Enzymology, 1994, Academic Press.

0153.0.1 The transfer of foreign genes into the genome of a plant is called transformation. In doing this the methods described for the transformation and regeneration of plants from plant tissues or plant cells are utilized for transient or stable transformation. Suitable methods are protoplast transformation by poly(ethylene glycol)-induced DNA uptake, the „biolistic“ method using the gene cannon – referred to as the particle bombardment method, electroporation, the incubation of dry embryos in DNA solution, microinjection and gene transfer mediated by Agrobacterium. Said methods are described by way of example in B. Jenes et al., Techniques for Gene Transfer, in: Transgenic Plants, Vol. 1, Engineering and Utilization, eds. S.D. Kung and R. Wu, Academic Press (1993) 128-143 and in Potrykus Annu. Rev. Plant Physiol. Plant Molec. Biol. 42 (1991) 205-225). The nucleic acids or the construct to be expressed is preferably cloned into a vector which is suitable for transforming Agrobacterium tumefaciens, for example pBin19 (Bevan et al., Nucl. Acids Res. 12 (1984) 8711). Agrobacteria transformed by such a vector can then be used in known manner for the transformation of plants, in particular of crop plants such as by way of example tobacco plants, for example by bathing bruised leaves or chopped leaves in an agrobacterial solution and then culturing them in suitable media. The transformation of plants by means of Agrobacterium tumefaciens is described, for example, by Höfgen and Willmitzer in Nucl. Acid Res. (1988) 16, 9877 or is known inter alia from F.F. White, Vectors for Gene Transfer in Higher Plants; in Transgenic Plants, Vol. 1, Engineering and Utilization, eds. S.D. Kung and R. Wu, Academic Press, 1993, pp. 15-38.

0154.0.1 Agrobacteria transformed by an expression vector according to the invention may likewise be used in known manner for the transformation of plants such as test plants like Arabidopsis or crop plants such as cereal crops, corn, oats, rye, barley, wheat, soybean, rice, cotton, sugar beet, canola, sunflower, flax, hemp, potatoes, tobacco, tomatoes, carrots, paprika, oilseed rape, tapioca, cassava, arrowroot, tagetes, alfalfa, lettuce and the various tree, nut and vine species, in particular of oil-containing crop plants such as soybean, peanut, castor oil plant, sunflower, corn, cotton, flax, oilseed rape, coconut, oil palm, safflower (Carthamus tinctorius) or cocoa bean, e.g. by bathing bruised leaves or chopped leaves in an agrobacterial solution and then culturing them in suitable media.

0155.0.1 The genetically modified plant cells may be regenerated by all of the methods known to those skilled in the art. Appropriate methods can be found in the publications referred to above by S.D. Kung and R. Wu, Potrykus or Höfgen and Willmitzer.

0156.0.1 Accordingly, a further aspect of the invention relates to transgenic organisms transformed by at least one nucleic acid sequence, expression cassette or vector according to the invention as well as cells, cell cultures, tissue, parts – such as, for example, leaves, roots, etc. in the case of plant organisms – or reproductive material derived from such organisms. The terms „host organism“, „host cell“, „recombinant (host) organism“ and „transgenic (host) cell“ are used here interchangeably. Of course these terms relate not only to the particular host organism or the particular target cell but also to the descendants or potential descendants of these organisms or cells. Since, due to mutation or environmental effects certain modifications may arise in successive generations, these descendants need not necessarily be identical with the parental cell but nevertheless are still encompassed by the term as used here.

0157.0.1 For the purposes of the invention „transgenic“ or „recombinant“ means with regard for example to a nucleic acid sequence, an expression cassette (= gene construct, nucleic acid construct) or a vector containing the nucleic acid sequence according to the invention or an organism transformed by the nucleic acid sequences, expression cassette or vector according to the invention all those constructions produced by genetic engineering methods in which either

a) the nucleic acid sequence depicted in Fig. 1a, 1b or 1c or its derivatives or parts thereof or

b) a genetic control sequence functionally linked to the nucleic acid sequence described under (a), for example a 3'- and/or 5'- genetic control sequence such as a promoter or terminator, or

c) (a) and (b)

are not found in their natural, genetic environment or have been modified by genetic engineering methods, wherein the modification may by way of example be a substitution, addition, deletion, inversion or insertion of one or more nucleotide residues. Natural genetic environment means the natural genomic or chromosomal locus in the organism of origin or inside the host organism or presence in a genomic library. In the case of a genomic library the natural genetic environment of the nucleic acid sequence is preferably retained at least in part. The environment borders the nucleic acid sequence at least on one side and has a sequence length of at least 50 bp, preferably at least 500 bp, particularly preferably at least 1,000 bp, most particularly preferably at least 5,000 bp. A naturally occurring expression cassette – for example the naturally occurring combination of the natural promoter of the nucleic acid sequence according to the invention with the corresponding Δ-8-desaturase, Δ-9-elongase and/or Δ-5-desaturase gene – turns into a transgenic expression cassette

when the latter is modified by unnatural, synthetic („artificial") methods such as by way of example a mutagenation. Appropriate methods are described by way of example in US 5,565,350 or WO 00/15815.

0158.0.1 Suitable organisms or host organisms for the nucleic acid, expression cassette or vector according to the invention are advantageously in principle all organisms, which are suitable for the expression of recombinant genes as described above. Further examples which may be mentioned are plants such as Arabidopsis, Asteraceae such as Calendula or crop plants such as soybean, peanut, castor oil plant, sunflower, flax, corn, cotton, flax, oilseed rape, coconut, oil palm, safflower (Carthamus tinctorius) or cocoa bean.

0159.0.1 A further object of the invention relates to the use of a nucleic acid construct, e.g. an expression cassette, containing DNA sequences encoding polypeptides of Fig. 1a, 1b or 1c or DNA sequences hybridizing therewith for the transformation of plant cells, tissues or parts of plants.

0160.0.1 In doing so, depending on the choice of promoter, the sequences Fig. 1a, 1b or 1c can be expressed specifically in the leaves, in the seeds, the nodules, in roots, in the stem or other parts of the plant. Those transgenic plants overproducing sequences **of Fig. 1a, 1b or 1c**, the reproductive material thereof, together with the plant cells, tissues or parts thereof are a further object of the present invention.

0161.0.1 The expression cassette or the nucleic acid sequences or construct according to the invention containing sequences of Fig. 1a, 1b or 1c can, moreover, also be employed for the transformation of the organisms identified by way of example above such as bacteria, yeasts, filamentous fungi and plants.

0162.0.1 Within the framework of the present invention, altering metabolic activity means, for example, the artificially acquired trait of increased biosynthetic performance due to functional over expression of sequences of Fig. 1a, 1b or 1c in the organisms according to the invention, advantageously in the transgenic plants according to the invention, by comparison with the nongenetically modified initial plants at least for the duration of at least one plant generation.

0163.0.1 A constitutive expression of the exogenous sequences of the Fig. 1a, 1b or 1c is, moreover, advantageous. On the other hand, however, an inducible expression may also appear desirable.

0164.0.1 The efficiency of the expression of the sequences of the Fig. 1a, 1b or 1c can be determined, for example, in vitro by shoot meristem propagation. In addition, an expression of the sequences of Fig. 1a, 1b or 1c modified in nature and level and its effect on the metabolic pathways performance can be tested on test plants in greenhouse trials.

0165.0.1 An additional object of the invention comprises transgenic organisms such as transgenic plants transformed by an expression cassette containing sequences of Fig. 1a, 1b or 1c according to the invention or DNA sequences hybridizing therewith, as well as transgenic cells, tissue, parts and reproduction material of such plants. Particular preference is given in this case to transgenic crop plants such as by way of example barley, wheat, rye, oats, corn, soybean, rice, cotton, sugar beet, oilseed rape and canola, sunflower, flax, hemp, thistle, potatoes, tobacco, tomatoes, tapioca, cassava, arrowroot, alfalfa, lettuce and the various tree, nut and vine species.

0166.0.1 For the purposes of the invention plants are mono- and dicotyledonous plants, mosses or algae.

0167.0.1 A further refinement according to the invention are transgenic plants as described above which contain a nucleic acid sequence or construct according to the invention or a expression cassette according to the invention.

0168.0.1 Furthermore, by derivatives is meant homologues of the sequences of Fig. 1a, 1b or 1c, for example eukaryotic homologues, truncated sequences, single-stranded DNA of the encoding and nonencoding DNA sequence or RNA of the encoding and nonencoding DNA sequence.

0169.0.1 In addition, by homologues of the sequences of Fig. 1a, 1b or 1c is meant derivatives such as by way of example promoter variants. These variants may be modified by one or more nucleotide exchanges, by insertion(s) and/or deletion(s) without, however, adversely affecting the functionality or efficiency of the promoters. Furthermore, the promoters can have their efficiency increased by altering their sequence or be completely replaced by more effective promoters even of foreign organisms.

0170.0.1 By derivatives is also advantageously meant variants whose nucleotide sequence has been altered in the region from –1 to –2000 ahead of the start codon in such a way that the gene expression and/or the protein expression is modified, preferably increased. Furthermore, by derivatives is also meant variants which have been modified at the 3' end.

0171.0.1 Suitable promoters in the expression cassette are in principle all promoters which can control the expression of foreign genes in organisms such as microorganisms like protozoa such as ciliates, algae such as green, brown, red or blue algae such as Euglenia, bacteria such as gram-positive or gram-negative bacteria, yeasts such as Saccharomyces, Pichia or Schizosaccharomyces or fungi such as Mortierella, Thraustochytrium or Schizochytrium or plants, advantageously in plants or fungi. Use is preferably made in particular of plant promoters or promoters derived from

a plant virus. Advantageous regulation sequences for the method according to the invention are found for example in promoters such as cos, tac, trp, tet, trp-tet, lpp, lac, lpp-lac, laclq-, T7, T5, T3, gal, trc, ara, SP6, λ-PR or in λ-PL promoters which are employed advantageously in gram-negative bacteria. Other advantageous regulation sequences are found, for example, in the gram-positive promoters amy and SPO2, in the yeast or fungal promoters ADC1, MFα, AC, P-60, CYC1, GAPDH, TEF, rp28, ADH or in the plant promoters CaMV/35S [Franck et al., Cell 21(1980) 285-294], SSU, OCS, lib4, STLS1, B33, nos (= Nopalin Synthase Promoter) or in the ubiquintin or phaseolin promoter. The expression cassette may also contain a chemically inducible promoter by means of which the expression of the exogenous sequences of the odd numbers of SEQ. ID No. 1-269 in the organisms can be controlled advantageously in the plants at a particular time. Advantageous plant promoters of this type are by way of example the PRP1 promoter [Ward et al., Plant.Mol. Biol.22(1993), 361-366], a promoter inducible by benzenesulfonamide (EP 388 186), a promoter inducible by tetracycline [Gatz et al., (1992) Plant J. 2,397-404], a promoter inducible by salicylic acid (WO 95/19443), a promoter inducible by abscisic acid (EP 335 528) and a promoter inducible by ethanol or cyclohexanone (WO93/21334). Other examples of plant promoters which can advantageously be used are the promoter of cytosolic FBPase from potato, the ST-LSI promoter from potato (Stockhaus et al., EMBO J. 8 (1989) 2445-245), the promoter of phosphoribosyl pyrophosphate amidotransferase from Glycine max (see also gene bank accession number U87999) or a nodiene-specific promoter as described in EP 249 676. Particularly advantageous are those plant promoters which ensure expression in tissues or plant parts/organs in which fatty acid biosynthesis or the precursor stages thereof occurs, as in endosperm or in the developing embryo for example. Particularly noteworthy are advantageous promoters which ensure seed-specific expression such as by way of example the USP promoter or derivatives thereof, the LEB4 promoter, the phaseolin promoter or the napin promoter. The particularly advantageous USP promoter cited according to the invention or its derivatives mediate very early gene expression in seed development [Baeumlein et al., Mol Gen Genet, 1991, 225 (3): 459-67]. Other advantageous seed-specific promoters which may be used for monocotylodonous or dicotylodonous plants are the promoters suitable for dicotylodons such as napin gene promoters, likewise cited by way of example, from oilseed rape (US 5,608,152), the oleosin promoter from Arabidopsis (WO 98/45461), the phaseolin promoter from Phaseolus vulgaris (US 5,504,200), the Bce4 promoter from Brassica (WO 91/13980) or the leguminous B4 promoter (LeB4, Baeumlein et al., Plant J., 2, 2, 1992: 233 – 239) or promoters suitable for monocotylodons such as the promoters of the lpt2 or lpt1 gene in barley (WO 95/15389

and WO 95/23230) or the promoters of the barley hordeine gene, the rice glutelin gene, the rice oryzin gene, the rice prolamin gene, the wheat gliadin gene, the white glutelin gene, the corn zein gene, the oats glutelin gene, the sorghum kasirin gene or the rye secalin gene which are described in WO99/16890.

0172.0.1 Furthermore, particularly preferred are those promoters, which ensure the expression in tissues, or plant parts in which, for example, the biosynthesis of fatty acids, oils and lipids or the precursor stages thereof takes place. Particularly noteworthy are promoters, which ensure a seed-specific expression. Noteworthy are the promoter of the napin gene from oilseed rape (US 5,608,152), the USP promoter from Vicia faba (USP = unknown seed protein, Baeumlein et al., Mol Gen Genet, 1991, 225 (3): 459-67), the promoter of the oleosin gene from Arabidopsis (WO98/45461), the phaseolin promoter (US 5,504,200) or the promoter of the legumin B4 gene (LeB4; Baeumlein et al., 1992, Plant Journal, 2 (2): 233-9). Other promoters to be mentioned are that of the lpt2 or lpt1 gene from barley (WO95/15389 and WO95/23230) which mediate seed-specific expression in monocotyledonous plants. Other advantageous seed specific promoters are promoters such as the promoters from rice, corn or wheat disclosed in WO 99/16890 or Amy32b, Amy6-6 or aleurain (US 5,677,474), Bce4 (rape, US 5,530,149), glycinin (soy bean, EP 571 741), phosphoenol pyruvat carboxylase (soy bean, JP 06/62870), ADR12-2 (soy bean, WO 98/08962), isocitratlyase (rape, US 5,689,040) or β–amylase (barley, EP 781 849).

0173.0.1 As described above, the expression construct (= gene construct, nucleic acid construct) may contain yet other genes, which are to be introduced into the organisms. These genes can be subject to separate regulation or be subject to the same regulation region as sequences Fig. 1a, 1b or 1c. These genes are by way of example other biosynthesis genes, advantageously for fatty acid biosynthesis, vitamin biosynthesis etc. that allow increased synthesis.

0174.0.1 In principle all natural promoters with their regulation sequences can be used like those named above for the expression cassette according to the invention and the method according to the invention. Over and above this, synthetic promoters may also advantageously be used.

0175.0.1 In the preparation of an expression cassette various DNA fragments can be manipulated in order to obtain a nucleotide sequence, which usefully reads in the correct direction and is equipped with a correct reading raster. To connect the DNA fragments (= nucleic acids according to the invention) to one another adaptors or linkers may be attached to the fragments.

0176.0.1 The promoter and the terminator regions can usefully be provided in the transcription direction with a linker or polylinker containing one or more restriction

points for the insertion of this sequence. Generally, the linker has 1 to 10, mostly 1 to 8, preferably 2 to 6, restriction points. In general the size of the linker inside the regulatory region is less than 100 bp, frequently less than 60 bp, but at least 5 bp. The promoter may be both native or homologous as well as foreign or heterologous to the host organism, for example to the host plant. In the 5'-3' transcription direction the expression cassette contains the promoter, a DNA sequence which encodes of Fig. 1a, 1b or 1c gene and a region for transcription termination. Different termination regions can be exchanged for one another in any desired fashion.

0177.0.1 Furthermore, manipulations which provide suitable restriction interfaces or which remove excess DNA or restriction interfaces can be employed. Where insertions, deletions or substitutions, such as transitions and transversions, come into consideration, in vitro mutagenesis, primer repair, restriction or ligation may be used. In suitable manipulations such as restriction, chewing back or filling of overhangs for blunt ends complementary ends of the fragments can be provided for the ligation.

0178.0.1 For an advantageous high expression the attachment of the specific ER retention signal SEKDEL inter alia can be of importance (Schouten, A. et al., Plant Mol. Biol. 30 (1996), 781-792). In this way the average expression level is tripled or even quadrupled. Other retention signals which occur naturally in plant and animal proteins located in the ER may also be employed for the construction of the cassette. In another preferred embodiment a plastidial targeting sequence is used as described by Napier J.A. [Targeting of foreign proteins to the chloroplast, Methods Mol. Biol., 49, 1995: 369 - 376]. A preferred used vector comprising said plastidial targeting sequence is disclosed by Colin Lazarus [Guerineau F., Woolston S., Brooks L., Mullineaux P. "An expression cassette for targeting foreign proteins into chloroplast; Nucleic. Acids Res., Dec 9, 16 (23), 1988: 11380].

0179.0.1 Preferred polyadenylation signals are plant polyadenylation signals, preferably those which substantially correspond to T-DNA polyadenylation signals from Agrobacterium tumefaciens, in particular gene 3 of the T-DNA (octopin synthase) of the Ti plasmid pTiACH5 (Gielen et al., EMBO J.3 (1984), 835 et seq.) or corresponding functional equivalents.

0180.0.1 An expression cassette is produced by fusion of a suitable promoter with suitable sequences of Fig. 1a, 1b or 1c together with a polyadenylation signal by common recombination and cloning techniques as described, for example, in T. Maniatis, E.F. Fritsch and J. Sambrook, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1989) as well as in T.J. Silhavy, M.L. Berman and L.W. Enquist, Experiments with Gene Fusions, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1984) and in Ausubel, F.M. et al., Current

Protocols in Molecular Biology, Greene Publishing Assoc. and Wiley-Interscience (1987).

0181.0.1 In the preparation of an expression cassette various DNA fragments can be manipulated to produce a nucleotide sequence which usefully reads in the correct direction and is equipped with a correct reading raster. Adapters or linkers can be attached to the fragments for joining the DNA fragments.

0182.0.1 The promoter and the terminator regions can usefully be provided in the transcription direction with a linker or polylinker containing one or more restriction points for the insertion of this sequence. Generally, the linker has 1 to 10, mostly 1 to 8, preferably 2 to 6, restriction points. In general the size of the linker inside the regulatory region is less than 100 bp, frequently less than 60 bp, but at least 5 bp. The promoter may be both native or homologous as well as foreign or heterologous to the host organism, for example to the host plant. In the 5'-3' transcription direction the expression cassette contains the promoter, a DNA sequence which either encodes gene of the odd numbers of SEQ. ID No. 1-269 and a region for transcription termination. Different termination regions can be exchanged for one another in any desired fashion.

0183.0.1 In the preparation of an expression cassette various DNA fragments can be manipulated to produce a nucleotide sequence which usefully reads in the correct direction and is equipped with a correct reading raster. Adapters or linkers can be attached to the fragments for joining the DNA fragments.

0184.0.1 The DNA sequences encoding the nucleic acid sequences used in the inventive processes such as the sequences of the Fig. 1a, 1b or 1c contain all the sequence characteristics needed to achieve correct localization of respective biosynthesis. Accordingly, no further targeting sequences are needed per se. However, such a localization may be desirable and advantageous and hence artificially modified or reinforced so that such fusion constructs are also a preferred advantageous embodiment of the invention.

0185.0.1 Particularly preferred are sequences which ensure targeting in plastids. Under certain circumstances targeting into other compartments (reported in: Kermode, Crit. Rev. Plant Sci. 15, 4 (1996), 285-423) may also be desirable, e.g. into vacuoles, the mitochondrium, the endoplasmic reticulum (ER), peroxisomes, lipid structures or due to lack of corresponding operative sequences retention in the compartment of origin, the cytosol.

0186.0.1 As used herein, the term "environmental stress" refers to any sub-optimal growing condition and includes, but is not limited to, sub-optimal conditions associated with salinity, drought, temperature, metal, chemical, pathogenic and

oxidative stresses, or combinations thereof. In preferred embodiments, the environmental stress can be salinity, drought, heat, or low temperature, or combinations thereof, and in particular, can be low water content or low temperature. Wherein drought stress means any environmental stress which leads to a lack of water in plants or reduction of water supply to plants, wherein low temperature stress means freezing of plants below + 4 °C as well as chilling of plants below 15 °C and wherein high temperature stress means for example a temperature above 35 °C. The range of stress and stress response depends on the different plants which are used for the invention, i.e. it differs for example between a plant such as wheat and a plant such as Arabidopsis. A common response of plants to environmental stress is the loss of yield or the loss of quality. It is also to be understood that as used in the specification and in the claims, "a" or "an" can mean one or more, depending upon the context in which it is used. Thus, for example, reference to "a cell" can mean that at least one cell can be utilized.

0187.0.1 As also used herein, the terms “nucleic acid” and “nucleic acid molecule” are intended to include DNA molecules (e.g., cDNA or genomic DNA) and RNA molecules (e.g., mRNA) and analogs of the DNA or RNA generated using nucleotide analogs. This term also encompasses untranslated sequence located at both the 3’ and 5’ ends of the coding region of the gene: at least about 1000 nucleotides of sequence upstream from the 5’ end of the coding region and at least about 200 nucleotides of sequence downstream from the 3’ end of the coding region of the gene. The nucleic acid molecule can be single-stranded or double-stranded, but preferably is double-stranded DNA.

0188.0.1 An “isolated” nucleic acid molecule is one that is substantially separated from other nucleic acid molecules, which are present in the natural source of the nucleic acid. That means other nucleic acid molecules are present in an amount less than 5% based on weight of the amount of the desired nucleic acid, preferably less than 2% by weight, more preferably less than 1% by weight, most preferably less than 0.5% by weight. Preferably, an “isolated” nucleic acid is free of some of the sequences that naturally flank the nucleic acid (i.e., sequences located at the 5’ and 3’ ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated stress related protein encoding nucleic acid molecule can contain less than about 5 kb, 4 kb, 3 kb, 2 kb, 1 kb, 0.5 kb or 0.1 kb of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell from which the nucleic acid is derived. Moreover, an “isolated” nucleic acid molecule, such as a cDNA molecule, can be free from some of the other cellular material with which it is naturally associated, or culture medium

when produced by recombinant techniques, or chemical precursors or other chemicals when chemically synthesized.

0189.0.1 A nucleic acid molecule of the present invention, e.g., a nucleic acid molecule encoding an SRP or a portion thereof which confers tolerance and/or resistance to environmental stress in plants, can be isolated using standard molecular biological techniques and the sequence information provided herein. For example, a Arabidopsis thaliana stress related protein encoding cDNA can be isolated from a A. thaliana c-DNA library using all or portion of one of the sequences of Fig. 1a, 1b or 1c. Moreover, a nucleic acid molecule encompassing all or a portion of one of the sequences of Fig. 1a, 1b or 1c can be isolated by the polymerase chain reaction using oligonucleotide primers designed based upon this sequence. For example, mRNA can be isolated from plant cells (e.g., by the guanidinium-thiocyanate extraction procedure of Chirgwin et al., 1979 Biochemistry 18:5294-5299) and cDNA can be prepared using reverse transcriptase (e.g., Moloney MLV reverse transcriptase, available from Gibco/BRL, Bethesda, MD; or AMV reverse transcriptase, available from Seikagaku America, Inc., St. Petersburg, FL). Synthetic oligonucleotide primers for polymerase chain reaction amplification can be designed based upon one of the nucleotide sequences shown in Fig. 1a, 1b or 1c. A nucleic acid molecule of the invention can be amplified using cDNA or, alternatively, genomic DNA, as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid molecule so amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore, oligonucleotides corresponding to a SRP encoding nucleotide sequence can be prepared by standard synthetic techniques, e.g., using an automated DNA synthesizer.

0190.0.1 In a preferred embodiment, an isolated nucleic acid molecule of the invention comprises one of the nucleotide sequences shown in sequences Fig. 1a, 1b or 1c encoding the SRP (i.e., the "coding region"), as well as 5' untranslated sequences and 3' untranslated sequences.

0191.0.1 Moreover, the nucleic acid molecule of the invention can comprise only a portion of the coding region of one of the sequences ôf the nucleic acid of Fig. 1a, 1b or 1c, for example, a fragment which can be used as a probe or primer or a fragment encoding a biologically active portion of a SRP.

0192.0.1 Portions of proteins encoded by the SRP encoding nucleic acid molecules of the invention are preferably biologically active portions described herein. As used herein, the term "biologically active portion of" a SRP is intended to include a portion, e.g., a domain/motif, of stress related protein that participates in a stress tolerance and/or resistance response in a plant. To determine whether a SRP, or a

biologically active portion thereof, results in increased stress tolerance in a plant, a stress analysis of a plant comprising the SRP may be performed. Such analysis methods are well known to those skilled in the art, as detailed in the Examples. More specifically, nucleic acid fragments encoding biologically active portions of a SRP can be prepared by isolating a portion of one of the sequences of the nucleic acid of Fig. 1a, 1b or 1c expressing the encoded portion of the SRP or peptide (e.g., by recombinant expression in vitro) and assessing the activity of the encoded portion of the SRP or peptide.

0193.0.1 Biologically active portions of a SRP are encompassed by the present invention and include peptides comprising amino acid sequences derived from the amino acid sequence of a SRP encoding gene, or the amino acid sequence of a protein homologous to a SRP, which include fewer amino acids than a full length SRP or the full length protein which is homologous to a SRP, and exhibits at least some enzymatic activity of a SRP. Typically, biologically active portions (e.g., peptides which are, for example, 5, 10, 15, 20, 30, 35, 36, 37, 38, 39, 40, 50, 100 or more amino acids in length) comprise a domain or motif with at least one activity of a SRP. Moreover, other biologically active portions in which other regions of the protein are deleted, can be prepared by recombinant techniques and evaluated for one or more of the activities described herein. Preferably, the biologically active portions of a SRP include one or more selected domains/motifs or portions thereof having biological activity.

0194.0.1 The term "biological active portion" or "biological activity" means a SRP or a portion of a SRP which still has at least 10 % or 20 %, preferably 20 %, 30 %, 40 % or 50 %, especially preferably 60 %, 70 % or 80 % of the enzymatic activity of the natural or starting enzyme.

0195.0.2 A nucleic acid molecule encompassing a complete sequence of the nucleic acid molecules used in the process, for example the polynucleotide of the invention, or a part thereof may additionally be isolated by polymerase chain reaction, oligonucleotide primers based on this sequence or on parts thereof being used. For example, a nucleic acid molecule comprising the complete sequence or part thereof can be isolated by polymerase chain reaction using oligonucleotide primers which have been generated on the basis of this sequence–For example, mRNA can be isolated from cells (for example by means of the guanidinium thiocyanate extraction method of Chirgwin et al. (1979) Biochemistry 18:5294-5299) and cDNA can be generated by means of reverse transcriptase (for example Moloney MLV reverse transcriptase, available from Gibco/BRL, Bethesda, MD, or AMV reverse transcriptase, obtainable from Seikagaku America, Inc., St.Petersburg, FL).

0196.0.2 Synthetic oligonucleotide primers for the amplification, e.g. as shown in **table 2,** by means of polymerase chain reaction can be generated on the basis of a sequence shown herein, for example the sequence shown in Fig. 1a, 1b or 1c or the sequences derived from polypeptides as shown in Fig. 1a, 1b or 1c.

0197.0.2 Moreover, it is possible to identify conserved regions from various organisms by carrying out protein sequence alignments with the polypeptide used in the process of the invention, in particular with sequences of the polypeptide of the invention, from which conserved regions, and in turn, degenerate primers can be derived. Conserved region for the polypeptide of the invention are indicated in the alignment shown in the figure Fig. 1a, 1b or 1c. Conserved regions are those, which show a very little variation in the amino acid in one particular position of several homologs from different origin. The consenus sequences shown in Fig. 2 are derived from said aligments.

0198.0.2 Degenerated primers can then be utilized by PCR for the amplification of fragments of novel proteins having above-mentioned activity, e.g. having an SPR activity or further functional homologs of the polypeptide of the invention from other organisms.

0199.0.2 These fragments can then be utilized as hybridization probe for isolating the complete gene sequence. As an alternative, the missing 5' and 3' sequences can be isolated by means of RACE-PCR (rapid amplification of cDNA ends). A nucleic acid molecule according to the invention can be amplified using cDNA or, as an alternative, genomic DNA as template and suitable oligonucleotide primers, following standard PCR amplification techniques. The nucleic acid molecule amplified thus can be cloned into a suitable vector and characterized by means of DNA sequence analysis. Oligonucleotides, which correspond to one of the nucleic acid molecules used in the process can be generated by standard synthesis methods, for example using an automatic DNA synthesizer.

0200.0.2 Nucleic acid molecules which are advantageously for the process according to the invention can be isolated based on their homology to the nucleic acid molecules disclosed herein using the sequences or part thereof as hybridization probe and following standard hybridization techniques under stringent hybridization conditions. In this context, it is possible to use, for example, isolated nucleic acid molecules of at least 15, 20, 25, 30, 35, 40, 50, 60 or more nucleotides, preferably of at least 15, 20 or 25 nucleotides in length which hybridize under stringent conditions with the above-described nucleic acid molecules, in particular with those which encompass a nucleotide sequence ofthe nucleic acid molecule used in the process of the invention or encoding a protein used in the invention or of the nucleic acid molecule of the

invention. Nucleic acid molecules with 30, 50, 100, 250 or more nucleotides may also be used.

0201.0.1 In addition to fragments of the SRP described herein, the present invention includes homologs and analogs of naturally occurring SRP and SRP encoding nucleic acids in a plant.

0202.0.1 "Homologs" are defined herein as two nucleic acids or proteins that have similar, or "homologous", nucleotide or amino acid sequences, respectively. Homologs include allelic variants, orthologs, paralogs, agonists and antagonists of SRP as defined hereafter. The term "homolog" further encompasses nucleic acid molecules that differ from one of the nucleotide sequences shown in sequences with SEQ ID No. **XXX** (and portions thereof) due to degeneracy of the genetic code and thus encode the same SRP as that encoded by the amino acid sequences shown in sequences with SEQ ID No. **XXX**. As used herein a "naturally occurring" SRP refers to a SRP amino acid sequence that occurs in nature.

0203.0.2 The term "homology" means that the respective nucleic acid molecules or encoded proteins are functionally and/or structurally equivalent. The nucleic acid molecules that are homologous to the nucleic acid molecules described above and that are derivatives of said nucleic acid molecules are, for example, variations of said nucleic acid molecules which represent modifications having the same biological function, in particular encoding proteins with the same or substantially the same biological function. They may be naturally occurring variations, such as sequences from other plant varieties or species, or mutations. These mutations may occur naturally or may be obtained by mutagenesis techniques. The allelic variations may be naturally occurring allelic variants as well as synthetically produced or genetically engineered variants. Structurally equivalents can, for example, be identified by testing the binding of said polypeptide to antibodies or computer based predictions. Structurally equivalent have the similar immunological characteristic, e.g. comprise similar epitopes.

0204.0.2 Functional equivalents derived from one of the polypeptides as shown in **SEQ ID NO: YYY** according to the invention by substitution, insertion or deletion have at least 30%, 35%, 40%, 45% or 50%, preferably at least 55%, 60%, 65% or 70% by preference at least 80%, especially preferably at least 85% or 90%, 91%, 92%, 93% or 94%, very especially preferably at least 95%, 97%, 98% or 99% homology with one of the polypeptides as shown in Fig. 1a, 1b or 1c according to the invention and are distinguished by essentially the same properties as the polypeptide as shown in Fig. 1a, 1b or 1c.

0205.0.2 Functional equivalents derived from the nucleic acid sequence as shown in SEQ ID NO: **YYY** according to the invention by substitution, insertion or deletion have at least 30%, 35%, 40%, 45% or 50%, preferably at least 55%, 60%, 65% or 70% by preference at least 80%, especially preferably at least 85% or 90%, 91%, 92%, 93% or 94%, very especially preferably at least 95%, 97%, 98% or 99% homology with one of the polypeptides as shown in Fig. 1a, 1b or 1c according to the invention and encode polypeptides having essentially the same properties as the polypeptide as shown in Fig. 1a, 1b or 1c.

0206.0.2 "Essentially the same properties" of a functional equivalent is above all understood as meaning that the functional equivalent has above mentioned acitivty, e.g conferring an increase in the fine chemical amount while increasing the amount of protein, activity or function of said functional equivalent in an organism, e.g. a microorgansim, a plant or plant or animal tissue, plant or animal cells or a part of the same.

0207.0.2 By "hybridizing" it is meant that such nucleic acid molecules hybridize under conventional hybridization conditions, preferably under stringent conditions such as described by, e.g., Sambrook (Molecular Cloning; A Laboratory Manual, 2nd Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY (1989)) or in Current Protocols in Molecular Biology, John Wiley & Sons, N. Y. (1989), 6.3.1-6.3.6.

0208.0.2 According to the invention, DNA as well as RNA molecules of the nucleic acid of the invention can be used as probes. Further, as template for the identification of functional homologues Northern blot assays as well as Southern blot assays can be performed. The Northern blot assay advantageously provides further informations about the expressed gene product: e.g. expression pattern, occurance of processing steps, like splicing and capping, etc. The Southern blot assay provides additional information about the chromosomal localization and organization of the gene encoding the nucleic acid molecule of the invention.

0209.0.2 A preferred, nonlimiting example of stringent hydridization conditions are hybridizations in 6 x sodium chloride/sodium citrate (= SSC) at approximately 45°C, followed by one or more wash steps in 0.2 x SSC, 0.1% SDS at 50 to 65°C, for example at 50°C, 55°C or 60°C. The skilled worker knows that these hybridization conditions differ as a function of the type of the nucleic acid and, for example when organic solvents are present, with regard to the temperature and concentration of the buffer. The temperature under "standard hybridization conditions" differs for example as a function of the type of the nucleic acid between 42°C and 58°C, preferably between 45°C and 50°C in an aqueous buffer with a concentration of 0.1 x 0.5 x, 1 x, 2x, 3x, 4x or 5 x SSC (pH 7.2). If organic solvent(s) is/are present in the

abovementioned buffer, for example 50% formamide, the temperature under standard conditions is approximately 40°C, 42°C or 45°C. The hybridization conditions for DNA:DNA hybrids are preferably for example 0.1 x SSC and 20°C, 25°C, 30°C, 35°C, 40°C or 45°C, preferably between 30°C and 45°C. The hybridization conditions for DNA:RNA hybrids are preferably for example 0.1 x SSC and 30°C, 35°C, 40°C, 45°C, 50°C or 55°C, preferably between 45°C and 55°C. The abovementioned hybridization temperatures are determined for example for a nucleic acid approximately 100 bp (= base pairs) in length and a G + C content of 50% in the absence of formamide. The skilled worker knows to determine the hybridization conditions required with the aid of textbooks, for example the ones mentioned above, or from the following textbooks: Sambrook et al., "Molecular Cloning", Cold Spring Harbor Laboratory, 1989; Hames and Higgins (Ed.) 1985, "Nucleic Acids Hybridization: A Practical Approach", IRL Press at Oxford University Press, Oxford; Brown (Ed.) 1991, "Essential Molecular Biology: A Practical Approach", IRL Press at Oxford University Press, Oxford.

0210.0.2 A further example of one such stringent hybridization condition is hybridization at 4XSSC at 65°C, followed by a washing in 0.1XSSC at 65°C for one hour. Alternatively, an exemplary stringent hybridization condition is in 50 % formamide, 4XSSC at 42°C. Further, the conditions during the wash step can be selected from the range of conditions delimited by low-stringency conditions (approximately 2X SSC at 50°C) and high-stringency conditions (approximately 0.2X SSC at 50°C, preferably at 65°C) (20X SSC: 0.3M sodium citrate, 3M NaCl, pH 7.0). In addition, the temperature during the wash step can be raised from low-stringency conditions at room temperature, approximately 22°C, to higher-stringency conditions at approximately 65°C. Both of the parameters salt concentration and temperature can be varied simultaneously, or else one of the two parameters can be kept constant while only the other is varied. Denaturants, for example formamide or SDS, may also be employed during the hybridization. In the presence of 50% formamide, hybridization is preferably effected at 42°C. Relevant factors like i) length of treatment, ii) salt conditions, iii) detergent conditions, iv) competitor DNAs, v) temperature and vi) probe selection can be combined case by case so that not all possibilities can be mentioned herein.

0211.0.2 Thus, in a preferred embodiment, Northern blots are prehybridized with Rothi-Hybri-Quick buffer (Roth, Karlsruhe) at 68°C for 2h. Hybridzation with radioactive labelled probe is done overnight at 68°C. Subsequent washing steps are performed at 68°C with 1xSSC.

0212.0.2 For Southern blot assays the membrane is prehybridized with Rothi-Hybri-Quick buffer (Roth, Karlsruhe) at 68°C for 2h. The hybridzation with radioactive

labelled probe is conducted over night at 68°C. Subsequently the hybridization buffer is discarded and the filter shortly washed using 2xSSC; 0,1% SDS. After discarding the washing buffer new 2xSSC; 0,1% SDS buffer is added and incubated at 68°C for 15 minutes. This washing step is performed twice followed by an additional washing step using 1xSSC; 0,1% SDS at 68°C for 10 min.

0213.0.2 Some further examples of conditions for DNA hybridization (Southern blot assays) and wash step are shown hereinbelow:

(1) Hybridization conditions can be selected, for example, from the following conditions:

a) 4X SSC at 65°C,

b) 6X SSC at 45°C,

c) 6X SSC, 100 mg/ml denatured fragmented fish sperm DNA at 68°C,

d) 6X SSC, 0.5% SDS, 100 mg/ml denatured salmon sperm DNA at 68°C,

e) 6X SSC, 0.5% SDS, 100 mg/ml denatured fragmented salmon sperm DNA, 50% formamide at 42°C,

f) 50% formamide, 4X SSC at 42°C,

g) 50% (vol/vol) formamide, 0.1% bovine serum albumin, 0.1% Ficoll, 0.1% polyvinylpyrrolidone, 50 mM sodium phosphate buffer pH 6.5, 750 mM NaCl, 75 mM sodium citrate at 42°C,

h) 2X or 4X SSC at 50°C (low-stringency condition), or

i) 30 to 40% formamide, 2X or 4X SSC at 42°C (low-stringency condition).

(2) Wash steps can be selected, for example, from the following conditions:

a) 0.015 M NaCl/0.0015 M sodium citrate/0.1% SDS at 50°C.

b) 0.1X SSC at 65°C.

c) 0.1X SSC, 0.5 % SDS at 68°C.

d) 0.1X SSC, 0.5% SDS, 50% formamide at 42°C.

e) 0.2X SSC, 0.1% SDS at 42°C.

f) 2X SSC at 65°C (low-stringency condition).

0214.0.1 In an other embodiment is meant by standard conditions, for example, depending on the nucleic acid in question temperatures between 42°C and 58°C in an aqueous buffer solution having a concentration of between 0.1 and 5 x SSC (1 X SSC = 0.15 M NaCl, 15 mM sodium citrate, pH 7.2) or additionally in the presence of 50 % formamide, such as by way of example 42°C in 5 x SSC, 50 % formamide. Hybridization conditions for DNA:DNA hybrids are advantageously 0.1 x SSC and temperatures between approximately 20°C and 45°C, preferably between

approximately 30 oC and 45 oC. For DNA:RNA hybrids the hybridization conditions are advantageously 0.1 x SSC and temperatures between approximately 30°C and 55°C, preferably between approximately 45°C and 55°C. These specified temperatures for hybridization are melting temperature values calculated by way of example for a nucleic acid having a length of approximately 100 nucleotides and a G + C content of 50 % in the absence of formamide. The experimental conditions for DNA hybridization are described in relevant genetics textbooks such as by way of example Sambrook et al., „Molecular Cloning", Cold Spring Harbor Laboratory, 1989, and may be calculated by formulae known to those skilled in the art, for example as a function of the length of the nucleic acids, the nature of the hybrids or the G + C content. Those skilled in the art may draw on the following textbooks for further information on hybridization: Ausubel et al. (eds), 1985, Current Protocols in Molecular Biology, John Wiley & Sons, New York; Hames and Higgins (eds), 1985, Nucleic Acids Hybridization: A Practical Approach, IRL Press at Oxford University Press, Oxford; Brown (ed), 1991, Essential Molecular Biology: A Practical Approach, IRL Press at Oxford University Press, Oxford.

0215.0.2 Polypeptides having above-mentioned activity, i.e. conferring the altered metabolic activity, derived from other organisms, can be encoded by other DNA sequences which hybridize to the sequences shown in Fig. 1a, 1b or 1c under relaxed hybridization conditions and which code on expression for peptides confering an altered metabolic activity.

0216.0.2 Further, some applications have to be performed at low stringency hybridisation conditions, without any consequences for the specificity of the hybridisation. For example, a Southern blot analysis of total DNA could be probed with a nucleic acid molecule of the present invention and washed at low stringency (55°C in 2xSSPE0,1% SDS). The hybridisation analysis could reveal a simple pattern of only genes encoding polypeptides of the present invention or used in the process of the invention, e.g. having herein-mentioned activity of increasing the fine chemical . A further example of such low-stringent hybridization conditions is 4XSSC at 50°C or hybridization with 30 to 40% formamide at 42°C. Such molecules comprise those which are fragments, analogues or derivatives of the polypeptide of the invention or used in the process of the invention and differ, for example, by way of amino acid and/or nucleotide deletion(s), insertion(s), substitution (s), addition(s) and/or recombination (s) or any other modification(s) known in the art either alone or in combination from the above-described amino acid sequences or their underlying nucleotide sequence(s). However, it is preferred to use high stringency hybridisation conditions.

0217.0.2 Hybridization should advantageously be carried out with fragments of at least 5, 10, 15, 20, 25, 30, 35 or 40 bp, advantageously at least 50, 60, 70 or 80 bp,

preferably at least 90, 100 or 110 bp. Most preferably are fragments of at least 15, 20, 25 or 30 bp. Preferably are also hybridizations with at least 100 bp or 200, very especially preferably at least 400 bp in length. In an especially preferred embodiment, the hybridization should be carried out with the entire nucleic acid sequence with conditions described above.

0218.0.2 The terms "fragment", "fragment of a sequence" or "part of a sequence" mean a truncated sequence of the original sequence referred to. The truncated sequence (nucleic acid or protein sequence) can vary widely in length; the minimum size being a sequence of sufficient size to provide a sequence with at least a comparable function and/or activity of the original sequence referred to or hybidizing with the nucleic acid molecule of the invention or used in the process of the invention under stringend conditions, while the maximum size is not critical. In some applications, the maximum size usually is not substantially greater than that required to provide the desired activity and/or function(s) of the original sequence.

0219.0.3 In addition to fragments and fusion polypeptides of the SRPs described herein, the present invention includes homologs and analogs of naturally occurring SRPs and SRP encoding nucleic acids in a plant. "Homologs" are defined herein as two nucleic acids or polypeptides that have similar, or substantially identical, nucleotide or amino acid sequences, respectively. Homologs include allelic variants, orthologs, paralogs, agonists and antagonists of SRPs as defined hereafter. The term "homolog" further encompasses nucleic acid molecules that differ from one of the nucleotide sequences shown in Fig. 1a, 1b or 1c (and portions thereof) due to degeneracy of the genetic code and thus encode the same SRP as that encoded by the nucleotide sequences shown in Fig. 1a, 1b or 1c. As used herein a "naturally occurring" SRP refers to a SRP amino acid sequence that occurs in nature. Preferably, a naturally occurring SRP comprises an amino acid sequence selected from the group consisting of polypeptides of Fig. 1a, 1b or 1c.

0220.0.3 An agonist of the SRP can retain substantially the same, or a subset, of the biological activities of the SRP. An antagonist of the SRP can inhibit one or more of the activities of the naturally occurring form of the SRP. For example, the SRP antagonist can competitively bind to a downstream or upstream member of the cell membrane component metabolic cascade that includes the SRP, or bind to a SRP that mediates transport of compounds across such membranes, thereby preventing translocation from taking place.

0221.0.3 Nucleic acid molecules corresponding to natural allelic variants and analogs, orthologs and paralogs of a SRP cDNA can be isolated based on their identity

to the *Saccharomyces cerevisiae, E.coli, Brassica napus, Glycine max*, or *Oryza sativa* SRP nucleic acids described herein using SRP cDNAs, or a portion thereof, as a hybridization probe according to standard hybridization techniques under stringent hybridization conditions. In an alternative embodiment, homologs of the SRP can be identified by screening combinatorial libraries of mutants, e.g., truncation mutants, of the SRP for SRP agonist or antagonist activity. In one embodiment, a variegated library of SRP variants is generated by combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A variegated library of SRP variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a degenerate set of potential SRP sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion polypeptides (e.g., for phage display) containing the set of SRP sequences therein. There are a variety of methods that can be used to produce libraries of potential SRP homologs from a degenerate oligonucleotide sequence. Chemical synthesis of a degenerate gene sequence can be performed in an automatic DNA synthesizer, and the synthetic gene is then ligated into an appropriate expression vector. Use of a degenerate set of genes allows for the provision, in one mixture, of all of the sequences encoding the desired set of potential SRP sequences. Methods for synthesizing degenerate oligonucleotides are known in the art. See, e.g., Narang, S.A., 1983, Tetrahedron 39:3; Itakura et al., 1984, Annu. Rev. Biochem. 53:323; Itakura et al., 1984, Science 198:1056; Ike et al., 1983, Nucleic Acid Res. 11:477.

0222.0.3 In addition, libraries of fragments of the SRP coding regions can be used to generate a variegated population of SRP fragments for screening and subsequent selection of homologs of a SRP. In one embodiment, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of a SRP coding sequence with a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double stranded DNA, which can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed duplexes by treatment with S1 nuclease, and ligating the resulting fragment library into an expression vector. By this method, an expression library can be derived which encodes N-terminal, C-terminal, and internal fragments of various sizes of the SRP.

0223.0.3 Several techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA libraries for gene products having a selected property. Such techniques are adaptable for rapid screening of the gene libraries generated by the combinatorial mutagenesis of SRP homologs. The most widely used techniques, which are amenable to high

through-put analysis, for screening large gene libraries typically include cloning the gene library into replicable expression vectors, transforming appropriate cells with the resulting library of vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates isolation of the vector encoding the gene whose product was detected. Recursive ensemble mutagenesis (REM), a new technique that enhances the frequency of functional mutants in the libraries, can be used in combination with the screening assays to identify SRP homologs (Arkin and Yourvan, 1992, PNAS 89:7811-7815; Delgrave et al., 1993, Polypeptide Engineering 6(3):327-331). In another embodiment, cell based assays can be exploited to analyze a variegated SRP library, using methods well known in the art. The present invention further provides a method of identifying a novel SRP, comprising (a) raising a specific antibody response to a SRP, or a fragment thereof, as described herein; (b) screening putative SRP material with the antibody, wherein specific binding of the antibody to the material indicates the presence of a potentially novel SRP; and (c) analyzing the bound material in comparison to known SRP, to determine its novelty.

0224.0.3 As stated above, the present invention includes SRPs and homologs thereof. To determine the percent sequence identity of two amino acid sequences (e.g., one of the sequences of Fig. 1a, 1b or 1c, and a mutant form thereof), the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in the sequence of one polypeptide for optimal alignment with the other polypeptide or nucleic acid). The amino acid residues at corresponding amino acid positions are then compared. When a position in one sequence (e.g., one of the sequences of Fig. 1a, 1b or 1c) is occupied by the same amino acid residue as the corresponding position in the other sequence (e.g., a mutant form of the sequence selected from the polypeptide of Fig. 1a, 1b or 1c), then the molecules are identical at that position. The same type of comparison can be made between two nucleic acid sequences.

0225.0.3 The percent sequence identity between the two sequences is a function of the number of identical positions shared by the sequences (i.e., percent sequence identity = numbers of identical positions/total numbers of positions x 100). Preferably, the isolated amino acid homologs included in the present invention are at least about 50-60%, preferably at least about 60-70%, and more preferably at least about 70-75%, 75-80%, 80-85%, 85-90% or 90-95%, and most preferably at least about 96%, 97%, 98%, 99% or more identical to an entire amino acid sequence shown in Fig. 1a, 1b or 1c. In yet another embodiment, the isolated amino acid homologs included in the present invention are at least about 50-60%, preferably at least about 60-70%, and more preferably at least about 70-75%, 75-80%, 80-85%, 85-90% or 90-95%, and most preferably at least about 96%, 97%, 98%, 99% or more identical to an entire amino

acid sequence encoded by a nucleic acid sequence shown in Fig. 1a, 1b or 1c. In other embodiments, the SRP amino acid homologs have sequence identity over at least 15 contiguous amino acid residues, more preferably at least 25 contiguous amino acid residues, and most preferably at least 35 contiguous amino acid residues of Fig. 1a, 1b or 1c.

0226.0.3 In another preferred embodiment, an isolated nucleic acid homolog of the invention comprises a nucleotide sequence which is at least about 50-60%, preferably at least about 60-70%, more preferably at least about 70-75%, 75-80%, 80-85%, 85-90% or 90-95%, and even more preferably at least about 95%, 96%, 97%, 98%, 99% or more identical to a nucleotide sequence shown Fig. 1a, 1b or 1c, or to a portion comprising at least 20, 30, 40, 50, 60 consecutive nucleotides thereof. The preferable length of sequence comparison for nucleic acids is at least 75 nucleotides, more preferably at least 100 nucleotides and most preferably the entire length of the coding region.

0227.0.3 It is further preferred that the isolated nucleic acid homolog of the invention encodes a SRP, or portion thereof, that is at least 85% identical to an amino acid sequence of Fig. 1a, 1b or 1c and that functions as a modulator of an environmental stress response in a plant. In a more preferred embodiment, overexpression of the nucleic acid homolog in a plant increases the tolerance of the plant to an environmental stress.

0228.0.3 For the purposes of the invention, the percent sequence identity between two nucleic acid or polypeptide sequences is determined using the Vector NTI 6.0 (PC) software package (InforMax, 7600 Wisconsin Ave., Bethesda, MD 20814). A gap opening penalty of 15 and a gap extension penalty of 6.66 are used for determining the percent identity of two nucleic acids. A gap opening penalty of 10 and a gap extension penalty of 0.1 are used for determining the percent identity of two polypeptides. All other parameters are set at the default settings. For purposes of a multiple alignment (Clustal W algorithm), the gap opening penalty is 10, and the gap extension penalty is 0.05 with blosum62 matrix. It is to be understood that for the purposes of determining sequence identity when comparing a DNA sequence to an RNA sequence, a thymidine nucleotide is equivalent to a uracil nucleotide.

0228.1.3 In another aspect, the invention provides an isolated nucleic acid comprising a polynucleotide that hybridizes to the polynucleotide of Fig. 1a, 1b or 1c under stringent conditions. More particularly, an isolated nucleic acid molecule of the invention is at least 15 nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule comprising a nucleotide sequence of Fig. 1a, 1b or 1c. In other embodiments, the nucleic acid is at least 30, 50, 100, 250 or more nucleotides in

length. Preferably, an isolated nucleic acid homolog of the invention comprises a nucleotide sequence which hybridizes under highly stringent conditions to the nucleotide sequence shown in Fig. 1a, 1b or 1c, and functions as a modulator of stress tolerance in a plant. In a further preferred embodiment, overexpression of the isolated nucleic acid homolog in a plant increases a plant's tolerance to an environmental stress.

0229.0.3 As used herein with regard to hybridization for DNA to DNA blot, the term "stringent conditions" refers in one embodiment to hybridization overnight at 60°C in 10X Denharts solution, 6X SSC, 0.5% SDS and 100 µg/ml denatured salmon sperm DNA. Blots are washed sequentially at 62°C for 30 minutes each time in 3X SSC/0.1% SDS, followed by 1X SSC/0.1% SDS and finally 0.1X SSC/0.1% SDS. As also used herein, "highly stringent conditions" refers to hybridization overnight at 65°C in 10X Denharts solution, 6X SSC, 0.5% SDS and 100 µg/ml denatured salmon sperm DNA. Blots are washed sequentially at 65°C for 30 minutes each time in 3X SSC/0.1% SDS, followed by 1X SSC/0.1% SDS and finally 0.1X SSC/0.1% SDS. Methods for nucleic acid hybridizations are described in Meinkoth and Wahl, 1984, Anal. Biochem. 138:267-284; Ausubel et al. eds, 1995, Current Protocols in Molecular Biology, Chapter 2, Greene Publishing and Wiley-Interscience, New York; and Tijssen, 1993, Laboratory Techniques in Biochemistry and Molecular Biology: Hybridization with Nucleic Acid Probes, Part I, Chapter 2, Elsevier, New York. Preferably, an isolated nucleic acid molecule of the invention that hybridizes under stringent or highly stringent conditions to a sequence of Fig. 1a, 1b or 1c corresponds to a naturally occurring nucleic acid molecule. As used herein, a "naturally occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (e.g., encodes a natural polypeptide). In one embodiment, the nucleic acid encodes a naturally occurring *Saccharomyces cerevisiae, E.coli, Brassica napus, Glycine max*, or *Oryza sativa* SRP.

0230.0.3 Using the above-described methods, and others known to those of skill in the art, one of ordinary skill in the art can isolate homologs of the SRPs comprising amino acid sequences shown in Fig. 1a, 1b or 1c. One subset of these homologs are allelic variants. As used herein, the term "allelic variant" refers to a nucleotide sequence containing polymorphisms that lead to changes in the amino acid sequences of a SRP and that exist within a natural population (e.g., a plant species or variety). Such natural allelic variations can typically result in 1-5% variance in a SRP nucleic acid. Allelic variants can be identified by sequencing the nucleic acid sequence of interest in a number of different plants, which can be readily carried out by using hybridization probes to identify the same SRP genetic locus in those plants. Any and

all such nucleic acid variations and resulting amino acid polymorphisms or variations in a SRP that are the result of natural allelic variation and that do not alter the functional activity of a SRP, are intended to be within the scope of the invention.

0231.0.3 An isolated nucleic acid molecule encoding a SRP having sequence identity with a polypeptide sequence of Fig. 1a, 1b or 1c can be created by introducing one or more nucleotide substitutions, additions or deletions into a nucleotide sequence of Fig. 1a, 1b or 1c, respectively, such that one or more amino acid substitutions, additions, or deletions are introduced into the encoded polypeptide. Mutations can be introduced into one of the sequences of Fig. 1a, 1b or 1c by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain.

0232.0.3 Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted nonessential amino acid residue in a SRP is preferably replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of a SRP coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for a SRP activity described herein to identify mutants that retain SRP activity. Following mutagenesis of one of the sequences of **SEQ ID NO:XXX,** the encoded polypeptide can be expressed recombinantly and the activity of the polypeptide can be determined by analyzing the stress tolerance of a plant expressing the polypeptide as described herein.

0233.0.3 Additionally, optimized SRP nucleic acids can be created. As used herein, "optimized" refers to a nucleic acid that is genetically engineered to increase its expression in a given plant or animal. To provide plant optimized SRP nucleic acids, the DNA sequence of the gene can be modified to 1) comprise codons preferred by highly expressed plant genes; 2) comprise an A+T content in nucleotide base composition to that substantially found in plants; 3) form a plant initiation sequence; or 4) eliminate sequences that cause destabilization, inappropriate polyadenylation, degradation, and termination of RNA, or that form secondary structure hairpins or RNA

splice sites. Increased expression of SRP nucleic acids in plants can be achieved by utilizing the distribution frequency of codon usage in plants in general or a particular plant. Methods for optimizing nucleic acid expression in plants can be found in EPA 0359472; EPA 0385962; PCT Application No. WO 91/16432; U.S. Patent No. 5,380,831; U.S. Patent No. 5,436,391; Perlack et al., 1991, Proc. Natl. Acad. Sci. USA 88:3324-3328; and Murray et al., 1989, Nucleic Acids Res. 17:477-498.

0234.0.3 As used herein, "frequency of preferred codon usage" refers to the preference exhibited by a specific host cell in usage of nucleotide codons to specify a given amino acid. To determine the frequency of usage of a particular codon in a gene, the number of occurrences of that codon in the gene is divided by the total number of occurrences of all codons specifying the same amino acid in the gene. Similarly, the frequency of preferred codon usage exhibited by a host cell can be calculated by averaging frequency of preferred codon usage in a large number of genes expressed by the host cell. It is preferable that this analysis be limited to genes that are highly expressed by the host cell. The percent deviation of the frequency of preferred codon usage for a synthetic gene from that employed by a host cell is calculated first by determining the percent deviation of the frequency of usage of a single codon from that of the host cell followed by obtaining the average deviation over all codons. As defined herein, this calculation includes unique codons (i.e., ATG and TGG). In general terms, the overall average deviation of the codon usage of an optimized gene from that of a host cell is calculated using the equation $1A = n = 1\ Z\ X_n - Y_n\ X_n$ times 100 Z where X_n = frequency of usage for codon n in the host cell; Y_n = frequency of usage for codon n in the synthetic gene; n represents an individual codon that specifies an amino acid; and the total number of codons is Z. The overall deviation of the frequency of codon usage, A, for all amino acids should preferably be less than about 25%, and more preferably less than about 10%.

0235.0.3 Hence, a SRP nucleic acid can be optimized such that its distribution frequency of codon usage deviates, preferably, no more than 25% from that of highly expressed plant genes and, more preferably, no more than about 10%. In addition, consideration is given to the percentage G+C content of the degenerate third base (monocotyledons appear to favor G+C in this position, whereas dicotyledons do not). It is also recognized that the XCG (where X is A, T, C, or G) nucleotide is the least preferred codon in dicots whereas the XTA codon is avoided in both monocots and dicots. Optimized SRP nucleic acids of this invention also preferably have CG and TA doublet avoidance indices closely approximating those of the chosen host plant (i.e., *Brassica napus*, *Glycine max*, or *Oryza sativa*). More preferably these indices deviate from that of the host by no more than about 10-15%.

0236.0.3 In addition to the nucleic acid molecules encoding the SRPs described above, another aspect of the invention pertains to isolated nucleic acid molecules that are antisense thereto. Antisense polynucleotides are thought to inhibit gene expression of a target polynucleotide by specifically binding the target polynucleotide and interfering with transcription, splicing, transport, translation, and/or stability of the target polynucleotide. Methods are described in the prior art for targeting the antisense polynucleotide to the chromosomal DNA, to a primary RNA transcript, or to a processed mRNA. Preferably, the target regions include splice sites, translation initiation codons, translation termination codons, and other sequences within the open reading frame.

0237.0.3 The term "antisense," for the purposes of the invention, refers to a nucleic acid comprising a polynucleotide that is sufficiently complementary to all or a portion of a gene, primary transcript, or processed mRNA, so as to interfere with expression of the endogenous gene. "Complementary" polynucleotides are those that are capable of base pairing according to the standard Watson-Crick complementarity rules. bpecifically, purines will base pair with pyrimidines to form a combination of guanine paired with cytosine (G:C) and adenine paired with either thymine (A:T) in the case of DNA, or adenine paired with uracil (A:U) in the case of RNA. It is understood that two polynucleotides may hybridize to each other even if they are not completely complementary to each other, provided that each has at least one region that is substantially complementary to the other. The term "antisense nucleic acid" includes single stranded RNA as well as double-stranded DNA expression cassettes that can be transcribed to produce an antisense RNA. "Active" antisense nucleic acids are antisense RNA molecules that are capable of selectively hybridizing with a primary transcript or mRNA encoding a polypeptide having at least 80% sequence identity with the polypeptide of Fig. 1a, 1b or 1c.

0238.0.3 The antisense nucleic acid can be complementary to an entire SRP coding strand, or to only a portion thereof. In one embodiment, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a nucleotide sequence encoding a SRP. The term "coding region" refers to the region of the nucleotide sequence comprising codons that are translated into amino acid residues. In another embodiment, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence encoding a SRP. The term "noncoding region" refers to 5' and 3' sequences that flank the coding region that are not translated into amino acids (i.e., also referred to as 5' and 3' untranslated regions). The antisense nucleic acid molecule can be complementary to the entire coding region of SRP mRNA, but more preferably is an oligonucleotide which is antisense to only a

portion of the coding or noncoding region of SRP mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of PKSRP mRNA. An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. Typically, the antisense molecules of the present invention comprise an RNA having 60-100% sequence identity with at least 14 consecutive nucleotides of one of the nucleic acid of Fig. 1a, 1b or 1c. Preferably, the sequence identity will be at least 70%, more preferably at least 75%, 80%, 85%, 90%, 95%, 98% and most preferably 99%.

0239.0.3 An antisense nucleic acid of the invention can be constructed using chemical synthesis and enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (e.g., an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, e.g., phosphorothioate derivatives and acridine substituted nucleotides can be used. Examples of modified nucleotides which can be used to generate the antisense nucleic acid include 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (i.e., RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

0240.0.3 In yet another embodiment, the antisense nucleic acid molecule of the invention is an α-anomeric nucleic acid molecule. An α-anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β-units, the strands run parallel to each other (Gaultier et al., 1987, Nucleic Acids. Res. 15:6625-6641). The antisense nucleic acid molecule can also comprise a

2'-o-methylribonucleotide (Inoue et al., 1987, Nucleic Acids Res. 15:6131-6148) or a chimeric RNA-DNA analogue (Inoue et al., 1987, FEBS Lett. 215:327-330).

0241.0.3 The antisense nucleic acid molecules of the invention are typically administered to a cell or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a SRP to thereby inhibit expression of the polypeptide, e.g., by inhibiting transcription and/or translation. The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule which binds to DNA duplexes, through specific interactions in the major groove of the double helix. The antisense molecule can be modified such that it specifically binds to a receptor or an antigen expressed on a selected cell surface, e.g., by linking the antisense nucleic acid molecule to a peptide or an antibody which binds to a cell surface receptor or antigen. The antisense nucleic acid molecule can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of the antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong prokaryotic, viral, or eukaryotic (including plant) promoter are preferred.

0242.0.3 As an alternative to antisense polynucleotides, ribozymes, sense polynucleotides, or double stranded RNA (dsRNA) can be used to reduce expression of a SRP polypeptide. By "ribozyme" is meant a catalytic RNA-based enzyme with ribonuclease activity which is capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which it has a complementary region. Ribozymes (e.g., hammerhead ribozymes described in Haselhoff and Gerlach, 1988, Nature 334:585-591) can be used to catalytically cleave SRP mRNA transcripts to thereby inhibit translation of SRP mRNA. A ribozyme having specificity for a SRP-encoding nucleic acid can be designed based upon the nucleotide sequence of a SRP cDNA, as disclosed herein (i.e., Fig. 1a, 1b or 1c) or on the basis of a heterologous sequence to be isolated according to methods taught in this invention. For example, a derivative of a Tetrahymena L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in a SRP-encoding mRNA. See, e.g., U.S. Patent Nos. 4,987,071 and 5,116,742 to Cech et al. Alternatively, SRP mRNA can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, e.g., Bartel, D. and Szostak, J.W., 1993, Science 261:1411-1418. In preferred embodiments, the ribozyme will contain a portion having at least 7, 8, 9, 10, 12, 14, 16, 18 or 20 nucleotides, and more preferably 7 or 8 nucleotides, that have 100% complementarity to a portion of the target RNA. Methods

for making ribozymes are known to those skilled in the art. See, e.g., U.S. Patent Nos. 6,025,167; 5,773,260; and 5,496,698.

0243.0.3 The term "dsRNA," as used herein, refers to RNA hybrids comprising two strands of RNA. The dsRNAs can be linear or circular in structure. In a preferred embodiment, dsRNA is specific for a polynucleotide encoding either the polypeptide of Fig. 1a, 1b or 1c or a polypeptide having at least 70% sequence identity with a polypeptide of Fig. 1a, 1b or 1c. The hybridizing RNAs may be substantially or completely complementary. By "substantially complementary," is meant that when the two hybridizing RNAs are optimally aligned using the BLAST program as described above, the hybridizing portions are at least 95% complementary. Preferably, the dsRNA will be at least 100 base pairs in length. Typically, the hybridizing RNAs will be of identical length with no over hanging 5' or 3' ends and no gaps. However, dsRNAs having 5' or 3' overhangs of up to 100 nucleotides may be used in the methods of the invention.

0244.0.3 The dsRNA may comprise ribonucleotides or ribonucleotide analogs, such as 2'-O-methyl ribosyl residues, or combinations thereof. See, e.g., U.S. Patent Nos. 4,130,641 and 4,024,222. A dsRNA polyriboinosinic acid:polyribocytidylic acid is described in U.S. patent 4,283,393. Methods for making and using dsRNA are known in the art. One method comprises the simultaneous transcription of two complementary DNA strands, either *in vivo*, or in a single *in vitro* reaction mixture. See, e.g., U.S. Patent No. 5,795,715. In one embodiment, dsRNA can be introduced into a plant or plant cell directly by standard transformation procedures. Alternatively, dsRNA can be expressed in a plant cell by transcribing two complementary RNAs.

0245.0.3 Other methods for the inhibition of endogenous gene expression, such as triple helix formation (Moser et al., 1987, Science 238:645-650 and Cooney et al., 1988, Science 241:456-459) and cosuppression (Napoli et al., 1990, The Plant Cell 2:279-289) are known in the art. Partial and full-length cDNAs have been used for the cosuppression of endogenous plant genes. See, e.g., U.S. Patent Nos. 4,801,340, 5,034,323, 5,231,020, and 5,283,184; Van der Kroll et al., 1990, The Plant Cell 2:291-299; Smith et al., 1990, Mol. Gen. Genetics 224:477-481 and Napoli et al., 1990, The Plant Cell 2:279-289.

0246.0.3 For sense suppression, it is believed that introduction of a sense polynucleotide blocks transcription of the corresponding target gene. The sense polynucleotide will have at least 65% sequence identity with the target plant gene or RNA. Preferably, the percent identity is at least 80%, 90%, 95% or more. The introduced sense polynucleotide need not be full length relative to the target gene or transcript. Preferably, the sense polynucleotide will have at least 65% sequence

identity with at least 100 consecutive nucleotides of one of the nucleic acids of Fig. 1a, 1b or 1c. The regions of identity can comprise introns and and/or exons and untranslated regions. The introduced sense polynucleotide may be present in the plant cell transiently, or may be stably integrated into a plant chromosome or extrachromosomal replicon.

0247.0.1 Moreover, nucleic acid molecules encoding SRP from the same or other species such as SRP analogs, orthologs and paralogs, are intended to be within the scope of the present invention. As used herein, the term "analogs" refers to two nucleic acids that have the same or similar function, but that have evolved separately in unrelated organisms. As used herein, the term "orthologs" refers to two nucleic acids from different species that have evolved from a common ancestral gene by speciation. Normally, orthologs encode proteins having the same or similar functions. As also used herein, the term "paralogs" refers to two nucleic acids that are related by duplication within a genome. Paralogs usually have different functions, but these functions may be related (Tatusov, R.L. et al. 1997 Science 278(5338):631-637). Analogs, orthologs and paralogs of a naturally occurring stress related protein can differ from the naturally occurring stress related protein by post-translational modifications, by amino acid sequence differences, or by both. Post-translational modifications include in vivo and in vitro chemical derivatization of polypeptides e.g., acetylation, carboxylation, phosphorylation or glycosylation, and such modifications may occur during polypeptide synthesis or processing or following treatment with isolated modifying enzymes. In particular, orthologs of the invention will generally exhibit at least 80-85%, more preferably 90%, 91%, 92%, 93%, 94%, and most preferably 95%, 96%, 97%, 98% or even 99% identity or homology with all or part of a naturally occurring stress related protein amino acid sequence and will exhibit a function similar to a stress related protein. Orthologs of the present invention are also preferably capable of participating in the stress response in plants.

0248.0.1 In addition to naturally-occurring variants of a stress related protein sequence that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into a nucleotide sequence of the Fig. 1a, 1b or 1c, thereby leading to changes in the amino acid sequence of the encoded stress related protein, without altering the functional ability of the stress related protein or enhancing the functional ability of the stress related protein. For example, nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues can be made in a sequence of Fig 1. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequence of one of stress related proteins without altering the activity thereof, whereas an "essential" amino acid residue is

required for stress related protein activity. Other amino acid residues, however, (e.g., those that are not conserved or only semi-conserved in the domain having SRP activity) may not be essential for activity and thus are likely to be amenable to alteration without altering SRP activity.

0249.0.1 Accordingly, another aspect of the invention pertains to nucleic acid molecules encoding stress related proteins that contain changes in amino acid residues that are not essential for stress related protein activity. Such SRP differ in amino acid sequence from a sequence Fig. 1a, 1b or 1c, yet retain at least one of the stress related protein activities described herein. In one embodiment, the isolated nucleic acid molecule comprises a nucleotide sequence encoding a protein, wherein the protein comprises an amino acid sequence at least about 50% homologous to an amino acid sequence of Fig. 1a, 1b or 1c. Preferably, the protein encoded by the nucleic acid molecule is at least about 50-60% homologous to one of the sequences of the Fig. 1a, 1b or 1c, more preferably at least about 60 - 70% homologous to one of the sequences of the Fig. 1a, 1b or 1c, even more preferably at least about 70 - 80%, 80 - 90%, more preferably 90%, 91%, 92%, 93%, 94% homologous to one of the sequences of the Fig. 1a, 1b or 1c and most preferably at least about 96%, 97%, 98%, or 99% homologous to one of the sequences of the Fig. 1a, 1b or 1c. The preferred stress related protein homologs of the present invention are preferably capable of participating in the stress tolerance response in a plant. The homology (= identity) was calculated over the entire amino acid range. The program used was PileUp (J. Mol. Evolution., 25 (1987), 351-360, Higgins et al., CABIOS, 5 1989: 151-153).

0250.0.1 Homologs of the sequences given in Fig. 1a, 1b or 1c are furthermore to be understood as meaning, for example, homologs, analogs, orthologs and paralogs which have at least 30% homology (= identity) at the derived amino acid level, preferably at least 50 %, 60 %, 70 % or 80 % homology, especially preferably at least 85 % homology, very especially preferably 90 % 91%, 92%, 93%, 94%homology, most preferably 95 %, 96 %, 97 %, 98 % or 99 % homology. The homology (= identity) was calculated over the entire amino acid range. The program used was PileUp (J. Mol. Evolution., 25 (1987), 351 – 360, Higgens et al., CABIOS, 5 1989: 151 – 153) or the program Gap and BestFit [Needleman and Wunsch (J. Mol. Biol. 48; 443 – 453 (1970) and Smith and Waterman respectively (Adv. Appl. Math. 2; 482 – 489 (1981)] which are part of the GCG software package [Genetics Computer Group, 575 Science Drive, Madison, Wisconsin, USA 53711 (1991)]. The above mentioned percentages of sequence homology are calculated with the program BestFit or Gap, preferably Gap, over the total sequence length with the following parameters used: Gap Weight: 8, Length Weight: 2.

0251.0.1 Variants shall also be encompassed, in particular, functional variants which can be obtained from the sequence shown in the Fig. 1a, 1b or 1c by means of deletion, insertion or substitution of nucleotides, the enzymatic activity of the derived synthetic proteins being retained or enhanced.

0252.0.1 An isolated nucleic acid molecule encoding a stress related protein homologous to a protein sequence of Fig. 1a, 1b or 1c can be created by introducing one or more nucleotide substitutions, additions or deletions into a nucleotide sequence of Fig. 1a, 1b or 1c such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein. Mutations can be introduced into one of the sequences of Fig. 1a, 1b or 1c by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Another route to the mutagenesis of enzymes, disclosed in the European Publication EP-A-0 909 821, is a method using the specific Escherichia coli strain XL1-Red to generate mutants and altered the enzyme activity.

0253.0.1 Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain.

0254.0.1 Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted nonessential amino acid residue in a stress related protein is preferably replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of a stress related protein coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for a stress related protein activity as described herein to identify mutants that retain stress related protein activity or show enhanced stress related protein activity. Following mutagenesis of one of the sequences of the nucleic acid of Fig. 1a, 1b or 1c, the encoded protein can be expressed recombinantly and the activity of the protein can be determined by analyzing the stress tolerance of a plant expressing the protein as described in the examples below.

0255.0.1 A useful method to ascertain the level of transcription of the gene (an indicator of the amount of mRNA available for translation to the gene product) is to perform a Northern blot (for reference see, for example, Ausubel et al., 1988 Current Protocols in Molecular Biology, Wiley: New York). This information at least partially demonstrates the degree of transcription of the gene. Total cellular RNA can be prepared from cells, tissues or organs by several methods, all well-known in the art, such as that described in Bormann, E.R. et al., 1992 Mol. Microbiol. 6:317-326. To assess the presence or relative quantity of protein translated from this mRNA, standard techniques, such as a Western blot, may be employed. These techniques are well known to one of ordinary skill in the art (see, for example, Ausubel et al., 1988 Current Protocols in Molecular Biology, Wiley: New York).

0256.0.1 The present invention also relates to a plant expression cassette comprising a SRP coding nucleic acid selected from the group comprising sequences of **SEQ IDs No. XXX** and/or homologs or parts thereof operatively linked to regulatory sequences and/or targeting sequences.

0257.0.1 Further, object of the invention is an expression vector comprising a SRP encoding nucleic acid selected from the group comprising sequences of the nucleic acid of Fig. 1a, 1b or 1c and/or homologs or parts thereof or a plant expression cassette as described above, whereby expression of the SRP coding nucleic acid in a host cell results in increased tolerance to environmental stress, which is preferably achieved by altering metabolic activity, as compared to a corresponding non-transformed wild type host cell.

0258.0.1 The invention further provides an isolated recombinant expression vector comprising a stress related protein encoding nucleic acid as described above, wherein expression of the vector or stress related protein encoding nucleic acid, respectively in a host cell results in increased tolerance and/or resistance to environmental stress, which is preferably achieved by altering metabolic activity, as compared to the corresponding non-transformed wild type of the host cell. As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Further types of vectors can be linearized nucleic acid sequences, such as transposons, which are pieces of DNA which can copy and insert themselves. There have been 2 types of transposons found: simple transposons, known as Insertion Sequences and composite transposons, which can have several genes as well as the genes that are required for transposition.

0259.0.1 Certain vectors are capable of autonomous replication in a host cell into which they are introduced (e.g., bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (e.g., non-episomal mammalian vectors) are integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they are operatively linked. Such vectors are referred to herein as "expression vectors". In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. In the present specification, "plasmid" and "vector" can be used interchangeably as the plasmid is the most commonly used form of vector. However, the invention is intended to include such other forms of expression vectors, such as viral vectors (e.g., replication defective retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

0260.0.1 A plant expression cassette preferably contains regulatory sequences capable of driving gene expression in plant cells and operably linked so that each sequence can fulfill its function, for example, termination of transcription by polyadenylation signals. Preferred polyadenylation signals are those originating from Agrobacterium tumefaciens T-DNA such as the gene 3 known as octopine synthase of the Ti-plasmid pTiACH5 (Gielen et al., 1984 EMBO J. 3:835) or functional equivalents thereof but also all other terminators functionally active in plants are suitable.

0261.0.1 As plant gene expression is very often not limited on transcriptional levels, a plant expression cassette preferably contains other operably linked sequences like translational enhancers such as the overdrive-sequence containing the 5´-untranslated leader sequence from tobacco mosaic virus enhancing the protein per RNA ratio (Gallie et al., 1987 Nucl. Acids Research 15:8693-8711).

0262.0.1 Plant gene expression has to be operably linked to an appropriate promoter conferring gene expression in a timely, cell or tissue specific manner. Preferred are promoters driving constitutive expression (Benfey et al., 1989 EMBO J. 8:2195-2202) like those derived from plant viruses like the 35S CaMV (Franck et al., 1980 Cell 21:285-294), the 19S CaMV (see also U.S. Patent No. 5352605 and PCT Application No. WO 8402913) or plant promoters like those from Rubisco small subunit described in U.S. Patent No. 4,962,028.

0263.0.1 Additional advantageous regulatory sequences are, for example, included in the plant promoters such as CaMV/35S [Franck et al., Cell 21 (1980) 285 - 294], PRP1 [Ward et al., Plant. Mol. Biol. 22 (1993)], SSU, OCS, lib4, usp, STLS1, B33, LEB4, nos or in the ubiquitin, napin or phaseolin promoter. Also advantageous in this connection are inducible promoters such as the promoters described in EP-A-0

388 186 (benzyl sulfonamide inducible), Plant J. 2, 1992: 397 - 404 (Gatz et al., Tetracyclin inducible), EP-A-0 335 528 (abscisic acid inducible) or WO 93/21334 (ethanol or cyclohexenol inducible). Additional useful plant promoters are the cytosolic FBPase promotor or ST-LSI promoter of the potato (Stockhaus et al., EMBO J. 8, 1989, 2445), the phosphorybosyl phyrophoshate amido transferase promoter of Glycine max (gene bank accession No. U87999) or the noden specific promoter described in EP-A-0 249 676. Additional particularly advantageous promoters are seed specific promoters which can be used for monokotyledones or dikotyledones and are described in US 5,608,152 (napin promoter from rapeseed), WO 98/45461 (phaseolin promoter from Arobidopsis), US 5,504,200 (phaseolin promoter from Phaseolus vulgaris), WO 91/13980 (Bce4 promoter from Brassica) and Baeumlein et al., Plant J., 2, 2, 1992: 233-239 (LEB4 promoter from leguminosa). Said promoters are useful in dikotyledones. The following promoters are useful for example in monokotyledones lpt-2- or lpt-1- promoter from barley (WO 95/15389 and WO 95/23230) or hordein promoter from barley. Other useful promoters are described in WO 99/16890.

0264.0.1 It is possible in principle to use all natural promoters with their regulatory sequences like those mentioned above for the novel process. It is also possible and advantageous in addition to use synthetic promoters.

0265.0.1 The gene construct may also comprise further genes which are to be inserted into the organisms and which are for example involved in stress resistance. It is possible and advantageous to insert and express in host organisms regulatory genes such as genes for inducers, repressors or enzymes which intervene by their enzymatic activity in the regulation, or one or more or all genes of a biosynthetic pathway. These genes can be heterologous or homologous in origin. The inserted genes may have their own promoter or else be under the control of same promoter as the sequences of the nucleic acid of Fig. 1a, 1b or 1c or their homologs.

0266.0.1 The gene construct advantageously comprises, for expression of the other genes present, additionally 3' and/or 5' terminal regulatory sequences to enhance expression, which are selected for optimal expression depending on the selected host organism and gene or genes.

0267.0.1 These regulatory sequences are intended to make specific expression of the genes and protein expression possible as mentioned above. This may mean, depending on the host organism, for example that the gene is expressed or overexpressed only after induction, or that it is immediately expressed and/or overexpressed.

0268.0.1 The regulatory sequences or factors may moreover preferably have a beneficial effect on expression of the introduced genes, and thus increase it. It is

possible in this way for the regulatory elements to be enhanced advantageously at the transcription level by using strong transcription signals such as promoters and/or enhancers. However, in addition, it is also possible to enhance translation by, for example, improving the stability of the mRNA.

0269.0.1 Other preferred sequences for use in plant gene expression cassettes are targeting-sequences necessary to direct the gene product in its appropriate cell compartment (for review see Kermode, 1996 Crit. Rev. Plant Sci. 15(4):285-423 and references cited therein) such as the vacuole, the nucleus, all types of plastids like amyloplasts, chloroplasts, chromoplasts, the extracellular space, mitochondria, the endoplasmic reticulum, oil bodies, peroxisomes and other compartments of plant cells.

0270.0.1 Plant gene expression can also be facilitated via an inducible promoter (for review see Gatz, 1997 Annu. Rev. Plant Physiol. Plant Mol. Biol. 48:89-108). Chemically inducible promoters are especially suitable if gene expression is wanted to occur in a time specific manner.

0271.0.1 Table 1 lists several examples of promoters that may be used to regulate transcription of the stress related protein nucleic acid coding sequences.

0272.0.1 Tab. 1: Examples of Tissue-specific and Stress inducible promoters in plants

Expression	Reference
Cor78- Cold, drought, salt, ABA, wounding-inducible	Ishitani, *et al.*, Plant Cell 9:1935-1949 (1997). Yamaguchi-Shinozaki and Shinozaki, Plant Cell 6:251-264 (1994).
Rci2A - Cold, dehydration-inducible	Capel *et al.*, Plant Physiol 115:569-576 (1997)
Rd22 - Drought, salt	Yamaguchi-Shinozaki and Shinozaki, Mol Gen Genet 238:17-25 (1993).
Cor15A - Cold, dehydration, ABA	Baker *et al.*, Plant Mol. Biol. 24:701-713 (1994).
GH3- Auxin inducible	Liu *et al.*, Plant Cell 6:645-657 (1994)
ARSK1-Root, salt inducible	Hwang and Goodman, Plant J 8:37-43 (1995).
PtxA - Root, salt inducible	GenBank accession X67427

SbHRGP3 - Root specific	Ahn *et al.*, Plant Cell 8:1477-1490 (1998).
KST1 - Guard cell specific	Plesch *et al.*, Plant Journal. 28(4):455-64, (2001)
KAT1 - Guard cell specific	Plesch *et al.*, Gene 249:83-89 (2000) Nakamura *et al.*, Plant Physiol. 109:371-374 (1995)
salicylic acid inducible	PCT Application No. WO 95/19443
tetracycline inducible	Gatz et al. Plant J. 2:397-404 (1992)
Ethanol inducible	PCT Application No. WO 93/21334
pathogen inducible PRP1	Ward et al., 1993 Plant. Mol. Biol. 22:361-366
heat inducible hsp80	U.S. Patent No. 5187267
cold inducible alpha-amylase	PCT Application No. WO 96/12814
Wound-inducible pinII	European Patent No. 375091
RD29A - salt-inducible	Yamaguchi-Shinozalei et al. (1993) Mol. Gen. Genet. 236:331-340
plastid-specific viral RNA-polymerase	PCT Application No. WO 95/16783 and. WO 97/06250

0273.0.1 Other promotors, e.g. superpromotor (Ni et al,., Plant Journal 7, 1995: 661-676), Ubiquitin promotor (Callis et al., J. Biol. Chem., 1990, 265: 12486-12493; US 5,510,474; US 6,020,190; Kawalleck et al., Plant. Molecular Biology, 1993, 21: 673-684) or 34S promotor (GenBank Accession numbers M59930 and X16673) were similar useful for the present invention and are known to a person skilled in the art.

0274.0.3 Developmental stage-preferred promoters are preferentially expressed at certain stages of development. Tissue and organ preferred promoters include those that are preferentially expressed in certain tissues or organs, such as leaves, roots, seeds, or xylem. Examples of tissue preferred and organ preferred promoters include, but are not limited to fruit-preferred, ovule-preferred, male tissue-preferred, seed-

preferred, integument-preferred, tuber-preferred, stalk-preferred, pericarp-preferred, and leaf-preferred, stigma-preferred, pollen-preferred, anther-preferred, a petal-preferred, sepal-preferred, pedicel-preferred, silique-preferred, stem-preferred, root-preferred promoters, and the like. Seed preferred promoters are preferentially expressed during seed development and/or germination. For example, seed preferred promoters can be embryo-preferred, endosperm preferred, and seed coat-preferred. See Thompson et al., 1989, BioEssays 10:108. Examples of seed preferred promoters include, but are not limited to, cellulose synthase (celA), Cim1, gamma-zein, globulin-1, maize 19 kD zein (cZ19B1), and the like.

0275.0.3 Other promoters useful in the expression cassettes of the invention include, but are not limited to, the major chlorophyll a/b binding protein promoter, histone promoters, the Ap3 promoter, the β-conglycin promoter, the napin promoter, the soybean lectin promoter, the maize 15kD zein promoter, the 22kD zein promoter, the 27kD zein promoter, the g-zein promoter, the waxy, shrunken 1, shrunken 2 and bronze promoters, the Zm13 promoter (U.S. Patent No. 5,086,169), the maize polygalacturonase promoters (PG) (U.S. Patent Nos. 5,412,085 and 5,545,546), and the SGB6 promoter (U.S. Patent No. 5,470,359), as well as synthetic or other natural promoters.

0276.0.3 Additional flexibility in controlling heterologous gene expression in plants may be obtained by using DNA binding domains and response elements from heterologous sources (*i.e.*, DNA binding domains from non-plant sources). An example of such a heterologous DNA binding domain is the LexA DNA binding domain (Brent and Ptashne, 1985, Cell 43:729-736).

0277.0.3 The invention further provides a recombinant expression vector comprising a SRP DNA molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operatively linked to a regulatory sequence in a manner that allows for expression (by transcription of the DNA molecule) of an RNA molecule that is antisense to a SRP mRNA. Regulatory sequences operatively linked to a nucleic acid molecule cloned in the antisense orientation can be chosen which direct the continuous expression of the antisense RNA molecule in a variety of cell types. For instance, viral promoters and/or enhancers, or regulatory sequences can be chosen which direct constitutive, tissue specific, or cell type specific expression of antisense RNA. The antisense expression vector can be in the form of a recombinant plasmid, phagemid, or attenuated virus wherein antisense nucleic acids are produced under the control of a high efficiency regulatory region. The activity of the regulatory region can be determined by the cell type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense

genes, see Weintraub, H. et al., 1986, Antisense RNA as a molecular tool for genetic analysis, Reviews - Trends in Genetics, Vol. 1(1), and Mol et al., 1990, FEBS Letters 268:427-430.

0279.0.3 Another aspect of the invention pertains to host cells into which a recombinant expression vector of the invention has been introduced. The terms "host cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but they also apply to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein. A host cell can be any prokaryotic or eukaryotic cell. For example, a SRP can be expressed in bacterial cells such as *C. glutamicum*, yeast, E.coli, insect cells, fungal cells, or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells), algae, ciliates, plant cells, fungi, or other microorganisms like *C. glutamicum*. Other suitable host cells are known to those skilled in the art.

0280.0.3 A host cell of the invention, such as a prokaryotic or eukaryotic host cell in culture, can be used to produce (i.e., express) a SRP. Accordingly, the invention further provides methods for producing SRPs using the host cells of the invention. In one embodiment, the method comprises culturing the host cell of invention (into which a recombinant expression vector encoding a SRP has been introduced, or into which genome has been introduced a gene encoding a wild-type or altered SRP) in a suitable medium until SRP is produced. In another embodiment, the method further comprises isolating SRPs from the medium or the host cell.

0281.0.3 Another aspect of the invention pertains to isolated SRPs, and biologically active portions thereof. An "isolated" or "purified" polypeptide or biologically active portion thereof is free of some of the cellular material when produced by recombinant DNA techniques, or chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of SRP in which the polypeptide is separated from some of the cellular components of the cells in which it is naturally or recombinantly produced. In one embodiment, the language "substantially free of cellular material" includes preparations of a SRP having less than about 30% (by dry weight) of non-SRP material (also referred to herein as a "contaminating polypeptide"), more preferably less than about 20% of non-SRP material, still more preferably less than about 10% of non-SRP material, and most preferably less than about 5% non-PKSRP material.

0282.0.3 When the SRP or biologically active portion thereof is recombinantly produced, it is also preferably substantially free of culture medium, i.e., culture medium represents less than about 20%, more preferably less than about 10%, and most preferably less than about 5% of the volume of the polypeptide preparation. The language "substantially free of chemical precursors or other chemicals" includes preparations of SRP in which the polypeptide is separated from chemical precursors or other chemicals that are involved in the synthesis of the polypeptide. In one embodiment, the language "substantially free of chemical precursors or other chemicals" includes preparations of a SRP having less than about 30% (by dry weight) of chemical precursors or non-SRP chemicals, more preferably less than about 20% chemical precursors or non-SRP chemicals, still more preferably less than about 10% chemical precursors or non-SRP chemicals, and most preferably less than about 5% chemical precursors or non-SRP chemicals. In preferred embodiments, isolated polypeptides, or biologically active portions thereof, lack contaminating polypeptides from the same organism from which the SRP is derived. Typically, such polypeptides are produced by recombinant expression of, for example, a *Saccharomyces cerevisiae*, E.coli, *Brassica napus*, *Glycine max*, or *Oryza sativa* SRP in plants other than *Saccharomyces cerevisiae*, E.coli, *Brassica napus*, *Glycine max*, or *Oryza sativa*, or microorganisms such as *C. glutamicum*, ciliates, algae or fungi.

0283.0.3 The nucleic acid molecules, polypeptides, polypeptide homologs, fusion polypeptides, primers, vectors, and host cells described herein can be used in one or more of the following methods: identification of *Saccharomyces cerevisiae, E.coli*, *Brassica napus*, *Glycine max*, or *Oryza sativa* and related organisms; mapping of genomes of organisms related to *Saccharomyces cerevisiae, E.coli, Brassica napus*, *Glycine max*, or *Oryza sativa*; identification and localization of *Saccharomyces cerevisiae, E.coli*, *Brassica napus*, *Glycine max*, or *Oryza sativa* sequences of interest; evolutionary studies; determination of SRP regions required for function; modulation of a SRP activity; modulation of the metabolism of one or more cell functions; modulation of the transmembrane transport of one or more compounds; modulation of stress resistance; and modulation of expression of SRP nucleic acids.

0284.0.3 The SRP nucleic acid molecules of the invention are also useful for evolutionary and polypeptide structural studies. The metabolic and transport processes in which the molecules of the invention participate are utilized by a wide variety of prokaryotic and eukaryotic cells; by comparing the sequences of the nucleic acid molecules of the present invention to those encoding similar enzymes from other organisms, the evolutionary relatedness of the organisms can be assessed. Similarly, such a comparison permits an assessment of which regions of the sequence are

conserved and which are not, which may aid in determining those regions of the polypeptide that are essential for the functioning of the enzyme. This type of determination is of value for polypeptide engineering studies and may give an indication of what the polypeptide can tolerate in terms of mutagenesis without losing function.

0285.0.3 Manipulation of the SRP nucleic acid molecules of the invention may result in the production of SRPs having functional differences from the wild-type SRPs. These polypeptides may be improved in efficiency or activity, may be present in greater numbers in the cell than is usual, or may be decreased in efficiency or activity.

0286.0.3 There are a number of mechanisms by which the alteration of a SRP of the invention may directly affect stress response and/or stress tolerance. In the case of plants expressing SRPs, increased transport can lead to improved salt and/or solute partitioning within the plant tissue and organs. By either increasing the number or the activity of transporter molecules which export ionic molecules from the cell, it may be possible to affect the salt tolerance of the cell.

0287.0.3 The effect of the genetic modification in plants, *C. glutamicum*, fungi, algae, or ciliates on stress tolerance can be assessed by growing the modified microorganism or plant under less than suitable conditions and then analyzing the growth characteristics and/or metabolism of the plant. Such analysis techniques are well known to one skilled in the art, and include dry weight, wet weight, polypeptide synthesis, carbohydrate synthesis, lipid synthesis, evapotranspiration rates, general plant and/or crop yield, flowering, reproduction, seed setting, root growth, respiration rates, photosynthesis rates, etc. (Applications of HPLC in Biochemistry in: Laboratory Techniques in Biochemistry and Molecular Biology, vol. 17; Rehm et al., 1993 Biotechnology, vol. 3, Chapter III: Product recovery and purification, page 469-714, VCH: Weinheim; Belter, P.A. et al., 1988, Bioseparations: downstream processing for biotechnology, John Wiley and Sons; Kennedy, J.F. and Cabral, J.M.S., 1992, Recovery processes for biological materials, John Wiley and Sons; Shaeiwitz, J.A. and Henry, J.D., 1988, Biochemical separations, in: Ulmann's Encyclopedia of Industrial Chemistry, vol. B3, Chapter 11, page 1-27, VCH: Weinheim; and Dechow, F.J., 1989, Separation and purification techniques in biotechnology, Noyes Publications).

0288.0.3 For example, yeast expression vectors comprising the nucleic acids disclosed herein, or fragments thereof, can be constructed and transformed into *Saccharomyces cerevisiae* using standard protocols. The resulting transgenic cells can then be assayed for fail or alteration of their tolerance to drought, salt, and temperature stress. Similarly, plant expression vectors comprising the nucleic acids disclosed herein, or fragments thereof, can be constructed and transformed into an appropriate

plant cell such as *Arabidopsis*, soy, rape, maize, wheat, *Medicago truncatula*, etc., using standard protocols. The resulting transgenic cells and/or plants derived therefrom can then be assayed for fail or alteration of their tolerance to drought, salt, temperature stress, and lodging.

0289.0.3 The engineering of one or more SRP genes of the invention may also result in SRPs having altered activities which indirectly impact the stress response and/or stress tolerance of algae, plants, ciliates, or fungi, or other microorganisms like *C. glutamicum*. For example, the normal biochemical processes of metabolism result in the production of a variety of products (e.g., hydrogen peroxide and other reactive oxygen species) which may actively interfere with these same metabolic processes. For example, peroxynitrite is known to nitrate tyrosine side chains, thereby inactivating some enzymes having tyrosine in the active site (Groves, J.T., 1999, Curr. Opin. Chem. Biol. 3(2):226-235). While these products are typically excreted, cells can be genetically altered to transport more products than is typical for a wild-type cell. By optimizing the activity of one or more PKSRPs of the invention which are involved in the export of specific molecules, such as salt molecules, it may be possible to improve the stress tolerance of the cell.

0290.0.3 Additionally, the sequences disclosed herein, or fragments thereof, can be used to generate knockout mutations in the genomes of various organisms, such as bacteria, mammalian cells, yeast cells, and plant cells (Girke, T., 1998, The Plant Journal 15:39-48). The resultant knockout cells can then be evaluated for their ability or capacity to tolerate various stress conditions, their response to various stress conditions, and the effect on the phenotype and/or genotype of the mutation. For other methods of gene inactivation, see U.S. Patent No. 6,004,804 "Non-Chimeric Mutational Vectors" and Puttaraju et al., 1999, Spliceosome-mediated RNA *trans*-splicing as a tool for gene therapy, Nature Biotechnology 17:246-252.

0291.0.3 The aforementioned mutagenesis strategies for SRPs resulting in increased stress resistance are not meant to be limiting; variations on these strategies will be readily apparent to one skilled in the art. Using such strategies, and incorporating the mechanisms disclosed herein, the nucleic acid and polypeptide molecules of the invention may be utilized to generate algae, ciliates, plants, fungi, or other microorganisms like *C. glutamicum* expressing mutated PKSRP nucleic acid and polypeptide molecules such that the stress tolerance is improved.

0292.0.3 The present invention also provides antibodies that specifically bind to a SRP, or a portion thereof, as encoded by a nucleic acid described herein. Antibodies can be made by many well-known methods (See, e.g. Harlow and Lane, "Antibodies; A Laboratory Manual," Cold Spring Harbor Laboratory, Cold Spring Harbor, New York,

(1988)). Briefly, purified antigen can be injected into an animal in an amount and in intervals sufficient to elicit an immune response. Antibodies can either be purified directly, or spleen cells can be obtained from the animal. The cells can then fused with an immortal cell line and screened for antibody secretion. The antibodies can be used to screen nucleic acid clone libraries for cells secreting the antigen. Those positive clones can then be sequenced. See, for example, Kelly et al., 1992, Bio/Technology 10:163-167; Bebbington et al., 1992, Bio/Technology 10:169-175.

0293.0.3 The phrases "selectively binds" and "specifically binds" with the polypeptide refer to a binding reaction that is determinative of the presence of the polypeptide in a heterogeneous population of polypeptides and other biologics. Thus, under designated immunoassay conditions, the specified antibodies bound to a particular polypeptide do not bind in a significant amount to other polypeptides present in the sample. Selective binding of an antibody under such conditions may require an antibody that is selected for its specificity for a particular polypeptide. A variety of immunoassay formats may be used to select antibodies that selectively bind with a particular polypeptide. For example, solid-phase ELISA immunoassays are routinely used to select antibodies selectively immunoreactive with a polypeptide. See Harlow and Lane, "Antibodies, A Laboratory Manual," Cold Spring Harbor Publications, New York, (1988), for a description of immunoassay formats and conditions that could be used to determine selective binding.

0294.0.3 In some instances, it is desirable to prepare monoclonal antibodies from various hosts. A description of techniques for preparing such monoclonal antibodies may be found in Stites et al., eds., "Basic and Clinical Immunology," (Lange Medical Publications, Los Altos, Calif., Fourth Edition) and references cited therein, and in Harlow and Lane, "Antibodies, A Laboratory Manual," Cold Spring Harbor Publications, New York, (1988).

0295.0.1 Gene expression in plants is regulated by the interaction of protein transcription factors with specific nucleotide sequences within the regulatory region of a gene. A common type of transcription factor contains zinc finger (ZF) motifs. Each ZF module is approximately 30 amino acids long folded around a zinc ion. The DNA recognition domain of a ZF protein is a α-helical structure that inserts into the major grove of the DNA double helix. The module contains three amino acids that bind to the DNA with each amino acid contacting a single base pair in the target DNA sequence. ZF motifs are arranged in a modular repeating fashion to form a set of fingers that recognize a contiguous DNA sequence. For example, a three-fingered ZF motif will recognize 9 bp of DNA. Hundreds of proteins have been shown to contain ZF motifs with between 2 and 37 ZF modules in each protein (Isalan M, et al., 1998 Biochemistry

37(35):12026-33; Moore M, et al., 2001 Proc. Natl. Acad. Sci. USA 98(4):1432-1436 and 1437-1441; US patents US 6007988 and US 6013453).

0296.0.1 The regulatory region of a plant gene contains many short DNA sequences (cis-acting elements) that serve as recognition domains for transcription factors, including ZF proteins. Similar recognition domains in different genes allow the coordinate expression of several genes encoding enzymes in a metabolic pathway by common transcription factors. Variation in the recognition domains among members of a gene family facilitates differences in gene expression within the same gene family, for example, among tissues and stages of development and in response to environmental conditions.

0297.0.1 Typical ZF proteins contain not only a DNA recognition domain but also a functional domain that enables the ZF protein to activate or repress transcription of a specific gene. Experimentally, an activation domain has been used to activate transcription of the target gene (US patent 5789538 and patent application WO9519431), but it is also possible to link a transcription repressor domain to the ZF and thereby inhibit transcription (patent applications WO00/47754 and WO2001002019). It has been reported that an enzymatic function such as nucleic acid cleavage can be linked to the ZF (patent application WO00/20622)

0298.0.1 The invention provides a method that allows one skilled in the art to isolate the regulatory region of one or more stress related protein encoding genes from the genome of a plant cell and to design zinc finger transcription factors linked to a functional domain that will interact with the regulatory region of the gene. The interaction of the zinc finger protein with the plant gene can be designed in such a manner as to alter expression of the gene and preferably thereby alter metabolic activity to confer increased (or decreased) tolerance of abiotic stress such as drought. The invention provides a method of producing a transgenic plant with a transgene encoding this designed transcription factor, or alternatively a natural transcription factor, that modifies transcription of the Stress-Related Protein, particularly stress related protein gene to provide increased tolerance of environmental stress, which is preferably achieved by altering metabolic activity. Such a regulation of plant genes by artificial polydactyl zinc fingers has been demonstrated by Ordiz et al.(Regulation of transgene Expression in plants with polydactyl zinc finger transcription factors, Ordiz et al., PNAS ,99 (20) 13290-13295, 2002) or Guan et al. (Hertiable endogenous gene regulation in plants with designed polydactyl zinc finger transcription factos, PNAS, Vol. 99 (20), 13296-13301 (2002)).

0299.0.1 In particular, the invention provides a method of producing a transgenic plant with a stress related protein coding nucleic acid, wherein expression of the

nucleic acid(s) in the plant results in increased tolerance to environmental stress, which is preferably achieved by altering metabolic activity, as compared to a wild type plant comprising: (a) transforming a plant cell with an expression vector comprising a stress related protein encoding nucleic acid, and (b) generating from the plant cell a transgenic plant with an increased tolerance to environmental stress as compared to a wild type plant. For such plant transformation, binary vectors such as pBinAR can be used (Höfgen and Willmitzer, 1990 Plant Science 66:221-230). Moreover suitable binary vectors are for example pBIN19, pBI101, pGPTV or pPZP (Hajukiewicz, P. et al., 1994, Plant Mol. Biol., 25: 989-994).

0300.0.1 Construction of the binary vectors can be performed by ligation of the cDNA into the T-DNA. 5' to the cDNA a plant promoter activates transcription of the cDNA. A polyadenylation sequence is located 3' to the cDNA. Tissue-specific expression can be achieved by using a tissue specific promoter as listed above. Also, any other promoter element can be used. For constitutive expression within the whole plant, the CaMV 35S promoter can be used. The expressed protein can be targeted to a cellular compartment using a signal peptide, for example for plastids, mitochondria or endoplasmic reticulum (Kermode, 1996 Crit. Rev. Plant Sci. 4(15):285-423). The signal peptide is cloned 5' in frame to the cDNA to archive subcellular localization of the fusion protein. Additionally, promoters that are responsive to abiotic stresses can be used with, such as the Arabidopsis promoter RD29A. One skilled in the art will recognize that the promoter used should be operatively linked to the nucleic acid such that the promoter causes transcription of the nucleic acid which results in the synthesis of a mRNA which encodes a polypeptide.

0301.0.1 Alternate methods of transfection include the direct transfer of DNA into developing flowers via electroporation or Agrobacterium mediated gene transfer. Agrobacterium mediated plant transformation can be performed using for example the GV3101(pMP90) (Koncz and Schell, 1986 Mol. Gen. Genet. 204:383-396) or LBA4404 (Ooms et al., Plasmid, 1982, 7: 15-29; Hoekema et al., Nature, 1983, 303: 179-180) Agrobacterium tumefaciens strain. Transformation can be performed by standard transformation and regeneration techniques (Deblaere et al., 1994 Nucl. Acids. Res. 13:4777-4788; Gelvin and Schilperoort, Plant Molecular Biology Manual, 2nd Ed. - Dordrecht : Kluwer Academic Publ., 1995. - in Sect., Ringbuc Zentrale Signatur: BT11-P ISBN 0-7923-2731-4; Glick, B R and Thompson, J E, Methods in Plant Molecular Biology and Biotechnology, Boca Raton : CRC Press, 1993. - 360 S., ISBN 0-8493-5164-2). For example, rapeseed can be transformed via cotyledon or hypocotyl transformation (Moloney et al., 1989 Plant Cell Reports 8:238-242; De Block et al., 1989 Plant Physiol. 91:694-701). Use of antibiotics for Agrobacterium and plant

selection depends on the binary vector and the Agrobacterium strain used for transformation. Rapeseed selection is normally performed using kanamycin as selectable plant marker. Agrobacterium mediated gene transfer to flax can be performed using, for example, a technique described by Mlynarova et al., 1994 Plant Cell Report 13:282-285. Additionally, transformation of soybean can be performed using for example a technique described in European Patent No. 0424 047, U.S. Patent No. 5,322,783, European Patent No. 0397 687, U.S. Patent No. 5,376,543 or U.S. Patent No. 5,169,770. Transformation of maize can be achieved by particle bombardment, polyethylene glycol mediated DNA uptake or via the silicon carbide fiber technique (see, for example, Freeling and Walbot "The maize handbook" Springer Verlag: New York (1993) ISBN 3-540-97826-7). A specific example of maize transformation is found in U.S. Patent No. 5,990,387 and a specific example of wheat transformation can be found in PCT Application No. WO 93/07256.

0302.0.1 The stress related protein encoding nucleic acid molecules of the invention have a variety of uses. Most importantly, the nucleic acid and amino acid sequences of the present invention can be used to transform plant cells or plants, thereby inducing tolerance to stresses such as drought, high salinity and cold. The present invention therefore provides a transgenic plant transformed by a stress related protein encoding nucleic acid (coding or antisense), wherein expression of the nucleic acid sequence in the plant results in increased tolerance to environmental stress as compared to a wild type plant. The increased stress tolerance is apparent as an increase in the yield or quality of the plant. The transgenic plant can be a monocot or a dicot or a gymnosperm plant. The invention further provides that the transgenic plant can be selected from maize, wheat, rye, oat, triticale, rice, barley, soybean, peanut, cotton, borage, sufflower, linseed, primrose, rapeseed, canola and turnip rape, manihot, pepper, sunflower, tagetes, solanaceous plant such as potato, tobacco, eggplant and tomato, Vicia species, pea, alfalfa, bushy plants such as coffee, cacao, tea, Salix species, trees such as oil palm, coconut, perennial grass, such as ryegrass and fescue, and forage crops, such as alfalfa and clover and Arabidopsis thaliana. Further the transgenic plant can be selected from spruce, pine or fir for example.

0303.0.1 In particular, the present invention describes using the expression of stress related proteins to engineer drought-tolerant, salt-tolerant and/or cold-tolerant plants. This strategy has herein been demonstrated for Arabidopsis thaliana, Ryegrass, Alfalfa, Rapeseed/Canola, Soybean, Corn and Wheat but its application is not restricted to these plants. Accordingly, the invention provides a transgenic plant containing a stress related protein encoding gene selected from the nucleic acid of Fig. 1a, 1b or 1c and/or homologs of the afore mentioned sequences, wherein the

environmental stress is drought, increased salt or decreased or increased temperature but its application is not restricted to these adverse environments. Protection against other adverse conditions such as heat, air pollution, heavy metals and chemical toxicants, for example, may be obtained. In preferred embodiments, the environmental stress is drought.

0304.0.1 The present invention also provides methods of modifying stress tolerance of a plant comprising, modifying the expression of a stress related protein encoding gene in the plant. The invention provides that this method can be performed such that the stress tolerance is increased. This can for example be done by the use of transcription factors. In particular, the present invention provides methods of producing a transgenic plant having an increased tolerance to environmental stress as compared to a wild type plant due to increased expression of a stress related protein in the plant.

0305.0.1 Growing the modified plants under stress conditions and then screening and analyzing the growth characteristics and/or metabolic activity assess the effect of the genetic modification in plants on stress tolerance and/or resistance. Such analysis techniques are well known to one skilled in the art. They include next to screening (Römpp Lexikon Biotechnologie, Stuttgart/New York: Georg Thieme Verlag 1992, "screening" p. 701) dry weight, wet weight, protein synthesis, carbohydrate synthesis, lipid synthesis, evapotranspiration rates, general plant and/or crop yield, flowering, reproduction, seed setting, root growth, respiration rates, photosynthesis rates, etc. (Applications of HPLC in Biochemistry in: Laboratory Techniques in Biochemistry and Molecular Biology, vol. 17; Rehm et al., 1993 Biotechnology, vol. 3, Chapter III: Product recovery and purification, page 469-714, VCH: Weinheim; Belter, P.A. et al., 1988 Bioseparations: downstream processing for biotechnology, John Wiley and Sons; Kennedy, J.F. and Cabral, J.M.S., 1992 Recovery processes for biological materials, John Wiley and Sons; Shaeiwitz, J.A. and Henry, J.D., 1988 Biochemical separations, in: Ulmann's Encyclopedia of Industrial Chemistry, vol. B3, Chapter 11, page 1-27, VCH: Weinheim; and Dechow, F.J. (1989) Separation and purification techniques in biotechnology, Noyes Publications).

0306.0.1 The engineering of one or more stress related protein encoding genes of the invention may also result in stress related proteins having altered activities which indirectly impact the stress response and/or stress tolerance of plants. For example, the normal biochemical processes of metabolism result in the production of a variety of products (e.g., hydrogen peroxide and other reactive oxygen species) which may actively interfere with these same metabolic processes (for example, peroxynitrite is known to react with tyrosine side chains, thereby inactivating some enzymes having tyrosine in the active site (Groves, J.T., 1999 Curr. Opin. Chem. Biol. 3(2):226-235). By

optimizing the activity of one or more stress related proteins (enzymes) of the invention, it may be possible to improve the stress tolerance of the cell.

0307.0.1 Throughout this application, various publications are referenced. The disclosures of all of these publications and those references cited within those publications in their entireties are hereby incorporated by reference into this application in order to more fully describe the state of the art to which this invention pertains.

0308.0.1 It should also be understood that the foregoing relates to preferred embodiments of the present invention and that numerous changes and variations may be made therein without departing from the scope of the invention. The invention is further illustrated by the following examples, which are not to be construed in any way as limiting. On the contrary, it is to be clearly understood that various other embodiments, modifications and equivalents thereof, which, after reading the description herein, may suggest themselves to those skilled in the art without departing from the spirit of the present invention and/or the scope of the claims.

0309.0.1 The invention also pertains to the use of SRP encoding nucleic acid selected form the group comprising the nucleic acid of Fig. 1a, 1b or 1c and/or homologs of the afore mentioned sequences for preparing a plant cell with increased environmental stress tolerance, which is preferably achieved by altering metabolic activity. The said sequences can also be used for preparing a plant with increased environmental stress tolerance.

0310.0.1 Object of the invention is further the use of altered metabolic activity and/or a SRP encoding nucleic acid selected form the group of sequences of the nucleic acid of Fig. 1a, 1b or 1c and/or homologs of the afore mentioned sequences or parts thereof as markers for selection of plants with increased tolerance to environmental stress or as markers for detection of stress in plants or plant cells.

0311.0.1 Example 1

0312.0.1 Engineering stress-tolerant Arabidopsis plants by over-expressing stress related protein genes.

0313.0.1 Gene cloning and transformation of Arabidopsis thaliana

0314.0.1 Amplification

0315.0.1 The standard protocol of Pfu DNA polymerase or a Pfu/Taq DNA polymerase mix (Herculase) was used for the amplification procedure. Amplified ORF fragments were analysed by gel electrophoresis. Each primer consists of a universal 5 `end and ORF specific 3` end whereby the universal sequences differ for the forward and reverse primers (forward primer sequence contains an EcoRI for yeast or SmaI for E.coli and the reverse primer sequence a SmaI for yeast or SacI for E.coli restriction site) allowing generally a unidirectional cloning success.

0316.0.1 Amplification using the protocol of Pfu or Herculase DNA polymerase (Stratagene). Conditions: 1x PCR buffer, 0.2 mM dNTP, 100 ng genomic DNA Saccharomyces cerevisiae (S288C) or 60 ng genomic DNA Escherichia coli K-12 (MG1655), 25 pmol forward primer, 25 pmol reverse primer, 2.5 u Pfu or Herculase DNA polymerase. 1st cycle for 3` for yeast of 2` for E.coli at 94 °C, followed by 25 cycles for 30`` at 94 °C, 30`` 55°C for yeast or 60°C for E.coli and 5-6` 72 °C, followed by 1 cycle for 610` at 72 °C, final for 4 °C at ∞.

0317.0.1 Table 2: Forward and reverse primer sequences used for ORF amplification

Gene	Forward Seq
YGL263W	GGAATTCCAGCTGACCACCATGGATGGAGCCAAATTTGAAAATAC
YGR004W	GGAATTCCAGCTGACCACCATGAGCGAAATAAATAATGAAAATCTAG
YGR014W	GGAATTCCAGCTGACCACCATGCAGTTTCCATTCGCTTGTCTC
YGL239C	GGAATTCCAGCTGACCACCATGAAATTTTTGAAGAACAAAGCACC
YBL060W	GGAATTCCAGCTGACCACCATGTGCGCCAGTTTAAACGAGGTA
YGL166W	GGAATTCCAGCTGACCACCATGGTCGTAATTAACGGGGTCAAAT
YDL202W	GGAATTCCAGCTGACCACCATGTTGCAGCTAAGGTTTATGCCT
YAL046C	GGAATTCCAGCTGACCACCATGAAGCTCCCACAGACCATGCT
YDR101C	GGAATTCCAGCTGACCACCATGGCTCTAGCTATCTCCCACGA
YDR108W	GGAATTCCAGCTGACCACCATGGTTTTTTCTTATGAGCACTATATG
YAL064W	GGAATTCCAGCTGACCACCATGCGATATACTGCAACTTTTCGG
YDR134C	GGAATTCCAGCTGACCACCATGCAATTCTCTACCGTCGCTTCT
YFL031w	GGAATTCCAGCTGACCACCATGAATAGCGAGTACGATTACCTGT
YFL052W	GGAATTCCAGCTGACCACCATGGCCCGCAATAGACAAGCGT
YFL042C	GGAATTCCAGCTGACCACCATGTCGGATGTAGATAACTGGGAA
YBR025C	GGAATTCCAGCTGACCACCATGCCTCCAAAGAAGCAAGTCGAA
YER174C	GGAATTCCAGCTGACCACCATGACTGTGGTTGAAATAAAAAGCC
YBR051W	GGAATTCCAGCTGACCACCATGCACATTCTTTTCTTGTTTATTTTC
YER175C	GGAATTCCAGCTGACCACCATGTCTACCTTTTCTGCTTCTGATT
YDR521W	GGAATTCCAGCTGACCACCATGAAAGGTTCAAAATCGCACCTTG
YER167W	GGAATTCCAGCTGACCACCATGCCGAAGAATAGTCACCACCAT
YER123W	GGAATTCCAGCTGACCACCATGTCCCAACGATCTTCACAACAC
YDR415C	GGAATTCCAGCTGACCACCATGGCCGATGAGGAACGTTTAAAG
YEL052W	GGAATTCCAGCTGACCACCATGATCGCTTTGAAGCCCAATGCT
YDR536W	GGAATTCCAGCTGACCACCATGAAGGATTTAAAATTATCGAATTTCA
YDR513W	GGAATTCCAGCTGACCACCATGGAGACCAATTTTTCCTTCGACT
YEL045C	GGAATTCCAGCTGACCACCATGAAATGTCACGCGAAACGGAC
YEL041W	GGAATTCCAGCTGACCACCATGAAAACTGATAGATTACTGATTAAC
YDL238C	GGAATTCCAGCTGACCACCATGACAAAAAGTGATTTATTATTTGATAA
YBR282W	GGAATTCCAGCTGACCACCATGAAAGGCTCACCCATTTCTCAAT
YBR258C	GGAATTCCAGCTGACCACCATGGCGTATAATCAAGAAGATAGTAA
YCL001W-A	GGAATTCCAGCTGACCACCATGACCTTTTTACAATTTATCAATAATAATA

YBR274W	GGAATTCCAGCTGACCACCATGAGTCTCTCGCAGGTGTCAC
YHR090C	GGAATTCCAGCTGACCACCATGGATCCAAGTTTAGTTTTAGAGC
YGR121C	GGAATTCCAGCTGACCACCATGGAGAGTCGAACTACAGGGC
YGR127W	GGAATTCCAGCTGACCACCATGTGCATTTTAATGGCCACAAGG
YGR150C	GGAATTCCAGCTGACCACCATGTACATGGCCAGATGTGGCC
YKL037W	GGAATTCCAGCTGACCACCATGCAGACAATGGGCGGGGAG
YKL051W	GGAATTCCAGCTGACCACCATGATTCAATTTAAAAGTCCAGGTAAC
YKL120W	GGAATTCCAGCTGACCACCATGTCATCTGACAACTCTAAACAAG
YKL011C	GGAATTCCAGCTGACCACCATGTCGACAGCACAGAAAGCTAAG
YKL017C	GGAATTCCAGCTGACCACCATGAACAAAGAATTGGCTTCTAAGTT
YKL049C	GGAATTCCAGCTGACCACCATGGAAACTGAAGTACCTGCACCA
YKL132C	GGAATTCCAGCTGACCACCATGGATGATATAAGCGGAAGGCAAA
YGR126W	GGAATTCCAGCTGACCACCATGCCTGTCCCATCTGTTACTGT
YKL070W	GGAATTCCAGCTGACCACCATGTACATTCCTAAACATTTTGAGTC
YKL058W	GGAATTCCAGCTGACCACCATGGCAGTACCCGGGTATTACGA
YHR130C	GGAATTCCAGCTGACCACCATGACTAAAAGTATATATATTATCATCG
YIL070C	GGAATTCCAGCTGACCACCATGTTCTTAAGAAGCGTTAACCGTG
YHR195W	GGAATTCCAGCTGACCACCATGACTCGTCCCCCATTGGTTC
YIR022W	GGAATTCCAGCTGACCACCATGAATCTAAGATTTGAATTGCAGAAA
YJL089W	GGAATTCCAGCTGACCACCATGGCCAAGAGGAAATATGGCAG
YJL172W	GGAATTCCAGCTGACCACCATGATCGCCTTACCAGTAGAGAAG
YHR113W	GGAATTCCAGCTGACCACCATGTTCAGGATACAACTGAGAACTA
YHR175W	GGAATTCCAGCTGACCACCATGGATGATAAGAAAACATGGAGTAC
YGR212W	GGAATTCCAGCTGACCACCATGAATCTTAAACTTTCTGCTATTGAA
YJL024C	GGAATTCCAGCTGACCACCATGATTCATGCAGTTCTAATATGTATG
YGR180c	GGAATTCCAGCTGACCACCATGGAAGCACATAACCAATTTTTGAA
YJL179W	GGAATTCCAGCTGACCACCATGTCACAGATAGCACAAGAAATGA
YJL001W	GGAATTCCAGCTGACCACCATGAATGGAATTCAAGTGGACATCA
YJL208C	GGAATTCCAGCTGACCACCATGTGCAGTAGGATACTCTTGTCC
YJL152W	GGAATTCCAGCTGACCACCATGCCGCATTTAGCCGCCGAAG
YJL131C	GGAATTCCAGCTGACCACCATGTTAAAAGTTCCTTTGAGTGATGT
YJL151C	GGAATTCCAGCTGACCACCATGGACAGAGACCATATTAATGACC
YLR441C	GGAATTCCAGCTGACCACCATGGCTGTCGGAAAGAATAAGAGA
YLR415C	GGAATTCCAGCTGACCACCATGTATCTCAGTGCCCAGCTTATG
YLR212C	GGAATTCCAGCTGACCACCATGGGTGGAGAAATTATTACTTTGC
YLR029C	GGAATTCCAGCTGACCACCATGGGTGCCTACAAATATTTGGAAG
YLL041C	GGAATTCCAGCTGACCACCATGTTGAACGTGCTATTGAGAAGGA
YLR105C	GGAATTCCAGCTGACCACCATGTCTAAAGGGAGGGTCAATCAG
YIL136W	GGAATTCCAGCTGACCACCATGTCATCAAGAATAATTGTCGGCA
YLR215C	GGAATTCCAGCTGACCACCATGTCCTCACAAGAATATACAACTTT
YLR321C	GGAATTCCAGCTGACCACCATGTCGCACCAAAACCAGCTTATT
YMR260C	GGAATTCCAGCTGACCACCATGGGTAAGAAAAACACTAAAGGTG
YNL120C	GGAATTCCAGCTGACCACCATGATAAAAGTCGATACTTCCGATG
YLR407W	GGAATTCCAGCTGACCACCATGACTGTTTCTACTTCCAAGACC
YMR197C	GGAATTCCAGCTGACCACCATGAGTTCCCTATTAATATCATACGA
YMR100W	GGAATTCCAGCTGACCACCATGAGAGACTCTAATCATCGATCAT

YMR210W	GGAATTCCAGCTGACCACCATGCGTCTAAAAGAATTGTTACCTAA
YMR318C	GGAATTCCAGCTGACCACCATGTCTTATCCTGAGAAATTTGAAGG
YMR069W	GGAATTCCAGCTGACCACCATGCGTTCTTCGGTATATAGTGAGA
YNL076W	GGAATTCCAGCTGACCACCATGTCGCGGGAGGCATTTGATGT
YNL024C	GGAATTCCAGCTGACCACCATGGAGAGTATATTTGGTGGGTTTG
YNL125C	GGAATTCCAGCTGACCACCATGTCAACGCACTCAAACGACTAC
YNL029C	GGAATTCCAGCTGACCACCATGTTGCTAATAAGAAGGACGATAAA
YMR115W	GGAATTCCAGCTGACCACCATGCTTTTACAAGGAATGCGTTTATC
YNL244C	GGAATTCCAGCTGACCACCATGTCCATTGAGAATCTGAAATCATT
YNL334C	GGAATTCCAGCTGACCACCATGACCGTCGTTATCGGAGTCTT
YNR018W	GGAATTCCAGCTGACCACCATGAAGATTTTAACCCAAGACGAAAT
YNL277W	GGAATTCCAGCTGACCACCATGTCGCATACTTTAAAATCGAAAAC
YOL118C	GGAATTCCAGCTGACCACCATGTCTTTTAGAAAGAAAAAACTCAAAC
YOL123W	GGAATTCCAGCTGACCACCATGAGCTCTGACGAAGAAGATTTCA
YOR020C	GGAATTCCAGCTGACCACCATGTCCACCCTTTTGAAGTCTGCT
YOL116W	GGAATTCCAGCTGACCACCATGGCAAGTAACCAGCACATAGGA
YOR305w	GGAATTCCAGCTGACCACCATGATAAAAAACTATTTGGGACGAAG
YPL267W	GGAATTCCAGCTGACCACCATGATATCACCATCAAAAAAGAGAAC
YPL229w	GGAATTCCAGCTGACCACCATGATGCCCTACAACACCCCTC
YPL038W	GGAATTCCAGCTGACCACCATGAAACTGGCGCAAGACATGAAT
YPR047W	GGAATTCCAGCTGACCACCATGGAGGTAACTTCAATGTTTCTCA
YPL011C	GGAATTCCAGCTGACCACCATGACTACAAATAATGACTTCTATTTTG
YPR148C	GGAATTCCAGCTGACCACCATGTCTGGTTATTTTTCAGGGTTTTC
YOL103W	GGAATTCCAGCTGACCACCATGGCTGAAATGAAGAATTCGACAG
YOR016C	GGAATTCCAGCTGACCACCATGCGCGTTTTTTACTTTGATTGCGA
YPL079W	GGAATTCCAGCTGACCACCATGGGTAAATCGTATGTCCATATAAC
YOR260W	GGAATTCCAGCTGACCACCATGTCAATTCAGGCTTTTGTCTTTTG
YOR360C	GGAATTCCAGCTGACCACCATGTCCACCCTTTTTCTGATTGGAA
YDL060W	GGAATTCCAGCTGACCACCATGGCAGGTCATTCACACAGGTC
YDL005C	GGAATTCCAGCTGACCACCATGGTAGTACAAAATAGCCCAGTTT
YPL210C	GGAATTCCAGCTGACCACCATGAAAGAAAGCAAAAAAATGGCTAAA
YMR118C	GGAATTCCAGCTGACCACCATGAAAGCAACCATTCAAAGAGTAAC
YPR052C	GGAATTCCAGCTGACCACCATGGTCACCCCAAGAGAACCTAA
YLR224W	GGAATTCCAGCTGACCACCATGAATCAGAGCGATAGCAGCTTG
YLR275W	GGAATTCCAGCTGACCACCATGTCGTATGTTTGATCTTAACCATT
YMR154C	GGAATTCCAGCTGACCACCATGAATGATTGGCATGAGTTCAATG
YDR205w	GGAATTCCAGCTGACCACCATGGATAGAGGCAGGTGGTGTTT
YPR037C	GGAATTCCAGCTGACCACCATGAAACAGATAGTCAAAAGAAGCC
YNR008W	GGAATTCCAGCTGACCACCATGGGCACACTGTTTCGAAGAAAT
YOR084W	GGAATTCCAGCTGACCACCATGGAACAGAACAGGTTCAAGAAAG
YGR054W	GGAATTCCAGCTGACCACCATGTCATCTCAGTTTTTCCTGAAAAC
YGL106W	GGAATTCCAGCTGACCACCATGTCAGCCACCAGAGCCAATAAA
YAL067C	GGAATTCCAGCTGACCACCATGTATTCAATTGTTAAAGAGATTATTG
YIL023c	GGAATTCCAGCTGACCACCATGAAGGCGTCGCACATTTGCTC
YBR064W	GGAATTCCAGCTGACCACCATGGATATGGTATCACCAGTCTTGA
b0019	TTGCTCTTCCATGAAACATCTGCATCGATTCTTTAG

b2148	TTGCTCTTCCATGAGTGCGTTAAATAAGAAAAG
b2796	TTGCTCTTCCATGGAAACGACTCAAACCAGCAC
b2082	TTGCTCTTCCATGTTTCATTGTCCTTTATGCCAGC
b0124	TTGCTCTTCCATGGCAATTAACAATACAGGCTCG
b3116	TTGCTCTTCCATGAGTACTTCAGATAGCATTGTATC
b1830	TTGCTCTTCCATGAACATGTTTTTTAGGCTTACC
b1453	TTGCTCTTCCATGTTCATGGCAACTTATATGACTTTT
b2664	TTGCTCTTCCATGATCAGGAGTCACACCATGA
b2799	TTGCTCTTCCATGATGGCTAACAGAATGATTCTGA
b3327	TTGCTCTTCCATGAATTATCGCTATCGCGCCA
b0970	TTGCTCTTCCATGGATCGTATTGTTAGTTCTTCAC
YER003C	GGAATTCCAGCTGACCACCATGTCCAACAAGCTGTTCAGGTTA
YCL027W	GGAATTCCAGCTGACCACCATGGTAGCAACAATAATGCAGACGA
YBR112C	GGAATTCCAGCTGACCACCATGAATCCGGGCGGTGAACAAAC
YNL079C	GGAATTCCAGCTGACCACCATGGACAAAATCAGAGAAAAGCTAAG
YFR042W	GGAATTCCAGCTGACCACCATGGCAGGTATCAAGTTGACGCAT
YER137C	GGAATTCCAGCTGACCACCATGTGTGAATCATCAAATAAGACTGA
YKL103C	GGAATTCCAGCTGACCACCATGGAGGAACAACGTGAAATACTG
YNL090W	GGAATTCCAGCTGACCACCATGTCTGAAAAGGCCGTTAGAAGG
YGR161C	GGAATTCCAGCTGACCACCATGATCGCTACCTCCAGAGCCG
YDR071C	GGAATTCCAGCTGACCACCATGGCCTCCTCAAGTAGCACGC

Gene	Reverse Seq
YGL263W	GATCCCCGGGAATTGCCATGTTACACATCATTGCAAGCTGATTGT
YGR004W	GATCCCCGGGAATTGCCATGTTATAGAGAAGGAGACATTGAAACAT
YGR014W	GATCCCCGGGAATTGCCATGTCAAACTTCGTTCCAACCCAGGG
YGL239C	GATCCCCGGGAATTGCCATGTCAATTGCAGGGATTATGGAATAAAA
YBL060W	GATCCCCGGGAATTGCCATGTTAGAACTGAACAGAACCCATGGC
YGL166W	GATCCCCGGGAATTGCCATGTTATTGTGAATGTGAGTTATGCGAAG
YDL202W	GATCCCCGGGAATTGCCATGTTACTTTGATCCCTTCGATTCTGCA
YAL046C	GATCCCCGGGAATTGCCATGTCATGATGATGCCGGACCCTTC
YDR101C	GATCCCCGGGAATTGCCATGCTACATTTTCATGGTTTCTTCAACTC
YDR108W	GATCCCCGGGAATTGCCATGTCATCCAATAAAGCTAACACTTGTTC
YAL064W	GATCCCCGGGAATTGCCATGCTATGGTTCGCTATTCAATATTAGAA
YDR134C	GATCCCCGGGAATTGCCATGTTACAACAATAAAGCGGCAGCACC
YFL031w	GATCCCCGGGAATTGCCATGTCAACAGCAGCCCCCACCGGT
YFL052W	GATCCCCGGGAATTGCCATGTTAAGGAAGCGCATCTACATCTTCT
YFL042C	GATCCCCGGGAATTGCCATGTCAACCATACCTTTGATCCAACTG
YBR025C	GATCCCCGGGAATTGCCATGTCAATTCTTACCAGCACCAGCTCT
YER174C	GATCCCCGGGAATTGCCATGTTACTGTAGAGCATGTTGGAAATATT
YBR051W	GATCCCCGGGAATTGCCATGTTATATATGGCATGTCTTCGCATGT
YER175C	GATCCCCGGGAATTGCCATGTCAGACCCTTTTGCCAAGTTTGTAA

YDR521W	GATCCCCGGGAATTGCCATGTTACTCACCATTAAAACATCTTTCCC
YER167W	GATCCCCGGGAATTGCCATGTTAGTTGCTATTATCAAAATAAAAAGAC
YER123W	GATCCCCGGGAATTGCCATGTCAAAAAAAAAAAGGAAAAAGAGAAAAG
YDR415C	GATCCCCGGGAATTGCCATGTCACATTTTTCTAAATTCACTTAGCAC
YEL052W	GATCCCCGGGAATTGCCATGTTAGTATGTAGGCTTAGTAACCCAA
YDR536W	GATCCCCGGGAATTGCCATGTCAACCCTCAAAATTTGCTTTATCG
YDR513W	GATCCCCGGGAATTGCCATGCTATTGAAATACCGGCTTCAATATTT
YEL045C	GATCCCCGGGAATTGCCATGCTAGGAAAGGAGGTGGTTACGAA
YEL041W	GATCCCCGGGAATTGCCATGTTAGATTGCAAAATGAGCCTGACGA
YDL238C	GATCCCCGGGAATTGCCATGCTAAATCTGGTAGACTTGCTGGC
YBR282W	GATCCCCGGGAATTGCCATGTTATCCACGCTCCTTATAACATGAA
YBR258C	GATCCCCGGGAATTGCCATGTTACGTACTTCCATTTGCTTCCTCT
YCL001W-A	GATCCCCGGGAATTGCCATGTCAGTTCATCAAAATTGAAATTTCTAACCA
YBR274W	GATCCCCGGGAATTGCCATGTCAGTTGGGAATTAGGATAATATCC
YHR090C	GATCCCCGGGAATTGCCATGTCAGTTACGTTTTCTTTTCAGTTTGT
YGR121C	GATCCCCGGGAATTGCCATGTTACCTATTGGCAGGATCTTCTTGA
YGR127W	GATCCCCGGGAATTGCCATGTTACAATTTGAATTTAAACCTTTTTTCC
YGR150C	GATCCCCGGGAATTGCCATGCTACATGTTAAGTTCTTGTTCCTCC
YKL037W	GATCCCCGGGAATTGCCATGTTATATACTCAATCCAAAACAGGGAA
YKL051W	GATCCCCGGGAATTGCCATGTCATACGACTACTTGAATAGATTCG
YKL120W	GATCCCCGGGAATTGCCATGTTAATTATGGCCTAAAACTCTCGAC
YKL011C	GATCCCCGGGAATTGCCATGTTAGTCATTGTTGTAAGTGTTCTGC
YKL017C	GATCCCCGGGAATTGCCATGTTACAAATAATCGTCAATGTTGGGG
YKL049C	GATCCCCGGGAATTGCCATGCTAAATAAACTGTCCCCTGATTCTT
YKL132C	GATCCCCGGGAATTGCCATGCTATACTGGCAAGTGACAGTTGTG
YGR126W	GATCCCCGGGAATTGCCATGTTAATCGAAAATTCTATGAAAAAACCC
YKL070W	GATCCCCGGGAATTGCCATGTCAGAAACGCTCCACTTTACTTCG
YKL058W	GATCCCCGGGAATTGCCATGTTACTCGCTCTTTTTTGAGTTACATG
YHR130C	GATCCCCGGGAATTGCCATGCTAATTCCTGATGCCAAGTAACGA
YIL070C	GATCCCCGGGAATTGCCATGTTAGTGGAAAAACTTCTTCATCTTTTC
YHR195W	GATCCCCGGGAATTGCCATGTTAGTATCTAAATGGTTGAGAGTATG
YIR022W	GATCCCCGGGAATTGCCATGCTACTCGCCCCCCAGCAGAG
YJL089W	GATCCCCGGGAATTGCCATGTTAGAAGGTCGAGTTCAAAATATTCT
YJL172W	GATCCCCGGGAATTGCCATGTTAAGCGTATTCGTTAACATTAACGA
YHR113W	GATCCCCGGGAATTGCCATGTTAGACAACAATTTCAGATTCTATGG
YHR175W	GATCCCCGGGAATTGCCATGTTAATGGCAGGCGAGGGAGCTG
YGR212W	GATCCCCGGGAATTGCCATGCTAGTATAAATTTAAGTAATCTTTCATAT
YJL024C	GATCCCCGGGAATTGCCATGTTATTGCCCCGTTGCCCATTGTG
YGR180c	GATCCCCGGGAATTGCCATGTTAGAAGTCATCATCAAAGTTAATTTC
YJL179W	GATCCCCGGGAATTGCCATGTTAATTCTTCATCAATGCCTTTAGATT
YJL001W	GATCCCCGGGAATTGCCATGTTATAGTTGTTCATATTCATCAGGGT
YJL208C	GATCCCCGGGAATTGCCATGTCAATTCCTTTTTTTTGGAGGAGGT
YJL152W	GATCCCCGGGAATTGCCATGTCACGCAGACATGCGACTGCG
YJL131C	GATCCCCGGGAATTGCCATGTTACATTTCATTCATTTTTTTTCTCTGA
YJL151C	GATCCCCGGGAATTGCCATGCTAAGTACGGCCGGAAGAGAGC
YLR441C	GATCCCCGGGAATTGCCATGTTACACAGTTTCCAAGACTTCGTC

YLR415C	GATCCCCGGGAATTGCCATGCTACTTCCAAACAACTGGTCCAGA
YLR212C	GATCCCCGGGAATTGCCATGTTATACTAATTTATGATCACCGTCGG
YLR029C	GATCCCCGGGAATTGCCATGTTATTTTCTGTATCTCCACAAGGAC
YLL041C	GATCCCCGGGAATTGCCATGCTAGGCAAATGCCAAAGATTTCTTA
YLR105C	GATCCCCGGGAATTGCCATGCTAGTCTCTATTTCTTCCGGGAAC
YIL136W	GATCCCCGGGAATTGCCATGCTAGTCCTTTTTCGAGCTCCAGAA
YLR215C	GATCCCCGGGAATTGCCATGCTAAGTTTCATTCTCACTATCACTG
YLR321C	GATCCCCGGGAATTGCCATGCTACATTCTCATTGTGGTTTCTAAG
YMR260C	GATCCCCGGGAATTGCCATGTTAATCATAAATAGTTTCATAAGTGTGT
YNL120C	GATCCCCGGGAATTGCCATGTCACTTCCTATGCAAAATGCTTAATA
YLR407W	GATCCCCGGGAATTGCCATGTCAGTCATGGCATGCCTTGGCA
YMR197C	GATCCCCGGGAATTGCCATGCTAAAATGAAGACAGCCACAATCTG
YMR100W	GATCCCCGGGAATTGCCATGCTATTGATTGTTTGTTCCACGGACT
YMR210W	GATCCCCGGGAATTGCCATGTTATGAAGTCCATGGTAAATTCGTG
YMR318C	GATCCCCGGGAATTGCCATGTTACATGAGGTTCATGTTCATGTTAG
YMR069W	GATCCCCGGGAATTGCCATGTTATTTTTTACTTAATTTCATCCATTTAG
YNL076W	GATCCCCGGGAATTGCCATGTTATGTATCACAACTATTAAATTCAGTT
YNL024C	GATCCCCGGGAATTGCCATGTTAATCTCTTTCAAAACAGACAGCAA
YNL125C	GATCCCCGGGAATTGCCATGCTATTTTTCACTTTGGCTGTTGCC
YNL029C	GATCCCCGGGAATTGCCATGTTAACTCTCTTGTCCCGATTTCTC
YMR115W	GATCCCCGGGAATTGCCATGTTAGTTTCTCAAGTGACTATTGTGAA
YNL244C	GATCCCCGGGAATTGCCATGTTACGAATCAGTCCGATTGGACTT
YNL334C	GATCCCCGGGAATTGCCATGTTAAGCTGGAAGAGCCAATCTCTT
YNR018W	GATCCCCGGGAATTGCCATGTTATTTCAAAGTCTTCAACAATTTTTCT
YNL277W	GATCCCCGGGAATTGCCATGTTAGTCTTCATGCTTATCACAGAAC
YOL118C	GATCCCCGGGAATTGCCATGTCACTTCAAAGTCTCTGGAATATGA
YOL123W	GATCCCCGGGAATTGCCATGTTATTCGTCTTCTTCCAAAGTTTGAG
YOR020C	GATCCCCGGGAATTGCCATGCTATGAGCGATCCCGTTTTGTGAA
YOL116W	GATCCCCGGGAATTGCCATGTTAATAATTGAATTTAATTTTACTTCTGTT
YOR305w	GATCCCCGGGAATTGCCATGTCACCGACTCATTTTGTTAAGCTTG
YPL267W	GATCCCCGGGAATTGCCATGTTACTCATCTTCATAGACGTGGAAG
YPL229w	GATCCCCGGGAATTGCCATGCTAACATTTCTTATTATCTCTATATATC
YPL038W	GATCCCCGGGAATTGCCATGCTAACTGCTTTTTTCGTGTTGAGTA
YPR047W	GATCCCCGGGAATTGCCATGTCATTTTTGTCCCTTTATATCAATTTTT
YPL011C	GATCCCCGGGAATTGCCATGTTAGCGTTTTTTTTTGCCCTTCTTC
YPR148C	GATCCCCGGGAATTGCCATGCTAAATTTCCAAACCATTTAGAACTTT
YOL103W	GATCCCCGGGAATTGCCATGCTAAGACTTGAAATTAATTAATTCGGG
YOR016C	GATCCCCGGGAATTGCCATGTCACTGTATCTCGCTGTCACAATC
YPL079W	GATCCCCGGGAATTGCCATGCTATTGTAATTCCCTTATAGTGTTCA
YOR260W	GATCCCCGGGAATTGCCATGTTATTTAAGCTCGAAATGGCTATTGA
YOR360C	GATCCCCGGGAATTGCCATGTCATTGTGGAAGAGGTCTTCTAGG
YDL060W	GATCCCCGGGAATTGCCATGTTACATACCATTCCAAGGTAACGAA
YDL005C	GATCCCCGGGAATTGCCATGCTATATATTGAAGCCGCTGAGGTC
YPL210C	GATCCCCGGGAATTGCCATGCTACTTACGTACTAAAATAGTCTCTT
YMR118C	GATCCCCGGGAATTGCCATGTTACTGAGCCAGTAAATACGTTCCT
YPR052C	GATCCCCGGGAATTGCCATGCTAAGCCAAAGTGGCGTTATATAAC

YLR224W	GATCCCCGGGAATTGCCATGTCATCTTCGAAGATAAGGGGTATTC
YLR275W	GATCCCCGGGAATTGCCATGTTACTCAACAGGGGTTTTTAACACA
YMR154C	GATCCCCGGGAATTGCCATGTTATTTTGGTATCACATCATCGGAG
YDR205w	GATCCCCGGGAATTGCCATGTCAATTTGCTATAGGCTGTAGCGG
YPR037C	GATCCCCGGGAATTGCCATGTTAGAACTGAATTATTTCACATTGTCT
YNR008W	GATCCCCGGGAATTGCCATGTTACATTGGGAAGGGCATCTGAGA
YOR084W	GATCCCCGGGAATTGCCATGTTACAGTTTTTGTTTAGTCGTTTTAAC
YGR054W	GATCCCCGGGAATTGCCATGTTATTCATCCTTCCAACCCAACTTT
YGL106W	GATCCCCGGGAATTGCCATGTCATTGTCTCAAAACATCTTCGATG
YAL067C	GATCCCCGGGAATTGCCATGTTATTTTTCATCAGATACTGATAAGGT
YIL023c	GATCCCCGGGAATTGCCATGTCAATGCTCATCCATGAGCGCCA
YBR064W	GATCCCCGGGAATTGCCATGCTAAAATATGGAGGAACTAGGTTTAA
b0019	TTGCTCTTCGTTAAACTGATGGACGCAAACGAACG
b2148	TTGCTCTTCGTTATTTCTTACGCGCGTATTTCAGTG
b2796	TTGCTCTTCGTTAGCTGAACAGAGAGTAGAAGATT
b2082	TTGCTCTTCGTTACATCCACATAATTTGCTGCCC
b0124	TTGCTCTTCGTTACTTCACATCATCCGGCAGCG
b3116	TTGCTCTTCGTTAAAACAGTTTGTATACGATGTTCAG
b1830	TTGCTCTTCGTTACTTGACGGGAGCGGGTTGT
b1453	TTGCTCTTCGTTAACTCGCCGTTTCAGGCTTAAA
b2664	TTGCTCTTCGTTAATTGCCAGCCATCGCCTG
b2799	TTGCTCTTCGTTACCAGGCGGTATGGTAAAGCT
b3327	TTGCTCTTCGTTAATTAATCATTGAGTTAAGTTGAAGA
b0970	TTGCTCTTCGTTAATCGCGGCTAGCGAAGCCC
YER003C	GATCCCCGGGAATTGCCATGCTAATTTGGTTCCACAAAGGCTCTA
YCL027W	GATCCCCGGGAATTGCCATGTCAGTCGTATTCTTGGAGACAGTC
YBR112C	GATCCCCGGGAATTGCCATGTTAGTCGTCGTAGTTTTCATCTTCT
YNL079C	GATCCCCGGGAATTGCCATGTCACAAGTTTTCCAGAGATGCAGC
YFR042W	GATCCCCGGGAATTGCCATGTCATTTTGTTAATAGTTTTTTGTATGCT
YER137C	GATCCCCGGGAATTGCCATGTTATTTCTTGGGTATAACTGTCAGTC
YKL103C	GATCCCCGGGAATTGCCATGTCACAACTCGCCGAATTCATCGTA
YNL090W	GATCCCCGGGAATTGCCATGTTATAAAATTATGCAACAGTTAGCCC
YGR161C	GATCCCCGGGAATTGCCATGCTATTTCAATGAACCAGTTTGGAATC
YDR071C	GATCCCCGGGAATTGCCATGCTAGTTGTCGTATTCTTCCTTAATTA

0318.0.1 Vector preparation

0319.0.1 The preferred binary vector 1bxbigResgen for yeast and 1bxSuperCoLic for E.coli, which is based on the modified pPZP binary vector backbone (comprising the kanamycin-gene for bacterial selection; Hajukiewicz, P. et al., 1994, Plant Mol. Biol., 25: 989-994) carried the selection marker bar-gene (De Block et al., 1987, EMBO J. 6, 2513-2518) driven by the mas1´promotor (Velten et al., 1984, EMBO J. 3, 2723-2730; Mengiste, Amedeo and Paszkowski, 1997, Plant J., 12, 945-948) on its T-DNA. In addition the T-DNA contained the strong double 35S(Kay et al., 1987, Science 236,

1299-1302) for yeast or Super promotor (Ni et al., 1995, Plant Journal 7, 661-676) for E.coli in front of a cloning cassette followed by the nos-terminator (Depicker A. Stachel S. Dhaese P. Zambryski P. Goodman HM. Nopaline synthase: transcript mapping and DNA sequence. Journal of Molecular & Applied Genetics. 1(6):561-73, 1982.). The cloning cassette consists of the following sequence:

0320.0.1 `Yeast: 5`-GGAATTCCAGCTGACCACCATGGCAATTCCCGGGGATC-3 or

0321.0.1 E.coli: 5`-TTG CTC TTC CAT GGC AAT GAT TAA TTA ACG AAG AGC AA-3´, respectively.

0322.0.1 Other selection marker systems, like the AHAS marker or other promotors, e.g. superpromotor (see above), 35S promotor (see above) , Ubiquitin promotor (Callis et al., J. Biol. Chem., 1990, 265: 12486-12493; US 5,510,474; US 6,020,190; Kawalleck et al., Plant. Molecular Biology, 1993, 21: 673-684) or 34S promotor (GenBank Accession numbers M59930 and X16673) were similar useful for the instant invention and are known to a person skilled in the art. The vector was linearised with EcoR and SmaI for yeast or SmaI and SacI for E.coli using the standard protocol provided by the supplier (MBI Fermentas, Germany) and purified using Qiagen columns (Qiagen, Hilden, Germany).

0323.0.1 **Ligation and transformation**

0324.0.1 Present ORF fragments (~ 100 ng) were digested by EcoRI and SmaI for yeast and SmaI and SacI for E.coli using the standard protocol provided by the supplier (MBI Fermentas, Germany), purified using Qiagen columns (Qiagen, Hilden, Germany) and were ligated into the cloning cassette of the binary vector systems (~ 30 ng) using standard procedures (Maniatis et al.).

0325.0.1 In the case of internal EcoRI, SmaI and SacI restriction sites a blunt end cloning procedure was applied. The undigested ORF fragments were directly purified and ligated into the cloning cassette of the binary vector. In this case the EcoRI site was refilled by Klenow reaction and the SacI site blunted Pfu DNA polymerase.

0326.0.1 Ligation products were transformed into E.coli (DH5alpha) using a standard heat shock protocol (Maniatis et al.). Transformed colonies were grown on LB media and selected by respective antibiotica (Km) for 16h at 37 °C. Positive clones were identified by control PCR reactions using a combination of a vector specific and the respective ORF specific primers.

0327.0.1 **Plasmidpreparation**

0328.0.1 Plasmid DNA was prepared from positive clones using standard protocols (Qiagen Hilden, Germany).

0329.0.1 Transformation of Agrobacteria

0330.0.1 Plasmids were transformed into Agrobacterium tumefaciens (GV3101pMP90; Koncz and Schell, 1986, Mol. Gen. Genet. 204: 383-396) using heat shock or electroporation protocols. Transformed colonies were grown on YEP media and selected by respective antibiotics (Rif/Gent/Km) for 2d at 28 °C. These Agrobacterium cultures were used for the plant transformation.

0331.0.1 Arabidopsis thaliana was grown and transformed according to standard conditions Bechtold 1993 (Bechtold, N., Ellis, J., Pelletier, G. 1993. In planta Agrobacterium mediated gene transfer by infiltration of Arabidopsis thaliana plantsC.R. Acad.Sci.Paris. 316:1194-1199); Bent et al. 1994 (Bent, A., Kunkel, B.N., Dahlbeck, D., Brown, K.L., Schmidt, R., Giraudat, J., Leung, J., and Staskawicz, B.J. 1994; PPCS2 of Arabidopsis thaliana: A leucin-rich repeat class of plant disease resistant genes; Science 265: 1856-1860).

0332.0.1 Transgenic A. thaliana plants were grown individually in pots containing a 4:1 (v/v) mixture of soil and quartz sand in a York growth chamber. Standard growth conditions were: photoperiod of 16 h light and 8 h dark, 20 °C, 60% relative humidity, and a photon flux density of 150 µE. To induce germination, sown seeds were kept at 4 °C, in the dark, for 3 days. Plants were watered daily until they were approximately 3 weeks old at which time drought was imposed by withholding water. Parallely, the relative humidity was reduced in 10% increments every second day to 20%. After approximately 12 days of withholding water, most plants showed visual symptoms of injury, such as wilting and leaf browning, whereas tolerant plants were identified as being visually turgid and healthy green in color. Plants were scored for symptoms of drought injury in comparison to neighbouring plants for 3 days in succession.

0333.0.1 Three successive experiments were conducted. In the first experiment, 10 independent T2 lines were sown for each gene being tested. The percentage of plants not showing visual symptoms of injury was determined. In the second experiment, the lines that had been scored as tolerant in the first experiment were put through a confirmation screen according to the same experimental procedures. In this experiment, plants of each tolerant line were grown and treated as before. In the third experiment, at least 7 replicates of the most tolerant line were grown and treated as before. The average and maximum number of days of drought survival after wild-type control had visually died were determined. Additionally measurements of chlorophyll fluorescence were made in stressed and non-stressed plants using a Mini-PAM (Heinz Walz GmbH, Effeltrich, Germany).

0334.0.1 In the first experiment, after 12 days of drought, the control, non-transgenic Arabidopsis thaliana and most transgenic lines expressing other transgenes

in the test showed extreme visual symptoms of stress including necrosis and cell death. Several plants expressing the genes retained viability as shown by their turgid appearance and maintenance of green color.

0335.0.1 The second experiment compared a smaller number of independent transgenic lines for each gene but a greater number of progeny within each independent transformation event. This experiment confirmed the previous results. Those lines containing the specific SRP encoding yeast genes survived longer than the controls. In some cases the transgenic line survived more than 3 days after the controls had died.

0336.0.1 According to the results of the first and second experiments some major lines containing the specific SRP encoding yeast genes were identified, which showed the best results with regard to the average days of survival after wild type and/or the hit percentage.

0337.0.1 In a third experiment these major lines were tested with multiple replicates (4-80 plants per line). The average number of days the plants of the major line survived longer than wild-type was measured. I.e., the number '1' means that, on average, the plants overexpressing this ORF, on averaged survived 1 day longer than wild-type. The value for WT in this column is '0'. The results are summmarised in table 3.

0338.0.1 Table 3: Drought tolerance of transgenic *Arabidopsis thaliana* expressing the various SRP encoding genes from *Saccharomyces cerevisiae* or *E. coli* after imposition of drought stress on 3 week old plants in a third experiment using several plants from one transgenic line (experiment 3). Drought tolerance is measured for the indicated number of transgenic plants (Plants tested) as the average number of days (Average days of survival after WT) that the transgenic plants survived after the control (untransformed wild type). The hit percentage indicates the fraction of the tested plants of the major line that was actually resistant, i.e. the number '50' indicates that half of the tested plants were resistant (survived longer than WT). For WT, this column has the value '0'.

Sequ. ID No.	Gene	Plants tested	Average days of survival after WT
1	YGL263W	12	1,17
3	YGR004W	11	1,36
5	YGR014W	11	0,82
7	YGL239C	13	2,4
9	YBL060W	14	1,6
11	YGL166W	14	1,07
13	YDL202W	15	0,47

15	YAL046C	14	1,9
17	YDR101C	14	3,57
19	YDR108W	14	0,5
21	YAL064W	33	2,29
23	YDR134C	13	0,8
25	YFL031w	13	1,3
27	YFL052W	14	1,1
29	YFL042C	11	1,3
31	YBR025C	11	1,4
33	YER174C	22	1,05
35	YBR051W	10	1,2
37	YER175C	11	1,7
39	YDR521W	14	0,5
41	YER167W	35	0,66
43	YER123W	11	2,2
45	YDR415C	7	2,71
47	YEL052W	4	1,5
49	YDR536W	14	1,5
51	YDR513W	7	3,14
53	YEL045C	14	1,64
55	YEL041W	13	1,77
57	YDL238C	35	1,2
59	YBR282W	14	1,79
61	YBR258C	9	3,4
63	YCL001W-A	36	1,78
65	YBR274W	14	2
67	YHR090C	8	4,5
69	YGR121C	40	1,6
71	YGR127W	8	1,4
73	YGR150C	12	2,6
75	YKL037W	14	0,79
77	YKL051W	16	2,4
79	YKL120W	14	0,64
81	YKL011C	12	1,9
83	YKL017C	10	1,8
85	YKL049C	80	1,92
87	YKL132C	33	1,82
89	YGR126W	8	2,3
91	YKL070W	14	2,1
93	YKL058W	9	1,44
95	YHR130C	9	1,8
97	YIL070C	13	0,69

99	YHR195W	14	1,9
101	YIR022W	14	1,07
103	YJL089W	14	0,86
105	YJL172W	11	0,82
107	YHR113W	15	2
109	YHR175W	9	0,78
111	YGR212W	13	1,46
113	YJL024C	13	0,69
115	YGR180c	14	2,9
117	YJL179W	18	1,3
119	YJL001W	14	1,6
121	YJL208C	12	1,4
123	YJL152W	13	1,3
125	YJL131C	14	0,6
127	YJL151C	14	1,9
129	YLR441C	10	2
131	YLR415C	14	1,6
133	YLR212C	13	0,64
135	YLR029C	14	1,56
137	YLL041C	13	0,92
139	YLR105C	14	0,86
141	YIL136W	8	2,25
143	YLR215C	13	1,77
145	YLR321C	14	1,29
147	YMR260C	11	2,09
149	YNL120C	7	2
151	YLR407W	12	1,17
153	YMR197C	14	0,57
155	YMR100W	12	1,25
157	YMR210W	10	1,1
159	YMR318C	13	0,85
161	YMR069W	8	1,25
163	YNL076W	13	1,31
165	YNL024C	13	1,08
167	YNL125C	4	1,75
169	YNL029C	13	1,92
171	YMR115W	12	0,75
173	YNL244C	11	1,55
175	YNL334C	14	1,5
177	YNR018W	14	1,29
179	YNL277W	14	1,14
181	YOL118C	14	1,71

183	YOL123W	14	0,71
185	YOR020C	12	1,83
187	YOL116W	13	1,08
189	YOR305w	15	1,2
191	YPL267W	6	2,5
193	YPL229w	5	2
195	YPL038W	10	1,3
197	YPR047W	11	1
199	YPL011C	12	0,75
201	YPR148C	10	1,1
203	YOL103W	12	0,75
205	YOR016C	14	0,79
207	YPL079W	15	1,33
209	YOR260W	7	1,29
211	YOR360C	15	1,53
213	YDL060W	15	0,67
215	YDL005C	15	1
217	YPL210C	15	1,13
219	YMR118C	14	1,14
221	YPR052C	14	1,07
223	YLR224W	10	2,1
225	YLR275W	9	2,44
227	YMR154C	15	1,27
229	YDR205w	12	1,08
231	YPR037C	12	2,17
233	YNR008W	14	2,29
235	YOR084W	10	2,2
237	YGR054W	14	1,5
239	YGL106W	13	3,46
241	YAL067C	13	1,62
243	YIL023c	15	1,73
245	YBR064W	15	1,13
247	b0020	13	0,78
249	b2148	15	3,13
251	b2796	15	2,33
253	b2082	14	2,43
255	b0124	15	2,87
257	b3116	15	1,07
259	b1830	15	2,07
261	b1453	14	2,29
263	b2664	13	1,85
265	b2799	15	1,87

267	b3327	15	1,47
269	b0970	15	1,33
271	YER003C	5	1
273	YCL027W	9	0.56
275	YBR112C	10	0.5
277	YNL079C	9	0.67
279	YFR042W	9	0.78
281	YER137C	3	0
283	YKL103C	9	1
285	YNL090W	6	0.83
287	YGR161C	7	0.86
289	YDR071C	9	0.78

0339.0.1 In a further experiment, for individual major lines, other lines containing the same gene contruct, but resulting from a different transformation event were tested. In these lines, the specific SRP encoding yeast genes is incorporated at a different site in the plant genom. The results are summmarised in table 4 in accordance to table 3. The resuls demonstrate the dependence of the stress tolerance and/or resistance in plants on the expression of the SRP, rather than the insertion event.

0340.0.1 Table 4: Drought tolerance of transgenic Arabidopsis thaliana expressing selected SRP encoding genes from Saccharomyces cerevisiae or E. coli after imposition of drought stress on 3 week old plants in a third experiment using one plant from severalindependent transgenic lines each (experiment 3). Drought tolerance is measured for the indicated number of transgenic plants (Plants tested) as the average number of days (Average days of survival after WT) that the transgenic plants survived after the control (untransformed wild type). The hit percentage indicates the fraction of the tested plants of the major line that was actually resistant, i.e. the number '50' indicates that half of the tested plants were resistant (survived longer than WT). For WT, this column has the value '0'.

Sequ. ID No.	Gene	Number other lines tested	Average days of survival after WT
1	YGL263W	7	1,43
3	YGR004W	8	1
5	YGR014W	8	0,75
7	YGL239C	5	1
9	YBL060W	8	2
11	YGL166W	8	0,63
13	YDL202W	8	0,25

15	YAL046C	7	1,3
17	YDR101C	9	1,1
19	YDR108W	9	0,22
21	YAL064W	8	3
23	YDR134C	6	2,2
25	YFL031w	9	2,3
27	YFL052W	5	1,4
31	YBR025C	5	1,2
33	YER174C	9	0,5
35	YBR051W	6	1,3
37	YER175C	4	1,4
39	YDR521W	3	0,7
43	YER123W	6	0,3
45	YDR415C	7	1,4
47	YEL052W	3	1,33
49	YDR536W	8	1,25
51	YDR513W	4	1,5
53	YEL045C	5	1,2
55	YEL041W	8	0,88
57	YDL238C	6	0,17
59	YBR282W	9	2,2
61	YBR258C	7	1,7
63	YCL001W-A	7	0,57
65	YBR274W	9	0,78
67	YHR090C	6	2,7
69	YGR121C	9	0,8
71	YGR127W	6	2,5
73	YGR150C	5	3
75	YKL037W	9	0,78
77	YKL051W	5	1,8
79	YKL120W	8	0,63
81	YKL011C	5	1,4
83	YKL017C	5	0,6
85	YKL049C	9	1,4
87	YKL132C	7	0,7
89	YGR126W	6	1,3
91	YKL070W	6	2
93	YKL058W	8	0,88
95	YHR130C	9	2,1
97	YIL070C	7	0,71
99	YHR195W	9	2,1
101	YIR022W	9	1,22
103	YJL089W	7	0,6
105	YJL172W	4	1
107	YHR113W	7	1,6
109	YHR175W	3	1

111	YGR212W	8	0,88
113	YJL024C	6	1,33
115	YGR180c	8	2,7
117	YJL179W	8	1,8
119	YJL001W	9	0,7
121	YJL208C	6	1,7
123	YJL152W	8	0,3
125	YJL131C	6	1
127	YJL151C	8	1,6
129	YLR441C	7	2,6
131	YLR415C	9	0,3
133	YLR212C	7	2,14
135	YLR029C	8	0,25
137	YLL041C	7	0,86
139	YLR105C	7	0,29
141	YIL136W	9	1,75
143	YLR215C	8	1,25
145	YLR321C	7	0,86
147	YMR260C	8	0,88
149	YNL120C	9	1,56
151	YLR407W	5	0,4
153	YMR197C	9	1,22
155	YMR100W	8	0,88
157	YMR210W	8	0,88
159	YMR318C	8	0,63
161	YMR069W	9	0,44
163	YNL076W	4	1,75
165	YNL024C	9	1,78
167	YNL125C	7	2,14
169	YNL029C	9	1,88
171	YMR115W	9	1,44
173	YNL244C	8	0,25
175	YNL334C	9	1,33
177	YNR018W	9	1,22
179	YNL277W	8	1
181	YOL118C	9	0,89
183	YOL123W	8	0,88
185	YOR020C	9	0,44
187	YOL116W	9	1,67
189	YOR305w	7	0,28
191	YPL267W	4	0,75
193	YPL229w	5	1,6
195	YPL038W	5	0,4
197	YPR047W	2	1
199	YPL011C	6	0,5
201	YPR148C	9	0,33

203	YOL103W	9	0,33
205	YOR016C	9	0,56
211	YOR360C	8	0,38
213	YDL060W	8	0,5
215	YDL005C	9	0,44
217	YPL210C	8	1,5
219	YMR118C	10	1,1
221	YPR052C	7	0,86
223	YLR224W	9	1,22
225	YLR275W	8	1,75
227	YMR154C	9	1,11
229	YDR205w	4	1
231	YPR037C	5	3,4
233	YNR008W	8	0,75
235	YOR084W	6	0,5
239	YGL106W	7	2,14
241	YAL067C	6	1,83
243	YIL023c	1	3
245	YBR064W	7	0,71
247	b0020	4	1,5
249	b2148	10	0,1
251	b2796	11	0,72
253	b2082	9	1,22
255	b0124	9	3,3
257	b3116	8	1
259	b1830	7	1,71
261	b1453	8	1,13
263	b2664	9	1
267	b3327	10	0,8
269	b0970	8	1,5
271	YER003C	12	2,08
273	YCL027W	14	2,14
275	YBR112C	11	3,3
277	YNL079C	13	2,69
279	YFR042W	7	2,3
281	YER137C	13	2,2
283	YKL103C	10	2,8
285	YNL090W	12	4,33
287	YGR161C	12	2,7
289	YDR071C	11	3

0341.0.1 Chlorophyll fluorescence measurements of photosynthetic yield confirmed that severe drought stress completely inhibited photosynthesis in the control

plants, but the transgenic major lines maintained photosynthetic function longer (Table 5).

0342.0.1 Table 5: Drought tolerance of transgenic Arabidopsis thaliana expressing the various SRP encoding genes from Saccharomyces cerevisiae or E. coli after imposition of drought stress on 3 week old plants in a third experiment using several plants from one transgenic line (experiment 3). Drought tolerance is reported as photosynthetic yield measured by chlorophyll fluorescence measured at three different time point during the drought stress experiment, and compared to the untransformed wild type control. For each transgenic line, the average of 5 replicate plants is indicated, the wild type value is the average of 20-25 plants measured in the same experiment.

Sequ. ID No.	Gene	Photosynthetic yield 6 days after final watering	*wild type*	Photosynthetic yield 10 days after final watering	*wild type*	Photosynthetic yield 14 days after final watering	*wild type*
1	YGL263W	751	*766*	765	*654*	264	*106*
3	YGR004W	759	*766*	755	*654*	246	*106*
5	YGR014W	759	*766*	752	*654*		
7	YGL239C	782	*757*	786	*610*		
9	YBL060W	743	*757*	782	*610*	108	*16*
11	YGL166W	752	*736*	747	*709*		
13	YDL202W	790	*766*	508	*548*		
15	YAL046C	788	*760*	756	*549*	216	*20*
19	YDR108W	756	*736*	739	*709*	0	*20*
23	YDR134C	757	*760*	765	*549*	273	*20*
25	YFL031w	763	*760*	766	*549*	784	*20*
27	YFL052W	757	*757*	753	*610*		
29	YFL042C	743	*757*	780	*610*		
31	YBR025C	763	*760*	762	*549*	631	*20*
35	YBR051W	741	*760*	696	*549*	456	*20*
37	YER175C	749	*757*	627	*610*	140	*16*
43	YER123W	767	*757*	780	*610*	147	*16*
47	YEL052W	750	*736*	773	*710*	177	*20*
49	YDR536W	753	*736*	772	*709*	293	*20*
51	YDR513W	782	*794*	660	*413*	411	*54*
53	YEL045C	755	*736*	553	*709*	147	*20*
55	YEL041W	758	*736*	769	*709*	129	*20*

59	YBR282W	759	*760*	724	*549*	221	*20*
61	YBR258C	759	*757*	772	*610*	144	*16*
65	YBR274W	749	*736*	769	*709*	146	*20*
67	YHR090C	749	*760*	765	*549*	620	*20*
71	YGR127W	740	*549*	576	*20*		
73	YGR150C	771	*760*	742	*549*	618	*20*
75	YKL037W	761	*736*	760	*709*	134	*20*
77	YKL051W	733	*760*	740	*549*	153	*20*
79	YKL120W	759	*736*	518	*709*		
81	YKL011C	750	*760*	694	*549*	434	*20*
83	YKL017C	744	*549*	734	*549*	754	*20*
89	YGR126W	784	*760*	750	*549*	159	*20*
91	YKL070W	774	*760*	734	*549*	244	*20*
93	YKL058W	752	*766*	765	*654*	495	*20*
95	YHR130C	772	*760*	756	*549*	147	*20*
97	YIL070C	768	*766*	755	*654*		
99	YHR195W	753	*757*	693	*610*	141	*16*
101	YIR022W	761	*736*	771	*709*		
105	YJL172W	756	*766*	758	*654*	293	*20*
107	YHR113W	749	*760*	754	*549*	142	*20*
109	YHR175W	768	*766*	758	*654*	465	*106*
111	YGR212W	777	*766*	748	*654*		
113	YJL024C	762	*766*	758	*654*	736	*106*
115	YGR180c	763	*757*	779	*610*		
117	YJL179W	744	*760*	606	*549*	310	*20*
119	YJL001W	748	*757*	519	*610*	135	*16*
121	YJL208C	685	*549*	49	*20*		
123	YJL152W	754	*757*	726	*610*		
125	YJL131C	750	*757*	758	*610*		
127	YJL151C	755	*760*	764	*549*	152	*20*
129	YLR441C	745	*760*	762	*549*	277	*20*
131	YLR415C	739	*757*	503	*610*	144	*16*
133	YLR212C	740	*736*	759	*709*	103	*20*
135	YLR029C	746	*736*	780	*709*	292	*20*
139	YLR105C	751	*736*	764	*709*		
141	YIL136W	749	*736*	779	*710*	422	*20*
143	YLR215C	752	*736*	774	*709*	151	*20*
145	YLR321C	749	*736*	767	*709*	145	*20*
147	YMR260C	774	*766*	763	*654*	691	*106*
149	YNL120C	764	*766*	740	*654*	298	*20*
151	YLR407W	774	*766*	640	*654*	138	*106*
153	YMR197C	751	*736*	723	*709*	63	*20*
155	YMR100W	770	*766*	596	*654*	171	*20*
157	YMR210W	753	*766*	755	*654*	733	*20*
159	YMR318C	761	*736*	780	*709*	135	*20*
161	YMR069W	756	*766*	750	*654*	519	*20*

163	YNL076W	765	*766*	757	*654*	244	*20*
165	YNL024C	767	*766*	761	*654*	279	*20*
167	YNL125C	761	*766*	750	*654*	283	*20*
169	YNL029C	764	*766*	758	*654*		
171	YMR115W	755	*736*	739	*709*		
173	YNL244C	774	*766*	696	*654*	94	*20*
175	YNL334C	751	*736*	756	*709*		
177	YNR018W	756	*736*	749	*709*		
181	YOL118C	727	*736*	756	*709*	280	*20*
183	YOL123W	747	*736*			140	*20*
185	YOR020C	764	*766*	748	*654*	207	*20*
187	YOL116W	774	*766*	735	*654*	135	*20*
189	YOR305w	773	*769*	565	*245*		
191	YPL267W	757	*767*	756	*548*		
193	YPL229w	781	*769*	752	*245*		
197	YPR047W	761	*769*	597	*245*		
199	YPL011C	766	*769*	582	*245*		
201	YPR148C	771	*769*	401	*245*		
203	YOL103W	789	*769*	237	*245*		
205	YOR016C	770	*769*	523	*245*		
211	YOR360C	771	*769*	651	*245*		
215	YDL005C	782	*769*	702	*245*		
217	YPL210C	794	*769*	735	*245*		
219	YMR118C	777	*768*	499	*272*		
221	YPR052C	772	*768*	298	*272*		
223	YLR224W	767	*768*	434	*272*		
225	YLR275W	741	*768*	780	*272*		
227	YMR154C	760	*768*	734	*272*		
229	YDR205w	787	*768*	241	*272*		
231	YPR037C	759	*768*	740	*272*		
233	YNR008W	746	*768*	782	*272*		
235	YOR084W	758	*768*	765	*272*		
237	YGR054W	766	*768*	140	*272*		
239	YGL106W	760	*768*	477	*272*		
241	YAL067C	759	*768*	681	*272*		
243	YIL023c	769		814			
245	YBR064W	745	*750*	770	*576*	117	*31*
249	b2148	736	*768*	740	*272*		
251	b2796	761	*768*	319	*272*		
253	b2082	756	*768*	706	*272*		
255	b0124	756	*768*	571	*272*		
257	b3116	765	*768*	600	*272*		
259	b1830	757	*768*	772	*272*		
261	b1453	750	*768*	648	*272*		
263	b2664	764	*768*	521	*272*		
265	b2799	763	*768*	615	*272*		

267	b3327	766	*768*	499	*272*		
269	b0970	764	*768*	560	*272*		
271	YER003C	758	*760*	769	*549*	729	*20*
273	YCL027W	749	*760*	770	*549*	145	*20*
275	YBR112C	760	*760*	760	*549*	731	*20*
277	YNL079C	763	*766*	762	*654*	216	*20*
279	YFR042W	789	*760*	739	*549*	232	*20*
281	YER137C	760	*760*	728	*549*	458	*20*
283	YKL103C	747	*760*	763	*549*	791	*20*
285	YNL090W	757	*760*	783	*549*	403	*20*
287	YGR161C	742	*760*	753	*549*	225	*20*
289	YDR071C	737	*757*	793	*610*	707	*16*

0343.0.4 Metabolic analysis of transgenic plants

The described metabolic changes in transgenic plants were identified using the following experimental procedure:

0344.0.4 a) Growth and treatment of plants

0345.0.4 Plants were grown in climate chambers under standard conditions on pot soil for three weeks (see above). Eight days prior to harvest, water was withheld for part of the plants (8-day treatment). Four days prior to harvest, water was withheld for another group of plants (4-day treatment). The plants of "control treatment" were normally watered throughout the growth period. Plants due to be analysed in the same analytical sequence were grown side-by-side to avoid environmental influences.

0346.0.4 b) Sampling and storage of samples

03470.4 Sampling took place in the climate chamber. Green parts were cut with a pair of scissors, quickly weighed, and immediately put into a liquid nitrogen pre-cooled extraction thimble. Racks with extraction thimbles were stored at –80°C until extraction.

0348.0.4 c) Freeze-drying

Plants were not allowed to thaw or reach temperatures > -40°C until either the first contact with solvents or the removal of water by freeze-drying.

0349.0.4 The sample rack with extraction thimbles was put into the pre-cooled (-40°C) freeze-dryer. The starting temperature for the main drying phase was –35°C, pressure was 0.120 mbar. For the drying process, parameters were changed according to a pressure and temperature program. The final temperature (after 12 hours) was +30°C, pressure was 0.001 - 0.004 mbar. After shutting down the vacuum pump and cooling machine, the system was aired with dried air or Argon.

0350.0.4 d) Extraction

0351.0.4 Extraction thimbles with plant material were transferred to 5 mL extraction cells on the ASE (Accelerated Solvent Extractor ASE 200 with Solvent Controller and AutoASE-Software (DIONEX)) immediately after freeze-drying.

0352.0.4 Polar substances were extracted with approximately 10 mL Methanol/Water (80/20, v/v) at T = 70 °C und p = 140 bar, 5 min heating phase, 1 min static Extraction. Lipid substances were extracted with approximately 10 mL Methanol/Dichlormethan (40/60, v/v) at T = 70 °C und p = 140 bar, 5 min heating phase, 1 min static Extraction. Both extracts were collected in one extraction vial (Centrifuge tubes, 50 mL with screw-on lid and Septum for ASE (DIONEX)).

0353.0.4 The following internal standards were added to the extracts: LC-Standards L-Methionine-d3, Boc-Ala-Gly-Gly-Gly-OH, L-Tryptophan-d5, Arginine$^{13}C_6{}^{15}N_4$, CoEnzyme Q1,2,4 and ribitol, L-glycine-2,2-d2. L-alanine-2,3,3,3-d4, alpha-methyl-glucopyranoside, nonadecanoic acid methyl ester, undecanoic acid methyl ester, tridecanoic acid, pentadecanoic acid, nonacosanoic acid. To the resulting mixture, 8 mL water were added. The solid residues of plant and extraction thimble were discarded.

0354.0.4 The extract was centrifuged at 1400 g for 5-10 minutes to speed-up phase-separation. For GC and LC analysis, 1 mL each was taken from the colourless methanol/water upper (polar) phase. The remaining upper phase was discarded. Of the dark-green, organic bottom phase 0.5 mL was taken for GC and LC analysis, respectively. All sample aliquots were evaporated using a IR-Dancer Infrared vacuum evaporator (Hettich), using a temperature maximum of 40°C and a maximum pressure of 10 mbar.

0355.0.4 e) LC/MS- and LC/MS/MS-Analysis

HPLC mobile phase was added to the lipid and polar residues, respectively (volume adjusted to the weighted sample) and an HPLC analysis using gradient elution was performed.

0356.0.4 f) Derivatisation of the lipid phase for GC/MS-Analysis

0357.0.4 For transmethanolysis, a mixture of 140 µl chloroform, 38 µL HCl (37% HCl in water), 320 µl methanol and 20 µl toluol was added to the residue. The sample container was carefully closed and reaction was carried out at 100°C for 2 hours. Subsequently, the solution was evaporated and the pellet was dried completely.

0358.0.4 The methoximation of carbonyl groups was achieved by a reaction with 100 µL methoxyamine-hydrochloride (5 mg/mL in Pyridine) for 1.5 hours at 60°C, in a closed vial. 20 µL of a mixture of linear, odd-numbered fatty acids was added to provide a time standard. Finally, derivatisation with 100 µL N-Methyl-N-(trimethylsilyl)-

2,2,2-trifluoracetamide (MSTFA) took place in a closed vial for 30 minutes at 60°C. The final volume for GC injection was 220 µl.

0359.0.4 **g) Derivatisation of the polar phase for GC/MS-Analysis**

0360.0.4 The methoximation of carbonyl groups was achieved by a reaction with 50 µL methoxyamine-hydrochloride (5 mg/mL in Pyridine) for 1.5 hours at 60°C, in a closed vial. 10 µL of a mixture of linear, odd-numbered fatty acids was added to provide a time standard. Finally, derivatisation with 50 µL N-methyl-N-(trimethylsilyl)-2,2,2-trifluoracetamide (MSTFA) took place in a closed vial for 30 minutes at 60°C. The final volume for GC injection was 110 µl.

0361.0.4 **h) Analysis of different plant samples**

0362.0.4 Samples were measured in sequences of 20. Each sequence contained 5 wild type and 5 transgenic plants grown under control conditions, as well as 5 wild type and 5 transgenic plants from either the 4 day or 8 day drought treatment.

0363.0.4 The peak height or peak area of each analyte (metabolite) was divided through the peak area of the respective internal standards. Data was normalised using the individual sample fresh weight. The resulting values were divided by the mean values found for wild type plants grown under control conditions and analysed in the same sequence, resulting in the so-called X-folds or ratios (see table 7 - 14), which represent values independent of the analytical sequence. These ratios indicate the behavior of the metabolite concentration of the target plants in comparison to the concentration in the wild type control plants.

0364.0.4 In table **6** the results of the metabolite screening for the plants transformed in genes YCL027W, YBR112C, YNL079C, YER137C, YKL103C, YNL090W, YGR161C, YDR071C are shown.

0365.0.4 Tables **6**: Details on screening of metabolic activity.

	wild type			**YDR071C**		
metabolite	control	4 days	8 days	control	4 days	8 days
2,3-dimethyl-5-phytylquinol	1,00	0,50	0,54			
2-hydroxy-palmitic acid	1,00	1,11	1,25	1,18		
3,4-dihydroxyphenylalanine (=dopa)	1,00	1,83	3,37			
3-hydroxy-palmitic acid	1,00					
5-oxoproline	1,00	1,56	1,81			
alanine	1,00	0,64	0,64			
alpha linolenic acid (c18:3 (c9, c12, c15))	1,00	1,24	1,40			
alpha-tocopherol	1,00	1,05	1,14			
aminoadipic acid	1,00	1,73	1,65			
anhydroglucose	1,00	1,02	1,16			
arginine	1,00	0,39	0,33			
aspartic acid	1,00	2,72	2,96			

beta-apo-8' carotenal	1,00	1,21	1,22			
beta-carotene	1,00	1,25	1,26			
beta-sitosterol	1,00	1,39	1,51			
beta-tocopherol	1,00	0,54	0,60			
palmitic acid	1,00	1,07	1,25			
delta-7-cis,10-cis-hexadecadienic acid (c16:2 me)	1,00	1,01	1,04			
hexadecatrienic acid (c16:3 me)	1,00	1,19	1,29			
margaric acid (c17:0 me)	1,00	1,19	1,28			
delta-15-cis-tetracosenic acid (c24:1 me)	1,00	1,16	1,34			
campesterol	1,00	1,32	1,65			
cerotic acid (c26:0)	1,00	0,74	1,00			
citrulline	1,00	0,51	0,33			
cryptoxanthine	1,00	1,00	0,90			
eicosenoic acid (20:1)	1,00	0,81	0,81			
ferulic acid	1,00	1,37	1,47			
fructose	1,00	14,10	19,78			
fumarate	1,00	5,19	9,33			
galactose	1,00	1,29	1,42	0,98		
g-aminobutyric acid	1,00	1,16	1,32			
gamma-tocopherol	1,00	0,54	0,60			
gluconic acid	1,00	2,24	3,08			
glucose	1,00	14,97	20,73			
glutamine	1,00	0,98	1,17			
glutamic acid	1,00	2,01	2,69			
glycerate	1,00	1,87	2,04			
glycerinaldehyd	1,00	1,11	1,12			
glycerol	1,00	1,22	1,29			
glycerol-3-phosphate	1,00	1,86	2,41			
glycine	1,00	0,25	0,26			
homoserine	1,00	0,61	0,69			
inositol	1,00	4,19	6,32			
isoleucine	1,00	1,28	1,66			
iso-maltose	1,00	2,63	3,02			
isopentenyl pyrophosphate	1,00	1,80	2,62			
leucine	1,00	1,34	1,74			
lignoceric acid (c24:0)	1,00	0,91	1,02			
linoleic acid (c18:2 (c9, c12))	1,00	1,19	1,38			
luteine	1,00	1,26	1,33			
malate	1,00	2,91	3,46			
mannose	1,00	16,40	17,80			
triacontanoic acid	1,00	1,26	1,23			
methionine	1,00	1,13	1,12			
methylgalactofuranoside	1,00	1,24	1,49			

methylgalactopyranoside	1,00	1,25	1,36			
ornithine						
palmitic acid (c16:0)	1,00	1,16	1,38			
phenylalanine	1,00	0,92	1,10			
phosphate	1,00	2,15	2,73			
proline	1,00	1,23	4,77			
putrescine	1,00		0,39			
pyruvate	1,00	1,30	1,21			
raffinose	1,00	17,04	74,78			
ribonic acid	1,00	2,32	3,43			
serine	1,00	0,98	1,13			
shikimate	1,00	1,11	1,07			
sinapine acid	1,00	2,74	3,44			
stearic acid (c18:0)	1,00	1,18	1,35			
succinate	1,00	2,98	3,49			
sucrose	1,00	1,42	1,70			
threonine	1,00	1,26	1,68			
tryptophane	1,00	1,13	1,89			
tyrosine	1,00	1,56	2,01			
ubichinone	1,00	1,02	1,20			
udp-glucose	1,00	1,53	1,94			
valine	1,00	0,98	1,18			
zeaxanthine	1,00	1,27	1,34			

	wild type			**YER137C**		
metabolite	Control	4 days	8 days	Control	4 days	8 days
2,3-dimethyl-5-phytylquinol	1,00	0,50	0,54	2,15		5,57
2-hydroxy-palmitic acid	1,00	1,11	1,25			
3,4-dihydroxyphenylalanine (=dopa)	1,00	1,83	3,37			
3-hydroxy-palmitic acid	1,00					
5-oxoproline	1,00	1,56	1,81	1,55		1,73
alanine	1,00	0,64	0,64	1,32		0,94
alpha linolenic acid (c18:3 (c9, c12, c15))	1,00	1,24	1,40			
alpha-tocopherol	1,00	1,05	1,14			
aminoadipic acid	1,00	1,73	1,65			
anhydroglucose	1,00	1,02	1,16		1,26	0,63
arginine	1,00	0,39	0,33			
aspartic acid	1,00	2,72	2,96			
beta-apo-8' carotenal	1,00	1,21	1,22			
beta-carotene	1,00	1,25	1,26			
beta-sitosterol	1,00	1,39	1,51	0,88	1,17	1,35
beta-tocopherol	1,00	0,54	0,60	2,78		5,83
palmitic acid	1,00	1,07	1,25			
delta-7-cis,10-cis-hexadecadienic acid	1,00	1,01	1,04			

(c16:2 me)						
hexadecatrienic acid (c16:3 me)	1,00	1,19	1,29			
margaric acid (c17:0 me)	1,00	1,19	1,28			
delta-15-cis-tetracosenic acid (c24:1 me)	1,00	1,16	1,34			
campesterol	1,00	1,32	1,65		1,10	1,28
cerotic acid (c26:0)	1,00	0,74	1,00	3,24	1,78	
citrulline	1,00	0,51	0,33			
cryptoxanthine	1,00	1,00	0,90			
eicosenoic acid (20:1)	1,00	0,81	0,81			
ferulic acid	1,00	1,37	1,47			
fructose	1,00	14,10	19,78			
fumarate	1,00	5,19	9,33			
galactose	1,00	1,29	1,42			
g-aminobutyric acid	1,00	1,16	1,32	4,44		10,51
gamma-tocopherol	1,00	0,54	0,60	2,78		5,83
gluconic acid	1,00	2,24	3,08			
glucose	1,00	14,97	20,73			
glutamine	1,00	0,98	1,17			
glutamic acid	1,00	2,01	2,69			
glycerate	1,00	1,87	2,04	1,17	2,32	
glycerinaldehyd	1,00	1,11	1,12			
glycerol	1,00	1,22	1,29			
glycerol-3-phosphate	1,00	1,86	2,41	1,12	1,57	2,05
glycine	1,00	0,25	0,26			
homoserine	1,00	0,61	0,69			
inositol	1,00	4,19	6,32			
isoleucine	1,00	1,28	1,66			
iso-maltose	1,00	2,63	3,02			
isopentenyl pyrophosphate	1,00	1,80	2,62			
leucine	1,00	1,34	1,74			
lignoceric acid (c24:0)	1,00	0,91	1,02	2,01	1,74	2,03
linoleic acid (c18:2 (c9, c12))	1,00	1,19	1,38			
luteine	1,00	1,26	1,33			
malate	1,00	2,91	3,46	1,67	5,70	6,01
mannose	1,00	16,40	17,80			
triacontanoic acid	1,00	1,26	1,23			
methionine	1,00	1,13	1,12			
methylgalactofuranoside	1,00	1,24	1,49			
methylgalactopyranoside	1,00	1,25	1,36			
ornithine						
palmitic acid (c16:0)	1,00	1,16	1,38			
phenylalanine	1,00	0,92	1,10			
phosphate	1,00	2,15	2,73			
proline	1,00	1,23	4,77			

putrescine	1,00		0,39			
pyruvate	1,00	1,30	1,21			
raffinose	1,00	17,04	74,78			
ribonic acid	1,00	2,32	3,43			
serine	1,00	0,98	1,13			
shikimate	1,00	1,11	1,07		1,40	1,50
sinapine acid	1,00	2,74	3,44			
stearic acid (c18:0)	1,00	1,18	1,35			
succinate	1,00	2,98	3,49			
sucrose	1,00	1,42	1,70			
threonine	1,00	1,26	1,68			
tryptophane	1,00	1,13	1,89			
tyrosine	1,00	1,56	2,01			
ubichinone	1,00	1,02	1,20			
udp-glucose	1,00	1,53	1,94			
valine	1,00	0,98	1,18			
zeaxanthine	1,00	1,27	1,34			

	wild type			YBR112C		
metabolite	Control	4 days	8 days	Control	4 days	8 days
2,3-dimethyl-5-phytylquinol	1,00	0,50	0,54	0,63		
2-hydroxy-palmitic acid	1,00	1,11	1,25			
3,4-dihydroxyphenylalanine (=dopa)	1,00	1,83	3,37			
3-hydroxy-palmitic acid	1,00					
5-oxoproline	1,00	1,56	1,81			
alanine	1,00	0,64	0,64			
alpha linolenic acid (c18:3 (c9, c12, c15))	1,00	1,24	1,40	1,12		1,42
alpha-tocopherol	1,00	1,05	1,14			
aminoadipic acid	1,00	1,73	1,65	3,90	12,95	
anhydroglucose	1,00	1,02	1,16			
arginine	1,00	0,39	0,33			
aspartic acid	1,00	2,72	2,96			
beta-apo-8' carotenal	1,00	1,21	1,22			
beta-carotene	1,00	1,25	1,26	1,35		
beta-sitosterol	1,00	1,39	1,51	1,19		
beta-tocopherol	1,00	0,54	0,60	0,70		
palmitic acid	1,00	1,07	1,25			
delta-7-cis,10-cis-hexadecadienic acid (c16:2 me)	1,00	1,01	1,04			
hexadecatrienic acid (c16:3 me)	1,00	1,19	1,29			
margaric acid (c17:0 me)	1,00	1,19	1,28			
delta-15-cis-tetracosenic acid (c24:1 me)	1,00	1,16	1,34			
campesterol	1,00	1,32	1,65	1,42		
cerotic acid (c26:0)	1,00	0,74	1,00			

citrulline	1,00	0,51	0,33			
cryptoxanthine	1,00	1,00	0,90			
eicosenoic acid (20:1)	1,00	0,81	0,81			
ferulic acid	1,00	1,37	1,47	1,20		
fructose	1,00	14,10	19,78			
fumarate	1,00	5,19	9,33			
galactose	1,00	1,29	1,42			
g-aminobutyric acid	1,00	1,16	1,32			
gamma-tocopherol	1,00	0,54	0,60	0,70		
gluconic acid	1,00	2,24	3,08			
glucose	1,00	14,97	20,73			
glutamine	1,00	0,98	1,17			
glutamic acid	1,00	2,01	2,69			
glycerate	1,00	1,87	2,04			
glycerinaldehyd	1,00	1,11	1,12			
glycerol	1,00	1,22	1,29			
glycerol-3-phosphate	1,00	1,86	2,41			
glycine	1,00	0,25	0,26			
homoserine	1,00	0,61	0,69			
inositol	1,00	4,19	6,32			
isoleucine	1,00	1,28	1,66			
iso-maltose	1,00	2,63	3,02			
isopentenyl pyrophosphate	1,00	1,80	2,62			
leucine	1,00	1,34	1,74			
lignoceric acid (c24:0)	1,00	0,91	1,02			
linoleic acid (c18:2 (c9, c12))	1,00	1,19	1,38			
luteine	1,00	1,26	1,33	1,17		
malate	1,00	2,91	3,46			
mannose	1,00	16,40	17,80			
triacontanoic acid	1,00	1,26	1,23			
methionine	1,00	1,13	1,12			
methylgalactofuranoside	1,00	1,24	1,49			
methylgalactopyranoside	1,00	1,25	1,36			
ornithine						
palmitic acid (c16:0)	1,00	1,16	1,38	1,11		
phenylalanine	1,00	0,92	1,10			
phosphate	1,00	2,15	2,73			
proline	1,00	1,23	4,77			
putrescine	1,00		0,39			
pyruvate	1,00	1,30	1,21			
raffinose	1,00	17,04	74,78			
ribonic acid	1,00	2,32	3,43			
serine	1,00	0,98	1,13			
shikimate	1,00	1,11	1,07			

sinapine acid	1,00	2,74	3,44			
stearic acid (c18:0)	1,00	1,18	1,35			
succinate	1,00	2,98	3,49			
sucrose	1,00	1,42	1,70			
threonine	1,00	1,26	1,68			
tryptophane	1,00	1,13	1,89			
tyrosine	1,00	1,56	2,01			
ubichinone	1,00	1,02	1,20			
udp-glucose	1,00	1,53	1,94			
valine	1,00	0,98	1,18			
zeaxanthine	1,00	1,27	1,34			

	wild type			**YGR161C**		
metabolite	Control	4 days	8 days	Control	4 days	8 days
2,3-dimethyl-5-phytylquinol	1,00	0,50	0,54			
2-hydroxy-palmitic acid	1,00	1,11	1,25			
3,4-dihydroxyphenylalanine (=dopa)	1,00	1,83	3,37			
3-hydroxy-palmitic acid	1,00					
5-oxoproline	1,00	1,56	1,81			
alanine	1,00	0,64	0,64			
alpha linolenic acid (c18:3 (c9, c12, c15))	1,00	1,24	1,40			
alpha-tocopherol	1,00	1,05	1,14			
aminoadipic acid	1,00	1,73	1,65			
anhydroglucose	1,00	1,02	1,16			
arginine	1,00	0,39	0,33			
aspartic acid	1,00	2,72	2,96			
beta-apo-8' carotenal	1,00	1,21	1,22			
beta-carotene	1,00	1,25	1,26			
beta-sitosterol	1,00	1,39	1,51			
beta-tocopherol	1,00	0,54	0,60			
palmitic acid	1,00	1,07	1,25			
delta-7-cis,10-cis-hexadecadienic acid (c16:2 me)	1,00	1,01	1,04	1,14		
hexadecatrienic acid (c16:3 me)	1,00	1,19	1,29			
margaric acid (c17:0 me)	1,00	1,19	1,28	1,22		
delta-15-cis-tetracosenic acid (c24:1 me)	1,00	1,16	1,34			
campesterol	1,00	1,32	1,65			
cerotic acid (c26:0)	1,00	0,74	1,00			
citrulline	1,00	0,51	0,33			
cryptoxanthine	1,00	1,00	0,90			
eicosenoic acid (20:1)	1,00	0,81	0,81			
ferulic acid	1,00	1,37	1,47			

fructose	1,00	14,10	19,78			
fumarate	1,00	5,19	9,33			
galactose	1,00	1,29	1,42	1,15		
g-aminobutyric acid	1,00	1,16	1,32			
gamma-tocopherol	1,00	0,54	0,60			
gluconic acid	1,00	2,24	3,08			
glucose	1,00	14,97	20,73			
glutamine	1,00	0,98	1,17			
glutamic acid	1,00	2,01	2,69			
glycerate	1,00	1,87	2,04			
glycerinaldehyd	1,00	1,11	1,12			
glycerol	1,00	1,22	1,29			
glycerol-3-phosphate	1,00	1,86	2,41			
glycine	1,00	0,25	0,26			
homoserine	1,00	0,61	0,69			
inositol	1,00	4,19	6,32			
isoleucine	1,00	1,28	1,66			
iso-maltose	1,00	2,63	3,02			
isopentenyl pyrophosphate	1,00	1,80	2,62			
leucine	1,00	1,34	1,74			
lignoceric acid (c24:0)	1,00	0,91	1,02			
linoleic acid (c18:2 (c9, c12))	1,00	1,19	1,38			
luteine	1,00	1,26	1,33			
malate	1,00	2,91	3,46			
mannose	1,00	16,40	17,80			
triacontanoic acid	1,00	1,26	1,23			
methionine	1,00	1,13	1,12			
methylgalactofuranoside	1,00	1,24	1,49			
methylgalactopyranoside	1,00	1,25	1,36	1,18		
ornithine						
palmitic acid (c16:0)	1,00	1,16	1,38			
phenylalanine	1,00	0,92	1,10			
phosphate	1,00	2,15	2,73			
proline	1,00	1,23	4,77			
putrescine	1,00		0,39			
pyruvate	1,00	1,30	1,21			
raffinose	1,00	17,04	74,78			
ribonic acid	1,00	2,32	3,43			
serine	1,00	0,98	1,13			
shikimate	1,00	1,11	1,07			
sinapine acid	1,00	2,74	3,44			
stearic acid (c18:0)	1,00	1,18	1,35			
succinate	1,00	2,98	3,49			
sucrose	1,00	1,42	1,70			

threonine	1,00	1,26	1,68			
tryptophane	1,00	1,13	1,89			
tyrosine	1,00	1,56	2,01			
ubichinone	1,00	1,02	1,20			
udp-glucose	1,00	1,53	1,94			
valine	1,00	0,98	1,18			
zeaxanthine	1,00	1,27	1,34			

				YKL103C		
metabolite	Control	4 days	8 days	Control	4 days	8 days
2,3-dimethyl-5-phytylquinol	1,00	0,50	0,54			
2-hydroxy-palmitic acid	1,00	1,11	1,25			
3,4-dihydroxyphenylalanine (=dopa)	1,00	1,83	3,37			
3-hydroxy-palmitic acid	1,00					
5-oxoproline	1,00	1,56	1,81			
alanine	1,00	0,64	0,64			
alpha linolenic acid (c18:3 (c9, c12, c15))	1,00	1,24	1,40			
alpha-tocopherol	1,00	1,05	1,14			
aminoadipic acid	1,00	1,73	1,65			
anhydroglucose	1,00	1,02	1,16			
arginine	1,00	0,39	0,33			
aspartic acid	1,00	2,72	2,96			
beta-apo-8' carotenal	1,00	1,21	1,22			
beta-carotene	1,00	1,25	1,26			
beta-sitosterol	1,00	1,39	1,51			
beta-tocopherol	1,00	0,54	0,60			
palmitic acid	1,00	1,07	1,25			
delta-7-cis,10-cis-hexadecadienic acid (c16:2 me)	1,00	1,01	1,04	1,18	1,16	1,30
hexadecatrienic acid (c16:3 me)	1,00	1,19	1,29			
margaric acid (c17:0 me)	1,00	1,19	1,28			
delta-15-cis-tetracosenic acid (c24:1 me)	1,00	1,16	1,34			
campesterol	1,00	1,32	1,65			
cerotic acid (c26:0)	1,00	0,74	1,00			
citrulline	1,00	0,51	0,33			
cryptoxanthine	1,00	1,00	0,90			
eicosenoic acid (20:1)	1,00	0,81	0,81			
ferulic acid	1,00	1,37	1,47			
fructose	1,00	14,10	19,78			
fumarate	1,00	5,19	9,33			
galactose	1,00	1,29	1,42			
g-aminobutyric acid	1,00	1,16	1,32			
gamma-tocopherol	1,00	0,54	0,60			
gluconic acid	1,00	2,24	3,08			

glucose	1,00	14,97	20,73			
glutamine	1,00	0,98	1,17			
glutamic acid	1,00	2,01	2,69			
glycerate	1,00	1,87	2,04			
glycerinaldehyd	1,00	1,11	1,12			
glycerol	1,00	1,22	1,29			
glycerol-3-phosphate	1,00	1,86	2,41			
glycine	1,00	0,25	0,26			
homoserine	1,00	0,61	0,69			
inositol	1,00	4,19	6,32			
isoleucine	1,00	1,28	1,66			
iso-maltose	1,00	2,63	3,02			
isopentenyl pyrophosphate	1,00	1,80	2,62			
leucine	1,00	1,34	1,74			
lignoceric acid (c24:0)	1,00	0,91	1,02			
linoleic acid (c18:2 (c9, c12))	1,00	1,19	1,38			
luteine	1,00	1,26	1,33			
malate	1,00	2,91	3,46			
mannose	1,00	16,40	17,80			
triacontanoic acid	1,00	1,26	1,23			
methionine	1,00	1,13	1,12			
methylgalactofuranoside	1,00	1,24	1,49			
methylgalactopyranoside	1,00	1,25	1,36			
ornithine					1,70	1,52
palmitic acid (c16:0)	1,00	1,16	1,38			
phenylalanine	1,00	0,92	1,10			
phosphate	1,00	2,15	2,73			
proline	1,00	1,23	4,77			
putrescine	1,00		0,39			
pyruvate	1,00	1,30	1,21			
raffinose	1,00	17,04	74,78			
ribonic acid	1,00	2,32	3,43			
serine	1,00	0,98	1,13			
shikimate	1,00	1,11	1,07			
sinapine acid	1,00	2,74	3,44			
stearic acid (c18:0)	1,00	1,18	1,35			
succinate	1,00	2,98	3,49			
sucrose	1,00	1,42	1,70			
threonine	1,00	1,26	1,68			
tryptophane	1,00	1,13	1,89			
tyrosine	1,00	1,56	2,01			
ubichinone	1,00	1,02	1,20			
udp-glucose	1,00	1,53	1,94			
valine	1,00	0,98	1,18			

zeaxanthine	1,00	1,27	1,34			

				YCL027W		
metabolite	Control	4 days	8 days	Control	4 days	8 days
2,3-dimethyl-5-phytylquinol	1,00	0,50	0,54			
2-hydroxy-palmitic acid	1,00	1,11	1,25			
3,4-dihydroxyphenylalanine (=dopa)	1,00	1,83	3,37			
3-hydroxy-palmitic acid	1,00					
5-oxoproline	1,00	1,56	1,81			
alanine	1,00	0,64	0,64			
alpha linolenic acid (c18:3 (c9, c12, c15))	1,00	1,24	1,40			
alpha-tocopherol	1,00	1,05	1,14			
aminoadipic acid	1,00	1,73	1,65			
anhydroglucose	1,00	1,02	1,16			
arginine	1,00	0,39	0,33			
aspartic acid	1,00	2,72	2,96			
beta-apo-8' carotenal	1,00	1,21	1,22			
beta-carotene	1,00	1,25	1,26			
beta-sitosterol	1,00	1,39	1,51			
beta-tocopherol	1,00	0,54	0,60			
palmitic acid	1,00	1,07	1,25			
delta-7-cis,10-cis-hexadecadienic acid (c16:2 me)	1,00	1,01	1,04			
hexadecatrienic acid (c16:3 me)	1,00	1,19	1,29			
margaric acid (c17:0 me)	1,00	1,19	1,28			
delta-15-cis-tetracosenic acid (c24:1 me)	1,00	1,16	1,34			
campesterol	1,00	1,32	1,65			
cerotic acid (c26:0)	1,00	0,74	1,00			
citrulline	1,00	0,51	0,33			
cryptoxanthine	1,00	1,00	0,90			
eicosenoic acid (20:1)	1,00	0,81	0,81			
ferulic acid	1,00	1,37	1,47	0,79	0,74	0,80
fructose	1,00	14,10	19,78			
fumarate	1,00	5,19	9,33			
galactose	1,00	1,29	1,42			
g-aminobutyric acid	1,00	1,16	1,32			
gamma-tocopherol	1,00	0,54	0,60			
gluconic acid	1,00	2,24	3,08			
glucose	1,00	14,97	20,73			
glutamine	1,00	0,98	1,17			
glutamic acid	1,00	2,01	2,69			
glycerate	1,00	1,87	2,04			
glycerinaldehyd	1,00	1,11	1,12			
glycerol	1,00	1,22	1,29			

glycerol-3-phosphate	1,00	1,86	2,41			
glycine	1,00	0,25	0,26			
homoserine	1,00	0,61	0,69			
inositol	1,00	4,19	6,32			
isoleucine	1,00	1,28	1,66			
iso-maltose	1,00	2,63	3,02			
isopentenyl pyrophosphate	1,00	1,80	2,62			
leucine	1,00	1,34	1,74			
lignoceric acid (c24:0)	1,00	0,91	1,02			
linoleic acid (c18:2 (c9, c12))	1,00	1,19	1,38			
luteine	1,00	1,26	1,33			
malate	1,00	2,91	3,46			
mannose	1,00	16,40	17,80			
triacontanoic acid	1,00	1,26	1,23			
methionine	1,00	1,13	1,12			
methylgalactofuranoside	1,00	1,24	1,49			
methylgalactopyranoside	1,00	1,25	1,36			
ornithine						
palmitic acid (c16:0)	1,00	1,16	1,38			
phenylalanine	1,00	0,92	1,10			
phosphate	1,00	2,15	2,73			
proline	1,00	1,23	4,77			
putrescine	1,00		0,39			
pyruvate	1,00	1,30	1,21			
raffinose	1,00	17,04	74,78			
ribonic acid	1,00	2,32	3,43			
serine	1,00	0,98	1,13			
shikimate	1,00	1,11	1,07			
sinapine acid	1,00	2,74	3,44			
stearic acid (c18:0)	1,00	1,18	1,35			
succinate	1,00	2,98	3,49			
sucrose	1,00	1,42	1,70			
threonine	1,00	1,26	1,68			
tryptophane	1,00	1,13	1,89			
tyrosine	1,00	1,56	2,01			
ubichinone	1,00	1,02	1,20			
udp-glucose	1,00	1,53	1,94			
valine	1,00	0,98	1,18			
zeaxanthine	1,00	1,27	1,34			

	YNL079C					
metabolite	Control	4 days	8 days	Control	4 days	8 days
2,3-dimethyl-5-phytylquinol	1,00	0,50	0,54	0,59		
2-hydroxy-palmitic acid	1,00	1,11	1,25			

3,4-dihydroxyphenylalanine (=dopa)	1,00	1,83	3,37			
3-hydroxy-palmitic acid	1,00		!			
5-oxoproline	1,00	1,56	1,81			
alanine	1,00	0,64	0,64			
alpha linolenic acid (c18:3 (c9, c12, c15))	1,00	1,24	1,40		1,53	1,56
alpha-tocopherol	1,00	1,05	1,14		2,64	3,66
aminoadipic acid	1,00	1,73	1,65			
anhydroglucose	1,00	1,02	1,16			
arginine	1,00	0,39	0,33			
aspartic acid	1,00	2,72	2,96			
beta-apo-8' carotenal	1,00	1,21	1,22			
beta-carotene	1,00	1,25	1,26		1,26	1,20
beta-sitosterol	1,00	1,39	1,51			
beta-tocopherol	1,00	0,54	0,60	0,73		0,56
palmitic acid	1,00	1,07	1,25			
delta-7-cis,10-cis-hexadecadienic acid (c16:2 me)	1,00	1,01	1,04			
hexadecatrienic acid (c16:3 me)	1,00	1,19	1,29			
margaric acid (c17:0 me)	1,00	1,19	1,28	1,22	1,53	1,36
delta-15-cis-tetracosenic acid (c24:1 me)	1,00	1,16	1,34			
campesterol	1,00	1,32	1,65		1,79	1,82
cerotic acid (c26:0)	1,00	0,74	1,00			
citrulline	1,00	0,51	0,33			
cryptoxanthine	1,00	1,00	0,90			
eicosenoic acid (20:1)	1,00	0,81	0,81			
ferulic acid	1,00	1,37	1,47			
fructose	1,00	14,10	19,78			
fumarate	1,00	5,19	9,33			
galactose	1,00	1,29	1,42			
g-aminobutyric acid	1,00	1,16	1,32			
gamma-tocopherol	1,00	0,54	0,60			
gluconic acid	1,00	2,24	3,08			
glucose	1,00	14,97	20,73			
glutamine	1,00	0,98	1,17			
glutamic acid	1,00	2,01	2,69			
glycerate	1,00	1,87	2,04			
glycerinaldehyd	1,00	1,11	1,12			
glycerol	1,00	1,22	1,29			
glycerol-3-phosphate	1,00	1,86	2,41			
glycine	1,00	0,25	0,26			
homoserine	1,00	0,61	0,69			
inositol	1,00	4,19	6,32		4,73	6,12
isoleucine	1,00	1,28	1,66			
iso-maltose	1,00	2,63	3,02		4,42	4,93

isopentenyl pyrophosphate	1,00	1,80	2,62			
leucine	1,00	1,34	1,74		1,51	2,19
lignoceric acid (c24:0)	1,00	0,91	1,02			
linoleic acid (c18:2 (c9, c12))	1,00	1,19	1,38			
luteine	1,00	1,26	1,33			
malate	1,00	2,91	3,46	1,49		5,72
mannose	1,00	16,40	17,80			
triacontanoic acid	1,00	1,26	1,23			
methionine	1,00	1,13	1,12			
methylgalactofuranoside	1,00	1,24	1,49			
methylgalactopyranoside	1,00	1,25	1,36			
ornithine						
palmitic acid (c16:0)	1,00	1,16	1,38			
phenylalanine	1,00	0,92	1,10			
phosphate	1,00	2,15	2,73			
proline	1,00	1,23	4,77			
putrescine	1,00		0,39			
pyruvate	1,00	1,30	1,21			
raffinose	1,00	17,04	74,78			
ribonic acid	1,00	2,32	3,43			
serine	1,00	0,98	1,13			
shikimate	1,00	1,11	1,07			
sinapine acid	1,00	2,74	3,44		3,89	2,79
stearic acid (c18:0)	1,00	1,18	1,35			
succinate	1,00	2,98	3,49			
sucrose	1,00	1,42	1,70			
threonine	1,00	1,26	1,68			
tryptophane	1,00	1,13	1,89		2,68	2,98
tyrosine	1,00	1,56	2,01			
ubichinone	1,00	1,02	1,20		0,88	1,02
udp-glucose	1,00	1,53	1,94			
valine	1,00	0,98	1,18			
zeaxanthine	1,00	1,27	1,34			

	wild type			YNL090W		
metabolite	Control	4 days	8 days	Control	4 days	8 days
2,3-dimethyl-5-phytylquinol	1,00	0,50	0,54			
2-hydroxy-palmitic acid	1,00	1,11	1,25	1,15	1,25	
3,4-dihydroxyphenylalanine (=dopa)	1,00	1,83	3,37			
3-hydroxy-palmitic acid	1,00					
5-oxoproline	1,00	1,56	1,81			
alanine	1,00	0,64	0,64			
alpha linolenic acid (c18:3 (c9, c12, c15))	1,00	1,24	1,40			

alpha-tocopherol	1,00	1,05	1,14	1,30		5,28
aminoadipic acid	1,00	1,73	1,65			
anhydroglucose	1,00	1,02	1,16			
arginine	1,00	0,39	0,33		0,85	
aspartic acid	1,00	2,72	2,96			
beta-apo-8' carotenal	1,00	1,21	1,22			
beta-carotene	1,00	1,25	1,26	1,15		1,91
beta-sitosterol	1,00	1,39	1,51			
beta-tocopherol	1,00	0,54	0,60			
palmitic acid	1,00	1,07	1,25			
delta-7-cis,10-cis-hexadecadienic acid (c16:2 me)	1,00	1,01	1,04			
hexadecatrienic acid (c16:3 me)	1,00	1,19	1,29			
margaric acid (c17:0 me)	1,00	1,19	1,28			
delta-15-cis-tetracosenic acid (c24:1 me)	1,00	1,16	1,34			
campesterol	1,00	1,32	1,65			
cerotic acid (c26:0)	1,00	0,74	1,00	2,98	3,93	
citrulline	1,00	0,51	0,33			
cryptoxanthine	1,00	1,00	0,90			
eicosenoic acid (20:1)	1,00	0,81	0,81			
ferulic acid	1,00	1,37	1,47			
fructose	1,00	14,10	19,78			
fumarate	1,00	5,19	9,33	0,76		
galactose	1,00	1,29	1,42			
g-aminobutyric acid	1,00	1,16	1,32			
gamma-tocopherol	1,00	0,54	0,60			1,69
gluconic acid	1,00	2,24	3,08			
glucose	1,00	14,97	20,73			
glutamine	1,00	0,98	1,17			
glutamic acid	1,00	2,01	2,69			
glycerate	1,00	1,87	2,04			
glycerinaldehyd	1,00	1,11	1,12			
glycerol	1,00	1,22	1,29			
glycerol-3-phosphate	1,00	1,86	2,41			
glycine	1,00	0,25	0,26			
homoserine	1,00	0,61	0,69			
inositol	1,00	4,19	6,32	1,46		9,70
isoleucine	1,00	1,28	1,66		3,54	4,86
iso-maltose	1,00	2,63	3,02	3,59	20,72	14,65
isopentenyl pyrophosphate	1,00	1,80	2,62	1,79		
leucine	1,00	1,34	1,74			
lignoceric acid (c24:0)	1,00	0,91	1,02			
linoleic acid (c18:2 (c9, c12))	1,00	1,19	1,38			

luteine	1,00	1,26	1,33			
malate	1,00	2,91	3,46	2,12		14,49
mannose	1,00	16,40	17,80			
triacontanoic acid	1,00	1,26	1,23			
methionine	1,00	1,13	1,12			
methylgalactofuranoside	1,00	1,24	1,49			
methylgalactopyranoside	1,00	1,25	1,36			
ornithine						
palmitic acid (c16:0)	1,00	1,16	1,38			
phenylalanine	1,00	0,92	1,10			
phosphate	1,00	2,15	2,73			
proline	1,00	1,23	4,77			
putrescine	1,00		0,39			
pyruvate	1,00	1,30	1,21			
raffinose	1,00	17,04	74,78			
ribonic acid	1,00	2,32	3,43			
serine	1,00	0,98	1,13			
shikimate	1,00	1,11	1,07			
sinapine acid	1,00	2,74	3,44			
stearic acid (c18:0)	1,00	1,18	1,35			
succinate	1,00	2,98	3,49			
sucrose	1,00	1,42	1,70			
threonine	1,00	1,26	1,68			
tryptophane	1,00	1,13	1,89			
tyrosine	1,00	1,56	2,01			
ubichinone	1,00	1,02	1,20			
udp-glucose	1,00	1,53	1,94			
valine	1,00	0,98	1,18	1,13	1,55	1,80
zeaxanthine	1,00	1,27	1,34			

0366.0.1 Example 2

0367.0.1 Engineering stress-tolerant Arabidopsis plants by over-expressing stress related protein encoding genes from *Saccharomyces cereviesae* or *E. coli* or *Brassica napus*, *Glycine max*, and *Oryza sativa* using stress-inducible and tissue-specific promoters.

0368.0.1 Transgenic Arabidopsis plants were created as in example 1 to express the stress related protein encoding transgenes under the control of either a tissue-specific or stress-inducible promoter. Constitutive expression of a transgene may cause deleterious side effects. Stress inducible expression was achieved using promoters selected from those listed above in Table 1.

0369.0.1 T2 generation plants were produced and treated with drought stress in two experiments. For the first drought experiment, the plants were deprived of water until the plant and soil were desiccated. At various times after withholding water, a normal watering schedule was resumed and the plants were grown to maturity. Seed yield was determined as seeds per plant. At an equivalent degree of drought stress, tolerant plants were able to resume normal growth and produced more seeds than non-transgenic control plants. Proline content of the leaves and stomatal aperture were also measured at various times during the drought stress. Tolerant plants maintained a lower proline content and a greater stomatal aperture than the non-transgenic control plants.

0370.0.1 An alternative method to impose water stress on the transgenic plants was by treatment with water containing an osmolyte such as polyethylene glycol (PEG) at specific water potential. Since PEG may be toxic, the plants were given only a short term exposure and then normal watering was resumed. As above, seed yields were measured from the mature plants. The response was measured during the stress period by physical measurements, such as stomatal aperture or osmotic potential, or biochemical measurements, such as accumulation of proline. Tolerant plants had higher seed yields, maintained their stomatal aperture and showed only slight changes in osmotic potential and proline levels, whereas the susceptible non-transgenic control plants closed their stomata and exhibited increased osmotic potential and proline levels.

0371.0.1 The transgenic plants with a constitutive promoter controlling transcription of the transgene were compared to those plants with a drought-inducible promoter in the absence of stress. The results indicated that the metabolite and gene expression changes did not occur when plants with the stress-inducible promoter were grown in the absence of stress. These plants also had higher seed yields than those with the constitutive promoter.

0372.0.1 Example 3

0373.0.1 Over-expression of stress related genes from *Saccharomyces cerevisiae* or *E. coli* or *Brassica napus*, *Glycine max*, and *Oryza sativa* provides tolerance of multiple abiotic stresses.

0374.0.1 Plants that exhibit tolerance of one abiotic stress often exhibit tolerance of another environmental stress or an oxygen free radical generating herbicide. This phenomenon of cross-tolerance is not understood at a mechanistic level (McKersie and Leshem, 1994). Nonetheless, it is reasonable to expect that plants exhibiting enhanced drought tolerance due to the expression of a transgene might also exhibit tolerance of low temperatures, freezing, salt, air pollutants such as ozone, and other abiotic

stresses. In support of this hypothesis, the expression of several genes are up or down-regulated by multiple abiotic stress factors including cold, salt, osmoticum, ABA, etc (e.g. Hong et al. (1992) Developmental and organ-specific expression of an ABA- and stress-induced protein in barley. Plant Mol Biol 18: 663-674; Jagendorf and Takabe (2001) Inducers of glycinebetaine synthesis in barley. Plant Physiol 127: 1827-1835); Mizoguchi et al. (1996) A gene encoding a mitogen-activated protein kinase is induced simultaneously with genes for a mitogen-activated protein kinase and an S6 ribosomal protein kinase by touch, cold, and water stress in Arabidopsis thaliana. Proc Natl Acad Sci U S A 93: 765-769; Zhu (2001) Cell signaling under salt, water and cold stresses. Curr Opin Plant Biol 4: 401-406).

0375.0.1 To determine salt tolerance, seeds of Arabidopsis thaliana were sterilized (100% bleach, 0.1% TritonX for five minutes two times and rinsed five times with ddH2O). Seeds were plated on non-selection media (1/2 MS, 0.6% phytagar, 0.5g/L MES, 1% sucrose, 2 µg/ml benamyl). Seeds are allowed to germinate for approximately ten days. At the 4-5 leaf stage, transgenic plants were potted into 5.5cm diameter pots and allowed to grow (22 °C, continuous light) for approximately seven days, watering as needed. To begin the assay, two liters of 100 mM NaCl and 1/8 MS was added to the tray under the pots. To the tray containing the control plants, three liters of 1/8 MS was added. The concentrations of NaCl supplementation were increased stepwise by 50 mM every 4 days up to 200 mM. After the salt treatment with 200 mM, fresh and dry weights of the plants as well as seed yields were determined.

0376.0.1 To determine cold tolerance, seeds of the transgenic and cold lines were germinated and grown for approximately 10 days to the 4-5 leaf stage as above. The plants were then transferred to cold temperatures (5 °C) and grown through the flowering and seed set stages of development. Photosynthesis was measured using chlorophyll fluorescence as an indicator of photosynthetic fitness and integrity of the photosystems. Seed yield and plant dry weight were measured as an indictor of plant biomass production.

0377.0.1 Plants that had tolerance to salinity or cold had higher seed yields, photosynthesis and dry matter production than susceptible plants.

0378.0.1 Example 4

0379.0.1 Engineering stress-tolerant alfalfa plants by over-expressing stress related genes from Saccharomyces cerevisiae or *E. coli* or *Brassica napus*, *Glycine max*, and *Oryza sativa*

0380.0.1 A regenerating clone of alfalfa (Medicago sativa) was transformed using the method of (McKersie et al., 1999 Plant Physiol 119: 839–847). Regeneration and transformation of alfalfa is genotype dependent and therefore a regenerating plant is

required. Methods to obtain regenerating plants have been described. For example, these can be selected from the cultivar Rangelander (Agriculture Canada) or any other commercial alfalfa variety as described by Brown DCW and A Atanassov (1985. Plant Cell Tissue Organ Culture 4: 111-112). Alternatively, the RA3 variety (University of Wisconsin) has been selected for use in tissue culture (Walker et al., 1978 Am J Bot 65:654-659).

0381.0.1 Petiole explants were cocultivated with an overnight culture of Agrobacterium tumefaciens C58C1 pMP90 (McKersie et al., 1999 Plant Physiol 119: 839–847) or LBA4404 containing a binary vector. Many different binary vector systems have been described for plant transformation (e.g. An, G. in Agrobacterium Protocols. Methods in Molecular Biology vol 44, pp 47-62, Gartland KMA and MR Davey eds. Humana Press, Totowa, New Jersey). Many are based on the vector pBIN19 described by Bevan (Nucleic Acid Research. 1984. 12:8711-8721) that includes a plant gene expression cassette flanked by the left and right border sequences from the Ti plasmid of Agrobacterium tumefaciens. A plant gene expression cassette consists of at least two genes – a selection marker gene and a plant promoter regulating the transcription of the cDNA or genomic DNA of the trait gene. Various selection marker genes can be used including the Arabidopsis gene encoding a mutated acetohydroxy acid synthase (AHAS) enzyme (US patents 57673666 and 6225105). Similarly, various promoters can be used to regulate the trait gene that provides constitutive, developmental, tissue or environmental regulation of gene transcription. In this example, the 34S promoter (GenBank Accession numbers M59930 and X16673) was used to provide constitutive expression of the trait gene.

0382.0.1 The explants were cocultivated for 3 d in the dark on SH induction medium containing 288 mg/ L Pro, 53 mg/ L thioproline, 4.35 g/ L K2SO4, and 100 µm acetosyringinone. The explants were washed in half-strength Murashige-Skoog medium (Murashige and Skoog, 1962) and plated on the same SH induction medium without acetosyringinone but with a suitable selection agent and suitable antibiotic to inhibit Agrobacterium growth. After several weeks, somatic embryos were transferred to BOi2Y development medium containing no growth regulators, no antibiotics, and 50 g/ L sucrose. Somatic embryos were subsequently germinated on half-strength Murashige-Skoog medium. Rooted seedlings were transplanted into pots and grown in a greenhouse.

0383.0.1 The T0 transgenic plants were propagated by node cuttings and rooted in Turface growth medium. The plants were defoliated and grown to a height of about 10 cm (approximately 2 weeks after defoliation). The plants were then subjected to drought stress in two experiments.

0384.0.1 For the first drought experiment, the seedlings received no water for a period up to 3 weeks at which time the plant and soil were desiccated. At various times after withholding water, a normal watering schedule was resumed. At one week after resuming watering, the fresh and dry weights of the shoots was determined. At an equivalent degree of drought stress, tolerant plants were able to resume normal growth whereas susceptible plants had died or suffered significant injury resulting in less dry matter. Proline content of the leaves and stomatal aperture were also measured at various times during the drought stress. Tolerant plants maintained a lower proline content and a greater stomatal aperture than the non-transgenic control plants.

0385.0.1 An alternative method to impose water stress on the transgenic plants was by treatment with a solution at specific water potential, containing an osmolyte such as polyethylene glycol (PEG). The PEG treatment was given to either detached leaves (e.g. Djilianov et al., 1997 Plant Science 129: 147-156) or to the roots (Wakabayashi et al., 1997 Plant Physiol 113: 967-973). Since PEG may be toxic, the plants were given only a short term exposure. The response was measured as physical measurements such as stomatal aperture or osmotic potential, or biochemical measurements such as accumulation of proline. Tolerant plants maintained their stomatal aperture and showed only slight changes in osmotic potential, whereas the susceptible non-transgenic control plants closed their stomata and exhibited increased osmotic potential. In addition the changes in proline and other metabolites were less in the tolerant transgenic plants than in the non-transgenic control plants.

0386.0.1 Tolerance of salinity and cold were measured using methods as described in example 3. Plants that had tolerance to salinity or cold had higher seed yields, photosynthesis and dry matter production than susceptible plants.

0387.0.1 **Example 5**

0388.0.1 **Engineering stress-tolerant ryegrass plants by over-expressing stress related genes from Saccharomyces cerevisiae or E. coli or *Brassica napus*, *Glycine max*, and *Oryza sativa***

0389.0.1 Seeds of several different ryegrass varieties may be used as explant sources for transformation, including the commercial variety Gunne available from Svalof Weibull seed company or the variety Affinity. Seeds were surface-sterilized sequentially with 1% Tween-20 for 1 minute, 100 % bleach for 60 minutes, 3 rinses with 5 minutes each with de-ionized and distilled H2O, and then germinated for 3-4 days on moist, sterile filter paper in the dark. Seedlings were further sterilized for 1 minute with 1% Tween-20, 5 minutes with 75% bleach, and rinsed 3 times with ddH2O, 5 min each.

0390.0.1 Surface-sterilized seeds were placed on the callus induction medium containing Murashige and Skoog basal salts and vitamins, 20 g/l sucrose, 150 mg/l asparagine, 500 mg/l casein hydrolysate, 3 g/l Phytagel, 10 mg/l BAP, and 5 mg/l dicamba. Plates were incubated in the dark at 25C for 4 weeks for seed germination and embryogenic callus induction.

0391.0.1 After 4 weeks on the callus induction medium, the shoots and roots of the seedlings were trimmed away, the callus was transferred to fresh media, maintained in culture for another 4 weeks, and then transferred to MSO medium in light for 2 weeks. Several pieces of callus (11-17 weeks old) were either strained through a 10 mesh sieve and put onto callus induction medium, or cultured in 100 ml of liquid ryegrass callus induction media (same medium as for callus induction with agar) in a 250 ml flask. The flask was wrapped in foil and shaken at 175 rpm in the dark at 23 C for 1 week. Sieving the liquid culture with a 40-mesh sieve collected the cells. The fraction collected on the sieve was plated and cultured on solid ryegrass callus induction medium for 1 week in the dark at 25C. The callus was then transferred to and cultured on MS medium containing 1% sucrose for 2 weeks.

0392.0.1 Transformation can be accomplished with either Agrobacterium of with particle bombardment methods. An expression vector is created containing a constitutive plant promoter and the cDNA of the gene in a pUC vector. The plasmid DNA was prepared from E. coli cells using with Qiagen kit according to manufacturer's instruction. Approximately 2 g of embryogenic callus was spread in the center of a sterile filter paper in a Petri dish. An aliquot of liquid MSO with 10 g/l sucrose was added to the filter paper. Gold particles (1.0 µm in size) were coated with plasmid DNA according to method of Sanford et al., 1993 and delivered to the embryogenic callus with the following parameters: 500 µg particles and 2 µg DNA per shot, 1300 psi and a target distance of 8.5 cm from stopping plate to plate of callus and 1 shot per plate of callus.

0393.0.1 After the bombardment, calli were transferred back to the fresh callus development medium and maintained in the dark at room temperature for a 1-week period. The callus was then transferred to growth conditions in the light at 25 °C to initiate embryo differentiation with the appropriate selection agent, e.g. 250 nM Arsenal, 5 mg/l PPT or 50 mg/L kanamycin. Shoots resistant to the selection agent appeared and once rotted were transferred to soil.

0394.0.1 Samples of the primary transgenic plants (T0) are analyzed by PCR to confirm the presence of T-DNA. These results are confirmed by Southern hybridization in which DNA is electrophoresed on a 1% agarose gel and transferred to a positively charged nylon membrane (Roche Diagnostics). The PCR DIG Probe Synthesis Kit

(Roche Diagnostics) is used to prepare a digoxigenin-labelled probe by PCR, and used as recommended by the manufacturer.

0395.0.1 Transgenic T0 ryegrass plants were propagated vegetatively by excising tillers. The transplanted tillers were maintained in the greenhouse for 2 months until well established. The shoots were defoliated and allowed to grow for 2 weeks.

0396.0.1 The first drought experiment was conducted in a manner similar to that described in example 3. The seedlings received no water for a period up to 3 weeks at which time the plant and soil were desiccated. At various times after withholding water, a normal watering schedule was resumed. At one week after resuming watering, the lengths of leaf blades, and the fresh and dry weights of the shoots was determined. At an equivalent degree of drought stress, tolerant plants were able to resume normal growth whereas susceptible plants had died or suffered significant injury resulting in shorter leaves and less dry matter. Proline content of the leaves and stomatal aperture were also measured at various times during the drought stress. Tolerant plants maintained a lower proline content and a greater stomatal aperture than the non-transgenic control plants.

0397.0.1 A second experiment imposing drought stress on the transgenic plants was by treatment with a solution of PEG as described in the previous examples. Tolerance of salinity and cold were measured using methods as described in example 3. Plants that had tolerance to salinity or cold had higher seed yields, photosynthesis and dry matter production than susceptible plants.

0398.0.1 **Example 6**

0399.0.1 **Engineering stress-tolerant soybean plants by over-expressing stress related genes from *Saccharomyces cerevisiae or E. coli* or *Brassica napus*, *Glycine max*, and *Oryza sativa***

0400.0.1 Soybean was transformed according to the following modification of the method described in the Texas A&M patent US 5,164,310. Several commercial soybean varieties are amenable to transformation by this method. The cultivar Jack (available from the Illinois Seed Foundation) is a commonly used for transformation. Seeds were sterilized by immersion in 70% (v/v) ethanol for 6 min and in 25 % commercial bleach (NaOCl) supplemented with 0.1% (v/v) Tween for 20 min, followed by rinsing 4 times with sterile double distilled water. Seven-day seedlings were propagated by removing the radicle, hypocotyl and one cotyledon from each seedling. Then, the epicotyl with one cotyledon was transferred to fresh germination media in petri dishes and incubated at 25 °C under a 16-hr photoperiod (approx. 100 µE-m-2s-1) for three weeks. Axillary nodes (approx. 4 mm in length) were cut from 3 – 4 week-old plants. Axillary nodes were excised and incubated in Agrobacterium LBA4404 culture.

0401.0.1 Many different binary vector systems have been described for plant transformation (e.g. An, G. in Agrobacterium Protocols. Methods in Molecular Biology vol 44, pp 47-62, Gartland KMA and MR Davey eds. Humana Press, Totowa, New Jersey). Many are based on the vector pBIN19 described by Bevan (Nucleic Acid Research. 1984. 12:8711-8721) that includes a plant gene expression cassette flanked by the left and right border sequences from the Ti plasmid of Agrobacterium tumefaciens. A plant gene expression cassette consists of at least two genes – a selection marker gene and a plant promoter regulating the transcription of the cDNA or genomic DNA of the trait gene. Various selection marker genes can be used including the Arabidopsis gene encoding a mutated acetohydroxy acid synthase (AHAS) enzyme (US patents 57673666 and 6225105). Similarly, various promoters can be used to regulate the trait gene to provide constitutive, developmental, tissue or environmental regulation of gene transcription. In this example, the 34S promoter (GenBank Accession numbers M59930 and X16673) was used to provide constitutive expression of the trait gene.

0402.0.1 After the co-cultivation treatment, the explants were washed and transferred to selection media supplemented with 500 mg/L timentin. Shoots were excised and placed on a shoot elongation medium. Shoots longer than 1 cm were placed on rooting medium for two to four weeks prior to transplanting to soil.

0403.0.1 The primary transgenic plants (T0) were analyzed by PCR to confirm the presence of T-DNA. These results were confirmed by Southern hybridization in which DNA is electrophoresed on a 1 % agarose gel and transferred to a positively charged nylon membrane (Roche Diagnostics). The PCR DIG Probe Synthesis Kit (Roche Diagnostics) is used to prepare a digoxigenin-labelled probe by PCR, and used as recommended by the manufacturer.

0404.0.1 Tolerant plants had higher seed yields, maintained their stomatal aperture and showed only slight changes in osmotic potential and proline levels, whereas the susceptible non-transgenic control plants closed their stomata and exhibited increased osmotic potential and proline levels.

0405.0.1 Tolerance of drought, salinity and cold were measured using methods as described in example3. Plants that had tolerance to salinity or cold had higher seed yields, photosynthesis and dry matter production than susceptible plants.

0406.0.1 **Example 7**

0407.0.1 **Engineering stress-tolerant Rapeseed/Canola plants by over-expressing stress related genes from *Saccharomyces cerevisiae or E. coli* or *Brassica napus*, *Glycine max*, and *Oryza sativa***

0408.0.1 Cotyledonary petioles and hypocotyls of 5-6 day-old young seedlings were used as explants for tissue culture and transformed according to Babic et al.(1998, Plant Cell Rep 17: 183-188). The commercial cultivar Westar (Agriculture Canada) is the standard variety used for transformation, but other varieties can be used.

0409.0.1 Agrobacterium tumefaciens LBA4404 containing a binary vector was used for canola transformation. Many different binary vector systems have been described for plant transformation (e.g. An, G. in Agrobacterium Protocols. Methods in Molecular Biology vol 44, pp 47-62, Gartland KMA and MR Davey eds. Humana Press, Totowa, New Jersey). Many are based on the vector pBIN19 described by Bevan (Nucleic Acid Research. 1984. 12:8711-8721) that includes a plant gene expression cassette flanked by the left and right border sequences from the Ti plasmid of Agrobacterium tumefaciens. A plant gene expression cassette consists of at least two genes – a selection marker gene and a plant promoter regulating the transcription of the cDNA or genomic DNA of the trait gene. Various selection marker genes can be used including the Arabidopsis gene encoding a mutated acetohydroxy acid synthase (AHAS) enzyme (US patents 57673666 and 6225105). Similarly, various promoters can be used to regulate the trait gene to provide constitutive, developmental, tissue or environmental regulation of gene transcription. In this example, the 34S promoter (GenBank Accession numbers M59930 and X16673) was used to provide constitutive expression of the trait gene.

0410.0.1 Canola seeds were surface-sterilized in 70% ethanol for 2 min., and then in 30% Clorox with a drop of Tween-20 for 10 min, followed by three rinses with sterilized distilled water. Seeds were then germinated in vitro 5 days on half strength MS medium without hormones, 1% sucrose, 0.7% Phytagar at 23oC, 16 hr. light. The cotyledon petiole explants with the cotyledon attached were excised from the in vitro seedlings, and inoculated with Agrobacterium by dipping the cut end of the petiole explant into the bacterial suspension. The explants were then cultured for 2 days on MSBAP-3 medium containing 3 mg/l BAP, 3 % sucrose, 0.7 % Phytagar at 23 °C, 16 hr light. After two days of co-cultivation with Agrobacterium, the petiole explants were transferred to MSBAP-3 medium containing 3 mg/l BAP, cefotaxime, carbenicillin, or timentin (300 mg/l) for 7 days, and then cultured on MSBAP-3 medium with cefotaxime, carbenicillin, or timentin and selection agent until shoot regeneration. When the shoots were 5 – 10 mm in length, they were cut and transferred to shoot elongation medium (MSBAP-0.5, containing 0.5 mg/l BAP). Shoots of about 2 cm in length were transferred to the rooting medium (MS0) for root induction.

0411.0.1 Samples of the primary transgenic plants (T0) were analyzed by PCR to confirm the presence of T-DNA. These results were confirmed by Southern hybridization in which DNA is electrophoresed on a 1 % agarose gel and transferred to a positively charged nylon membrane (Roche Diagnostics). The PCR DIG Probe Synthesis Kit (Roche Diagnostics) is used to prepare a digoxigenin-labelled probe by PCR, and used as recommended by the manufacturer.

0412.0.1 The transgenic plants were then evaluated for their improved stress tolerance according to the method described in Example 3. Tolerant plants had higher seed yields, maintained their stomatal aperture and showed only slight changes in osmotic potential and proline levels, whereas the susceptible non-transgenic control plants closed their stomata and exhibited increased osmotic potential and proline levels.

0413.0.1 Tolerance of drought, salinity and cold were measured using methods as described in the previous example 3. Plants that had tolerance to salinity or cold had higher seed yields, photosynthesis and dry matter production than susceptible plants.

0414.0.1 **Example 8**

0415.0.1 **Engineering stress-tolerant corn plants by over-expressing stress related genes from Saccharomyces cerevisiae or E. coli or *Brassica napus*, *Glycine max*, and *Oryza sativa***

0416.0.1 Transformation of maize (Zea Mays L.) is performed with a modification of the method described by Ishida et al. (1996. Nature Biotech 14745-50). Transformation is genotype-dependent in corn and only specific genotypes are amenable to transformation and regeneration. The inbred line A188 (University of Minnesota) or hybrids with A188 as a parent are good sources of donor material for transformation (Fromm et al. 1990 Biotech 8:833-839), but other genotypes can be used successfully as well. Ears are harvested from corn plants at approximately 11 days after pollination (DAP) when the length of immature embryos is about 1 to 1.2 mm. Immature embryos are co-cultivated with Agrobacterium tumefaciens that carry "super binary" vectors and transgenic plants are recovered through organogenesis. The super binary vector system of Japan Tobacco is described in WO patents WO94/00977 and WO95/06722. Vectors were constructed as described. Various selection marker genes can be used including the maize gene encoding a mutated acetohydroxy acid synthase (AHAS) enzyme (US patent 6025541). Similarly, various promoters can be used to regulate the trait gene to provide constitutive, developmental, tissue or environmental regulation of gene transcription. In this example, the 34S promoter (GenBank Accession numbers M59930 and X16673) was used to provide constitutive expression of the trait gene.

0417.0.1 Excised embryos are grown on callus induction medium, then maize regeneration medium, containing imidazolinone as a selection agent. The Petri plates are incubated in the light at 25 °C for 2-3 weeks, or until shoots develop. The green shoots are transferred from each embryo to maize rooting medium and incubated at 25 °C for 2-3 weeks, until roots develop. The rooted shoots are transplanted to soil in the greenhouse. T1 seeds are produced from plants that exhibit tolerance to the imidazolinone herbicides and which are PCR positive for the transgenes.

0418.0.1 The T1 transgenic plants were then evaluated for their improved stress tolerance according to the method described in Example 3. The T1 generation of single locus insertions of the T-DNA will segregate for the transgene in a 3:1 ratio. Those progeny containing one or two copies of the transgene are tolerant of the imidazolinone herbicide, and exhibit greater tolerance of drought stress than those progeny lacking the transgenes. Tolerant plants had higher seed yields, maintained their stomatal aperture and showed only slight changes in osmotic potential and proline levels, whereas the susceptible non-transgenic control plants closed their stomata and exhibited increased osmotic potential and proline levels. Homozygous T2 plants exhibited similar phenotypes. Hybrid plants (F1 progeny) of homozygous transgenic plants and non-transgenic plants also exhibited increased environmental stress tolerance.

0419.0.1 Tolerance of salinity and cold were measured using methods as described in the previous example 3. Plants that had tolerance to drought, salinity or cold had higher seed yields, photosynthesis and dry matter production than susceptible plants.

0420.0.1 **Example 9**

0421.0.1 **Engineering stress-tolerant wheat plants by over-expressing stress related genes from *Saccharomyces cerevisiae or E. coli*, *Brassica napus*, *Glycine max*, or *Oryza sativa***

0422.0.1 Transformation of wheat is performed with the method described by Ishida et al. (1996 Nature Biotech. 14745-50). The cultivar Bobwhite (available from CYMMIT, Mexico) is commonly used in transformation. Immature embryos are co-cultivated with Agrobacterium tumefaciens that carry "super binary" vectors, and transgenic plants are recovered through organogenesis. The super binary vector system of Japan Tobacco is described in WO patents WO94/00977 and WO95/06722. Vectors were constructed as described. Various selection marker genes can be used including the maize gene encoding a mutated acetohydroxy acid synthase (AHAS) enzyme (US patent 6025541). Similarly, various promoters can be used to regulate the trait gene to provide constitutive, developmental, tissue or environmental regulation of

gene transcription. In this example, the 34S promoter (GenBank Accession numbers M59930 and X16673) was used to provide constitutive expression of the trait gene.

0423.0.1 After incubation with Agrobacterium, the embryos are grown on callus induction medium, then regeneration medium, containing imidazolinone as a selection agent. The Petri plates are incubated in the light at 25 °C for 2-3 weeks, or until shoots develop. The green shoots are transferred from each embryo to rooting medium and incubated at 25 °C for 2-3 weeks, until roots develop. The rooted shoots are transplanted to soil in the greenhouse. T1 seeds are produced from plants that exhibit tolerance to the imidazolinone herbicides and which are PCR positive for the transgenes.

0424.0.1 The T1 transgenic plants were then evaluated for their improved stress tolerance according to the method described in the previous example 3. The T1 generation of single locus insertions of the T-DNA will segregate for the transgene in a 3:1 ratio. Those progeny containing one or two copies of the transgene are tolerant of the imidazolinone herbicide, and exhibit greater tolerance of drought stress than those progeny lacking the transgenes. Tolerant plants had higher seed yields, maintained their stomatal aperture and showed only slight changes in osmotic potential and proline levels, whereas the susceptible non-transgenic control plants closed their stomata and exhibited increased osmotic potential and proline levels. Homozygous T2 plants exhibited similar phenotypes. Tolerance of salinity and cold were measured using methods as described in the previous examples. Plants that had tolerance to drought, salinity or cold had higher seed yields, photosynthesis and dry matter production than susceptible plants.

0425.0.3 **Example 14**

0426.0.3 **Identification of Identical and Heterologous Genes**

0427.0.3 Gene sequences can be used to identify identical or heterologous genes from cDNA or genomic libraries. Identical genes (e. g. full-length cDNA clones) can be isolated via nucleic acid hybridization using for example cDNA libraries. Depending on the abundance of the gene of interest, 100,000 up to 1,000,000 recombinant bacteriophages are plated and transferred to nylon membranes. After denaturation with alkali, DNA is immobilized on the membrane by e. g. UV cross linking. Hybridization is carried out at high stringency conditions. In aqueous solution, hybridization and washing is performed at an ionic strength of 1 M NaCl and a temperature of 68°C. Hybridization probes are generated by e.g. radioactive (^{32}P) nick transcription labeling (High Prime, Roche, Mannheim, Germany). Signals are detected by autoradiography.

0428.0.3 Partially identical or heterologous genes that are related but not identical can be identified in a manner analogous to the above-described procedure using low

stringency hybridization and washing conditions. For aqueous hybridization, the ionic strength is normally kept at 1 M NaCl while the temperature is progressively lowered from 68 to 42°C.

0429.0.3 Isolation of gene sequences with homology (or sequence identity/similarity) only in a distinct domain of (for example 10-20 amino acids) can be carried out by using synthetic radio labeled oligonucleotide probes. Radiolabeled oligonucleotides are prepared by phosphorylation of the 5-prime end of two complementary oligonucleotides with T4 polynucleotide kinase. The complementary oligonucleotides are annealed and ligated to form concatemers. The double stranded concatemers are than radiolabeled by, for example, nick transcription. Hybridization is normally performed at low stringency conditions using high oligonucleotide concentrations.

Oligonucleotide hybridization solution:
6 x SSC
0.01 M sodium phosphate
1 mM EDTA (pH 8)
0.5 % SDS
100 µg/ml denatured salmon sperm DNA
0.1 % nonfat dried milk

0430.0.3 During hybridization, temperature is lowered stepwise to 5-10°C below the estimated oligonucleotide T_m or down to room temperature followed by washing steps and autoradiography. Washing is performed with low stringency such as 3 washing steps using 4 x SSC. Further details are described by Sambrook, J. et al., 1989, "Molecular Cloning: A Laboratory Manual," Cold Spring Harbor Laboratory Press or Ausubel, F.M. et al., 1994, "Current Protocols in Molecular Biology," John Wiley & Sons.

0431.0.3 Example 15

0432.0.3 Identification of Identical Genes by Screening Expression Libraries with Antibodies

0433.0.3 c-DNA clones can be used to produce recombinant polypeptide for example in *E. coli* (e.g. Qiagen QIAexpress pQE system). Recombinant polypeptides are then normally affinity purified via Ni-NTA affinity chromatography (Qiagen). Recombinant polypeptides are then used to produce specific antibodies for example by using standard techniques for rabbit immunization. Antibodies are affinity purified using a Ni-NTA column saturated with the recombinant antigen as described by Gu et al., 1994, BioTechniques 17:257-262. The antibody can than be used to screen expression cDNA libraries to identify identical or heterologous genes via an immunological screening (Sambrook, J. et al., 1989, "Molecular Cloning: A Laboratory

Manual," Cold Spring Harbor Laboratory Press or Ausubel, F.M. et al., 1994, "Current Protocols in Molecular Biology", John Wiley & Sons).

0434.0.3 Example 16

0435.0.3 In vivo Mutagenesis

0436.0.3 *In vivo* mutagenesis of microorganisms can be performed by passage of plasmid (or other vector) DNA through *E. coli* or other microorganisms (e.g. *Bacillus* spp. or yeasts such as *Saccharomyces cerevisiae*) which are impaired in their capabilities to maintain the integrity of their genetic information. Typical mutator strains have mutations in the genes for the DNA repair system (e.g., mutHLS, mutD, mutT, etc.; for reference, see Rupp, W.D., 1996, DNA repair mechanisms, in: *Escherichia coli* and *Salmonella*, p. 2277-2294, ASM: Washington.) Such strains are well known to those skilled in the art. The use of such strains is illustrated, for example, in Greener, A. and Callahan, M., 1994, Strategies 7: 32-34. Transfer of mutated DNA molecules into plants is preferably done after selection and testing in microorganisms. Transgenic plants are generated according to various examples within the exemplification of this document.

0437.0.3 Example 17

0438.0.3 Identification and Analysis of YNL090W Homologs

0439.0.3 Transgenic Arabidopsis plants overexpressing YNL 090W (ORF 3165) lived 4.33 days longer than the wild type control under drought conditions. The protein sequence of YNL090W was used to identify related gene sequences of expressed sequence tags (ESTs) proprietary libraries constructed from *Oryza sativa* cv. Noppon-Brarre (a japonica rice), *Brassica napus* cv. "AC Excel" "Quantum" and "Cresor" (canola), and *Glycine max* cv. Resuick (soybean) by Blast analysis (Altschul SF, Gish W, Miller W, Myers EW, Lipman DJ. 1990 J Mol Biol 21593:403-10).

0440.0.3 The plant cDNA sequences were translated into a predicated amino acid sequences, and relationship among the amino acids sequences was determined by sequence alignment using the clustal W alogorithm in Vector NTI Version 7 (**Figure 2**). They have 75% similarity overall. In general, proteins having conserved domains referred to as I (GXXXGKT), II (DXXG), III (VGTK), IV (EXSS), and E (FXXXYXX), are classified as small GTPases. All five domains in the proteins in Figure 1 are more conserved than in other known small GTPases, particularly Domain I (KXVXXGDXXXGKT), Domain E (FXXXYXXTV), Domain II (WDTAGQE) and Domain III (VGTKXDL). In addition, polybasic amino acids in C terminus are shown in the Figure 2, as well as a C-terminal CAAL domain (wherein A is an aliphatic amino acid), which is the signature sequence for post translational modification by the enzyme geranylgeranyltransferase I. Another important Rho-specific feature was shown in

most proteins in Figure 1 is the highly conserved amino ácids between Domain II and Domain III.

SEQUENCES

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<120> Nucleic acid sequences encoding proteins associated with abiotic stress response and plant cells and plants with increased tolerance to environmental stress

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<222> (1)..(1143)

<400> 1

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1 5 10 15

ata ttt gat tgc tac aat tcc acg cta ccc aag aat gta ttc cga agt 96
Ile Phe Asp Cys Tyr Asn Ser Thr Leu Pro Lys Asn Val Phe Arg Ser
20 25 30

ttt gtt acc tgg tcc tgc tat gag aaa ttc aat tcc tta gaa ttc cgc 144
Phe Val Thr Trp Ser Cys Tyr Glu Lys Phe Asn Ser Leu Glu Phe Arg
35 40 45

act tgg cta tta atg tgg tta cca ctc att att gcg tgg aaa ata cgt 192
Thr Trp Leu Leu Met Trp Leu Pro Leu Ile Ile Ala Trp Lys Ile Arg
50 55 60

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Gly Lys Arg His Tyr Leu Val Ile Val Thr Ala Leu Met Phe Glu Val
65 70 75 80

ctg tat ttc tta tgg aca tat tcg tac ata ttc cga gaa cgc acc tta 288
Leu Tyr Phe Leu Trp Thr Tyr Ser Tyr Ile Phe Arg Glu Arg Thr Leu
85 90 95

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Gly Lys Gln Val Ser Gln Phe Ala Lys Glu Ile Ile Thr Asn Thr Pro
100 105 110

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Gly Ile Asp Thr Glu Asp Trp Glu Arg Val Ala Val Asn Phe Asn Ser
115 120 125

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130 135 140

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145 150 155 160

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180 185 190

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Ser Ile Ala Tyr Leu Asn Gly Leu Leu Thr Ile Pro Arg Leu Arg Asn
245 250 255

tca ctg cat atc ctc tat gta tgt gca gtt ctt tca tct atg ata att 816
Ser Leu His Ile Leu Tyr Val Cys Ala Val Leu Ser Ser Met Ile Ile
260 265 270

gaa tat tta ata ggg atc gac aaa ttc agg ttc aaa tca atg aat ctg 864
Glu Tyr Leu Ile Gly Ile Asp Lys Phe Arg Phe Lys Ser Met Asn Leu
275 280 285

ata cat aaa cta cag ttc ttg tca tat att aca tgt gga cac gag aag 912
Ile His Lys Leu Gln Phe Leu Ser Tyr Ile Thr Cys Gly His Glu Lys
290 295 300

tct gat gca act aat tgg tct caa att gcg aag agg acg aat act tac 960
Ser Asp Ala Thr Asn Trp Ser Gln Ile Ala Lys Arg Thr Asn Thr Tyr
305 310 315 320

atg ttt gag cag aaa att tgg aat tcg cca ata ctg ttc tca gat ggt 1008
Met Phe Glu Gln Lys Ile Trp Asn Ser Pro Ile Leu Phe Ser Asp Gly
325 330 335

att gat tgt gaa aag ttt ttt aaa tgg tat ttc agt acc cct gta tct 1056
Ile Asp Cys Glu Lys Phe Phe Lys Trp Tyr Phe Ser Thr Pro Val Ser
340 345 350

tcg caa gcg tct ttg tca gtt ggt tcc act gat ttt gaa ctc tgg cca 1104
Ser Gln Ala Ser Leu Ser Val Gly Ser Thr Asp Phe Glu Leu Trp Pro
355 360 365

tat ata aaa gaa gca caa tca gct tgc aat gat gtg taa 1143
Tyr Ile Lys Glu Ala Gln Ser Ala Cys Asn Asp Val
370 375 380

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Phe Val Thr Trp Ser Cys Tyr Glu Lys Phe Asn Ser Leu Glu Phe Arg
35 40 45

Thr Trp Leu Leu Met Trp Leu Pro Leu Ile Ile Ala Trp Lys Ile Arg
50 55 60

Gly Lys Arg His Tyr Leu Val Ile Val Thr Ala Leu Met Phe Glu Val
65 70 75 80

Leu Tyr Phe Leu Trp Thr Tyr Ser Tyr Ile Phe Arg Glu Arg Thr Leu
85 90 95

Gly Lys Gln Val Ser Gln Phe Ala Lys Glu Ile Ile Thr Asn Thr Pro
100 105 110

Gly Ile Asp Thr Glu Asp Trp Glu Arg Val Ala Val Asn Phe Asn Ser
115 120 125

Tyr Leu Tyr Glu Asn Lys Leu Trp Asn Thr Glu Tyr Phe Phe Phe Asp
130 135 140

Gly Ser Ser Cys Gln Glu Ala Phe Arg Lys Met Leu Leu Glu Pro Phe
145 150 155 160

Ser Leu Lys Lys Asn Asp Phe Ala Asn Ala Lys Val Pro Asp Gly Ser
165 170 175

Val Cys Tyr Thr Glu Lys Ala Leu Gln Val Tyr Phe Thr Gln Ile Glu
180 185 190

Arg Lys Trp His Trp Ile Asn Ser Glu Gly Phe Leu His Asn Lys Thr
195 200 205

Thr Gln Ser Val Gln Phe Ser Lys His Gly Tyr Gly Ser Lys Leu Leu
210 215 220

Trp Ala Phe Lys Glu Val Thr Ile Met Asn Ser Arg Phe Ala Phe Phe
225 230 235 240

Ser Ile Ala Tyr Leu Asn Gly Leu Leu Thr Ile Pro Arg Leu Arg Asn
245 250 255

Ser Leu His Ile Leu Tyr Val Cys Ala Val Leu Ser Ser Met Ile Ile
260 265 270

Glu Tyr Leu Ile Gly Ile Asp Lys Phe Arg Phe Lys Ser Met Asn Leu
275 280 285

Ile His Lys Leu Gln Phe Leu Ser Tyr Ile Thr Cys Gly His Glu Lys
290 295 300

Ser Asp Ala Thr Asn Trp Ser Gln Ile Ala Lys Arg Thr Asn Thr Tyr
305 310 315 320

Met Phe Glu Gln Lys Ile Trp Asn Ser Pro Ile Leu Phe Ser Asp Gly
325 330 335

Ile Asp Cys Glu Lys Phe Phe Lys Trp Tyr Phe Ser Thr Pro Val Ser
340 345 350

Ser Gln Ala Ser Leu Ser Val Gly Ser Thr Asp Phe Glu Leu Trp Pro
355 360 365

Tyr Ile Lys Glu Ala Gln Ser Ala Cys Asn Asp Val
370 375 380

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gct gag tct aca gaa agc aag aat aaa cac att cgt agc gct tta aga 96
Ala Glu Ser Thr Glu Ser Lys Asn Lys His Ile Arg Ser Ala Leu Arg
20 25 30

aaa cga aga ggt aaa tta agc gcc caa act tat gag gaa gat caa gag 144
Lys Arg Arg Gly Lys Leu Ser Ala Gln Thr Tyr Glu Glu Asp Gln Glu
35 40 45

gct att tta tca tct cct tta ttg act tca aca cct aaa aca gtc tcc 192
Ala Ile Leu Ser Ser Pro Leu Leu Thr Ser Thr Pro Lys Thr Val Ser
50 55 60

agg tca tta gtg agg tta tac cca tat tta att gtt gtg gat aac ttt 240
Arg Ser Leu Val Arg Leu Tyr Pro Tyr Leu Ile Val Val Asp Asn Phe
65 70 75 80

cta agt atc atc act tgg tcc aat gac aat gtc tct gca aac ttg ctt 288
Leu Ser Ile Ile Thr Trp Ser Asn Asp Asn Val Ser Ala Asn Leu Leu
85 90 95

gga ata ttc tta ttt acg gtt tgt gtt cta tat ttt gga ttt att aca 336
Gly Ile Phe Leu Phe Thr Val Cys Val Leu Tyr Phe Gly Phe Ile Thr
100 105 110

agg tat ttt gga cat tta atg atc gtt ggt ata ata tgg gta tat ctt 384
Arg Tyr Phe Gly His Leu Met Ile Val Gly Ile Ile Trp Val Tyr Leu
115 120 125

tta att gac aag cac gtt caa gaa aca atg gca tct tgc cct tca ttg 432
Leu Ile Asp Lys His Val Gln Glu Thr Met Ala Ser Cys Pro Ser Leu
130 135 140

gat gat ata ata cac gtt atg gat agg gtt tct atg aaa tct agc gct 480
Asp Asp Ile Ile His Val Met Asp Arg Val Ser Met Lys Ser Ser Ala
145 150 155 160

gtg tta tct cct att acg att ttg agc gct cag gat gtt aga aga ctg 528

Val Leu Ser Pro Ile Thr Ile Leu Ser Ala Gln Asp Val Arg Arg Leu
165 170 175

tta ttt acc att gcc ttc cta tcc cca gtt tat att ttt cta aca gtg 576
Leu Phe Thr Ile Ala Phe Leu Ser Pro Val Tyr Ile Phe Leu Thr Val
180 185 190

ttt gtg cta tct cca aac tat tta atg tta ata ggg ggt ctg tat gtg 624
Phe Val Leu Ser Pro Asn Tyr Leu Met Leu Ile Gly Gly Leu Tyr Val
195 200 205

ctt acg tac cat tct aaa cta atc cga aga atg aga aga tac ttg tgg 672
Leu Thr Tyr His Ser Lys Leu Ile Arg Arg Met Arg Arg Tyr Leu Trp
210 215 220

aaa ttt cgc gtt gtt aga tta ctt gta ttt ttc ata aca gga tta gac 720
Lys Phe Arg Val Val Arg Leu Leu Val Phe Phe Ile Thr Gly Leu Asp
225 230 235 240

ctt ggt gga cca gat aat aat agg cgc ttg ttt gct tct gtc aat aag 768
Leu Gly Gly Pro Asp Asn Asn Arg Arg Leu Phe Ala Ser Val Asn Lys
245 250 255

aaa ata agg tcc ttt gtt tgg aat gag gta ggg aac aca tct aac act 816
Lys Ile Arg Ser Phe Val Trp Asn Glu Val Gly Asn Thr Ser Asn Thr
260 265 270

aaa aag act gta ctt ttc aag gtt gct ctg ttt gaa aac cag cgc cgc 864
Lys Lys Thr Val Leu Phe Lys Val Ala Leu Phe Glu Asn Gln Arg Arg
275 280 285

tgg ctt ggc atc gga tgg aca tca act atg ttg agt tat gag cgc gca 912
Trp Leu Gly Ile Gly Trp Thr Ser Thr Met Leu Ser Tyr Glu Arg Ala
290 295 300

tct tgg aca gat gaa ttc cta aat act tct cca agc cca gaa gtg ttt 960
Ser Trp Thr Asp Glu Phe Leu Asn Thr Ser Pro Ser Pro Glu Val Phe
305 310 315 320

act tta cca gag gag cag tcg gga atg gct tgg gaa tgg cac gat aaa 1008
Thr Leu Pro Glu Glu Gln Ser Gly Met Ala Trp Glu Trp His Asp Lys
325 330 335

gat tgg atg ctt gac cta aca aat gat ggg atc att caa ctt cct gct 1056
Asp Trp Met Leu Asp Leu Thr Asn Asp Gly Ile Ile Gln Leu Pro Ala
340 345 350

tct gct gct aag aca aaa gtt aag cca ggt gca gat gaa ggt ttc ata 1104
Ser Ala Ala Lys Thr Lys Val Lys Pro Gly Ala Asp Glu Gly Phe Ile
355 360 365

tat tat gat aac acc tgg aat aat ccc tct gca acg gac aca tat aaa 1152
Tyr Tyr Asp Asn Thr Trp Asn Asn Pro Ser Ala Thr Asp Thr Tyr Lys
370 375 380

aag tac aca aga aga agg agg tgg atc agg act gca aca gta aca aca 1200
Lys Tyr Thr Arg Arg Arg Arg Trp Ile Arg Thr Ala Thr Val Thr Thr
385 390 395 400

acg tat gac gat gag ccc act gta gaa aaa gct aca ccg aat tct cat 1248
Thr Tyr Asp Asp Glu Pro Thr Val Glu Lys Ala Thr Pro Asn Ser His
405 410 415

gct ctg aag agt gaa gaa aat aat aga gtt aga aaa aga aaa gtg tca 1296
Ala Leu Lys Ser Glu Glu Asn Asn Arg Val Arg Lys Arg Lys Val Ser
420 425 430

ttt agt aca gca aat gaa gtg cat atc ata cct tcc tcg gac agt agc 1344
Phe Ser Thr Ala Asn Glu Val His Ile Ile Pro Ser Ser Asp Ser Ser
435 440 445

aaa tta ata caa ata tct gat gtt tca atg tct cct tct cta taa 1389
Lys Leu Ile Gln Ile Ser Asp Val Ser Met Ser Pro Ser Leu
450 455 460

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35 40 45

Ala Ile Leu Ser Ser Pro Leu Leu Thr Ser Thr Pro Lys Thr Val Ser
50 55 60

Arg Ser Leu Val Arg Leu Tyr Pro Tyr Leu Ile Val Val Asp Asn Phe
65 70 75 80

Leu Ser Ile Ile Thr Trp Ser Asn Asp Asn Val Ser Ala Asn Leu Leu
85 90 95

Gly Ile Phe Leu Phe Thr Val Cys Val Leu Tyr Phe Gly Phe Ile Thr
100 105 110

Arg Tyr Phe Gly His Leu Met Ile Val Gly Ile Ile Trp Val Tyr Leu
115 120 125

Leu Ile Asp Lys His Val Gln Glu Thr Met Ala Ser Cys Pro Ser Leu
130 135 140

Asp Asp Ile Ile His Val Met Asp Arg Val Ser Met Lys Ser Ser Ala
145 150 155 160

Val Leu Ser Pro Ile Thr Ile Leu Ser Ala Gln Asp Val Arg Arg Leu
165 170 175

Leu Phe Thr Ile Ala Phe Leu Ser Pro Val Tyr Ile Phe Leu Thr Val
180 185 190

Phe Val Leu Ser Pro Asn Tyr Leu Met Leu Ile Gly Gly Leu Tyr Val
195 200 205

Leu Thr Tyr His Ser Lys Leu Ile Arg Arg Met Arg Arg Tyr Leu Trp
210 215 220

Lys Phe Arg Val Val Arg Leu Leu Val Phe Phe Ile Thr Gly Leu Asp

225 230 235 240

Leu Gly Gly Pro Asp Asn Asn Arg Arg Leu Phe Ala Ser Val Asn Lys
245 250 255

Lys Ile Arg Ser Phe Val Trp Asn Glu Val Gly Asn Thr Ser Asn Thr
260 265 270

Lys Lys Thr Val Leu Phe Lys Val Ala Leu Phe Glu Asn Gln Arg Arg
275 280 285

Trp Leu Gly Ile Gly Trp Thr Ser Thr Met Leu Ser Tyr Glu Arg Ala
290 295 300

Ser Trp Thr Asp Glu Phe Leu Asn Thr Ser Pro Ser Pro Glu Val Phe
305 310 315 320

Thr Leu Pro Glu Glu Gln Ser Gly Met Ala Trp Glu Trp His Asp Lys
325 330 335

Asp Trp Met Leu Asp Leu Thr Asn Asp Gly Ile Ile Gln Leu Pro Ala
340 345 350

Ser Ala Ala Lys Thr Lys Val Lys Pro Gly Ala Asp Glu Gly Phe Ile
355 360 365

Tyr Tyr Asp Asn Thr Trp Asn Asn Pro Ser Ala Thr Asp Thr Tyr Lys
370 375 380

Lys Tyr Thr Arg Arg Arg Arg Trp Ile Arg Thr Ala Thr Val Thr Thr
385 390 395 400

Thr Tyr Asp Asp Glu Pro Thr Val Glu Lys Ala Thr Pro Asn Ser His
405 410 415

Ala Leu Lys Ser Glu Glu Asn Asn Arg Val Arg Lys Arg Lys Val Ser
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435 440 445

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450 455 460

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1               5                   10                  15

tca ttg gcc cgg gcc agc ccc ttc gac ttt ata ttc ggc aat gga acg        96
Ser Leu Ala Arg Ala Ser Pro Phe Asp Phe Ile Phe Gly Asn Gly Thr
            20                  25                  30

caa caa gct cag agc caa agc gag agt caa ggt caa gtt tct ttc acc       144
Gln Gln Ala Gln Ser Gln Ser Glu Ser Gln Gly Gln Val Ser Phe Thr
        35                  40                  45

aat gaa gct tct cag gat agt tcc acc acc tct ttg gta aca gcc tat       192
Asn Glu Ala Ser Gln Asp Ser Ser Thr Thr Ser Leu Val Thr Ala Tyr
    50                  55                  60

tct caa ggt gtt cat tcg cac cag tct gca aca ata gtg agt gcc aca       240
Ser Gln Gly Val His Ser His Gln Ser Ala Thr Ile Val Ser Ala Thr
65                  70                  75                  80

atc tct tcc ctc cca tct act tgg tat gat gcg agc tcc act tcc cag       288
Ile Ser Ser Leu Pro Ser Thr Trp Tyr Asp Ala Ser Ser Thr Ser Gln
                85                  90                  95

act tct gtg tca tat gcc agt caa gaa tcc gac tat gcc gtt aat caa       336
Thr Ser Val Ser Tyr Ala Ser Gln Glu Ser Asp Tyr Ala Val Asn Gln
            100                 105                 110
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aac tct tgg agc gcg tct act aat caa ctg cca tct acc agt acg aca 384
Asn Ser Trp Ser Ala Ser Thr Asn Gln Leu Pro Ser Thr Ser Thr Thr
115 120 125

agc tac tat gcg cca acc ttc agt aca tcg gcc gat ttt gct gct tct 432
Ser Tyr Tyr Ala Pro Thr Phe Ser Thr Ser Ala Asp Phe Ala Ala Ser
130 135 140

agt gta aat gca gct tct gat gtc tcc act gcc agt gtt ccc att gat 480
Ser Val Asn Ala Ala Ser Asp Val Ser Thr Ala Ser Val Pro Ile Asp
145 150 155 160

acg agt gct aat tct atc cct ttc aca act aca agt aac ata gag act 528
Thr Ser Ala Asn Ser Ile Pro Phe Thr Thr Thr Ser Asn Ile Glu Thr
165 170 175

aca acg agt gca cct ctc act tcg gac act cca ctt att tcc act agt 576
Thr Thr Ser Ala Pro Leu Thr Ser Asp Thr Pro Leu Ile Ser Thr Ser
180 185 190

acg atg tcc gca gct gat aac gta ttt tcg tca gca aac cct att tct 624
Thr Met Ser Ala Ala Asp Asn Val Phe Ser Ser Ala Asn Pro Ile Ser
195 200 205

gcc tcc cta aca acc acc gat agt tca gaa agt ttt gac caa act tcg 672
Ala Ser Leu Thr Thr Thr Asp Ser Ser Glu Ser Phe Asp Gln Thr Ser
210 215 220

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Thr Ala Gly Ala Ile Pro Val Gln Ser Ser Ala Asp Phe Ser Ser Ser
225 230 235 240

agt gaa att tta gta caa agt tcg gcg gat ttc agt agc cct agt tct 768
Ser Glu Ile Leu Val Gln Ser Ser Ala Asp Phe Ser Ser Pro Ser Ser
245 250 255

cca act act acc gat ata tcg cta tca gct gcc cca ctg caa aca agt 816
Pro Thr Thr Thr Asp Ile Ser Leu Ser Ala Ala Pro Leu Gln Thr Ser
260 265 270

gaa tca agc agt ttt acc act gca tca gca gct cta cca gta agt tca 864
Glu Ser Ser Ser Phe Thr Thr Ala Ser Ala Ala Leu Pro Val Ser Ser

275 280 285

aca gac gtt gat ggc tca agc gcc tca cct gta gtg agc atg agc gcc 912
Thr Asp Val Asp Gly Ser Ser Ala Ser Pro Val Val Ser Met Ser Ala
290 295 300

gca gga caa ata gct agc tca agc agc aca gat aat cca act atg tca 960
Ala Gly Gln Ile Ala Ser Ser Ser Ser Thr Asp Asn Pro Thr Met Ser
305 310 315 320

gaa acc ttt tcg tta aca tct aca gaa gtt gat ggt tcc gat gtt tca 1008
Glu Thr Phe Ser Leu Thr Ser Thr Glu Val Asp Gly Ser Asp Val Ser
325 330 335

tca aca gtg agc gca tta tta tcg gct cct ttt tta caa aca agt act 1056
Ser Thr Val Ser Ala Leu Leu Ser Ala Pro Phe Leu Gln Thr Ser Thr
340 345 350

tcc aac agt ttc agc att gtt agc cca tcg gta tct ttt gtt cca tca 1104
Ser Asn Ser Phe Ser Ile Val Ser Pro Ser Val Ser Phe Val Pro Ser
355 360 365

cag agt tcc tca gac gtt gct agc tcc agt act gca aat gta gtt agt 1152
Gln Ser Ser Ser Asp Val Ala Ser Ser Ser Thr Ala Asn Val Val Ser
370 375 380

tca tcc ttt tct gat att cca ccg caa act agt acc tca ggg agc gta 1200
Ser Ser Phe Ser Asp Ile Pro Pro Gln Thr Ser Thr Ser Gly Ser Val
385 390 395 400

gtt tcg gta gcg caa tcc gca tct gcc ctc gca ttt caa agt tca aca 1248
Val Ser Val Ala Gln Ser Ala Ser Ala Leu Ala Phe Gln Ser Ser Thr
405 410 415

gag gta tat ggt gcc agt gcc tcg agc aca atg agt tca tta tta tca 1296
Glu Val Tyr Gly Ala Ser Ala Ser Ser Thr Met Ser Ser Leu Leu Ser
420 425 430

act act tcg cta cag tct act act ttg gat agc tca agt tta gct agc 1344
Thr Thr Ser Leu Gln Ser Thr Thr Leu Asp Ser Ser Ser Leu Ala Ser
435 440 445

tcc tct gcg tcg agt tca gac ctt aca gat tat ggc gtc tcc agt aca 1392
Ser Ser Ala Ser Ser Ser Asp Leu Thr Asp Tyr Gly Val Ser Ser Thr
450 455 460

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465 470 475 480

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Ser Phe Ser Val Val Ser Pro Ser Val Ser Phe Val Pro Ser Gln Ser
485 490 495

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Ser Ser Asp Val Ala Ser Thr Ser Ala Pro Ser Val Val Ser Ser Ser
500 505 510

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Phe Ser Tyr Thr Ser Leu Gln Ala Gly Gly Ser Ser Met Thr Asn Pro
515 520 525

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Ser Ser Ser Thr Ile Val Tyr Ser Ser Ser Thr Gly Ser Ser Glu Glu
530 535 540

tcc gct gca tct aca gct tct gca aca ctg tcg ggc tcc tcg tct act 1680
Ser Ala Ala Ser Thr Ala Ser Ala Thr Leu Ser Gly Ser Ser Ser Thr
545 550 555 560

tat atg gca gga aat ttg caa tca cag cct cca tcc act tca agt ttg 1728
Tyr Met Ala Gly Asn Leu Gln Ser Gln Pro Pro Ser Thr Ser Ser Leu
565 570 575

ctt tcg gag tct caa gct aca agc act tca gct gtg cta gct agc agt 1776
Leu Ser Glu Ser Gln Ala Thr Ser Thr Ser Ala Val Leu Ala Ser Ser
580 585 590

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Ser Val Ser Thr Thr Ser Pro Tyr Thr Thr Ala Gly Gly Ala Ser Thr
595 600 605

gag gcc tca tcc ctc ata tca tct aca tct gcg gaa act tcc cag gta 1872
Glu Ala Ser Ser Leu Ile Ser Ser Thr Ser Ala Glu Thr Ser Gln Val

610 615 620

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Ser Tyr Ser Gln Ser Thr Thr Ala Leu Gln Thr Ser Ser Phe Ala Ser
625 630 635 640

tct tca aca aca gaa gga agt gaa aca tct agt caa ggt ttt tct acc 1968
Ser Ser Thr Thr Glu Gly Ser Glu Thr Ser Ser Gln Gly Phe Ser Thr
645 650 655

agc tct gtt tta gtt caa atg cct tct tcg att tcc agc gaa ttc tca 2016
Ser Ser Val Leu Val Gln Met Pro Ser Ser Ile Ser Ser Glu Phe Ser
660 665 670

ccc tct cag acg aca act caa atg aat tct gca agc tca tca tct cag 2064
Pro Ser Gln Thr Thr Thr Gln Met Asn Ser Ala Ser Ser Ser Ser Gln
675 680 685

tac act ata tca tcc act ggt ata ctt tct cag gtt tca gac aca tcg 2112
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690 695 700

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Val Ser Tyr Thr Thr Ser Ser Ser Ser Val Ser Gln Val Ser Asp Thr
705 710 715 720

cca gtt tct tat aca act tca agt tcg tct gtt tct caa gtt tca gac 2208
Pro Val Ser Tyr Thr Thr Ser Ser Ser Ser Val Ser Gln Val Ser Asp
725 730 735

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740 745 750

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755 760 765

tca gac aca ccg gtt tct tat aca act tca agt tcg tcc gtt tct caa 2352
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770 775 780

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785 790 795 800

caa gtc tca gac act ccg gtg cct tct aca agt tca agg tcg tcc gtt 2448
Gln Val Ser Asp Thr Pro Val Pro Ser Thr Ser Ser Arg Ser Ser Val
805 810 815

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Ser Gln Thr Ser Ser Ser Leu Gln Pro Thr Thr Thr Ser Ser Gln Arg
820 825 830

ttc acc att tcc act cat gga gcg ctt tct gaa agt agt tct gtt agc 2544
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835 840 845

caa caa gct tct gag att act agc tca atc aat gca aca gct tcc gaa 2592
Gln Gln Ala Ser Glu Ile Thr Ser Ser Ile Asn Ala Thr Ala Ser Glu
850 855 860

tac cat agc atc cag aca acc gcg gct act caa tcc aca act cta tct 2640
Tyr His Ser Ile Gln Thr Thr Ala Ala Thr Gln Ser Thr Thr Leu Ser
865 870 875 880

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Phe Thr Asp Ala Asn Ser Ser Ser Ala Ser Ala Pro Leu Glu Val Ala
885 890 895

acg tct acg cca acc cca tct tca aag gca tcc tct ctg ttg ctt aca 2736
Thr Ser Thr Pro Thr Pro Ser Ser Lys Ala Ser Ser Leu Leu Leu Thr
900 905 910

cca tca aca tcc tct tta agt cag gtt gct aca aat act aat gta cag 2784
Pro Ser Thr Ser Ser Leu Ser Gln Val Ala Thr Asn Thr Asn Val Gln
915 920 925

acg agt tta aca acg gaa tcg acg acc gtt tta gaa cca tca acg act 2832
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930 935 940

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945 950 955 960

tgg att cca act gag tta atc acg cag gca cca gaa gct gca tcc act 2928
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965 970 975

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Ala Ser Ser Thr Val Gly Gly Thr Gln Thr Met Thr Leu Pro His Ala
980 985 990

att gca gcc gcg aca caa gtt ccc gag cct gag ggc tac acc cta atc 3024
Ile Ala Ala Ala Thr Gln Val Pro Glu Pro Glu Gly Tyr Thr Leu Ile
995 1000 1005

aca ata ggg ttc aaa aaa gct ttg aac tac gaa ttt gtt gta tca 3069
Thr Ile Gly Phe Lys Lys Ala Leu Asn Tyr Glu Phe Val Val Ser
1010 1015 1020

gaa cca aaa tca tcg gct caa atc ttc gga tac ttg cct gaa gct 3114
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1025 1030 1035

ctg aac aca cct ttt aag aac gta ttc aca aac att acg gta cta 3159
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1040 1045 1050

caa ata gtg cca tta cag gat gac tca ctc aac tac tta gta agt 3204
Gln Ile Val Pro Leu Gln Asp Asp Ser Leu Asn Tyr Leu Val Ser
1055 1060 1065

gtt gct gaa gta tac ttt cca act gca gaa ata gag gag ctg tca 3249
Val Ala Glu Val Tyr Phe Pro Thr Ala Glu Ile Glu Glu Leu Ser
1070 1075 1080

aat cta att acc aac tct tca agc gct ttt tac acg gat gga atg 3294
Asn Leu Ile Thr Asn Ser Ser Ser Ala Phe Tyr Thr Asp Gly Met
1085 1090 1095

ggt aca gca aaa tct atg gct gca atg gtt gat tcc tca ata ccg 3339
Gly Thr Ala Lys Ser Met Ala Ala Met Val Asp Ser Ser Ile Pro
1100 1105 1110

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cta acg  ggc ctc tta cac gat  agt aac agc aac tct  ggc gga tct      3384
Leu Thr  Gly Leu Leu His Asp  Ser Asn Ser Asn Ser  Gly Gly Ser
    1115                 1120                 1125

tcg gac  gga tcc tcc tcc agt  aat tcg aac tca gga  tct tca ggt      3429
Ser Asp  Gly Ser Ser Ser Ser  Asn Ser Asn Ser Gly  Ser Ser Gly
    1130                 1135                 1140

tca gga  tct aat tcg aac tcc  ggt gtg tct tca tct  tcc gga aat      3474
Ser Gly  Ser Asn Ser Asn Ser  Gly Val Ser Ser Ser  Ser Gly Asn
    1145                 1150                 1155

tcc tat  caa gat gcc ggt act  ttg gaa tat tca tcc  aaa tct aac      3519
Ser Tyr  Gln Asp Ala Gly Thr  Leu Glu Tyr Ser Ser  Lys Ser Asn
    1160                 1165                 1170

tcc aac  gta tcc act tct agc  aaa tca aag aaa aaa  atc att ggt      3564
Ser Asn  Val Ser Thr Ser Ser  Lys Ser Lys Lys Lys  Ile Ile Gly
    1175                 1180                 1185

tta gtt  atc ggc gtt gtt gtt  ggt gga tgc tta tat  att tta ttc      3609
Leu Val  Ile Gly Val Val Val  Gly Gly Cys Leu Tyr  Ile Leu Phe
    1190                 1195                 1200

atg att  ttt gct ttc aag tat  atc ata aga agg cgg  att caa agt      3654
Met Ile  Phe Ala Phe Lys Tyr  Ile Ile Arg Arg Arg  Ile Gln Ser
    1205                 1210                 1215

caa gaa  att atc aag aac cca  gaa att tcc agt atc  agt tca agt      3699
Gln Glu  Ile Ile Lys Asn Pro  Glu Ile Ser Ser Ile  Ser Ser Ser
    1220                 1225                 1230

gaa ttt  ggt gga gag aaa aat  tac aat aat gaa aag  aga atg agc      3744
Glu Phe  Gly Gly Glu Lys Asn  Tyr Asn Asn Glu Lys  Arg Met Ser
    1235                 1240                 1245

gtt caa  gaa tcc ata aca caa  tct atg cga att caa  aat tgg atg      3789
Val Gln  Glu Ser Ile Thr Gln  Ser Met Arg Ile Gln  Asn Trp Met
    1250                 1255                 1260

gat gat  agt tac tat ggt cac  ggg ttg aca aat aat  gac tca act      3834
Asp Asp  Ser Tyr Tyr Gly His  Gly Leu Thr Asn Asn  Asp Ser Thr
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1265 1270 1275

cca acc agg cac aat aca tcg agt tcc ata cca aaa att tca aga 3879
Pro Thr Arg His Asn Thr Ser Ser Ser Ile Pro Lys Ile Ser Arg
1280 1285 1290

cca att gct agc caa aac tcc ctg ggt tgg aac gaa gtt tga 3921
Pro Ile Ala Ser Gln Asn Ser Leu Gly Trp Asn Glu Val
1295 1300 1305

<210> 6
<211> 1306
<212> PRT
<213> Saccharomyces cerevisiae

<400> 6

Met Gln Phe Pro Phe Ala Cys Leu Leu Ser Thr Leu Val Ile Ser Gly
1 5 10 15

Ser Leu Ala Arg Ala Ser Pro Phe Asp Phe Ile Phe Gly Asn Gly Thr
20 25 30

Gln Gln Ala Gln Ser Gln Ser Glu Ser Gln Gly Gln Val Ser Phe Thr
35 40 45

Asn Glu Ala Ser Gln Asp Ser Ser Thr Thr Ser Leu Val Thr Ala Tyr
50 55 60

Ser Gln Gly Val His Ser His Gln Ser Ala Thr Ile Val Ser Ala Thr
65 70 75 80

Ile Ser Ser Leu Pro Ser Thr Trp Tyr Asp Ala Ser Ser Thr Ser Gln
85 90 95

Thr Ser Val Ser Tyr Ala Ser Gln Glu Ser Asp Tyr Ala Val Asn Gln
100 105 110

Asn Ser Trp Ser Ala Ser Thr Asn Gln Leu Pro Ser Thr Ser Thr Thr
115 120 125

Ser Tyr Tyr Ala Pro Thr Phe Ser Thr Ser Ala Asp Phe Ala Ala Ser
130 135 140

Ser Val Asn Ala Ala Ser Asp Val Ser Thr Ala Ser Val Pro Ile Asp
145 150 155 160

Thr Ser Ala Asn Ser Ile Pro Phe Thr Thr Thr Ser Asn Ile Glu Thr
165 170 175

Thr Thr Ser Ala Pro Leu Thr Ser Asp Thr Pro Leu Ile Ser Thr Ser
180 185 190

Thr Met Ser Ala Ala Asp Asn Val Phe Ser Ser Ala Asn Pro Ile Ser
195 200 205

Ala Ser Leu Thr Thr Thr Asp Ser Ser Glu Ser Phe Asp Gln Thr Ser
210 215 220

Thr Ala Gly Ala Ile Pro Val Gln Ser Ser Ala Asp Phe Ser Ser Ser
225 230 235 240

Ser Glu Ile Leu Val Gln Ser Ser Ala Asp Phe Ser Ser Pro Ser Ser
245 250 255

Pro Thr Thr Thr Asp Ile Ser Leu Ser Ala Ala Pro Leu Gln Thr Ser
260 265 270

Glu Ser Ser Ser Phe Thr Thr Ala Ser Ala Ala Leu Pro Val Ser Ser
275 280 285

Thr Asp Val Asp Gly Ser Ser Ala Ser Pro Val Val Ser Met Ser Ala
290 295 300

Ala Gly Gln Ile Ala Ser Ser Ser Ser Thr Asp Asn Pro Thr Met Ser
305 310 315 320

Glu Thr Phe Ser Leu Thr Ser Thr Glu Val Asp Gly Ser Asp Val Ser
325 330 335

Ser Thr Val Ser Ala Leu Leu Ser Ala Pro Phe Leu Gln Thr Ser Thr
340 345 350

Ser Asn Ser Phe Ser Ile Val Ser Pro Ser Val Ser Phe Val Pro Ser
355 360 365

Gln Ser Ser Ser Asp Val Ala Ser Ser Ser Thr Ala Asn Val Val Ser
370 375 380

Ser Ser Phe Ser Asp Ile Pro Pro Gln Thr Ser Thr Ser Gly Ser Val
385 390 395 400

Val Ser Val Ala Gln Ser Ala Ser Ala Leu Ala Phe Gln Ser Ser Thr
405 410 415

Glu Val Tyr Gly Ala Ser Ala Ser Ser Thr Met Ser Ser Leu Leu Ser
420 425 430

Thr Thr Ser Leu Gln Ser Thr Thr Leu Asp Ser Ser Ser Leu Ala Ser
435 440 445

Ser Ser Ala Ser Ser Ser Asp Leu Thr Asp Tyr Gly Val Ser Ser Thr
450 455 460

Ala Ser Ile Pro Leu Leu Ser Ala Ser Glu Gln Ala Ser Thr Ser Ser
465 470 475 480

Ser Phe Ser Val Val Ser Pro Ser Val Ser Phe Val Pro Ser Gln Ser
485 490 495

Ser Ser Asp Val Ala Ser Thr Ser Ala Pro Ser Val Val Ser Ser Ser
500 505 510

Phe Ser Tyr Thr Ser Leu Gln Ala Gly Gly Ser Ser Met Thr Asn Pro
515 520 525

Ser Ser Ser Thr Ile Val Tyr Ser Ser Ser Thr Gly Ser Ser Glu Glu
530 535 540

Ser Ala Ala Ser Thr Ala Ser Ala Thr Leu Ser Gly Ser Ser Ser Thr
545 550 555 560

Tyr Met Ala Gly Asn Leu Gln Ser Gln Pro Pro Ser Thr Ser Ser Leu
565 570 575

Leu Ser Glu Ser Gln Ala Thr Ser Thr Ser Ala Val Leu Ala Ser Ser
580 585 590

Ser Val Ser Thr Thr Ser Pro Tyr Thr Thr Ala Gly Gly Ala Ser Thr
595 600 605

Glu Ala Ser Ser Leu Ile Ser Ser Thr Ser Ala Glu Thr Ser Gln Val
610 615 620

Ser Tyr Ser Gln Ser Thr Thr Ala Leu Gln Thr Ser Ser Phe Ala Ser
625 630 635 640

Ser Ser Thr Thr Glu Gly Ser Glu Thr Ser Ser Gln Gly Phe Ser Thr
645 650 655

Ser Ser Val Leu Val Gln Met Pro Ser Ser Ile Ser Ser Glu Phe Ser
660 665 670

Pro Ser Gln Thr Thr Thr Gln Met Asn Ser Ala Ser Ser Ser Ser Gln
675 680 685

Tyr Thr Ile Ser Ser Thr Gly Ile Leu Ser Gln Val Ser Asp Thr Ser
690 695 700

Val Ser Tyr Thr Thr Ser Ser Ser Ser Val Ser Gln Val Ser Asp Thr
705 710 715 720

Pro Val Ser Tyr Thr Thr Ser Ser Ser Ser Val Ser Gln Val Ser Asp
725 730 735

Thr Pro Val Ser Tyr Thr Thr Ser Ser Ser Ser Val Ser Gln Val Ser
740 745 750

Asp Thr Pro Val Ser Tyr Thr Thr Ser Ser Ser Ser Val Ser Gln Val
755 760 765

Ser Asp Thr Pro Val Ser Tyr Thr Thr Ser Ser Ser Ser Val Ser Gln
770 775 780

Val Ser Asp Thr Ser Val Pro Ser Thr Ser Ser Arg Ser Ser Val Ser
785 790 795 800

Gln Val Ser Asp Thr Pro Val Pro Ser Thr Ser Ser Arg Ser Ser Val
805 810 815

Ser Gln Thr Ser Ser Ser Leu Gln Pro Thr Thr Thr Ser Ser Gln Arg
820 825 830

Phe Thr Ile Ser Thr His Gly Ala Leu Ser Glu Ser Ser Ser Val Ser
835 840 845

Gln Gln Ala Ser Glu Ile Thr Ser Ser Ile Asn Ala Thr Ala Ser Glu
850 855 860

Tyr His Ser Ile Gln Thr Thr Ala Ala Thr Gln Ser Thr Thr Leu Ser
865 870 875 880

Phe Thr Asp Ala Asn Ser Ser Ser Ala Ser Ala Pro Leu Glu Val Ala
885 890 895

Thr Ser Thr Pro Thr Pro Ser Ser Lys Ala Ser Ser Leu Leu Leu Thr
900 905 910

Pro Ser Thr Ser Ser Leu Ser Gln Val Ala Thr Asn Thr Asn Val Gln
915 920 925

Thr Ser Leu Thr Thr Glu Ser Thr Thr Val Leu Glu Pro Ser Thr Thr
930 935 940

Asn Ser Ser Ser Thr Phe Ser Leu Val Thr Ser Ser Asp Asn Asn Trp
945 950 955 960

Trp Ile Pro Thr Glu Leu Ile Thr Gln Ala Pro Glu Ala Ala Ser Thr
965 970 975

Ala Ser Ser Thr Val Gly Gly Thr Gln Thr Met Thr Leu Pro His Ala
980 985 990

Ile Ala Ala Ala Thr Gln Val Pro Glu Pro Glu Gly Tyr Thr Leu Ile
995 1000 1005

Thr Ile Gly Phe Lys Lys Ala Leu Asn Tyr Glu Phe Val Val Ser
1010 1015 1020

Glu Pro Lys Ser Ser Ala Gln Ile Phe Gly Tyr Leu Pro Glu Ala
1025 1030 1035

Leu Asn Thr Pro Phe Lys Asn Val Phe Thr Asn Ile Thr Val Leu
1040 1045 1050

Gln Ile Val Pro Leu Gln Asp Asp Ser Leu Asn Tyr Leu Val Ser
1055 1060 1065

Val Ala Glu Val Tyr Phe Pro Thr Ala Glu Ile Glu Glu Leu Ser
1070 1075 1080

Asn Leu Ile Thr Asn Ser Ser Ser Ala Phe Tyr Thr Asp Gly Met
1085 1090 1095

Gly Thr Ala Lys Ser Met Ala Ala Met Val Asp Ser Ser Ile Pro
1100 1105 1110

Leu Thr Gly Leu Leu His Asp Ser Asn Ser Asn Ser Gly Gly Ser
1115 1120 1125

Ser Asp Gly Ser Ser Ser Ser Asn Ser Asn Ser Gly Ser Ser Gly
1130 1135 1140

Ser Gly Ser Asn Ser Asn Ser Gly Val Ser Ser Ser Ser Gly Asn
1145 1150 1155

Ser Tyr Gln Asp Ala Gly Thr Leu Glu Tyr Ser Ser Lys Ser Asn
1160 1165 1170

Ser Asn Val Ser Thr Ser Ser Lys Ser Lys Lys Lys Ile Ile Gly
1175 1180 1185

Leu Val Ile Gly Val Val Val Gly Gly Cys Leu Tyr Ile Leu Phe
1190 1195 1200

Met Ile Phe Ala Phe Lys Tyr Ile Ile Arg Arg Arg Ile Gln Ser
1205 1210 1215

Gln Glu Ile Ile Lys Asn Pro Glu Ile Ser Ser Ile Ser Ser Ser
1220 1225 1230

Glu Phe Gly Gly Glu Lys Asn Tyr Asn Asn Glu Lys Arg Met Ser
1235 1240 1245

Val Gln Glu Ser Ile Thr Gln Ser Met Arg Ile Gln Asn Trp Met
1250 1255 1260

Asp Asp Ser Tyr Tyr Gly His Gly Leu Thr Asn Asn Asp Ser Thr
1265 1270 1275

Pro Thr Arg His Asn Thr Ser Ser Ser Ile Pro Lys Ile Ser Arg
1280 1285 1290

Pro Ile Ala Ser Gln Asn Ser Leu Gly Trp Asn Glu Val
1295 1300 1305

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<211> 315
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(315)

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Met Lys Phe Leu Lys Asn Lys Ala Pro Ala Asn Leu Val Asp Asn Gly
1 5 10 15

agg ttt gtg gaa gca ata acg tgc aat aaa gtt aaa ccg aat cca tct 96
Arg Phe Val Glu Ala Ile Thr Cys Asn Lys Val Lys Pro Asn Pro Ser
20 25 30

tgc gtc tcc aac tgc ctc aaa ttt ctt tcc gaa gtt tta gcg gta gaa 144
Cys Val Ser Asn Cys Leu Lys Phe Leu Ser Glu Val Leu Ala Val Glu
35 40 45

gca ata act gat tcg gcc aga aat tta gct acg gtt tcc aaa tcg gac 192
Ala Ile Thr Asp Ser Ala Arg Asn Leu Ala Thr Val Ser Lys Ser Asp
50 55 60

atc cta cta ttt tct ctt cta caa ttg agt agc aat aaa cag agc ggg 240
Ile Leu Leu Phe Ser Leu Leu Gln Leu Ser Ser Asn Lys Gln Ser Gly
65 70 75 80

tcc tct ttg cca ctt ttt gat ctt gtg ttt ata cta ctt tca act ttt 288
Ser Ser Leu Pro Leu Phe Asp Leu Val Phe Ile Leu Leu Ser Thr Phe
85 90 95

ttt tta ttc cat aat ccc tgc aat tga 315
Phe Leu Phe His Asn Pro Cys Asn
100

<210> 8
<211> 104
<212> PRT
<213> Saccharomyces cerevisiae

<400> 8
Met Lys Phe Leu Lys Asn Lys Ala Pro Ala Asn Leu Val Asp Asn Gly
1 5 10 15

Arg Phe Val Glu Ala Ile Thr Cys Asn Lys Val Lys Pro Asn Pro Ser
20 25 30

Cys Val Ser Asn Cys Leu Lys Phe Leu Ser Glu Val Leu Ala Val Glu
35 40 45

Ala Ile Thr Asp Ser Ala Arg Asn Leu Ala Thr Val Ser Lys Ser Asp
50 55 60

Ile Leu Leu Phe Ser Leu Leu Gln Leu Ser Ser Asn Lys Gln Ser Gly
65 70 75 80

Ser Ser Leu Pro Leu Phe Asp Leu Val Phe Ile Leu Leu Ser Thr Phe
85 90 95

Phe Leu Phe His Asn Pro Cys Asn
100

<210> 9
<211> 2064
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(2064)

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Met Cys Ala Ser Leu Asn Glu Val Lys Lys Asn Asp Thr Tyr Gly Val
1 5 10 15

tca caa aag ggc tac aat gac aat ttc agt gaa agt gag ggc gtc ctt 96
Ser Gln Lys Gly Tyr Asn Asp Asn Phe Ser Glu Ser Glu Gly Val Leu
20 25 30

cat ggt agt aag tcg atg ccc act agc atg aaa aat atg cta cag tct 144
His Gly Ser Lys Ser Met Pro Thr Ser Met Lys Asn Met Leu Gln Ser
35 40 45

ccc acg atg gtc aac atg tgt gat att tta caa aac aag gaa gct gct 192
Pro Thr Met Val Asn Met Cys Asp Ile Leu Gln Asn Lys Glu Ala Ala
50 55 60

aat gac gaa aaa cct gtg ata cct act acg gat acc gcc act gcg ggg 240
Asn Asp Glu Lys Pro Val Ile Pro Thr Thr Asp Thr Ala Thr Ala Gly
65 70 75 80

act ggt act gaa gat att agc tcc act caa tcc gag gaa act gat cag 288
Thr Gly Thr Glu Asp Ile Ser Ser Thr Gln Ser Glu Glu Thr Asp Gln
85 90 95

aat agt cat ctt att gcc tca gag atc ttg gaa ggc act ttc aaa gat 336
Asn Ser His Leu Ile Ala Ser Glu Ile Leu Glu Gly Thr Phe Lys Asp
100 105 110

gta tct tac aag gaa tat gca aat ttc ttg gga aac gat aac aat aat 384
Val Ser Tyr Lys Glu Tyr Ala Asn Phe Leu Gly Asn Asp Asn Asn Asn
115 120 125

caa gtc ttg act gag ttt gta aag tta ttg agt cct ttg ccg tcg tca 432
Gln Val Leu Thr Glu Phe Val Lys Leu Leu Ser Pro Leu Pro Ser Ser
130 135 140

cta tta gaa acg ctt ttc aat tta tcg aaa agt ata tat ttc att gca 480
Leu Leu Glu Thr Leu Phe Asn Leu Ser Lys Ser Ile Tyr Phe Ile Ala
145 150 155 160

gaa gcg caa aat atc gac cgg ata cta gag tgc ttg agc ata gaa tgg 528
Glu Ala Gln Asn Ile Asp Arg Ile Leu Glu Cys Leu Ser Ile Glu Trp
165 170 175

ata gct tgc cac ccg aac aca cat tgg aag tca ggc tat aag tca tgt 576
Ile Ala Cys His Pro Asn Thr His Trp Lys Ser Gly Tyr Lys Ser Cys
180 185 190

cat ata gtc tta ttt tcc ctg ttg atc ctt aat tcg gat ttg cac aac 624
His Ile Val Leu Phe Ser Leu Leu Ile Leu Asn Ser Asp Leu His Asn
195 200 205

aac ttt caa gtt gac cat aaa aag att aag ttt tcc atg gtt gca ttt 672
Asn Phe Gln Val Asp His Lys Lys Ile Lys Phe Ser Met Val Ala Phe
210 215 220

atc aac aat aca ctg agg gca cta aga gag gaa aat gaa tac gaa gaa 720
Ile Asn Asn Thr Leu Arg Ala Leu Arg Glu Glu Asn Glu Tyr Glu Glu
225 230 235 240

ttg aaa ata tac tcc cgc gaa cat ttg atc atc gaa gaa ctt tcc gaa 768
Leu Lys Ile Tyr Ser Arg Glu His Leu Ile Ile Glu Glu Leu Ser Glu
245 250 255

tac tat aaa acg tta aat gaa acg cct tta ccg tta tgc aca gaa tct 816
Tyr Tyr Lys Thr Leu Asn Glu Thr Pro Leu Pro Leu Cys Thr Glu Ser
260 265 270

aga aca tca ata aat ata tca gat aac caa tct tcc ttg aaa agg ttc 864
Arg Thr Ser Ile Asn Ile Ser Asp Asn Gln Ser Ser Leu Lys Arg Phe
275 280 285

tct act cta gga tca cgg gaa ttt agt aca tca aat tta cgt agt gtt 912
Ser Thr Leu Gly Ser Arg Glu Phe Ser Thr Ser Asn Leu Arg Ser Val
290 295 300

aac tct aat tct act aca cta tat tca aga gat ggt caa gta tct gta 960
Asn Ser Asn Ser Thr Thr Leu Tyr Ser Arg Asp Gly Gln Val Ser Val
305 310 315 320

cga gaa atg agc gca aaa tca aat aaa aac ttt cac aat aat cac ccc 1008
Arg Glu Met Ser Ala Lys Ser Asn Lys Asn Phe His Asn Asn His Pro
325 330 335

atg gat gca ctc tac ctt aaa gag tct ttt gat gac ggt tta att acc 1056
Met Asp Ala Leu Tyr Leu Lys Glu Ser Phe Asp Asp Gly Leu Ile Thr
340 345 350

gaa aac ggc tcc agt tgg ttc atg gac gat tta att ctt ata agc aag 1104
Glu Asn Gly Ser Ser Trp Phe Met Asp Asp Leu Ile Leu Ile Ser Lys
355 360 365

aaa tct tta cca cgt aaa tat tct aaa aga gac aaa gat caa gtg gcg 1152
Lys Ser Leu Pro Arg Lys Tyr Ser Lys Arg Asp Lys Asp Gln Val Ala
370 375 380

gca cca aaa atg acc tct aag aga aac aaa tcg ttc ttc gga tgg cta 1200
Ala Pro Lys Met Thr Ser Lys Arg Asn Lys Ser Phe Phe Gly Trp Leu
385 390 395 400

aaa cca tct aaa acg act aca ctt att gag cac aca tct aga agg act 1248
Lys Pro Ser Lys Thr Thr Thr Leu Ile Glu His Thr Ser Arg Arg Thr
405 410 415

tct tta tcg tat ttg aat aag gat tct gaa tgg gag agg gtg aaa ata 1296
Ser Leu Ser Tyr Leu Asn Lys Asp Ser Glu Trp Glu Arg Val Lys Ile
420 425 430

cag gtc aag gag ggc aga att ttt att ttc aaa att aaa cca gat gtt 1344
Gln Val Lys Glu Gly Arg Ile Phe Ile Phe Lys Ile Lys Pro Asp Val
435 440 445

aag gat atc atc caa tca agt gaa aca gac agt gct acc atc gac tat 1392
Lys Asp Ile Ile Gln Ser Ser Glu Thr Asp Ser Ala Thr Ile Asp Tyr
450 455 460

ttc aaa gat atc agt agc tct tat ttt gct tac tca ctg ctt gaa gct 1440
Phe Lys Asp Ile Ser Ser Ser Tyr Phe Ala Tyr Ser Leu Leu Glu Ala
465 470 475 480

gaa gca cat gtc gtg caa gat aat ata att ata ggt agt gga gca atg 1488
Glu Ala His Val Val Gln Asp Asn Ile Ile Ile Gly Ser Gly Ala Met
485 490 495

aaa tca aat gtg tgt aac aaa aac acc aag agg aaa agt ggc aac ttt 1536
Lys Ser Asn Val Cys Asn Lys Asn Thr Lys Arg Lys Ser Gly Asn Phe
500 505 510

acc gtt agt ttt cca gag aat atc aac gga cca aag ctt gtt ctg gag 1584
Thr Val Ser Phe Pro Glu Asn Ile Asn Gly Pro Lys Leu Val Leu Glu
515 520 525

ttc cag acg aga agt gtt gaa gaa gcc cac aag ttt atg gac tgt atc 1632
Phe Gln Thr Arg Ser Val Glu Glu Ala His Lys Phe Met Asp Cys Ile
530 535 540

aac ttc tgg gca ggt agg att tct cca gtt cct tta aca caa ttc gaa 1680
Asn Phe Trp Ala Gly Arg Ile Ser Pro Val Pro Leu Thr Gln Phe Glu
545 550 555 560

gcc gta tct aac gca gaa tat gga tgg agt gac aag atc ttg aca gag 1728
Ala Val Ser Asn Ala Glu Tyr Gly Trp Ser Asp Lys Ile Leu Thr Glu
565 570 575

cac gct tcc ctc aat ctt aaa aat att gtt gta agt gaa tgg aag cca 1776
His Ala Ser Leu Asn Leu Lys Asn Ile Val Val Ser Glu Trp Lys Pro
580 585 590

cta ttg ggg cta gag cta cta tac gaa gat gcg aaa gat gta gag atg 1824

Leu Leu Gly Leu Glu Leu Leu Tyr Glu Asp Ala Lys Asp Val Glu Met
595 600 605

gtc gaa cta aaa gaa agg cta aag gaa ttg atg aac ttc acc aga cag 1872
Val Glu Leu Lys Glu Arg Leu Lys Glu Leu Met Asn Phe Thr Arg Gln
610 615 620

ctt ggt ata tgg ata gat aaa cat aac gaa ata aag gat aag ctg gtc 1920
Leu Gly Ile Trp Ile Asp Lys His Asn Glu Ile Lys Asp Lys Leu Val
625 630 635 640

gaa att tgg agc ttt gac gat aac tat ttt gaa gca gtc atg aat aat 1968
Glu Ile Trp Ser Phe Asp Asp Asn Tyr Phe Glu Ala Val Met Asn Asn
645 650 655

tgg aat tcg aga tat ttg tat atg aat aat caa tat aag aaa cga ctg 2016
Trp Asn Ser Arg Tyr Leu Tyr Met Asn Asn Gln Tyr Lys Lys Arg Leu
660 665 670

agc tac ttg aaa gct ttg caa aaa gcc atg ggt tct gtt cag ttc taa 2064
Ser Tyr Leu Lys Ala Leu Gln Lys Ala Met Gly Ser Val Gln Phe
675 680 685

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<211> 687
<212> PRT
<213> Saccharomyces cerevisiae

<400> 10

Met Cys Ala Ser Leu Asn Glu Val Lys Lys Asn Asp Thr Tyr Gly Val
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Ser Gln Lys Gly Tyr Asn Asp Asn Phe Ser Glu Ser Glu Gly Val Leu
20 25 30

His Gly Ser Lys Ser Met Pro Thr Ser Met Lys Asn Met Leu Gln Ser
35 40 45

Pro Thr Met Val Asn Met Cys Asp Ile Leu Gln Asn Lys Glu Ala Ala

50 55 60

Asn Asp Glu Lys Pro Val Ile Pro Thr Thr Asp Thr Ala Thr Ala Gly
65 70 75 80

Thr Gly Thr Glu Asp Ile Ser Ser Thr Gln Ser Glu Glu Thr Asp Gln
85 90 95

Asn Ser His Leu Ile Ala Ser Glu Ile Leu Glu Gly Thr Phe Lys Asp
100 105 110

Val Ser Tyr Lys Glu Tyr Ala Asn Phe Leu Gly Asn Asp Asn Asn Asn
115 120 125

Gln Val Leu Thr Glu Phe Val Lys Leu Leu Ser Pro Leu Pro Ser Ser
130 135 140

Leu Leu Glu Thr Leu Phe Asn Leu Ser Lys Ser Ile Tyr Phe Ile Ala
145 150 155 160

Glu Ala Gln Asn Ile Asp Arg Ile Leu Glu Cys Leu Ser Ile Glu Trp
165 170 175

Ile Ala Cys His Pro Asn Thr His Trp Lys Ser Gly Tyr Lys Ser Cys
180 185 190

His Ile Val Leu Phe Ser Leu Leu Ile Leu Asn Ser Asp Leu His Asn
195 200 205

Asn Phe Gln Val Asp His Lys Lys Ile Lys Phe Ser Met Val Ala Phe
210 215 220

Ile Asn Asn Thr Leu Arg Ala Leu Arg Glu Glu Asn Glu Tyr Glu Glu
225 230 235 240

Leu Lys Ile Tyr Ser Arg Glu His Leu Ile Ile Glu Glu Leu Ser Glu
245 250 255

Tyr Tyr Lys Thr Leu Asn Glu Thr Pro Leu Pro Leu Cys Thr Glu Ser
260 265 270

Arg Thr Ser Ile Asn Ile Ser Asp Asn Gln Ser Ser Leu Lys Arg Phe

275 280 285

Ser Thr Leu Gly Ser Arg Glu Phe Ser Thr Ser Asn Leu Arg Ser Val
290 295 300

Asn Ser Asn Ser Thr Thr Leu Tyr Ser Arg Asp Gly Gln Val Ser Val
305 310 315 320

Arg Glu Met Ser Ala Lys Ser Asn Lys Asn Phe His Asn Asn His Pro
325 330 335

Met Asp Ala Leu Tyr Leu Lys Glu Ser Phe Asp Asp Gly Leu Ile Thr
340 345 350

Glu Asn Gly Ser Ser Trp Phe Met Asp Asp Leu Ile Leu Ile Ser Lys
355 360 365

Lys Ser Leu Pro Arg Lys Tyr Ser Lys Arg Asp Lys Asp Gln Val Ala
370 375 380

Ala Pro Lys Met Thr Ser Lys Arg Asn Lys Ser Phe Phe Gly Trp Leu
385 390 395 400

Lys Pro Ser Lys Thr Thr Thr Leu Ile Glu His Thr Ser Arg Arg Thr
405 410 415

Ser Leu Ser Tyr Leu Asn Lys Asp Ser Glu Trp Glu Arg Val Lys Ile
420 425 430

Gln Val Lys Glu Gly Arg Ile Phe Ile Phe Lys Ile Lys Pro Asp Val
435 440 445

Lys Asp Ile Ile Gln Ser Ser Glu Thr Asp Ser Ala Thr Ile Asp Tyr
450 455 460

Phe Lys Asp Ile Ser Ser Ser Tyr Phe Ala Tyr Ser Leu Leu Glu Ala
465 470 475 480

Glu Ala His Val Val Gln Asp Asn Ile Ile Ile Gly Ser Gly Ala Met
485 490 495

Lys Ser Asn Val Cys Asn Lys Asn Thr Lys Arg Lys Ser Gly Asn Phe

500 505 510

Thr Val Ser Phe Pro Glu Asn Ile Asn Gly Pro Lys Leu Val Leu Glu
515 520 525

Phe Gln Thr Arg Ser Val Glu Glu Ala His Lys Phe Met Asp Cys Ile
530 535 540

Asn Phe Trp Ala Gly Arg Ile Ser Pro Val Pro Leu Thr Gln Phe Glu
545 550 555 560

Ala Val Ser Asn Ala Glu Tyr Gly Trp Ser Asp Lys Ile Leu Thr Glu
565 570 575

His Ala Ser Leu Asn Leu Lys Asn Ile Val Val Ser Glu Trp Lys Pro
580 585 590

Leu Leu Gly Leu Glu Leu Leu Tyr Glu Asp Ala Lys Asp Val Glu Met
595 600 605

Val Glu Leu Lys Glu Arg Leu Lys Glu Leu Met Asn Phe Thr Arg Gln
610 615 620

Leu Gly Ile Trp Ile Asp Lys His Asn Glu Ile Lys Asp Lys Leu Val
625 630 635 640

Glu Ile Trp Ser Phe Asp Asp Asn Tyr Phe Glu Ala Val Met Asn Asn
645 650 655

Trp Asn Ser Arg Tyr Leu Tyr Met Asn Asn Gln Tyr Lys Lys Arg Leu
660 665 670

Ser Tyr Leu Lys Ala Leu Gln Lys Ala Met Gly Ser Val Gln Phe
675 680 685

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<212> DNA
<213> Saccharomyces cerevisiae

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<221> CDS

<222> (1)..(678)

<400> 11

atg gtc gta att aac ggg gtc aaa tat gcc tgt gaa acg tgt atc agg 48
Met Val Val Ile Asn Gly Val Lys Tyr Ala Cys Glu Thr Cys Ile Arg
1 5 10 15

ggt cac agg gcg gcg cag tgt act cac act gat ggt ccg cta cag atg 96
Gly His Arg Ala Ala Gln Cys Thr His Thr Asp Gly Pro Leu Gln Met
20 25 30

atc aga cgc aag gga aga cca tcg acc aca tgt ggc cat tgt aaa gag 144
Ile Arg Arg Lys Gly Arg Pro Ser Thr Thr Cys Gly His Cys Lys Glu
35 40 45

ctg aga aga acc aag aac ttc aac cca tcc ggt ggg tgc atg tgt gcc 192
Leu Arg Arg Thr Lys Asn Phe Asn Pro Ser Gly Gly Cys Met Cys Ala
50 55 60

tct gca cga cgg cca gct gtt ggc agc aag gaa gat gaa aca cga tgt 240
Ser Ala Arg Arg Pro Ala Val Gly Ser Lys Glu Asp Glu Thr Arg Cys
65 70 75 80

cgt tgt gat gag ggt gaa cct tgt aaa tgt cat acc aag agg aaa agc 288
Arg Cys Asp Glu Gly Glu Pro Cys Lys Cys His Thr Lys Arg Lys Ser
85 90 95

agc cgg aaa tca aag gga ggg tca tgc cac aga agg gca aat gat gaa 336
Ser Arg Lys Ser Lys Gly Gly Ser Cys His Arg Arg Ala Asn Asp Glu
100 105 110

gca gcg cat gtc aat ggt ctc ggt att gca gat ctg gac gtt ctt ttg 384
Ala Ala His Val Asn Gly Leu Gly Ile Ala Asp Leu Asp Val Leu Leu
115 120 125

ggc cta aat ggt cgc tcg tcg gat gta gac atg aca acc aca ttg ccg 432
Gly Leu Asn Gly Arg Ser Ser Asp Val Asp Met Thr Thr Thr Leu Pro
130 135 140

agt ttg aag cca cct ctg caa aac gga gaa att aag gcc gac agc att 480
Ser Leu Lys Pro Pro Leu Gln Asn Gly Glu Ile Lys Ala Asp Ser Ile
145 150 155 160

gac aat ctt gat ttg gct tcc ctc gat ccg ctt gag caa agc cct agt 528
Asp Asn Leu Asp Leu Ala Ser Leu Asp Pro Leu Glu Gln Ser Pro Ser
165 170 175

ata tct atg gaa cct gtt agt atc aat gaa aca gga agc gca tat aca 576
Ile Ser Met Glu Pro Val Ser Ile Asn Glu Thr Gly Ser Ala Tyr Thr
180 185 190

act acg aac aca gca cta aac gat att gac att cca ttc tcc atc aat 624
Thr Thr Asn Thr Ala Leu Asn Asp Ile Asp Ile Pro Phe Ser Ile Asn
195 200 205

gag ttg aac gag cta tac aaa caa gta tct tcg cat aac tca cat tca 672
Glu Leu Asn Glu Leu Tyr Lys Gln Val Ser Ser His Asn Ser His Ser
210 215 220

caa taa 678
Gln
225

<210> 12
<211> 225
<212> PRT
<213> Saccharomyces cerevisiae

<400> 12

Met Val Val Ile Asn Gly Val Lys Tyr Ala Cys Glu Thr Cys Ile Arg
1 5 10 15

Gly His Arg Ala Ala Gln Cys Thr His Thr Asp Gly Pro Leu Gln Met
20 25 30

Ile Arg Arg Lys Gly Arg Pro Ser Thr Thr Cys Gly His Cys Lys Glu
35 40 45

Leu Arg Arg Thr Lys Asn Phe Asn Pro Ser Gly Gly Cys Met Cys Ala
50 55 60

Ser Ala Arg Arg Pro Ala Val Gly Ser Lys Glu Asp Glu Thr Arg Cys
65 70 75 80

Arg Cys Asp Glu Gly Glu Pro Cys Lys Cys His Thr Lys Arg Lys Ser
85 90 95

Ser Arg Lys Ser Lys Gly Gly Ser Cys His Arg Arg Ala Asn Asp Glu
100 105 110

Ala Ala His Val Asn Gly Leu Gly Ile Ala Asp Leu Asp Val Leu Leu
115 120 125

Gly Leu Asn Gly Arg Ser Ser Asp Val Asp Met Thr Thr Thr Leu Pro
130 135 140

Ser Leu Lys Pro Pro Leu Gln Asn Gly Glu Ile Lys Ala Asp Ser Ile
145 150 155 160

Asp Asn Leu Asp Leu Ala Ser Leu Asp Pro Leu Glu Gln Ser Pro Ser
165 170 175

Ile Ser Met Glu Pro Val Ser Ile Asn Glu Thr Gly Ser Ala Tyr Thr
180 185 190

Thr Thr Asn Thr Ala Leu Asn Asp Ile Asp Ile Pro Phe Ser Ile Asn
195 200 205

Glu Leu Asn Glu Leu Tyr Lys Gln Val Ser Ser His Asn Ser His Ser
210 215 220

Gln
225

<210> 13
<211> 750
<212> DNA
<213> Saccharomyces cerevisiae

<220>

<221> CDS

<222> (1)..(750)

<400> 13

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atg ttg cag cta agg ttt atg cct gga tgg gtc ccc aga aat ggt ttt      48
Met Leu Gln Leu Arg Phe Met Pro Gly Trp Val Pro Arg Asn Gly Phe
1               5                  10                  15

ttt ggt ttg aag gag aca att ggt aca gta cat aag aga ttt tat gct      96
Phe Gly Leu Lys Glu Thr Ile Gly Thr Val His Lys Arg Phe Tyr Ala
            20                  25                  30

ctg gct tct gaa caa ccc tca aga aag aca gta aag ccg ctg gac tcg     144
Leu Ala Ser Glu Gln Pro Ser Arg Lys Thr Val Lys Pro Leu Asp Ser
        35                  40                  45

agg aag acg ttt ctc atc gat aca tac aag cat tta atg gag aac agt     192
Arg Lys Thr Phe Leu Ile Asp Thr Tyr Lys His Leu Met Glu Asn Ser
    50                  55                  60

tct atg att ttt ttt gtc cat tac aat aat ctt tcc aaa aca gaa gat     240
Ser Met Ile Phe Phe Val His Tyr Asn Asn Leu Ser Lys Thr Glu Asp
65                  70                  75                  80

cac cat ttc aga ttc aag att aaa cag aca gga ggg aaa ctc aca aaa     288
His His Phe Arg Phe Lys Ile Lys Gln Thr Gly Gly Lys Leu Thr Lys
                85                  90                  95

gta aga aac aac ctg ttc gaa gtc tac ttg aga aat tcg cat ctg ccc     336
Val Arg Asn Asn Leu Phe Glu Val Tyr Leu Arg Asn Ser His Leu Pro
            100                 105                 110

gac cca tgt gga ttc gtg aag cgt aaa gag caa aac tgg aaa cat cca     384
Asp Pro Cys Gly Phe Val Lys Arg Lys Glu Gln Asn Trp Lys His Pro
        115                 120                 125

ctc ttg cca cta ctg aag ggt cct acg gcc aca att aca tac gaa gac     432
Leu Leu Pro Leu Leu Lys Gly Pro Thr Ala Thr Ile Thr Tyr Glu Asp
    130                 135                 140
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acc aac cct caa caa gta gcc aag cta ttg aag gtt ctg cag tca gca 480
Thr Asn Pro Gln Gln Val Ala Lys Leu Leu Lys Val Leu Gln Ser Ala
145 150 155 160

caa gac aag ctg atg gtg att ggt gca aaa gta gaa aac gaa gtt ttg 528
Gln Asp Lys Leu Met Val Ile Gly Ala Lys Val Glu Asn Glu Val Leu
165 170 175

aat gtg gaa aaa ata aac act ttt aag act ctc ccc aca aag ccg gaa 576
Asn Val Glu Lys Ile Asn Thr Phe Lys Thr Leu Pro Thr Lys Pro Glu
180 185 190

atg cag tcg cag tta gtc agc gtt ttg caa atg cta agt ggg ttg ggt 624
Met Gln Ser Gln Leu Val Ser Val Leu Gln Met Leu Ser Gly Leu Gly
195 200 205

ttg gtt cgt acg ttg gaa aac agt tca aat gca ttg tat tta aca cta 672
Leu Val Arg Thr Leu Glu Asn Ser Ser Asn Ala Leu Tyr Leu Thr Leu
210 215 220

aaa tct cac aat gac aac caa aaa cct aaa gag gat gtg gag tca act 720
Lys Ser His Asn Asp Asn Gln Lys Pro Lys Glu Asp Val Glu Ser Thr
225 230 235 240

aca gat gca gaa tcg aag gga tca aag taa 750
Thr Asp Ala Glu Ser Lys Gly Ser Lys
245

<210> 14
<211> 249
<212> PRT
<213> Saccharomyces cerevisiae

<400> 14

Met Leu Gln Leu Arg Phe Met Pro Gly Trp Val Pro Arg Asn Gly Phe
1 5 10 15

Phe Gly Leu Lys Glu Thr Ile Gly Thr Val His Lys Arg Phe Tyr Ala
20 25 30

Leu Ala Ser Glu Gln Pro Ser Arg Lys Thr Val Lys Pro Leu Asp Ser
35 40 45

Arg Lys Thr Phe Leu Ile Asp Thr Tyr Lys His Leu Met Glu Asn Ser
50 55 60

Ser Met Ile Phe Phe Val His Tyr Asn Asn Leu Ser Lys Thr Glu Asp
65 70 75 80

His His Phe Arg Phe Lys Ile Lys Gln Thr Gly Gly Lys Leu Thr Lys
85 90 95

Val Arg Asn Asn Leu Phe Glu Val Tyr Leu Arg Asn Ser His Leu Pro
100 105 110

Asp Pro Cys Gly Phe Val Lys Arg Lys Glu Gln Asn Trp Lys His Pro
115 120 125

Leu Leu Pro Leu Leu Lys Gly Pro Thr Ala Thr Ile Thr Tyr Glu Asp
130 135 140

Thr Asn Pro Gln Gln Val Ala Lys Leu Leu Lys Val Leu Gln Ser Ala
145 150 155 160

Gln Asp Lys Leu Met Val Ile Gly Ala Lys Val Glu Asn Glu Val Leu
165 170 175

Asn Val Glu Lys Ile Asn Thr Phe Lys Thr Leu Pro Thr Lys Pro Glu
180 185 190

Met Gln Ser Gln Leu Val Ser Val Leu Gln Met Leu Ser Gly Leu Gly
195 200 205

Leu Val Arg Thr Leu Glu Asn Ser Ser Asn Ala Leu Tyr Leu Thr Leu
210 215 220

Lys Ser His Asn Asp Asn Gln Lys Pro Lys Glu Asp Val Glu Ser Thr
225 230 235 240

Thr Asp Ala Glu Ser Lys Gly Ser Lys

<210> 15
<211> 357
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(357)

<400> 15

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Met Lys Leu Pro Gln Thr Met Leu Arg Ser Ile Ser Val Lys His Val
1 5 10 15

cgg tgg cca agg att ctg acg ggc tca aag ctt tgg tac tca acg cag 96
Arg Trp Pro Arg Ile Leu Thr Gly Ser Lys Leu Trp Tyr Ser Thr Gln
20 25 30

atg gca atg act ccg gag gag aag atg atc acc gat aaa cta caa cag 144
Met Ala Met Thr Pro Glu Glu Lys Met Ile Thr Asp Lys Leu Gln Gln
35 40 45

gaa ctg gaa cct gaa gtg tgt aaa gtg caa gac gtt tcc ggt ggc tgc 192
Glu Leu Glu Pro Glu Val Cys Lys Val Gln Asp Val Ser Gly Gly Cys
50 55 60

gga tcc atg ttt gct atc aac ata aca agc aag aag ttc aac gga ctg 240
Gly Ser Met Phe Ala Ile Asn Ile Thr Ser Lys Lys Phe Asn Gly Leu
65 70 75 80

agt ctc atc aag cag cac cag ctg gtg aac aga att ttg agg gac gat 288
Ser Leu Ile Lys Gln His Gln Leu Val Asn Arg Ile Leu Arg Asp Asp
85 90 95

att tcc aga tgg cat ggc cta caa ttg acc act aag aag tca act ggg 336
Ile Ser Arg Trp His Gly Leu Gln Leu Thr Thr Lys Lys Ser Thr Gly
100 105 110

aag ggt ccg gca tca tca tga 357
Lys Gly Pro Ala Ser Ser
115

<210> 16
<211> 118
<212> PRT
<213> Saccharomyces cerevisiae

<400> 16

Met Lys Leu Pro Gln Thr Met Leu Arg Ser Ile Ser Val Lys His Val
1 5 10 15

Arg Trp Pro Arg Ile Leu Thr Gly Ser Lys Leu Trp Tyr Ser Thr Gln
20 25 30

Met Ala Met Thr Pro Glu Glu Lys Met Ile Thr Asp Lys Leu Gln Gln
35 40 45

Glu Leu Glu Pro Glu Val Cys Lys Val Gln Asp Val Ser Gly Gly Cys
50 55 60

Gly Ser Met Phe Ala Ile Asn Ile Thr Ser Lys Lys Phe Asn Gly Leu
65 70 75 80

Ser Leu Ile Lys Gln His Gln Leu Val Asn Arg Ile Leu Arg Asp Asp
85 90 95

Ile Ser Arg Trp His Gly Leu Gln Leu Thr Thr Lys Lys Ser Thr Gly
100 105 110

Lys Gly Pro Ala Ser Ser
115

<210> 17

<211> 1782

<212> DNA

<213> Saccharomyces cerevisiae

<220>

<221> CDS

<222> (1)..(1782)

<400> 17

atg gct cta gct atc tcc cac gag gat act cag att ttg cta aag gac 48
Met Ala Leu Ala Ile Ser His Glu Asp Thr Gln Ile Leu Leu Lys Asp
1 5 10 15

aaa aat att cta cag gaa tcg gtc ttg aac aaa tac aga act gct gga 96
Lys Asn Ile Leu Gln Glu Ser Val Leu Asn Lys Tyr Arg Thr Ala Gly
20 25 30

caa atc gca caa act gct ttg aaa tat gtt act tct ttg atc aat gat 144
Gln Ile Ala Gln Thr Ala Leu Lys Tyr Val Thr Ser Leu Ile Asn Asp
35 40 45

tca tat cac tct aag acc aca cag cgc caa tta acc gtg cca gag cta 192
Ser Tyr His Ser Lys Thr Thr Gln Arg Gln Leu Thr Val Pro Glu Leu
50 55 60

tgt ttg ctt acc gat tct ttt att ttg acc cgg ttg gaa caa tat tat 240
Cys Leu Leu Thr Asp Ser Phe Ile Leu Thr Arg Leu Glu Gln Tyr Tyr
65 70 75 80

aaa aac aaa gtt aat gaa aga ggt att gcc att cca acc act att gat 288
Lys Asn Lys Val Asn Glu Arg Gly Ile Ala Ile Pro Thr Thr Ile Asp
85 90 95

atc gac caa att tct ggt gga tgg tgc ccc gaa ata gat gat act caa 336
Ile Asp Gln Ile Ser Gly Gly Trp Cys Pro Glu Ile Asp Asp Thr Gln
100 105 110

aat ttg tta aac tgg aat aag ggg aaa gac tcc act ttt gca tca tct 384
Asn Leu Leu Asn Trp Asn Lys Gly Lys Asp Ser Thr Phe Ala Ser Ser
115 120 125

gtc act ggg act ttg aga ccg ggg gat tta gtc aag att aca cta ggt 432
Val Thr Gly Thr Leu Arg Pro Gly Asp Leu Val Lys Ile Thr Leu Gly
130 135 140

gtt cat att gat ggt tac acc tct gaa gtt tct cat act atg gtt att 480
Val His Ile Asp Gly Tyr Thr Ser Glu Val Ser His Thr Met Val Ile
145 150 155 160

tac ccc gtt gat gaa acc aaa cct att ctt caa ccc act ggg cca cta 528
Tyr Pro Val Asp Glu Thr Lys Pro Ile Leu Gln Pro Thr Gly Pro Leu
165 170 175

cta ggt ggt aaa gcg gat gct gta gct gct gct cac att gct atg gaa 576
Leu Gly Gly Lys Ala Asp Ala Val Ala Ala Ala His Ile Ala Met Glu
180 185 190

aca gtt gtt gct tta tta gcc tgt gct ctg act cca gaa aag ctt cct 624
Thr Val Val Ala Leu Leu Ala Cys Ala Leu Thr Pro Glu Lys Leu Pro
195 200 205

gcc tca ctg gga gga act tca agt ggt atc aca ggc caa ttg att aga 672
Ala Ser Leu Gly Gly Thr Ser Ser Gly Ile Thr Gly Gln Leu Ile Arg
210 215 220

act ata gtg gat act att gcc aga tct tat aac tgt ggc gtt gtt cct 720
Thr Ile Val Asp Thr Ile Ala Arg Ser Tyr Asn Cys Gly Val Val Pro
225 230 235 240

ggt tct cgt gta aga agg att aga aga ttc ctg gca ggc caa aac gaa 768
Gly Ser Arg Val Arg Arg Ile Arg Arg Phe Leu Ala Gly Gln Asn Glu
245 250 255

ggt att gtt gcc gaa agg gaa tat aag ggt gtt gtt tgg aca gag tcc 816
Gly Ile Val Ala Glu Arg Glu Tyr Lys Gly Val Val Trp Thr Glu Ser
260 265 270

cat caa gaa gca gat ttg cta tct aat act gat gcc aag gat tta aca 864

His Gln Glu Ala Asp Leu Leu Ser Asn Thr Asp Ala Lys Asp Leu Thr
275 280 285

gtg gta gat cgt gga caa tcg act cca ttc act aat gtt tct gct att 912

Val Val Asp Arg Gly Gln Ser Thr Pro Phe Thr Asn Val Ser Ala Ile
290 295 300

cca agt gat gat ttc gtt gtt caa tca ggt gaa gtg tat tta att gat 960
Pro Ser Asp Asp Phe Val Val Gln Ser Gly Glu Val Tyr Leu Ile Asp
305 310 315 320

ttg aaa atg gca tct ttg gag cat tgt acc aaa aag ggt tta gta act 1008
Leu Lys Met Ala Ser Leu Glu His Cys Thr Lys Lys Gly Leu Val Thr
325 330 335

tta gaa acc gtt gac tct tac aca ggt aaa tct cat aag gct gga gaa 1056
Leu Glu Thr Val Asp Ser Tyr Thr Gly Lys Ser His Lys Ala Gly Glu
340 345 350

ttg att gca aga ccc ggt gca tat gtt aga gat ttt gct caa acc cat 1104
Leu Ile Ala Arg Pro Gly Ala Tyr Val Arg Asp Phe Ala Gln Thr His
355 360 365

att ctt aaa tta aaa act tct aga caa tta tta act aaa atc gat aaa 1152
Ile Leu Lys Leu Lys Thr Ser Arg Gln Leu Leu Thr Lys Ile Asp Lys
370 375 380

caa ggc gtt tat cca ttc aag tta tct cat tta tct tct aac ttt cct 1200
Gln Gly Val Tyr Pro Phe Lys Leu Ser His Leu Ser Ser Asn Phe Pro
385 390 395 400

ttc gtt cac gaa aat gaa gaa gaa ctc caa agc tta aag aaa gat ttg 1248
Phe Val His Glu Asn Glu Glu Glu Leu Gln Ser Leu Lys Lys Asp Leu
405 410 415

aaa tca ttt aga ctt ggg atg agt gag att tcc aac aac tac tta tgt 1296

Lys Ser Phe Arg Leu Gly Met Ser Glu Ile Ser Asn Asn Tyr Leu Cys
420 425 430

gtg gaa agt cca ata caa att gct aga tgg gtt cca tgg gac cat att 1344

Val Glu Ser Pro Ile Gln Ile Ala Arg Trp Val Pro Trp Asp His Ile
435 440 445

tta aag gct acc aat cca aac ggt aat tta agt tat gat gca acc tct 1392
Leu Lys Ala Thr Asn Pro Asn Gly Asn Leu Ser Tyr Asp Ala Thr Ser
450 455 460

aca tta aca tta cct ggg cat gag tta cct tta cca aaa ttg ggt gtt 1440
Thr Leu Thr Leu Pro Gly His Glu Leu Pro Leu Pro Lys Leu Gly Val
465 470 475 480

tca gcc atc aag ctt aaa tcc tta atg aat tca acc aag gaa tcg att 1488
Ser Ala Ile Lys Leu Lys Ser Leu Met Asn Ser Thr Lys Glu Ser Ile
485 490 495

tct tta cca gtt gct cgt gaa tgt aat acc atc gta tta tgt gac tct 1536
Ser Leu Pro Val Ala Arg Glu Cys Asn Thr Ile Val Leu Cys Asp Ser
500 505 510

agt gta agt aca acg gac aga ccc gaa tta ttg aga tta act ggt ggt 1584
Ser Val Ser Thr Thr Asp Arg Pro Glu Leu Leu Arg Leu Thr Gly Gly
515 520 525

tct aag acc tgt caa ccg agc tgg att cac tct cag cac gaa tta aat 1632
Ser Lys Thr Cys Gln Pro Ser Trp Ile His Ser Gln His Glu Leu Asn
530 535 540

cca caa gat tca att gtt caa ggg atc ttt caa tta gct act ttg gcc 1680
Pro Gln Asp Ser Ile Val Gln Gly Ile Phe Gln Leu Ala Thr Leu Ala
545 550 555 560

aag gat aag agg ttc ggt cta tta tta aag gaa acg cag cca atg aag 1728
Lys Asp Lys Arg Phe Gly Leu Leu Leu Lys Glu Thr Gln Pro Met Lys
565 570 575

cag aag agt gtt gag aca tca aat ggc gga gtt gaa gaa acc atg aaa 1776
Gln Lys Ser Val Glu Thr Ser Asn Gly Gly Val Glu Glu Thr Met Lys
580 585 590

atg tag 1782
Met

<210> 18
<211> 593
<212> PRT
<213> Saccharomyces cerevisiae

<400> 18

Met Ala Leu Ala Ile Ser His Glu Asp Thr Gln Ile Leu Leu Lys Asp
1 5 10 15

Lys Asn Ile Leu Gln Glu Ser Val Leu Asn Lys Tyr Arg Thr Ala Gly
20 25 30

Gln Ile Ala Gln Thr Ala Leu Lys Tyr Val Thr Ser Leu Ile Asn Asp
35 40 45

Ser Tyr His Ser Lys Thr Thr Gln Arg Gln Leu Thr Val Pro Glu Leu
50 55 60

Cys Leu Leu Thr Asp Ser Phe Ile Leu Thr Arg Leu Glu Gln Tyr Tyr
65 70 75 80

Lys Asn Lys Val Asn Glu Arg Gly Ile Ala Ile Pro Thr Thr Ile Asp
85 90 95

Ile Asp Gln Ile Ser Gly Gly Trp Cys Pro Glu Ile Asp Asp Thr Gln
100 105 110

Asn Leu Leu Asn Trp Asn Lys Gly Lys Asp Ser Thr Phe Ala Ser Ser
115 120 125

Val Thr Gly Thr Leu Arg Pro Gly Asp Leu Val Lys Ile Thr Leu Gly
130 135 140

Val His Ile Asp Gly Tyr Thr Ser Glu Val Ser His Thr Met Val Ile
145 150 155 160

Tyr Pro Val Asp Glu Thr Lys Pro Ile Leu Gln Pro Thr Gly Pro Leu
165 170 175

Leu Gly Gly Lys Ala Asp Ala Val Ala Ala Ala His Ile Ala Met Glu
180 185 190

Thr Val Val Ala Leu Leu Ala Cys Ala Leu Thr Pro Glu Lys Leu Pro
195 200 205

Ala Ser Leu Gly Gly Thr Ser Ser Gly Ile Thr Gly Gln Leu Ile Arg
210 215 220

Thr Ile Val Asp Thr Ile Ala Arg Ser Tyr Asn Cys Gly Val Val Pro
225 230 235 240

Gly Ser Arg Val Arg Arg Ile Arg Arg Phe Leu Ala Gly Gln Asn Glu
245 250 255

Gly Ile Val Ala Glu Arg Glu Tyr Lys Gly Val Val Trp Thr Glu Ser
260 265 270

His Gln Glu Ala Asp Leu Leu Ser Asn Thr Asp Ala Lys Asp Leu Thr
275 280 285

Val Val Asp Arg Gly Gln Ser Thr Pro Phe Thr Asn Val Ser Ala Ile
290 295 300

Pro Ser Asp Asp Phe Val Val Gln Ser Gly Glu Val Tyr Leu Ile Asp
305 310 315 320

Leu Lys Met Ala Ser Leu Glu His Cys Thr Lys Lys Gly Leu Val Thr
325 330 335

Leu Glu Thr Val Asp Ser Tyr Thr Gly Lys Ser His Lys Ala Gly Glu
340 345 350

Leu Ile Ala Arg Pro Gly Ala Tyr Val Arg Asp Phe Ala Gln Thr His
355 360 365

Ile Leu Lys Leu Lys Thr Ser Arg Gln Leu Leu Thr Lys Ile Asp Lys
370 375 380

Gln Gly Val Tyr Pro Phe Lys Leu Ser His Leu Ser Ser Asn Phe Pro
385 390 395 400

Phe Val His Glu Asn Glu Glu Glu Leu Gln Ser Leu Lys Lys Asp Leu
405 410 415

Lys Ser Phe Arg Leu Gly Met Ser Glu Ile Ser Asn Asn Tyr Leu Cys
420 425 430

Val Glu Ser Pro Ile Gln Ile Ala Arg Trp Val Pro Trp Asp His Ile
435 440 445

Leu Lys Ala Thr Asn Pro Asn Gly Asn Leu Ser Tyr Asp Ala Thr Ser
450 455 460

Thr Leu Thr Leu Pro Gly His Glu Leu Pro Leu Pro Lys Leu Gly Val
465 470 475 480

Ser Ala Ile Lys Leu Lys Ser Leu Met Asn Ser Thr Lys Glu Ser Ile
485 490 495

Ser Leu Pro Val Ala Arg Glu Cys Asn Thr Ile Val Leu Cys Asp Ser
500 505 510

Ser Val Ser Thr Thr Asp Arg Pro Glu Leu Leu Arg Leu Thr Gly Gly
515 520 525

Ser Lys Thr Cys Gln Pro Ser Trp Ile His Ser Gln His Glu Leu Asn
530 535 540

Pro Gln Asp Ser Ile Val Gln Gly Ile Phe Gln Leu Ala Thr Leu Ala
545 550 555 560

Lys Asp Lys Arg Phe Gly Leu Leu Leu Lys Glu Thr Gln Pro Met Lys
565 570 575

Gln Lys Ser Val Glu Thr Ser Asn Gly Gly Val Glu Glu Thr Met Lys
580 585 590

Met

<210> 19
<211> 2097
<212> DNA
<213> Saccharomyces cerevisiae

<220>

<221> CDS

<222> (1)..(2097)

<400> 19

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atg gtt ttt tct tat gag cac tat atg aat ctc ctt ttc cat ttg gat       48
Met Val Phe Ser Tyr Glu His Tyr Met Asn Leu Leu Phe His Leu Asp
1               5                  10                  15

aac agt aaa gaa acg gtg cct cca gag att gca aaa aga ata att tca       96
Asn Ser Lys Glu Thr Val Pro Pro Glu Ile Ala Lys Arg Ile Ile Ser
            20                  25                  30

aat gct ata gct cct gta ata aca gtt act tca act cct ctc ttc gac      144
Asn Ala Ile Ala Pro Val Ile Thr Val Thr Ser Thr Pro Leu Phe Asp
        35                  40                  45

aaa cat att caa gaa acg tac aaa gta gat tct ctc tat atg ctg ctg      192
Lys His Ile Gln Glu Thr Tyr Lys Val Asp Ser Leu Tyr Met Leu Leu
    50                  55                  60

cga ttc ttt ggc ggt tgt gtc tct gat aga gat caa gcc aat gaa gcg      240
Arg Phe Phe Gly Gly Cys Val Ser Asp Arg Asp Gln Ala Asn Glu Ala
65                  70                  75                  80

aag gtt gga cag cat gag cat gag gtt tgt gat gca agt gac tcg acg      288
Lys Val Gly Gln His Glu His Glu Val Cys Asp Ala Ser Asp Ser Thr
                85                  90                  95

gat tca att ccc aaa aat aaa aat ttg gaa gtg ccc aat tta tca aag      336
Asp Ser Ile Pro Lys Asn Lys Asn Leu Glu Val Pro Asn Leu Ser Lys
            100                 105                 110

aaa ggt agt cgc agt agg tcg aat agt ctt ttc cag agg gat tca acg      384
Lys Gly Ser Arg Ser Arg Ser Asn Ser Leu Phe Gln Arg Asp Ser Thr
        115                 120                 125

caa tct caa tat atc agg ttt aca agg cca tta ggt gac ttg atc gaa      432
Gln Ser Gln Tyr Ile Arg Phe Thr Arg Pro Leu Gly Asp Leu Ile Glu
    130                 135                 140
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aca aga gat gca aat gat atg tta ttc aat tac cat tct tta gag gta 480
Thr Arg Asp Ala Asn Asp Met Leu Phe Asn Tyr His Ser Leu Glu Val
145 150 155 160

ttc tta gat aat tat ttg aaa ttg gtt gca gca aat act gat gaa atg 528
Phe Leu Asp Asn Tyr Leu Lys Leu Val Ala Ala Asn Thr Asp Glu Met
165 170 175

gtt cct cat aat ctt ctt aag aaa tcc att tat cat agt ttc ttt tca 576
Val Pro His Asn Leu Leu Lys Lys Ser Ile Tyr His Ser Phe Phe Ser
180 185 190

cta gca att tca tcc aca aat aac tta tcg ccc tat gaa act ttt aat 624
Leu Ala Ile Ser Ser Thr Asn Asn Leu Ser Pro Tyr Glu Thr Phe Asn
195 200 205

cac cct att ctt tcc ttg att gct tta gat ata tca aat ggc gaa gtt 672
His Pro Ile Leu Ser Leu Ile Ala Leu Asp Ile Ser Asn Gly Glu Val
210 215 220

tat gag gat gca aga gat ctt tta gtc aat ttc aag aat ctt aat cat 720
Tyr Glu Asp Ala Arg Asp Leu Leu Val Asn Phe Lys Asn Leu Asn His
225 230 235 240

aat act gaa aac ttt cct atc ttc atg aat aca aat gaa atg ctt cca 768
Asn Thr Glu Asn Phe Pro Ile Phe Met Asn Thr Asn Glu Met Leu Pro
245 250 255

gtt ttc tta ctc tgc tac aat gac gat tcc caa gaa gaa ttc gaa aaa 816
Val Phe Leu Leu Cys Tyr Asn Asp Asp Ser Gln Glu Glu Phe Glu Lys
260 265 270

tgc cag gcg tta gct aag aaa cta aag aag cag ttg ttt gtt gag agt 864
Cys Gln Ala Leu Ala Lys Lys Leu Lys Lys Gln Leu Phe Val Glu Ser
275 280 285

atc tta cta gca ctc tgg aag gat tct ttt att tac gac gaa aat tca 912
Ile Leu Leu Ala Leu Trp Lys Asp Ser Phe Ile Tyr Asp Glu Asn Ser
290 295 300

gtc ata cag tta cac caa cca gta atg tca tcg ctt gaa gaa att ctc 960
Val Ile Gln Leu His Gln Pro Val Met Ser Ser Leu Glu Glu Ile Leu

305 310 315 320

ttc ttc ctt caa gct cca act caa aca aca ctc tct ctg gct ttg ata 1008
Phe Phe Leu Gln Ala Pro Thr Gln Thr Thr Leu Ser Leu Ala Leu Ile
325 330 335

aac tcg atc tat gat atg ctt gat tat ttg gtt tat gat tta atg ata 1056
Asn Ser Ile Tyr Asp Met Leu Asp Tyr Leu Val Tyr Asp Leu Met Ile
340 345 350

cca ttc atg aaa aga aaa gtg tca ttc tgg gaa gag aca att tta cag 1104
Pro Phe Met Lys Arg Lys Val Ser Phe Trp Glu Glu Thr Ile Leu Gln
355 360 365

cca aga aag tcg cta ttt aat ggt gca aag ttt ttc aaa aaa ttt atg 1152
Pro Arg Lys Ser Leu Phe Asn Gly Ala Lys Phe Phe Lys Lys Phe Met
370 375 380

aat aaa aat cct gtc aat ggt aat cac caa cat aat tct cta acg aga 1200
Asn Lys Asn Pro Val Asn Gly Asn His Gln His Asn Ser Leu Thr Arg
385 390 395 400

gac agc cag gga aat gaa tac ttc gca tcg tca tct tct gag ttt ttg 1248
Asp Ser Gln Gly Asn Glu Tyr Phe Ala Ser Ser Ser Ser Glu Phe Leu
405 410 415

atg aga aag tta gca gat tgg tct atg atg cta tcc gac ttc aaa act 1296
Met Arg Lys Leu Ala Asp Trp Ser Met Met Leu Ser Asp Phe Lys Thr
420 425 430

gct tat tcc aca tac gaa tcg ctt atg gat gac cta gat gca ttt cca 1344
Ala Tyr Ser Thr Tyr Glu Ser Leu Met Asp Asp Leu Asp Ala Phe Pro
435 440 445

aag tac ctg gca tca tgc atc gaa tgg tgc gcg gta tca cta ttg atg 1392
Lys Tyr Leu Ala Ser Cys Ile Glu Trp Cys Ala Val Ser Leu Leu Met
450 455 460

ggt gcg cag agc ata gtc acc gtg aaa atg atc aaa aac gat ata aat 1440
Gly Ala Gln Ser Ile Val Thr Val Lys Met Ile Lys Asn Asp Ile Asn
465 470 475 480

cct ctt atc gaa agg gca tta gcc aca tac gaa aac tgc tca cga ata 1488
Pro Leu Ile Glu Arg Ala Leu Ala Thr Tyr Glu Asn Cys Ser Arg Ile
485 490 495

caa cgt ggt aaa ggc aaa gaa tca aac tct ttg gat gtt aca gag cca 1536
Gln Arg Gly Lys Gly Lys Glu Ser Asn Ser Leu Asp Val Thr Glu Pro
500 505 510

gtg cgt tcg tat gag aca cgt tgt atg att ttg gca tct gaa ttg ttt 1584
Val Arg Ser Tyr Glu Thr Arg Cys Met Ile Leu Ala Ser Glu Leu Phe
515 520 525

tta tct tta agc aat acg tgg aca tct acc cca tac gct atc caa tat 1632
Leu Ser Leu Ser Asn Thr Trp Thr Ser Thr Pro Tyr Ala Ile Gln Tyr
530 535 540

tta gaa aca att cta gac gag tgc aag ttg gga cct tgt tca cag ata 1680
Leu Glu Thr Ile Leu Asp Glu Cys Lys Leu Gly Pro Cys Ser Gln Ile
545 550 555 560

atg gtt tgg gaa agg ctt agt gac tgc tat aat ttg aga gtt gac cct 1728
Met Val Trp Glu Arg Leu Ser Asp Cys Tyr Asn Leu Arg Val Asp Pro
565 570 575

aga atc aaa cat aga gtt gga gca atg aag aag gac gct aaa gac acc 1776
Arg Ile Lys His Arg Val Gly Ala Met Lys Lys Asp Ala Lys Asp Thr
580 585 590

gaa gat ctc cga ggt gag cat aag tat agc aca gat cat ttc aca gac 1824
Glu Asp Leu Arg Gly Glu His Lys Tyr Ser Thr Asp His Phe Thr Asp
595 600 605

gag gac ata tta tcg gaa ggg tta aca aga aga cgc aag gca gct ttt 1872
Glu Asp Ile Leu Ser Glu Gly Leu Thr Arg Arg Arg Lys Ala Ala Phe
610 615 620

ttt agg tta ata gca gct aag aag tgg gca gag caa aaa caa tgg aga 1920
Phe Arg Leu Ile Ala Ala Lys Lys Trp Ala Glu Gln Lys Gln Trp Arg
625 630 635 640

cag gtt tct tgg tgc tta aaa gat att gaa agt acc tat tca gag atc 1968
Gln Val Ser Trp Cys Leu Lys Asp Ile Glu Ser Thr Tyr Ser Glu Ile
645 650 655

aaa ttt ttg cat ggt aac ggt tta att tta agc aaa cta aaa aat caa 2016
Lys Phe Leu His Gly Asn Gly Leu Ile Leu Ser Lys Leu Lys Asn Gln
660 665 670

ctc aat tta aag gac gtg gat tct gca cca cgg ccc tcc gaa aag aat 2064
Leu Asn Leu Lys Asp Val Asp Ser Ala Pro Arg Pro Ser Glu Lys Asn
675 680 685

ctt aca aga aca agt gtt agc ttt att gga tga 2097
Leu Thr Arg Thr Ser Val Ser Phe Ile Gly
690 695

<210> 20
<211> 698
<212> PRT
<213> Saccharomyces cerevisiae

<400> 20

Met Val Phe Ser Tyr Glu His Tyr Met Asn Leu Leu Phe His Leu Asp
1 5 10 15

Asn Ser Lys Glu Thr Val Pro Pro Glu Ile Ala Lys Arg Ile Ile Ser
20 25 30

Asn Ala Ile Ala Pro Val Ile Thr Val Thr Ser Thr Pro Leu Phe Asp
35 40 45

Lys His Ile Gln Glu Thr Tyr Lys Val Asp Ser Leu Tyr Met Leu Leu
50 55 60

Arg Phe Phe Gly Gly Cys Val Ser Asp Arg Asp Gln Ala Asn Glu Ala

65 70 75 80

Lys Val Gly Gln His Glu His Glu Val Cys Asp Ala Ser Asp Ser Thr
85 90 95

Asp Ser Ile Pro Lys Asn Lys Asn Leu Glu Val Pro Asn Leu Ser Lys
100 105 110

Lys Gly Ser Arg Ser Arg Ser Asn Ser Leu Phe Gln Arg Asp Ser Thr
115 120 125

Gln Ser Gln Tyr Ile Arg Phe Thr Arg Pro Leu Gly Asp Leu Ile Glu
130 135 140

Thr Arg Asp Ala Asn Asp Met Leu Phe Asn Tyr His Ser Leu Glu Val
145 150 155 160

Phe Leu Asp Asn Tyr Leu Lys Leu Val Ala Ala Asn Thr Asp Glu Met
165 170 175

Val Pro His Asn Leu Leu Lys Lys Ser Ile Tyr His Ser Phe Phe Ser
180 185 190

Leu Ala Ile Ser Ser Thr Asn Asn Leu Ser Pro Tyr Glu Thr Phe Asn
195 200 205

His Pro Ile Leu Ser Leu Ile Ala Leu Asp Ile Ser Asn Gly Glu Val
210 215 220

Tyr Glu Asp Ala Arg Asp Leu Leu Val Asn Phe Lys Asn Leu Asn His
225 230 235 240

Asn Thr Glu Asn Phe Pro Ile Phe Met Asn Thr Asn Glu Met Leu Pro
245 250 255

Val Phe Leu Leu Cys Tyr Asn Asp Asp Ser Gln Glu Glu Phe Glu Lys
260 265 270

Cys Gln Ala Leu Ala Lys Lys Leu Lys Lys Gln Leu Phe Val Glu Ser
275 280 285

Ile Leu Leu Ala Leu Trp Lys Asp Ser Phe Ile Tyr Asp Glu Asn Ser
290 295 300

Val Ile Gln Leu His Gln Pro Val Met Ser Ser Leu Glu Glu Ile Leu
305 310 315 320

Phe Phe Leu Gln Ala Pro Thr Gln Thr Thr Leu Ser Leu Ala Leu Ile
325 330 335

Asn Ser Ile Tyr Asp Met Leu Asp Tyr Leu Val Tyr Asp Leu Met Ile
340 345 350

Pro Phe Met Lys Arg Lys Val Ser Phe Trp Glu Glu Thr Ile Leu Gln
355 360 365

Pro Arg Lys Ser Leu Phe Asn Gly Ala Lys Phe Phe Lys Lys Phe Met
370 375 380

Asn Lys Asn Pro Val Asn Gly Asn His Gln His Asn Ser Leu Thr Arg
385 390 395 400

Asp Ser Gln Gly Asn Glu Tyr Phe Ala Ser Ser Ser Ser Glu Phe Leu

405 410 415

Met Arg Lys Leu Ala Asp Trp Ser Met Met Leu Ser Asp Phe Lys Thr
420 425 430

Ala Tyr Ser Thr Tyr Glu Ser Leu Met Asp Asp Leu Asp Ala Phe Pro
435 440 445

Lys Tyr Leu Ala Ser Cys Ile Glu Trp Cys Ala Val Ser Leu Leu Met
450 455 460

Gly Ala Gln Ser Ile Val Thr Val Lys Met Ile Lys Asn Asp Ile Asn
465 470 475 480

Pro Leu Ile Glu Arg Ala Leu Ala Thr Tyr Glu Asn Cys Ser Arg Ile
485 490 495

Gln Arg Gly Lys Gly Lys Glu Ser Asn Ser Leu Asp Val Thr Glu Pro
500 505 510

Val Arg Ser Tyr Glu Thr Arg Cys Met Ile Leu Ala Ser Glu Leu Phe
515 520 525

Leu Ser Leu Ser Asn Thr Trp Thr Ser Thr Pro Tyr Ala Ile Gln Tyr
530 535 540

Leu Glu Thr Ile Leu Asp Glu Cys Lys Leu Gly Pro Cys Ser Gln Ile
545 550 555 560

Met Val Trp Glu Arg Leu Ser Asp Cys Tyr Asn Leu Arg Val Asp Pro
565 570 575

Arg Ile Lys His Arg Val Gly Ala Met Lys Lys Asp Ala Lys Asp Thr
580 585 590

Glu Asp Leu Arg Gly Glu His Lys Tyr Ser Thr Asp His Phe Thr Asp
595 600 605

Glu Asp Ile Leu Ser Glu Gly Leu Thr Arg Arg Arg Lys Ala Ala Phe
610 615 620

Phe Arg Leu Ile Ala Ala Lys Lys Trp Ala Glu Gln Lys Gln Trp Arg
625 630 635 640

Gln Val Ser Trp Cys Leu Lys Asp Ile Glu Ser Thr Tyr Ser Glu Ile
645 650 655

Lys Phe Leu His Gly Asn Gly Leu Ile Leu Ser Lys Leu Lys Asn Gln
660 665 670

Leu Asn Leu Lys Asp Val Asp Ser Ala Pro Arg Pro Ser Glu Lys Asn
675 680 685

Leu Thr Arg Thr Ser Val Ser Phe Ile Gly
690 695

<210> 21
<211> 327
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(327)

<400> 21

atg cga tat act gca act ttt cgg cct ttg caa cga ttt gta atg aat 48
Met Arg Tyr Thr Ala Thr Phe Arg Pro Leu Gln Arg Phe Val Met Asn
1 5 10 15

cct ttt gca tcg cta gaa gga caa gat aat att tct tct gtt ttt ttt 96
Pro Phe Ala Ser Leu Glu Gly Gln Asp Asn Ile Ser Ser Val Phe Phe
20 25 30

tta cat atg caa caa ttt gaa agt cag gtc aaa gac aga ttc cgg ttc 144
Leu His Met Gln Gln Phe Glu Ser Gln Val Lys Asp Arg Phe Arg Phe
35 40 45

ccc ata ttc aga ttg gag aga aaa act ttt ggc aac tca tgt tac caa 192
Pro Ile Phe Arg Leu Glu Arg Lys Thr Phe Gly Asn Ser Cys Tyr Gln
50 55 60

gtc gag acg ctt aaa gtt aag tgt cgg cca aga cac gca aaa tct tgt 240
Val Glu Thr Leu Lys Val Lys Cys Arg Pro Arg His Ala Lys Ser Cys
65 70 75 80

aat ctt tta acg ctg ctc ttc aaa tca cgg acg caa tca gta ctt gta 288
Asn Leu Leu Thr Leu Leu Phe Lys Ser Arg Thr Gln Ser Val Leu Val
85 90 95

cct aat ttt ggt ttt cta ata ttg aat agc gaa cca tag 327
Pro Asn Phe Gly Phe Leu Ile Leu Asn Ser Glu Pro
100 105

<210> 22
<211> 108
<212> PRT
<213> Saccharomyces cerevisiae

<400> 22

Met Arg Tyr Thr Ala Thr Phe Arg Pro Leu Gln Arg Phe Val Met Asn
1 5 10 15

Pro Phe Ala Ser Leu Glu Gly Gln Asp Asn Ile Ser Ser Val Phe Phe
20 25 30

Leu His Met Gln Gln Phe Glu Ser Gln Val Lys Asp Arg Phe Arg Phe
35 40 45

Pro Ile Phe Arg Leu Glu Arg Lys Thr Phe Gly Asn Ser Cys Tyr Gln
50 55 60

Val Glu Thr Leu Lys Val Lys Cys Arg Pro Arg His Ala Lys Ser Cys
65 70 75 80

Asn Leu Leu Thr Leu Leu Phe Lys Ser Arg Thr Gln Ser Val Leu Val
85 90 95

Pro Asn Phe Gly Phe Leu Ile Leu Asn Ser Glu Pro
100 105

<210> 23
<211> 411
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(411)

<400> 23
atg caa ttc tct acc gtc gct tct atc gct gct att gcc gct gtt gcc 48
Met Gln Phe Ser Thr Val Ala Ser Ile Ala Ala Ile Ala Ala Val Ala
1 5 10 15

tcc gcc gct tct aac att acc act gct act gtc aca gaa gaa tct acc 96
Ser Ala Ala Ser Asn Ile Thr Thr Ala Thr Val Thr Glu Glu Ser Thr

20 25 30

act ttg gtc act atc act tct tgt gag gac cac gtt tgt tct gaa aca 144
Thr Leu Val Thr Ile Thr Ser Cys Glu Asp His Val Cys Ser Glu Thr
35 40 45

gtt tcc cca gct ttg gtt tcc act gct acc gtc acc gta aat gac gtt 192
Val Ser Pro Ala Leu Val Ser Thr Ala Thr Val Thr Val Asn Asp Val
50 55 60

atc act taa tac acc acc tgg tgt cca ttg cca acc act gaa gca cca 240
Ile Thr Tyr Thr Thr Trp Cys Pro Leu Pro Thr Thr Glu Ala Pro
65 70 75

aag aat acc act tct cca gct cca act gaa aag cca acc gaa aag cca 288
Lys Asn Thr Thr Ser Pro Ala Pro Thr Glu Lys Pro Thr Glu Lys Pro
80 85 90 95

act gaa aag cca acc caa caa ggt tct agc act caa act gtt acc tcc 336
Thr Glu Lys Pro Thr Gln Gln Gly Ser Ser Thr Gln Thr Val Thr Ser
100 105 110

tac act ggt gcc gct gtt aag gct ttg cca gct gcc ggt gct ttg ttg 384
Tyr Thr Gly Ala Ala Val Lys Ala Leu Pro Ala Ala Gly Ala Leu Leu
115 120 125

gct ggt gct gcc gct tta ttg ttg taa 411
Ala Gly Ala Ala Ala Leu Leu Leu
130 135

<210> 24
<211> 66
<212> PRT
<213> Saccharomyces cerevisiae

<400> 24

Met Gln Phe Ser Thr Val Ala Ser Ile Ala Ala Ile Ala Ala Val Ala
1 5 10 15

Ser Ala Ala Ser Asn Ile Thr Thr Ala Thr Val Thr Glu Glu Ser Thr
20 25 30

Thr Leu Val Thr Ile Thr Ser Cys Glu Asp His Val Cys Ser Glu Thr
35 40 45

Val Ser Pro Ala Leu Val Ser Thr Ala Thr Val Thr Val Asn Asp Val
50 55 60

Ile Thr
65

<210> 25
<211> 69
<212> PRT
<213> Saccharomyces cerevisiae

<400> 25

Tyr Thr Thr Trp Cys Pro Leu Pro Thr Thr Glu Ala Pro Lys Asn Thr
1 5 10 15

Thr Ser Pro Ala Pro Thr Glu Lys Pro Thr Glu Lys Pro Thr Glu Lys
20 25 30

Pro Thr Gln Gln Gly Ser Ser Thr Gln Thr Val Thr Ser Tyr Thr Gly
35 40 45

Ala Ala Val Lys Ala Leu Pro Ala Ala Gly Ala Leu Leu Ala Gly Ala
50 55 60

Ala Ala Leu Leu Leu
65

<210> 26
<211> 693
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(693)

<400> 26

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atg gaa atg act gat ttt gaa cta act agt aat tcg caa tcg aac ttg        48
Met Glu Met Thr Asp Phe Glu Leu Thr Ser Asn Ser Gln Ser Asn Leu
1               5                  10                  15

gct atc cct acc aac ttc aag tcg act ctg cct cca agg aaa aga gcc        96
Ala Ile Pro Thr Asn Phe Lys Ser Thr Leu Pro Pro Arg Lys Arg Ala
            20                  25                  30

aag aca aaa gag gaa aag gaa cag cga agg atc gag cgt att ttg aga       144
Lys Thr Lys Glu Glu Lys Glu Gln Arg Arg Ile Glu Arg Ile Leu Arg
        35                  40                  45

aac aga aga gct gct cac cag agc aga gag aaa aaa aga cta cat ctg       192
Asn Arg Arg Ala Ala His Gln Ser Arg Glu Lys Lys Arg Leu His Leu
    50                  55                  60

cag tat ctc gag aga aaa tgt tct ctt ttg gaa aat tta ctg aac agc       240
Gln Tyr Leu Glu Arg Lys Cys Ser Leu Leu Glu Asn Leu Leu Asn Ser
65                  70                  75                  80

gtc aac ctt gaa aaa ctg gct gac cac gaa gac gcg ttg act tgc agc       288
Val Asn Leu Glu Lys Leu Ala Asp His Glu Asp Ala Leu Thr Cys Ser
                85                  90                  95

cac gac gct ttt gtt gct tct ctt gac gag tac agg gat ttc cag agc       336
His Asp Ala Phe Val Ala Ser Leu Asp Glu Tyr Arg Asp Phe Gln Ser
            100                 105                 110

acg agg ggc gct tca ctg gac acc agg gcc agt tcg cac tcg tcg tct       384
Thr Arg Gly Ala Ser Leu Asp Thr Arg Ala Ser Ser His Ser Ser Ser
```

115 120 125

gat acg ttc aca cct tca cct ctg aac tgt aca atg gag cct gcg act 432
Asp Thr Phe Thr Pro Ser Pro Leu Asn Cys Thr Met Glu Pro Ala Thr
130 135 140

ttg tcg ccc aag agt atg cgc gat tcc gcg tcg gac caa gag act tca 480
Leu Ser Pro Lys Ser Met Arg Asp Ser Ala Ser Asp Gln Glu Thr Ser
145 150 155 160

tgg gag ctg cag atg ttt aag acg gaa aat gta cca gag tcg acg acg 528
Trp Glu Leu Gln Met Phe Lys Thr Glu Asn Val Pro Glu Ser Thr Thr
165 170 175

cta cct gcc gta gac aac aac aat ttg ttt gat gcg gtg gcc tcg ccg 576
Leu Pro Ala Val Asp Asn Asn Asn Leu Phe Asp Ala Val Ala Ser Pro
180 185 190

ttg gca gac cca ctc tgc gac gat ata gcg gga aac agt cta ccc ttt 624
Leu Ala Asp Pro Leu Cys Asp Asp Ile Ala Gly Asn Ser Leu Pro Phe
195 200 205

gac aat tca att gat ctt gac aat tgg cgt aat cca gcc gtg att acg 672
Asp Asn Ser Ile Asp Leu Asp Asn Trp Arg Asn Pro Ala Val Ile Thr
210 215 220

atg acc agg aaa cta cag tga 693
Met Thr Arg Lys Leu Gln
225 230

<210> 27
<211> 230
<212> PRT
<213> Saccharomyces cerevisiae

<400> 27

Met Glu Met Thr Asp Phe Glu Leu Thr Ser Asn Ser Gln Ser Asn Leu
1 5 10 15

Ala Ile Pro Thr Asn Phe Lys Ser Thr Leu Pro Pro Arg Lys Arg Ala
20 25 30

Lys Thr Lys Glu Glu Lys Glu Gln Arg Arg Ile Glu Arg Ile Leu Arg
35 40 45

Asn Arg Arg Ala Ala His Gln Ser Arg Glu Lys Lys Arg Leu His Leu
50 55 60

Gln Tyr Leu Glu Arg Lys Cys Ser Leu Leu Glu Asn Leu Leu Asn Ser
65 70 75 80

Val Asn Leu Glu Lys Leu Ala Asp His Glu Asp Ala Leu Thr Cys Ser
85 90 95

His Asp Ala Phe Val Ala Ser Leu Asp Glu Tyr Arg Asp Phe Gln Ser
100 105 110

Thr Arg Gly Ala Ser Leu Asp Thr Arg Ala Ser Ser His Ser Ser Ser
115 120 125

Asp Thr Phe Thr Pro Ser Pro Leu Asn Cys Thr Met Glu Pro Ala Thr
130 135 140

Leu Ser Pro Lys Ser Met Arg Asp Ser Ala Ser Asp Gln Glu Thr Ser
145 150 155 160

Trp Glu Leu Gln Met Phe Lys Thr Glu Asn Val Pro Glu Ser Thr Thr
165 170 175

Leu Pro Ala Val Asp Asn Asn Asn Leu Phe Asp Ala Val Ala Ser Pro
180 185 190

Leu Ala Asp Pro Leu Cys Asp Asp Ile Ala Gly Asn Ser Leu Pro Phe
195 200 205

Asp Asn Ser Ile Asp Leu Asp Asn Trp Arg Asn Pro Ala Val Ile Thr
210 215 220

Met Thr Arg Lys Leu Gln
225 230

<210> 28
<211> 1398
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(1398)

<400> 28
atg gcc cgc aat aga caa gcg tgc gac tgt tgt tgc att cgt cga gta 48
Met Ala Arg Asn Arg Gln Ala Cys Asp Cys Cys Cys Ile Arg Arg Val
1 5 10 15

aag tgt gat cgt aaa aaa cca tgt aaa tgt tgt ctt caa cac aat ctg 96
Lys Cys Asp Arg Lys Lys Pro Cys Lys Cys Cys Leu Gln His Asn Leu
20 25 30

caa tgt aca tat ctt cga cct ttg aag aaa aga ggt cca aaa ccc gtc 144
Gln Cys Thr Tyr Leu Arg Pro Leu Lys Lys Arg Gly Pro Lys Pro Val
35 40 45

aag gtg aga aat tta aag aaa gta gat gat gta cag gta ttt agt aaa 192
Lys Val Arg Asn Leu Lys Lys Val Asp Asp Val Gln Val Phe Ser Lys
50 55 60

agt agt agt ggt ggc ata atg aag gtt cca aag gca cta att gat cag 240

Ser Ser Ser Gly Gly Ile Met Lys Val Pro Lys Ala Leu Ile Asp Gln
65 70 75 80

tgt ctg cgg ctc tat aat gat aag ttg tat gtg atc tgg cct ttg ctg 288
Cys Leu Arg Leu Tyr Asn Asp Lys Leu Tyr Val Ile Trp Pro Leu Leu
85 90 95

tgt tat gat gat ctt tac gaa ctt tta gag aaa aga tat gac gaa acc 336
Cys Tyr Asp Asp Leu Tyr Glu Leu Leu Glu Lys Arg Tyr Asp Glu Thr
100 105 110

tgt gtg tat tgg ttc ctg gta tct ctt tct gcc gcc acg ctt agc gat 384
Cys Val Tyr Trp Phe Leu Val Ser Leu Ser Ala Ala Thr Leu Ser Asp
115 120 125

ttg cag act gaa att gag tcg gaa gga ggg gtt acc ttt act ggg ata 432
Leu Gln Thr Glu Ile Glu Ser Glu Gly Gly Val Thr Phe Thr Gly Ile
130 135 140

cag tta tcc agt ttc tgc atg tca tca cgc caa gaa ttt gac gat ttt 480
Gln Leu Ser Ser Phe Cys Met Ser Ser Arg Gln Glu Phe Asp Asp Phe
145 150 155 160

aac ggt agt gat ata ttc aag att atg acg tac tat tgt cta aac cgc 528
Asn Gly Ser Asp Ile Phe Lys Ile Met Thr Tyr Tyr Cys Leu Asn Arg
165 170 175

tgc tac gca cag atg tcc aac tca aga act tcg tat cgg ctt tct tgt 576
Cys Tyr Ala Gln Met Ser Asn Ser Arg Thr Ser Tyr Arg Leu Ser Cys
180 185 190

gaa gcc gtg ggg ctc att aag ttg gcg ggg ttc cat cgc gag gaa act 624
Glu Ala Val Gly Leu Ile Lys Leu Ala Gly Phe His Arg Glu Glu Thr
195 200 205

ttg aaa ctt ctt cct ttc gat gag cag cag ctt gga agg aaa gtt tat 672
Leu Lys Leu Leu Pro Phe Asp Glu Gln Gln Leu Gly Arg Lys Val Tyr
210 215 220

tat ttg ctt ctc tta acg gaa aga tac ttt tct gtg tat acg cat tgc 720
Tyr Leu Leu Leu Leu Thr Glu Arg Tyr Phe Ser Val Tyr Thr His Cys
225 230 235 240

gcc acg agc ctg gat acc acg att gct cca cca caa ccg gag aac gta 768
Ala Thr Ser Leu Asp Thr Thr Ile Ala Pro Pro Gln Pro Glu Asn Val
245 250 255

acg gac ccc cga cta tct ctc gac agc ttc ttg gag atg att agg gta 816
Thr Asp Pro Arg Leu Ser Leu Asp Ser Phe Leu Glu Met Ile Arg Val
260 265 270

ttt act gta ccg gga aaa tgc ttc ttt gat gct cta gct acc gac tct 864
Phe Thr Val Pro Gly Lys Cys Phe Phe Asp Ala Leu Ala Thr Asp Ser
275 280 285

gct aat gta acc tgt act gaa gac tcc ctt aaa aag ata tgg agg gaa 912
Ala Asn Val Thr Cys Thr Glu Asp Ser Leu Lys Lys Ile Trp Arg Glu
290 295 300

ctt cat acg gtg cca ctt gag ata gaa cca tgg tct tac ggc tat gta 960
Leu His Thr Val Pro Leu Glu Ile Glu Pro Trp Ser Tyr Gly Tyr Val
305 310 315 320

gac ata tct ttt tca cgg cat tgg att aga aca ctt gct tgg aag cta 1008
Asp Ile Ser Phe Ser Arg His Trp Ile Arg Thr Leu Ala Trp Lys Leu
325 330 335

gtg ctt caa ata agc ggt atg cga atc agt ttc ctt tca aat agc aag 1056
Val Leu Gln Ile Ser Gly Met Arg Ile Ser Phe Leu Ser Asn Ser Lys
340 345 350

aat acg cat att cca gta gaa att gct aga gac atg tta gaa gac aca 1104
Asn Thr His Ile Pro Val Glu Ile Ala Arg Asp Met Leu Glu Asp Thr
355 360 365

ttt tta atc cca aaa aat ctt tat gca gtt cac ggt cca ggg ata tca 1152
Phe Leu Ile Pro Lys Asn Leu Tyr Ala Val His Gly Pro Gly Ile Ser
370 375 380

gtg aaa gca cta gaa ata gcc gac gca ttg gta gat gtt gtg aat cag 1200
Val Lys Ala Leu Glu Ile Ala Asp Ala Leu Val Asp Val Val Asn Gln
385 390 395 400

tac gat caa aat gca gag tcg gag gct tgg aat ttt ttg ttc gat ata 1248

Tyr Asp Gln Asn Ala Glu Ser Glu Ala Trp Asn Phe Leu Phe Asp Ile
405 410 415

tcc aaa ttt gtc ttc tct ctt aag cat tgt gat agc aca tta gtt gat 1296
Ser Lys Phe Val Phe Ser Leu Lys His Cys Asp Ser Thr Leu Val Asp
420 425 430

aag ttt acg aca aag tgt cag tgt gcg ctt atc acg ctt cct ctt tct 1344
Lys Phe Thr Thr Lys Cys Gln Cys Ala Leu Ile Thr Leu Pro Leu Ser
435 440 445

aat ccg ctt gaa tcg aca gat ggt tct aaa gaa gat gta gat gcg ctt 1392
Asn Pro Leu Glu Ser Thr Asp Gly Ser Lys Glu Asp Val Asp Ala Leu
450 455 460

cct taa 1398
Pro
465

<210> 29
<211> 465
<212> PRT
<213> Saccharomyces cerevisiae

<400> 29

Met Ala Arg Asn Arg Gln Ala Cys Asp Cys Cys Cys Ile Arg Arg Val
1 5 10 15

Lys Cys Asp Arg Lys Lys Pro Cys Lys Cys Cys Leu Gln His Asn Leu
20 25 30

Gln Cys Thr Tyr Leu Arg Pro Leu Lys Lys Arg Gly Pro Lys Pro Val
35 40 45

Lys Val Arg Asn Leu Lys Lys Val Asp Asp Val Gln Val Phe Ser Lys
50 55 60

Ser Ser Ser Gly Gly Ile Met Lys Val Pro Lys Ala Leu Ile Asp Gln
65 70 75 80

Cys Leu Arg Leu Tyr Asn Asp Lys Leu Tyr Val Ile Trp Pro Leu Leu
85 90 95

Cys Tyr Asp Asp Leu Tyr Glu Leu Leu Glu Lys Arg Tyr Asp Glu Thr
100 105 110

Cys Val Tyr Trp Phe Leu Val Ser Leu Ser Ala Ala Thr Leu Ser Asp
115 120 125

Leu Gln Thr Glu Ile Glu Ser Glu Gly Gly Val Thr Phe Thr Gly Ile
130 135 140

Gln Leu Ser Ser Phe Cys Met Ser Ser Arg Gln Glu Phe Asp Asp Phe
145 150 155 160

Asn Gly Ser Asp Ile Phe Lys Ile Met Thr Tyr Tyr Cys Leu Asn Arg
165 170 175

Cys Tyr Ala Gln Met Ser Asn Ser Arg Thr Ser Tyr Arg Leu Ser Cys
180 185 190

Glu Ala Val Gly Leu Ile Lys Leu Ala Gly Phe His Arg Glu Glu Thr
195 200 205

Leu Lys Leu Leu Pro Phe Asp Glu Gln Gln Leu Gly Arg Lys Val Tyr
210 215 220

Tyr Leu Leu Leu Leu Thr Glu Arg Tyr Phe Ser Val Tyr Thr His Cys

225 230 235 240

Ala Thr Ser Leu Asp Thr Thr Ile Ala Pro Pro Gln Pro Glu Asn Val
245 250 255

Thr Asp Pro Arg Leu Ser Leu Asp Ser Phe Leu Glu Met Ile Arg Val
260 265 270

Phe Thr Val Pro Gly Lys Cys Phe Phe Asp Ala Leu Ala Thr Asp Ser
275 280 285

Ala Asn Val Thr Cys Thr Glu Asp Ser Leu Lys Lys Ile Trp Arg Glu
290 295 300

Leu His Thr Val Pro Leu Glu Ile Glu Pro Trp Ser Tyr Gly Tyr Val
305 310 315 320

Asp Ile Ser Phe Ser Arg His Trp Ile Arg Thr Leu Ala Trp Lys Leu
325 330 335

Val Leu Gln Ile Ser Gly Met Arg Ile Ser Phe Leu Ser Asn Ser Lys
340 345 350

Asn Thr His Ile Pro Val Glu Ile Ala Arg Asp Met Leu Glu Asp Thr
355 360 365

Phe Leu Ile Pro Lys Asn Leu Tyr Ala Val His Gly Pro Gly Ile Ser
370 375 380

Val Lys Ala Leu Glu Ile Ala Asp Ala Leu Val Asp Val Val Asn Gln
385 390 395 400

Tyr Asp Gln Asn Ala Glu Ser Glu Ala Trp Asn Phe Leu Phe Asp Ile
405 410 415

Ser Lys Phe Val Phe Ser Leu Lys His Cys Asp Ser Thr Leu Val Asp
420 425 430

Lys Phe Thr Thr Lys Cys Gln Cys Ala Leu Ile Thr Leu Pro Leu Ser
435 440 445

Asn Pro Leu Glu Ser Thr Asp Gly Ser Lys Glu Asp Val Asp Ala Leu
450 455 460

Pro
465

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<211> 2025
<212> DNA
<213> Saccharomyces cerevisiae

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act gat tct gtg aaa caa ttg ggt ccc ccc ttt gag cat gca agt aac 96
Thr Asp Ser Val Lys Gln Leu Gly Pro Pro Phe Glu His Ala Ser Asn
20 25 30

aat gac aat gcc ggc gat act gaa gct gag tca ctg caa gaa gtg ccc 144

Asn Asp Asn Ala Gly Asp Thr Glu Ala Glu Ser Leu Gln Glu Val Pro
35 40 45

cta aat aca gag acc aac gac gta cgc aag aat tta gta gtg att aca 192
Leu Asn Thr Glu Thr Asn Asp Val Arg Lys Asn Leu Val Val Ile Thr
50 55 60

aac caa agt gcc gcc gat gaa cac cct aca gag atc aag cac gat caa 240
Asn Gln Ser Ala Ala Asp Glu His Pro Thr Glu Ile Lys His Asp Gln
65 70 75 80

tca agg act tct tcg acg tcc tcg ttc ttc agt gga atg atc tct tcg 288
Ser Arg Thr Ser Ser Thr Ser Ser Phe Phe Ser Gly Met Ile Ser Ser
85 90 95

ttt aag tca aac gtg cca tcc cca gtt tct aga tca act acg cca act 336
Phe Lys Ser Asn Val Pro Ser Pro Val Ser Arg Ser Thr Thr Pro Thr
100 105 110

tcg cca gtt tcg caa cca agc att ata tca cat aga agg gag cct tcc 384
Ser Pro Val Ser Gln Pro Ser Ile Ile Ser His Arg Arg Glu Pro Ser
115 120 125

atg ggg tcc aaa aga aga tca agc cgc cgt atc agt aat gcc aca att 432
Met Gly Ser Lys Arg Arg Ser Ser Arg Arg Ile Ser Asn Ala Thr Ile
130 135 140

gct gaa ata ggc tct ccc ttg caa cag gtg gaa aag cct gat gag gtc 480
Ala Glu Ile Gly Ser Pro Leu Gln Gln Val Glu Lys Pro Asp Glu Val
145 150 155 160

aag aca aga ctc act cct tcc caa atg aaa gaa gac aat tac gat cat 528
Lys Thr Arg Leu Thr Pro Ser Gln Met Lys Glu Asp Asn Tyr Asp His
165 170 175

aga cga ttc gtg gaa gaa cgt tac atg gac aca cct tat cac tat gcg 576
Arg Arg Phe Val Glu Glu Arg Tyr Met Asp Thr Pro Tyr His Tyr Ala
180 185 190

tct gag caa aga aat aaa gac ttt cat gag aca ttc aag tcc gtt cct 624
Ser Glu Gln Arg Asn Lys Asp Phe His Glu Thr Phe Lys Ser Val Pro
195 200 205

aaa gat gac aga cta ctg gat gat ttt aat tgt ggg ctg aat aga gag 672
Lys Asp Asp Arg Leu Leu Asp Asp Phe Asn Cys Gly Leu Asn Arg Glu
210 215 220

ctg ctt tac cag ggg aaa cta tac ata aca gaa acg cat ctc tgc ttc 720
Leu Leu Tyr Gln Gly Lys Leu Tyr Ile Thr Glu Thr His Leu Cys Phe
225 230 235 240

aac tcc aat gtt ctt ggt tgg att gct aaa gta ctg att gcg ttc gaa 768
Asn Ser Asn Val Leu Gly Trp Ile Ala Lys Val Leu Ile Ala Phe Glu
245 250 255

gat gtc acg ttt atg gaa aaa act tct gct gct ggg ttg ttc ccc agc 816
Asp Val Thr Phe Met Glu Lys Thr Ser Ala Ala Gly Leu Phe Pro Ser
260 265 270

gca ata tcc atc gaa aca aag atg ggc aaa act ctc ttt aat ggt ttt 864
Ala Ile Ser Ile Glu Thr Lys Met Gly Lys Thr Leu Phe Asn Gly Phe
275 280 285

ata tcc agg gat gct gca ttt gga tta atg aaa gaa gtg tgg tca aga 912
Ile Ser Arg Asp Ala Ala Phe Gly Leu Met Lys Glu Val Trp Ser Arg
290 295 300

acc ttg ttg cag aag gac atg gcc agc gaa aac atc aat act aaa gca 960
Thr Leu Leu Gln Lys Asp Met Ala Ser Glu Asn Ile Asn Thr Lys Ala
305 310 315 320

gaa aag tca gga aat ggc aaa gag att gat gat gca ata aac tcc atc 1008
Glu Lys Ser Gly Asn Gly Lys Glu Ile Asp Asp Ala Ile Asn Ser Ile
325 330 335

gat gag gaa aac aat gat aaa gac gct aat gat aat gac act aat gaa 1056
Asp Glu Glu Asn Asn Asp Lys Asp Ala Asn Asp Asn Asp Thr Asn Glu
340 345 350

aat gac gat gaa aat atc tct aca aat gag act acc ccc aat agt acg 1104
Asn Asp Asp Glu Asn Ile Ser Thr Asn Glu Thr Thr Pro Asn Ser Thr
355 360 365

agt tcc tcg ccg gat aaa gaa aaa gag aaa gcg tat aaa ctg cgt gcc 1152

Ser Ser Ser Pro Asp Lys Glu Lys Glu Lys Ala Tyr Lys Leu Arg Ala
370 375 380

gat tcc tcg tat cag tat gat ggt cca ata tat cat cat tca aca agc 1200
Asp Ser Ser Tyr Gln Tyr Asp Gly Pro Ile Tyr His His Ser Thr Ser
385 390 395 400

ttt ccg gct gaa cct atg gcc aat aac gag ttt gtt ctc aag gag tta 1248
Phe Pro Ala Glu Pro Met Ala Asn Asn Glu Phe Val Leu Lys Glu Leu
405 410 415

cca ttc gat tgt gca cct ggt ata ctt ttt gag atc atg ttc aac tca 1296
Pro Phe Asp Cys Ala Pro Gly Ile Leu Phe Glu Ile Met Phe Asn Ser
420 425 430

gag caa aac gaa ttt ctt cta gat ttt tta cgg ggt caa gaa ggt tca 1344
Glu Gln Asn Glu Phe Leu Leu Asp Phe Leu Arg Gly Gln Glu Gly Ser
435 440 445

caa att acc act att cca aat ttc acg agc att gac gga tct tcc atg 1392
Gln Ile Thr Thr Ile Pro Asn Phe Thr Ser Ile Asp Gly Ser Ser Met
450 455 460

act ttg aag cgt gag tat tca tac gag aaa gca ttg cac ttt cct gcg 1440
Thr Leu Lys Arg Glu Tyr Ser Tyr Glu Lys Ala Leu His Phe Pro Ala
465 470 475 480

ggg ccc aag tcc acg aca tgt tat gtt gct gag gta ata aag aga aaa 1488
Gly Pro Lys Ser Thr Thr Cys Tyr Val Ala Glu Val Ile Lys Arg Lys
485 490 495

gat cct gat act tac tat gag gtt atc agt agc ata cgc act ccg aac 1536
Asp Pro Asp Thr Tyr Tyr Glu Val Ile Ser Ser Ile Arg Thr Pro Asn
500 505 510

gtg ccc agt ggt ggt agt ttc tca act aag aca agg tat cta atc cgt 1584
Val Pro Ser Gly Gly Ser Phe Ser Thr Lys Thr Arg Tyr Leu Ile Arg
515 520 525

tgg aat gac gaa ata acg tgt ctg tta cgg gta tcc ttt tgg gtg gaa 1632
Trp Asn Asp Glu Ile Thr Cys Leu Leu Arg Val Ser Phe Trp Val Glu
530 535 540

tgg act ggt tcc agt tgg atc aaa ggt atg gtt gaa aat gga tgc aag 1680
Trp Thr Gly Ser Ser Trp Ile Lys Gly Met Val Glu Asn Gly Cys Lys
545 550 555 560

aat ggt caa ttg gag gct gcg caa tta atg gag cgt att ctt tcc aag 1728
Asn Gly Gln Leu Glu Ala Ala Gln Leu Met Glu Arg Ile Leu Ser Lys
565 570 575

ttc atc aag aac aat gtc gaa gag tgc caa att act atc agc aag gag 1776
Phe Ile Lys Asn Asn Val Glu Glu Cys Gln Ile Thr Ile Ser Lys Glu
580 585 590

gaa gag gag caa gat gat aaa gaa gta aaa aat aag ttg aaa gag gtt 1824
Glu Glu Glu Gln Asp Asp Lys Glu Val Lys Asn Lys Leu Lys Glu Val
595 600 605

gac ctt gaa caa cca aga gaa gcg gtt gtt acg gct ccc gca att gca 1872
Asp Leu Glu Gln Pro Arg Glu Ala Val Val Thr Ala Pro Ala Ile Ala
610 615 620

gag cag caa ggt ctc aag gtc acc atg gaa aca tgg ttg ttc tta tac 1920
Glu Gln Gln Gly Leu Lys Val Thr Met Glu Thr Trp Leu Phe Leu Tyr
625 630 635 640

ttg att gtg gtc gtt ttg cta ttg ttt aat ctg ttc tac ata cgt tca 1968
Leu Ile Val Val Val Leu Leu Leu Phe Asn Leu Phe Tyr Ile Arg Ser
645 650 655

att gct gtc tca tta cat caa ctg gtg aag ctg caa ttg gta gaa ctg 2016
Ile Ala Val Ser Leu His Gln Leu Val Lys Leu Gln Leu Val Glu Leu
660 665 670

aag ttg tga 2025
Lys Leu

<210> 31
<211> 674
<212> PRT
<213> Saccharomyces cerevisiae

<400> 31

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20 25 30

Asn Asp Asn Ala Gly Asp Thr Glu Ala Glu Ser Leu Gln Glu Val Pro
35 40 45

Leu Asn Thr Glu Thr Asn Asp Val Arg Lys Asn Leu Val Val Ile Thr
50 55 60

Asn Gln Ser Ala Ala Asp Glu His Pro Thr Glu Ile Lys His Asp Gln
65 70 75 80

Ser Arg Thr Ser Ser Thr Ser Ser Phe Phe Ser Gly Met Ile Ser Ser
85 90 95

Phe Lys Ser Asn Val Pro Ser Pro Val Ser Arg Ser Thr Thr Pro Thr
100 105 110

Ser Pro Val Ser Gln Pro Ser Ile Ile Ser His Arg Arg Glu Pro Ser
115 120 125

Met Gly Ser Lys Arg Arg Ser Ser Arg Arg Ile Ser Asn Ala Thr Ile
130 135 140

Ala Glu Ile Gly Ser Pro Leu Gln Gln Val Glu Lys Pro Asp Glu Val
145 150 155 160

Lys Thr Arg Leu Thr Pro Ser Gln Met Lys Glu Asp Asn Tyr Asp His
165 170 175

Arg Arg Phe Val Glu Glu Arg Tyr Met Asp Thr Pro Tyr His Tyr Ala
180 185 190

Ser Glu Gln Arg Asn Lys Asp Phe His Glu Thr Phe Lys Ser Val Pro
195 200 205

Lys Asp Asp Arg Leu Leu Asp Asp Phe Asn Cys Gly Leu Asn Arg Glu
210 215 220

Leu Leu Tyr Gln Gly Lys Leu Tyr Ile Thr Glu Thr His Leu Cys Phe
225 230 235 240

Asn Ser Asn Val Leu Gly Trp Ile Ala Lys Val Leu Ile Ala Phe Glu
245 250 255

Asp Val Thr Phe Met Glu Lys Thr Ser Ala Ala Gly Leu Phe Pro Ser
260 265 270

Ala Ile Ser Ile Glu Thr Lys Met Gly Lys Thr Leu Phe Asn Gly Phe
275 280 285

Ile Ser Arg Asp Ala Ala Phe Gly Leu Met Lys Glu Val Trp Ser Arg
290 295 300

Thr Leu Leu Gln Lys Asp Met Ala Ser Glu Asn Ile Asn Thr Lys Ala
305 310 315 320

Glu Lys Ser Gly Asn Gly Lys Glu Ile Asp Asp Ala Ile Asn Ser Ile
325 330 335

Asp Glu Glu Asn Asn Asp Lys Asp Ala Asn Asp Asn Asp Thr Asn Glu
340 345 350

Asn Asp Asp Glu Asn Ile Ser Thr Asn Glu Thr Thr Pro Asn Ser Thr
355 360 365

Ser Ser Ser Pro Asp Lys Glu Lys Glu Lys Ala Tyr Lys Leu Arg Ala
370 375 380

Asp Ser Ser Tyr Gln Tyr Asp Gly Pro Ile Tyr His His Ser Thr Ser
385 390 395 400

Phe Pro Ala Glu Pro Met Ala Asn Asn Glu Phe Val Leu Lys Glu Leu
405 410 415

Pro Phe Asp Cys Ala Pro Gly Ile Leu Phe Glu Ile Met Phe Asn Ser
420 425 430

Glu Gln Asn Glu Phe Leu Leu Asp Phe Leu Arg Gly Gln Glu Gly Ser
435 440 445

Gln Ile Thr Thr Ile Pro Asn Phe Thr Ser Ile Asp Gly Ser Ser Met
450 455 460

Thr Leu Lys Arg Glu Tyr Ser Tyr Glu Lys Ala Leu His Phe Pro Ala
465 470 475 480

Gly Pro Lys Ser Thr Thr Cys Tyr Val Ala Glu Val Ile Lys Arg Lys
485 490 495

Asp Pro Asp Thr Tyr Tyr Glu Val Ile Ser Ser Ile Arg Thr Pro Asn
500 505 510

Val Pro Ser Gly Gly Ser Phe Ser Thr Lys Thr Arg Tyr Leu Ile Arg
515 520 525

Trp Asn Asp Glu Ile Thr Cys Leu Leu Arg Val Ser Phe Trp Val Glu
530 535 540

Trp Thr Gly Ser Ser Trp Ile Lys Gly Met Val Glu Asn Gly Cys Lys
545 550 555 560

Asn Gly Gln Leu Glu Ala Ala Gln Leu Met Glu Arg Ile Leu Ser Lys
565 570 575

Phe Ile Lys Asn Asn Val Glu Glu Cys Gln Ile Thr Ile Ser Lys Glu
580 585 590

Glu Glu Glu Gln Asp Asp Lys Glu Val Lys Asn Lys Leu Lys Glu Val
595 600 605

Asp Leu Glu Gln Pro Arg Glu Ala Val Val Thr Ala Pro Ala Ile Ala
610 615 620

Glu Gln Gln Gly Leu Lys Val Thr Met Glu Thr Trp Leu Phe Leu Tyr
625 630 635 640

Leu Ile Val Val Val Leu Leu Leu Phe Asn Leu Phe Tyr Ile Arg Ser
645 650 655

Ile Ala Val Ser Leu His Gln Leu Val Lys Leu Gln Leu Val Glu Leu
660 665 670

Lys Leu

<210> 32
<211> 1185
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<213> Saccharomyces cerevisiae

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<221> CDS
<222> (1)..(1185)

<400> 32

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1               5                  10                  15

cca ggt aat aac ttg aaa gcc ggt att gtc ggt ttg gcc aat gtt ggt        96
Pro Gly Asn Asn Leu Lys Ala Gly Ile Val Gly Leu Ala Asn Val Gly
            20                  25                  30

aag tct acc ttt ttc caa gcc atc act aga tgt cca ttg ggt aac cca       144
Lys Ser Thr Phe Phe Gln Ala Ile Thr Arg Cys Pro Leu Gly Asn Pro
        35                  40                  45

gct aac tat cca ttc gct acc att gat cca gaa gaa gcc cgt gtt att       192
Ala Asn Tyr Pro Phe Ala Thr Ile Asp Pro Glu Glu Ala Arg Val Ile
    50                  55                  60

gtc cca tct cca aga ttt gat aag ttg tgt gaa atc tac aag aag aca       240
Val Pro Ser Pro Arg Phe Asp Lys Leu Cys Glu Ile Tyr Lys Lys Thr
65                  70                  75                  80

gct tcg gaa gtt cca gct cat ttg acc gtt tac gat att gct ggt ttg       288
Ala Ser Glu Val Pro Ala His Leu Thr Val Tyr Asp Ile Ala Gly Leu
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85 90 95

act aag ggt gcc tct gct ggt gaa ggt ttg ggt aat gct ttc ttg tct 336
Thr Lys Gly Ala Ser Ala Gly Glu Gly Leu Gly Asn Ala Phe Leu Ser
100 105 110

cac atc aga tca gtc gat tct atc tac caa gtc gtt cgt tgt ttc gat 384
His Ile Arg Ser Val Asp Ser Ile Tyr Gln Val Val Arg Cys Phe Asp
115 120 125

gat gct gaa att atc cac gtt gag ggt gac gtt gat cca gtt cgt gat 432
Asp Ala Glu Ile Ile His Val Glu Gly Asp Val Asp Pro Val Arg Asp
130 135 140

tta gaa att att aac caa gaa cta aga ttg aaa gat att gaa ttc gca 480
Leu Glu Ile Ile Asn Gln Glu Leu Arg Leu Lys Asp Ile Glu Phe Ala
145 150 155 160

caa aag gct ttg gaa ggt gct gaa aag att gcc aaa aga ggt ggt caa 528
Gln Lys Ala Leu Glu Gly Ala Glu Lys Ile Ala Lys Arg Gly Gly Gln
165 170 175

tct ttg gaa gtc aaa caa aag aag gaa gaa atg gat ttg att acg aaa 576
Ser Leu Glu Val Lys Gln Lys Lys Glu Glu Met Asp Leu Ile Thr Lys
180 185 190

atc att aaa ttg cta gag agt ggt caa aga gtt gct aat cac tcc tgg 624
Ile Ile Lys Leu Leu Glu Ser Gly Gln Arg Val Ala Asn His Ser Trp
195 200 205

act tca aaa gaa gtt gaa att atc aac tcc atg ttc ttg ttg act gct 672
Thr Ser Lys Glu Val Glu Ile Ile Asn Ser Met Phe Leu Leu Thr Ala
210 215 220

aag cca tgt atc tat ttg att aat tta tct gaa aga gat tac atc aga 720
Lys Pro Cys Ile Tyr Leu Ile Asn Leu Ser Glu Arg Asp Tyr Ile Arg
225 230 235 240

aag aaa aac aag cat ctg cta aga atc aag gaa tgg gta gac aag tac 768
Lys Lys Asn Lys His Leu Leu Arg Ile Lys Glu Trp Val Asp Lys Tyr
245 250 255

tct cca ggt gac ttg atc att cca ttc agt gtt tct cta gaa gaa aga 816
Ser Pro Gly Asp Leu Ile Ile Pro Phe Ser Val Ser Leu Glu Glu Arg
260 265 270

cta tct cat atg tcc cca gaa gat gct gaa gaa gaa ttg aag aaa ctg 864
Leu Ser His Met Ser Pro Glu Asp Ala Glu Glu Glu Leu Lys Lys Leu
275 280 285

cag aca ata tct gcc ttg cca aag att atc act acc atg aga caa aag 912
Gln Thr Ile Ser Ala Leu Pro Lys Ile Ile Thr Thr Met Arg Gln Lys
290 295 300

tta gat ttg att tcc ttt ttc acc tgc ggt cca gat gaa gtt cgt gaa 960
Leu Asp Leu Ile Ser Phe Phe Thr Cys Gly Pro Asp Glu Val Arg Glu
305 310 315 320

tgg acc atc aga aga ggt act aaa gct cca caa gct gct ggt gtt att 1008
Trp Thr Ile Arg Arg Gly Thr Lys Ala Pro Gln Ala Ala Gly Val Ile
325 330 335

cat aac gat tta atg aat acc ttt att ttg gct caa gtt atg aaa tgt 1056
His Asn Asp Leu Met Asn Thr Phe Ile Leu Ala Gln Val Met Lys Cys
340 345 350

gaa gat gtc ttc gaa tat aag gac gat tct gcc atc aag gcc gct ggt 1104
Glu Asp Val Phe Glu Tyr Lys Asp Asp Ser Ala Ile Lys Ala Ala Gly
355 360 365

aag ttg atg caa aag ggt aaa gac tat gtc gtt gaa gac ggt gat atc 1152
Lys Leu Met Gln Lys Gly Lys Asp Tyr Val Val Glu Asp Gly Asp Ile
370 375 380

att tac ttc aga gct ggt gct ggt aag aat tga 1185
Ile Tyr Phe Arg Ala Gly Ala Gly Lys Asn
385 390

<210> 33
<211> 394
<212> PRT
<213> Saccharomyces cerevisiae

<400> 33

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Pro Gly Asn Asn Leu Lys Ala Gly Ile Val Gly Leu Ala Asn Val Gly
20 25 30

Lys Ser Thr Phe Phe Gln Ala Ile Thr Arg Cys Pro Leu Gly Asn Pro
35 40 45

Ala Asn Tyr Pro Phe Ala Thr Ile Asp Pro Glu Glu Ala Arg Val Ile
50 55 60

Val Pro Ser Pro Arg Phe Asp Lys Leu Cys Glu Ile Tyr Lys Lys Thr
65 70 75 80

Ala Ser Glu Val Pro Ala His Leu Thr Val Tyr Asp Ile Ala Gly Leu
85 90 95

Thr Lys Gly Ala Ser Ala Gly Glu Gly Leu Gly Asn Ala Phe Leu Ser
100 105 110

His Ile Arg Ser Val Asp Ser Ile Tyr Gln Val Val Arg Cys Phe Asp
115 120 125

Asp Ala Glu Ile Ile His Val Glu Gly Asp Val Asp Pro Val Arg Asp
130 135 140

Leu Glu Ile Ile Asn Gln Glu Leu Arg Leu Lys Asp Ile Glu Phe Ala
145 150 155 160

Gln Lys Ala Leu Glu Gly Ala Glu Lys Ile Ala Lys Arg Gly Gly Gln
165 170 175

Ser Leu Glu Val Lys Gln Lys Lys Glu Glu Met Asp Leu Ile Thr Lys
180 185 190

Ile Ile Lys Leu Leu Glu Ser Gly Gln Arg Val Ala Asn His Ser Trp
195 200 205

Thr Ser Lys Glu Val Glu Ile Ile Asn Ser Met Phe Leu Leu Thr Ala
210 215 220

Lys Pro Cys Ile Tyr Leu Ile Asn Leu Ser Glu Arg Asp Tyr Ile Arg
225 230 235 240

Lys Lys Asn Lys His Leu Leu Arg Ile Lys Glu Trp Val Asp Lys Tyr
245 250 255

Ser Pro Gly Asp Leu Ile Ile Pro Phe Ser Val Ser Leu Glu Glu Arg
260 265 270

Leu Ser His Met Ser Pro Glu Asp Ala Glu Glu Glu Leu Lys Lys Leu
275 280 285

Gln Thr Ile Ser Ala Leu Pro Lys Ile Ile Thr Thr Met Arg Gln Lys
290 295 300

Leu Asp Leu Ile Ser Phe Phe Thr Cys Gly Pro Asp Glu Val Arg Glu
305 310 315 320

Trp Thr Ile Arg Arg Gly Thr Lys Ala Pro Gln Ala Ala Gly Val Ile

325 330 335

His Asn Asp Leu Met Asn Thr Phe Ile Leu Ala Gln Val Met Lys Cys
340 345 350

Glu Asp Val Phe Glu Tyr Lys Asp Asp Ser Ala Ile Lys Ala Ala Gly
355 360 365

Lys Leu Met Gln Lys Gly Lys Asp Tyr Val Val Glu Asp Gly Asp Ile
370 375 380

Ile Tyr Phe Arg Ala Gly Ala Gly Lys Asn
385 390

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<211> 735
<212> DNA
<213> Saccharomyces cerevisiae

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<221> CDS
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act aca aac gct gct aat aaa ctc att gtc tta tat ttt aaa gct caa 96
Thr Thr Asn Ala Ala Asn Lys Leu Ile Val Leu Tyr Phe Lys Ala Gln
20 25 30

tgg gct gat cct tgc aaa act atg agc cag gtg cta gaa gct gtt agt 144
Trp Ala Asp Pro Cys Lys Thr Met Ser Gln Val Leu Glu Ala Val Ser
35 40 45

gaa aaa gtt agg caa gag gat gtc cgg ttt tta tca ata gat gca gac 192
Glu Lys Val Arg Gln Glu Asp Val Arg Phe Leu Ser Ile Asp Ala Asp
50 55 60

gaa cat cca gaa ata tca gac ctt ttt gag att gca gcc gta cca tac 240
Glu His Pro Glu Ile Ser Asp Leu Phe Glu Ile Ala Ala Val Pro Tyr
65 70 75 80

ttc gtc ttc att caa aat ggt act att gta aaa gaa ata tca gcc gca 288
Phe Val Phe Ile Gln Asn Gly Thr Ile Val Lys Glu Ile Ser Ala Ala
85 90 95

gat cct aag gag ttt gtg aaa agc tta gaa att ctt tcg aat gct tct 336
Asp Pro Lys Glu Phe Val Lys Ser Leu Glu Ile Leu Ser Asn Ala Ser
100 105 110

gcc tca cta gcg aac aat gcc aag ggt cct aaa tct acg tct gat gag 384
Ala Ser Leu Ala Asn Asn Ala Lys Gly Pro Lys Ser Thr Ser Asp Glu
115 120 125

gaa agc agc ggg tct tcc gat gat gaa gag gac gaa act gaa gaa gaa 432
Glu Ser Ser Gly Ser Ser Asp Asp Glu Glu Asp Glu Thr Glu Glu Glu
130 135 140

ata aat gct agg ctg gtg aag cta gta caa gct gca cct gtg atg cta 480
Ile Asn Ala Arg Leu Val Lys Leu Val Gln Ala Ala Pro Val Met Leu
145 150 155 160

ttc atg aaa gga agc cca tca gaa cct aaa tgc gga ttt tct aga cag 528
Phe Met Lys Gly Ser Pro Ser Glu Pro Lys Cys Gly Phe Ser Arg Gln
165 170 175

tta gtt ggt atc ctc aga gaa cac caa ata agg ttc gga ttt ttt gat 576
Leu Val Gly Ile Leu Arg Glu His Gln Ile Arg Phe Gly Phe Phe Asp
180 185 190

ata tta aga gac gaa aac gtt aga caa agc ttg aag aag ttt tct gat 624
Ile Leu Arg Asp Glu Asn Val Arg Gln Ser Leu Lys Lys Phe Ser Asp
195 200 205

tgg cct act ttt cct cag tta tat atc aat ggg gag ttc cag gga ggt 672
Trp Pro Thr Phe Pro Gln Leu Tyr Ile Asn Gly Glu Phe Gln Gly Gly

210 215 220

ttg gat att atc aag gaa tct ata gaa gaa gat cct gaa tat ttc caa 720
Leu Asp Ile Ile Lys Glu Ser Ile Glu Glu Asp Pro Glu Tyr Phe Gln
225 230 235 240

cat gct cta cag taa 735
His Ala Leu Gln

<210> 35
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<212> PRT
<213> Saccharomyces cerevisiae

<400> 35

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Trp Ala Asp Pro Cys Lys Thr Met Ser Gln Val Leu Glu Ala Val Ser
35 40 45

Glu Lys Val Arg Gln Glu Asp Val Arg Phe Leu Ser Ile Asp Ala Asp
50 55 60

Glu His Pro Glu Ile Ser Asp Leu Phe Glu Ile Ala Ala Val Pro Tyr
65 70 75 80

Phe Val Phe Ile Gln Asn Gly Thr Ile Val Lys Glu Ile Ser Ala Ala
85 90 95

Asp Pro Lys Glu Phe Val Lys Ser Leu Glu Ile Leu Ser Asn Ala Ser
100 105 110

Ala Ser Leu Ala Asn Asn Ala Lys Gly Pro Lys Ser Thr Ser Asp Glu
115 120 125

Glu Ser Ser Gly Ser Ser Asp Asp Glu Glu Asp Glu Thr Glu Glu Glu
130 135 140

Ile Asn Ala Arg Leu Val Lys Leu Val Gln Ala Ala Pro Val Met Leu
145 150 155 160

Phe Met Lys Gly Ser Pro Ser Glu Pro Lys Cys Gly Phe Ser Arg Gln
165 170 175

Leu Val Gly Ile Leu Arg Glu His Gln Ile Arg Phe Gly Phe Phe Asp
180 185 190

Ile Leu Arg Asp Glu Asn Val Arg Gln Ser Leu Lys Lys Phe Ser Asp
195 200 205

Trp Pro Thr Phe Pro Gln Leu Tyr Ile Asn Gly Glu Phe Gln Gly Gly
210 215 220

Leu Asp Ile Ile Lys Glu Ser Ile Glu Glu Asp Pro Glu Tyr Phe Gln
225 230 235 240

His Ala Leu Gln

<210> 36

<211> 351
<212> DNA
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<220>
<221> CDS
<222> (1)..(351)

<400> 36

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atg cac att ctt ttc ttg ttt att ttc cac tgt ttg gca ttc aaa gac      48
Met His Ile Leu Phe Leu Phe Ile Phe His Cys Leu Ala Phe Lys Asp
1               5                  10                  15

ttg att ttt ttt aag caa tac gta cca ttt gca gcg gcg gga gga tat      96
Leu Ile Phe Phe Lys Gln Tyr Val Pro Phe Ala Ala Ala Gly Gly Tyr
            20                  25                  30

ccc ata tcg ttt cta ttc atc aaa gtt ctg acc gcc tca acg aat tta     144
Pro Ile Ser Phe Leu Phe Ile Lys Val Leu Thr Ala Ser Thr Asn Leu
        35                  40                  45

cta ctt tct tct tcc tct gga ggg tcc tgg aat aag tta tcc aaa gag     192
Leu Leu Ser Ser Ser Ser Gly Gly Ser Trp Asn Lys Leu Ser Lys Glu
    50                  55                  60

tcg caa tta ctc aaa gtc att ctc aca cac ttt ctt gtt cct att ttt     240
Ser Gln Leu Leu Lys Val Ile Leu Thr His Phe Leu Val Pro Ile Phe
65                  70                  75                  80

ttt ttc tta ttc caa tat att att tta tca gaa gac aga cag caa gaa     288
Phe Phe Leu Phe Gln Tyr Ile Ile Leu Ser Glu Asp Arg Gln Gln Glu
                85                  90                  95

cga cag cct aag ttt cga gac aac gct aaa ttt gac gga cat gcg aag     336
Arg Gln Pro Lys Phe Arg Asp Asn Ala Lys Phe Asp Gly His Ala Lys
            100                 105                 110

aca tgc cat ata taa                                                351
Thr Cys His Ile
        115
```

<210> 37
<211> 116
<212> PRT
<213> Saccharomyces cerevisiae

<400> 37

Met His Ile Leu Phe Leu Phe Ile Phe His Cys Leu Ala Phe Lys Asp
1 5 10 15

Leu Ile Phe Phe Lys Gln Tyr Val Pro Phe Ala Ala Ala Gly Gly Tyr
20 25 30

Pro Ile Ser Phe Leu Phe Ile Lys Val Leu Thr Ala Ser Thr Asn Leu
35 40 45

Leu Leu Ser Ser Ser Ser Gly Gly Ser Trp Asn Lys Leu Ser Lys Glu
50 55 60

Ser Gln Leu Leu Lys Val Ile Leu Thr His Phe Leu Val Pro Ile Phe
65 70 75 80

Phe Phe Leu Phe Gln Tyr Ile Ile Leu Ser Glu Asp Arg Gln Gln Glu
85 90 95

Arg Gln Pro Lys Phe Arg Asp Asn Ala Lys Phe Asp Gly His Ala Lys
100 105 110

Thr Cys His Ile
115

<210> 38

<211> 900
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(900)

<400> 38

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atg tct acc ttt tct gct tct gat ttc aac tca gaa aga tat tca tct        48
Met Ser Thr Phe Ser Ala Ser Asp Phe Asn Ser Glu Arg Tyr Ser Ser
1               5                  10                  15

tca aga cct tct tat ccc tcc gat ttt tac aag atg att gat gaa tac        96
Ser Arg Pro Ser Tyr Pro Ser Asp Phe Tyr Lys Met Ile Asp Glu Tyr
            20                  25                  30

cac gac gga gaa agg aaa tta ctc gta gat gtt ggc tgt gga cca ggt       144
His Asp Gly Glu Arg Lys Leu Leu Val Asp Val Gly Cys Gly Pro Gly
        35                  40                  45

act gcc act tta caa atg gct cag gag tta aaa cca ttc gaa caa att       192
Thr Ala Thr Leu Gln Met Ala Gln Glu Leu Lys Pro Phe Glu Gln Ile
    50                  55                  60

atc gga agc gat ctc tcc gct acc atg att aag act gca gaa gta ata       240
Ile Gly Ser Asp Leu Ser Ala Thr Met Ile Lys Thr Ala Glu Val Ile
65                  70                  75                  80

aag gaa gga agt cct gat aca tac aaa aac gtt tca ttt aag att tct       288
Lys Glu Gly Ser Pro Asp Thr Tyr Lys Asn Val Ser Phe Lys Ile Ser
                85                  90                  95

tca agt gat gat ttt aaa ttc cta ggc gcg gat tca gta gac aaa cag       336
Ser Ser Asp Asp Phe Lys Phe Leu Gly Ala Asp Ser Val Asp Lys Gln
            100                 105                 110

aaa att gat atg att acc gca gta gaa tgt gct cat tgg ttc gat ttc       384
Lys Ile Asp Met Ile Thr Ala Val Glu Cys Ala His Trp Phe Asp Phe
        115                 120                 125
```

gaa aaa ttt cag cga tct gct tat gcc aat ttg aga aaa gat ggt act 432
Glu Lys Phe Gln Arg Ser Ala Tyr Ala Asn Leu Arg Lys Asp Gly Thr
130 135 140

atc gct att tgg ggt tat gcg gac cca att ttc ccg gac tac cct gaa 480
Ile Ala Ile Trp Gly Tyr Ala Asp Pro Ile Phe Pro Asp Tyr Pro Glu
145 150 155 160

ttt gat gat ctg atg att gaa gtt cct tac ggg aag caa gga ctg gga 528
Phe Asp Asp Leu Met Ile Glu Val Pro Tyr Gly Lys Gln Gly Leu Gly
165 170 175

ccc tat tgg gaa caa ccg ggg aga tct cgc ctt cgt aat atg ctg aaa 576
Pro Tyr Trp Glu Gln Pro Gly Arg Ser Arg Leu Arg Asn Met Leu Lys
180 185 190

gac tct cac tta gac cca gaa ctt ttc cat gat ata caa gtt tca tat 624
Asp Ser His Leu Asp Pro Glu Leu Phe His Asp Ile Gln Val Ser Tyr
195 200 205

ttt tgt gca gaa gat gtg aga gac aaa gta aaa ctc cac cag cat aca 672
Phe Cys Ala Glu Asp Val Arg Asp Lys Val Lys Leu His Gln His Thr
210 215 220

aag aag cca ttg cta atc aga aag cag gtc acc cta gtg gag ttt gca 720
Lys Lys Pro Leu Leu Ile Arg Lys Gln Val Thr Leu Val Glu Phe Ala
225 230 235 240

gat tat gtc aga acc tgg agc gct tac cat cag tgg aag cag gat cca 768
Asp Tyr Val Arg Thr Trp Ser Ala Tyr His Gln Trp Lys Gln Asp Pro
245 250 255

aag aac aaa gat aaa gaa gat gta gca gat tgg ttt att aaa gag tca 816
Lys Asn Lys Asp Lys Glu Asp Val Ala Asp Trp Phe Ile Lys Glu Ser
260 265 270

cta agg agg agg ccg gaa ctt tcc acc aac acc aaa att gaa gtt gtt 864
Leu Arg Arg Arg Pro Glu Leu Ser Thr Asn Thr Lys Ile Glu Val Val
275 280 285

tgg aat act ttt tac aaa ctt ggc aaa agg gtc tga 900
Trp Asn Thr Phe Tyr Lys Leu Gly Lys Arg Val

290 295

<210> 39
<211> 299
<212> PRT
<213> Saccharomyces cerevisiae

<400> 39

Met Ser Thr Phe Ser Ala Ser Asp Phe Asn Ser Glu Arg Tyr Ser Ser
1 5 10 15

Ser Arg Pro Ser Tyr Pro Ser Asp Phe Tyr Lys Met Ile Asp Glu Tyr
20 25 30

His Asp Gly Glu Arg Lys Leu Leu Val Asp Val Gly Cys Gly Pro Gly
35 40 45

Thr Ala Thr Leu Gln Met Ala Gln Glu Leu Lys Pro Phe Glu Gln Ile
50 55 60

Ile Gly Ser Asp Leu Ser Ala Thr Met Ile Lys Thr Ala Glu Val Ile
65 70 75 80

Lys Glu Gly Ser Pro Asp Thr Tyr Lys Asn Val Ser Phe Lys Ile Ser
85 90 95

Ser Ser Asp Asp Phe Lys Phe Leu Gly Ala Asp Ser Val Asp Lys Gln
100 105 110

Lys Ile Asp Met Ile Thr Ala Val Glu Cys Ala His Trp Phe Asp Phe
115 120 125

Glu Lys Phe Gln Arg Ser Ala Tyr Ala Asn Leu Arg Lys Asp Gly Thr
130 135 140

Ile Ala Ile Trp Gly Tyr Ala Asp Pro Ile Phe Pro Asp Tyr Pro Glu
145 150 155 160

Phe Asp Asp Leu Met Ile Glu Val Pro Tyr Gly Lys Gln Gly Leu Gly
165 170 175

Pro Tyr Trp Glu Gln Pro Gly Arg Ser Arg Leu Arg Asn Met Leu Lys
180 185 190

Asp Ser His Leu Asp Pro Glu Leu Phe His Asp Ile Gln Val Ser Tyr
195 200 205

Phe Cys Ala Glu Asp Val Arg Asp Lys Val Lys Leu His Gln His Thr
210 215 220

Lys Lys Pro Leu Leu Ile Arg Lys Gln Val Thr Leu Val Glu Phe Ala
225 230 235 240

Asp Tyr Val Arg Thr Trp Ser Ala Tyr His Gln Trp Lys Gln Asp Pro
245 250 255

Lys Asn Lys Asp Lys Glu Asp Val Ala Asp Trp Phe Ile Lys Glu Ser
260 265 270

Leu Arg Arg Arg Pro Glu Leu Ser Thr Asn Thr Lys Ile Glu Val Val
275 280 285

Trp Asn Thr Phe Tyr Lys Leu Gly Lys Arg Val
290 295

<210> 40

<211> 336

<212> DNA

<213> Saccharomyces cerevisiae

<220>

<221> CDS

<222> (1)..(336)

<400> 40

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atg aaa ggt tca aaa tcg cac ctt gtc ttc act ctc ctg caa gta tca        48
Met Lys Gly Ser Lys Ser His Leu Val Phe Thr Leu Leu Gln Val Ser
1               5                  10                  15

caa cta aat gtt ttt ctt ttc ttt cta ggt ttt ttg ttg cca tta ttc        96
Gln Leu Asn Val Phe Leu Phe Phe Leu Gly Phe Leu Leu Pro Leu Phe
            20                  25                  30

tta gga ctg ttc gtt tca ctg cgc tct ttg gct ctt gca cta tcc tct       144
Leu Gly Leu Phe Val Ser Leu Arg Ser Leu Ala Leu Ala Leu Ser Ser
        35                  40                  45

ggg tgg ttt att atg gat ctg ata cta ttt cgc acc ttt cca gaa gca       192
Gly Trp Phe Ile Met Asp Leu Ile Leu Phe Arg Thr Phe Pro Glu Ala
    50                  55                  60

gaa tta tat cca gca gtc atc ggt aaa cca tct ggt ctg ggg ctt act       240
Glu Leu Tyr Pro Ala Val Ile Gly Lys Pro Ser Gly Leu Gly Leu Thr
65                  70                  75                  80

gag gca ttt gag ttt ata tcc att ttt ttc cct gat gtt cag caa acc       288
Glu Ala Phe Glu Phe Ile Ser Ile Phe Phe Pro Asp Val Gln Gln Thr
                85                  90                  95

gaa aga aat ata aaa tac aac tgg gaa aga tgt ttt aat ggt gag taa       336
Glu Arg Asn Ile Lys Tyr Asn Trp Glu Arg Cys Phe Asn Gly Glu
            100                 105                 110
```

<210> 41
<211> 111
<212> PRT
<213> Saccharomyces cerevisiae

<400> 41

Met Lys Gly Ser Lys Ser His Leu Val Phe Thr Leu Leu Gln Val Ser
1 5 10 15

Gln Leu Asn Val Phe Leu Phe Phe Leu Gly Phe Leu Leu Pro Leu Phe
20 25 30

Leu Gly Leu Phe Val Ser Leu Arg Ser Leu Ala Leu Ala Leu Ser Ser
35 40 45

Gly Trp Phe Ile Met Asp Leu Ile Leu Phe Arg Thr Phe Pro Glu Ala
50 55 60

Glu Leu Tyr Pro Ala Val Ile Gly Lys Pro Ser Gly Leu Gly Leu Thr
65 70 75 80

Glu Ala Phe Glu Phe Ile Ser Ile Phe Phe Pro Asp Val Gln Gln Thr
85 90 95

Glu Arg Asn Ile Lys Tyr Asn Trp Glu Arg Cys Phe Asn Gly Glu
100 105 110

<210> 42
<211> 2556
<212> DNA
<213> Saccharomyces cerevisiae

<220>

<221> CDS

<222> (1)..(2556)

<400> 42

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atg ccg aag aat agt cac cac cat cgt tcc agt tcg gtt aat tcc aca        48
Met Pro Lys Asn Ser His His His Arg Ser Ser Ser Val Asn Ser Thr
1               5                  10                  15

aag agt cgt tct acg gaa tct acg aat aaa tgg aaa att ccg cac tat        96
Lys Ser Arg Ser Thr Glu Ser Thr Asn Lys Trp Lys Ile Pro His Tyr
            20                  25                  30

tat cgc aga tcc gct agc ggc agc aca caa gct tcg ccg gac agg aac       144
Tyr Arg Arg Ser Ala Ser Gly Ser Thr Gln Ala Ser Pro Asp Arg Asn
        35                  40                  45

tcc tca aca ggc tca tgt agc act cca gta tta cct act atg aat gtt       192
Ser Ser Thr Gly Ser Cys Ser Thr Pro Val Leu Pro Thr Met Asn Val
    50                  55                  60

atg tct agc ccg aaa aaa gtt ttg cta gag gat ccc aga gac aac cat       240
Met Ser Ser Pro Lys Lys Val Leu Leu Glu Asp Pro Arg Asp Asn His
65                  70                  75                  80

act aag gcg aag aag agt agt aga aag aaa tca ggt gaa atg gtc ttc       288
Thr Lys Ala Lys Lys Ser Ser Arg Lys Lys Ser Gly Glu Met Val Phe
                85                  90                  95

gtc aat tat act gta cag gac acg gct aac gaa aat gat act gac ttg       336
Val Asn Tyr Thr Val Gln Asp Thr Ala Asn Glu Asn Asp Thr Asp Leu
            100                 105                 110

caa acc cag ccg gtt tct gtg cca gca cca aag gcg aaa tta aag aag       384
Gln Thr Gln Pro Val Ser Val Pro Ala Pro Lys Ala Lys Leu Lys Lys
        115                 120                 125

aaa tcc tcc aaa agg aga atg ctg aag ata ttt gga tcg tca aag aac       432
Lys Ser Ser Lys Arg Arg Met Leu Lys Ile Phe Gly Ser Ser Lys Asn
    130                 135                 140

gaa cac ata gag gac atc gtt gaa gag caa cca atg gtg ctt caa atg       480
Glu His Ile Glu Asp Ile Val Glu Glu Gln Pro Met Val Leu Gln Met
```

145 150 155 160

gat tca gaa tct aaa ccc ctt tcg gga acc cct atc tca gaa agc gga 528
Asp Ser Glu Ser Lys Pro Leu Ser Gly Thr Pro Ile Ser Glu Ser Gly
165 170 175

atc gac gcc tcg tca cta aca acc aaa aga tct tat aac tcg ttc tta 576
Ile Asp Ala Ser Ser Leu Thr Thr Lys Arg Ser Tyr Asn Ser Phe Leu
180 185 190

aaa cac aat agg cta aac ggt aaa act ccg ttc tct gga aac ttg tcc 624
Lys His Asn Arg Leu Asn Gly Lys Thr Pro Phe Ser Gly Asn Leu Ser
195 200 205

ttt cca tca tta aac atg atg ggt aac act act gat ctg cct att gac 672
Phe Pro Ser Leu Asn Met Met Gly Asn Thr Thr Asp Leu Pro Ile Asp
210 215 220

aat aac gat ttt tgt tcc gag aaa gaa gtc gtt ccg aaa tca act cat 720
Asn Asn Asp Phe Cys Ser Glu Lys Glu Val Val Pro Lys Ser Thr His
225 230 235 240

gat cct tca cta gca aaa ccg cca tca agg ttc act gaa agc gaa aca 768
Asp Pro Ser Leu Ala Lys Pro Pro Ser Arg Phe Thr Glu Ser Glu Thr
245 250 255

aat tct act ccc aac tta tca agt ata cct ctc atg aac aca aaa aat 816
Asn Ser Thr Pro Asn Leu Ser Ser Ile Pro Leu Met Asn Thr Lys Asn
260 265 270

aca aga ttg aag tac aat aaa gtg gcg cct cag agt tca gac cga caa 864
Thr Arg Leu Lys Tyr Asn Lys Val Ala Pro Gln Ser Ser Asp Arg Gln
275 280 285

aag tca cag gaa agt ggg cta tat cat tct acc gaa tca ttc aac ttc 912
Lys Ser Gln Glu Ser Gly Leu Tyr His Ser Thr Glu Ser Phe Asn Phe
290 295 300

aaa gat caa aac tac agt aac aat aaa tcc tct tta agt ctg aac tcc 960
Lys Asp Gln Asn Tyr Ser Asn Asn Lys Ser Ser Leu Ser Leu Asn Ser
305 310 315 320

gat tta agt aca ccc cac ttt gca aag cat tca cct gat tca cca aga 1008
Asp Leu Ser Thr Pro His Phe Ala Lys His Ser Pro Asp Ser Pro Arg
325 330 335

act tca aga tct ttc aac tgc gga gac tca caa agt aaa gtt aaa tta 1056
Thr Ser Arg Ser Phe Asn Cys Gly Asp Ser Gln Ser Lys Val Lys Leu
340 345 350

ccg gaa gaa aat gac gct tct att gca ttt agt aag atg ttt act aga 1104
Pro Glu Glu Asn Asp Ala Ser Ile Ala Phe Ser Lys Met Phe Thr Arg
355 360 365

aaa cga gcc aac act ggc ggg tcc acg tgt tcg cta gcc tca ccc act 1152
Lys Arg Ala Asn Thr Gly Gly Ser Thr Cys Ser Leu Ala Ser Pro Thr
370 375 380

att gca caa act att cag caa tca aat ata aaa gtt aat aaa ttg cca 1200
Ile Ala Gln Thr Ile Gln Gln Ser Asn Ile Lys Val Asn Lys Leu Pro
385 390 395 400

act cag cga acc act tca gtt ggc tca tta tca tcc atg tca aat cgt 1248
Thr Gln Arg Thr Thr Ser Val Gly Ser Leu Ser Ser Met Ser Asn Arg
405 410 415

tat tca cca ata aga gtt gca tcg cca gga aga gca aga tcc gca act 1296
Tyr Ser Pro Ile Arg Val Ala Ser Pro Gly Arg Ala Arg Ser Ala Thr
420 425 430

cgt ggg tct tcc ctt tat aga tta tcc aga gac ctt aat tct tta cca 1344
Arg Gly Ser Ser Leu Tyr Arg Leu Ser Arg Asp Leu Asn Ser Leu Pro
435 440 445

agc gtc act gat cta cca gaa atg gat agt aca acc cca gtt aac gaa 1392
Ser Val Thr Asp Leu Pro Glu Met Asp Ser Thr Thr Pro Val Asn Glu
450 455 460

ata ttc ttg gat ggc caa cca cag cat aaa agt ggc agt gtc aaa gga 1440
Ile Phe Leu Asp Gly Gln Pro Gln His Lys Ser Gly Ser Val Lys Gly
465 470 475 480

ggg cat agg aag aaa caa gaa tct atc tct gat gct caa aga att caa 1488
Gly His Arg Lys Lys Gln Glu Ser Ile Ser Asp Ala Gln Arg Ile Gln

485 490 495

cat tct aat tcg tac att aca aca cct tca tct tct ctg gtg act cct 1536
His Ser Asn Ser Tyr Ile Thr Thr Pro Ser Ser Ser Leu Val Thr Pro
500 505 510

cct tac tac atg aca ggt tac aca tta cca agt tct gca tct gct tct 1584
Pro Tyr Tyr Met Thr Gly Tyr Thr Leu Pro Ser Ser Ala Ser Ala Ser
515 520 525

tca act cca aat gtg ctt gaa aca cac aat atg aac ttt gtt cca agt 1632
Ser Thr Pro Asn Val Leu Glu Thr His Asn Met Asn Phe Val Pro Ser
530 535 540

acc agt act gtt aca agt tat cgc cca tct agc aat ttt tcc tca ttt 1680
Thr Ser Thr Val Thr Ser Tyr Arg Pro Ser Ser Asn Phe Ser Ser Phe
545 550 555 560

gac aaa gaa tac agt aac gaa aac gac gct agt ggg gaa ttc tct gct 1728
Asp Lys Glu Tyr Ser Asn Glu Asn Asp Ala Ser Gly Glu Phe Ser Ala
565 570 575

ttc aat act cca atg gag aat ata ccg gca cta aaa ggt ata cct aga 1776
Phe Asn Thr Pro Met Glu Asn Ile Pro Ala Leu Lys Gly Ile Pro Arg
580 585 590

tcc acg tta gaa gaa aat gaa gaa gag gat gtc cta gta caa gat att 1824
Ser Thr Leu Glu Glu Asn Glu Glu Glu Asp Val Leu Val Gln Asp Ile
595 600 605

ccg aat acg gca cac ttc caa aga agg gat att atg ggg atg gat act 1872
Pro Asn Thr Ala His Phe Gln Arg Arg Asp Ile Met Gly Met Asp Thr
610 615 620

cac aga aag gat gac agt tta gat ttt aac tct ttg atg cca cac ggt 1920
His Arg Lys Asp Asp Ser Leu Asp Phe Asn Ser Leu Met Pro His Gly
625 630 635 640

agt aca act agt agc agc atc gta gat tct gtt atg acg aac tca ata 1968
Ser Thr Thr Ser Ser Ser Ile Val Asp Ser Val Met Thr Asn Ser Ile
645 650 655

tcc act aca aca agc aac gcg acc gga aac tac ttt caa gat caa gat 2016
Ser Thr Thr Thr Ser Asn Ala Thr Gly Asn Tyr Phe Gln Asp Gln Asp
660 665 670

aag tat aca ttg gta aat acg gga ttg gga ttg agt gat gca aac ctc 2064
Lys Tyr Thr Leu Val Asn Thr Gly Leu Gly Leu Ser Asp Ala Asn Leu
675 680 685

gat cat ttt att aga tct caa tgg aaa cac gct tct cga tca gaa tcc 2112
Asp His Phe Ile Arg Ser Gln Trp Lys His Ala Ser Arg Ser Glu Ser
690 695 700

aat aat aat acc gga aat cgc gtt tct tac agt ggc tca aca cca aac 2160
Asn Asn Asn Thr Gly Asn Arg Val Ser Tyr Ser Gly Ser Thr Pro Asn
705 710 715 720

aat gtt gat aca aca aag act aat ttg caa gtg tat acc gag ttc gat 2208
Asn Val Asp Thr Thr Lys Thr Asn Leu Gln Val Tyr Thr Glu Phe Asp
725 730 735

ttt gaa aac cca gag tcg ttt ttc cat gag caa tcg aag cta cta ggt 2256
Phe Glu Asn Pro Glu Ser Phe Phe His Glu Gln Ser Lys Leu Leu Gly
740 745 750

gag atg ggc cac agc aat aac aac agc aac agc gcc atc aac atg aat 2304
Glu Met Gly His Ser Asn Asn Asn Ser Asn Ser Ala Ile Asn Met Asn
755 760 765

gaa ccc aag tct gcg gat aca tac att gga aat ata tct ccg gat act 2352
Glu Pro Lys Ser Ala Asp Thr Tyr Ile Gly Asn Ile Ser Pro Asp Thr
770 775 780

tca gca act gtt tca tta ggc gac ctg atg ggc tca aac gtt tca aac 2400
Ser Ala Thr Val Ser Leu Gly Asp Leu Met Gly Ser Asn Val Ser Asn
785 790 795 800

aac agt gaa aga aat ttt tac gat ggt cat act ttc gtt cca cag tat 2448
Asn Ser Glu Arg Asn Phe Tyr Asp Gly His Thr Phe Val Pro Gln Tyr
805 810 815

cag gcg aac tca tct gtg gaa aac tca aat aat caa aat gca gca cca 2496
Gln Ala Asn Ser Ser Val Glu Asn Ser Asn Asn Gln Asn Ala Ala Pro

820 825 830

att gca aat aac gac att gat aat aat tta cag tct ttt tat ttt gat 2544
Ile Ala Asn Asn Asp Ile Asp Asn Asn Leu Gln Ser Phe Tyr Phe Asp
835 840 845

aat agc aac taa 2556
Asn Ser Asn
850

<210> 43
<211> 851
<212> PRT
<213> Saccharomyces cerevisiae

<400> 43

Met Pro Lys Asn Ser His His His Arg Ser Ser Ser Val Asn Ser Thr
1 5 10 15

Lys Ser Arg Ser Thr Glu Ser Thr Asn Lys Trp Lys Ile Pro His Tyr
20 25 30

Tyr Arg Arg Ser Ala Ser Gly Ser Thr Gln Ala Ser Pro Asp Arg Asn
35 40 45

Ser Ser Thr Gly Ser Cys Ser Thr Pro Val Leu Pro Thr Met Asn Val
50 55 60

Met Ser Ser Pro Lys Lys Val Leu Leu Glu Asp Pro Arg Asp Asn His
65 70 75 80

Thr Lys Ala Lys Lys Ser Ser Arg Lys Lys Ser Gly Glu Met Val Phe
85 90 95

Val Asn Tyr Thr Val Gln Asp Thr Ala Asn Glu Asn Asp Thr Asp Leu
100 105 110

Gln Thr Gln Pro Val Ser Val Pro Ala Pro Lys Ala Lys Leu Lys Lys
115 120 125

Lys Ser Ser Lys Arg Arg Met Leu Lys Ile Phe Gly Ser Ser Lys Asn
130 135 140

Glu His Ile Glu Asp Ile Val Glu Glu Gln Pro Met Val Leu Gln Met
145 150 155 160

Asp Ser Glu Ser Lys Pro Leu Ser Gly Thr Pro Ile Ser Glu Ser Gly
165 170 175

Ile Asp Ala Ser Ser Leu Thr Thr Lys Arg Ser Tyr Asn Ser Phe Leu
180 185 190

Lys His Asn Arg Leu Asn Gly Lys Thr Pro Phe Ser Gly Asn Leu Ser
195 200 205

Phe Pro Ser Leu Asn Met Met Gly Asn Thr Thr Asp Leu Pro Ile Asp
210 215 220

Asn Asn Asp Phe Cys Ser Glu Lys Glu Val Val Pro Lys Ser Thr His
225 230 235 240

Asp Pro Ser Leu Ala Lys Pro Pro Ser Arg Phe Thr Glu Ser Glu Thr
245 250 255

Asn Ser Thr Pro Asn Leu Ser Ser Ile Pro Leu Met Asn Thr Lys Asn

260 265 270

Thr Arg Leu Lys Tyr Asn Lys Val Ala Pro Gln Ser Ser Asp Arg Gln
275 280 285

Lys Ser Gln Glu Ser Gly Leu Tyr His Ser Thr Glu Ser Phe Asn Phe
290 295 300

Lys Asp Gln Asn Tyr Ser Asn Asn Lys Ser Ser Leu Ser Leu Asn Ser
305 310 315 320

Asp Leu Ser Thr Pro His Phe Ala Lys His Ser Pro Asp Ser Pro Arg
325 330 335

Thr Ser Arg Ser Phe Asn Cys Gly Asp Ser Gln Ser Lys Val Lys Leu
340 345 350

Pro Glu Glu Asn Asp Ala Ser Ile Ala Phe Ser Lys Met Phe Thr Arg
355 360 365

Lys Arg Ala Asn Thr Gly Gly Ser Thr Cys Ser Leu Ala Ser Pro Thr
370 375 380

Ile Ala Gln Thr Ile Gln Gln Ser Asn Ile Lys Val Asn Lys Leu Pro
385 390 395 400

Thr Gln Arg Thr Thr Ser Val Gly Ser Leu Ser Ser Met Ser Asn Arg
405 410 415

Tyr Ser Pro Ile Arg Val Ala Ser Pro Gly Arg Ala Arg Ser Ala Thr
420 425 430

Arg Gly Ser Ser Leu Tyr Arg Leu Ser Arg Asp Leu Asn Ser Leu Pro
435 440 445

Ser Val Thr Asp Leu Pro Glu Met Asp Ser Thr Thr Pro Val Asn Glu
450 455 460

Ile Phe Leu Asp Gly Gln Pro Gln His Lys Ser Gly Ser Val Lys Gly
465 470 475 480

Gly His Arg Lys Lys Gln Glu Ser Ile Ser Asp Ala Gln Arg Ile Gln
485 490 495

His Ser Asn Ser Tyr Ile Thr Thr Pro Ser Ser Ser Leu Val Thr Pro
500 505 510

Pro Tyr Tyr Met Thr Gly Tyr Thr Leu Pro Ser Ser Ala Ser Ala Ser
515 520 525

Ser Thr Pro Asn Val Leu Glu Thr His Asn Met Asn Phe Val Pro Ser
530 535 540

Thr Ser Thr Val Thr Ser Tyr Arg Pro Ser Ser Asn Phe Ser Ser Phe
545 550 555 560

Asp Lys Glu Tyr Ser Asn Glu Asn Asp Ala Ser Gly Glu Phe Ser Ala
565 570 575

Phe Asn Thr Pro Met Glu Asn Ile Pro Ala Leu Lys Gly Ile Pro Arg
580 585 590

Ser Thr Leu Glu Glu Asn Glu Glu Glu Asp Val Leu Val Gln Asp Ile

595 600 605

Pro Asn Thr Ala His Phe Gln Arg Arg Asp Ile Met Gly Met Asp Thr
610 615 620

His Arg Lys Asp Asp Ser Leu Asp Phe Asn Ser Leu Met Pro His Gly
625 630 635 640

Ser Thr Thr Ser Ser Ser Ile Val Asp Ser Val Met Thr Asn Ser Ile
645 650 655

Ser Thr Thr Thr Ser Asn Ala Thr Gly Asn Tyr Phe Gln Asp Gln Asp
660 665 670

Lys Tyr Thr Leu Val Asn Thr Gly Leu Gly Leu Ser Asp Ala Asn Leu
675 680 685

Asp His Phe Ile Arg Ser Gln Trp Lys His Ala Ser Arg Ser Glu Ser
690 695 700

Asn Asn Asn Thr Gly Asn Arg Val Ser Tyr Ser Gly Ser Thr Pro Asn
705 710 715 720

Asn Val Asp Thr Thr Lys Thr Asn Leu Gln Val Tyr Thr Glu Phe Asp
725 730 735

Phe Glu Asn Pro Glu Ser Phe Phe His Glu Gln Ser Lys Leu Leu Gly
740 745 750

Glu Met Gly His Ser Asn Asn Asn Ser Asn Ser Ala Ile Asn Met Asn
755 760 765

Glu Pro Lys Ser Ala Asp Thr Tyr Ile Gly Asn Ile Ser Pro Asp Thr
770 775 780

Ser Ala Thr Val Ser Leu Gly Asp Leu Met Gly Ser Asn Val Ser Asn
785 790 795 800

Asn Ser Glu Arg Asn Phe Tyr Asp Gly His Thr Phe Val Pro Gln Tyr
805 810 815

Gln Ala Asn Ser Ser Val Glu Asn Ser Asn Asn Gln Asn Ala Ala Pro
820 825 830

Ile Ala Asn Asn Asp Ile Asp Asn Asn Leu Gln Ser Phe Tyr Phe Asp
835 840 845

Asn Ser Asn
850

<210> 44
<211> 1575
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(1575)

<400> 44
atg tcc caa cga tct tca caa cac att gta ggt att cat tat gct gta 48
Met Ser Gln Arg Ser Ser Gln His Ile Val Gly Ile His Tyr Ala Val
1 5 10 15

gga cct aag att ggc gaa ggg tct ttc gga gta ata ttt gag gga gag 96

Gly Pro Lys Ile Gly Glu Gly Ser Phe Gly Val Ile Phe Glu Gly Glu
20 25 30

aac att ctt cat tct tgt caa gcg cag acc ggt agc aag agg gac tct 144
Asn Ile Leu His Ser Cys Gln Ala Gln Thr Gly Ser Lys Arg Asp Ser
35 40 45

agt ata ata atg gcg aac gag cca gtc gca att aaa ttc gaa ccg cga 192
Ser Ile Ile Met Ala Asn Glu Pro Val Ala Ile Lys Phe Glu Pro Arg
50 55 60

cat tcg gac gca ccc cag ttg cgt gac gaa ttt aga gcc tat agg ata 240
His Ser Asp Ala Pro Gln Leu Arg Asp Glu Phe Arg Ala Tyr Arg Ile
65 70 75 80

ttg aat ggc tgc gtt gga att ccc cat gct tat tat ttt ggt caa gaa 288
Leu Asn Gly Cys Val Gly Ile Pro His Ala Tyr Tyr Phe Gly Gln Glu
85 90 95

ggt atg cac aac atc ttg att atc gat tta cta ggg cca tca ttg gaa 336
Gly Met His Asn Ile Leu Ile Ile Asp Leu Leu Gly Pro Ser Leu Glu
100 105 110

gat ctc ttt gag tgg tgt ggt aga aaa ttt tca gtg aaa aca acc tgt 384
Asp Leu Phe Glu Trp Cys Gly Arg Lys Phe Ser Val Lys Thr Thr Cys
115 120 125

atg gtt gcc aag caa atg att gat aga gtt aga gca att cat gat cac 432
Met Val Ala Lys Gln Met Ile Asp Arg Val Arg Ala Ile His Asp His
130 135 140

gac tta atc tat cgc gat att aaa ccc gat aac ttt tta att tct caa 480
Asp Leu Ile Tyr Arg Asp Ile Lys Pro Asp Asn Phe Leu Ile Ser Gln
145 150 155 160

tat caa aga att tca cct gaa gga aaa gtc att aaa tca tgt gcc tcc 528
Tyr Gln Arg Ile Ser Pro Glu Gly Lys Val Ile Lys Ser Cys Ala Ser
165 170 175

tct tct aat aat gat ccc aat tta ata tac atg gtt gac ttt ggt atg 576
Ser Ser Asn Asn Asp Pro Asn Leu Ile Tyr Met Val Asp Phe Gly Met
180 185 190

gca aaa caa tat aga gat cca aga acg aaa caa cat ata cca tac cgt 624
Ala Lys Gln Tyr Arg Asp Pro Arg Thr Lys Gln His Ile Pro Tyr Arg
195 200 205

gaa cga aaa tca ttg agc ggt acc gcc aga tat atg tct att aat act 672
Glu Arg Lys Ser Leu Ser Gly Thr Ala Arg Tyr Met Ser Ile Asn Thr
210 215 220

cat ttt gga aga gaa cag tca cgt agg gat gat tta gaa tcg cta ggt 720
His Phe Gly Arg Glu Gln Ser Arg Arg Asp Asp Leu Glu Ser Leu Gly
225 230 235 240

cac gtt ttt ttt tat ttc ttg agg gga tcc ttg cca tgg caa ggt ttg 768
His Val Phe Phe Tyr Phe Leu Arg Gly Ser Leu Pro Trp Gln Gly Leu
245 250 255

aaa gca cca aac aac aaa ctg aag tat gaa aag att ggt atg act aaa 816
Lys Ala Pro Asn Asn Lys Leu Lys Tyr Glu Lys Ile Gly Met Thr Lys
260 265 270

cag aaa ttg aat cct gat gat ctt tta ttg aat aat gct att cct tat 864
Gln Lys Leu Asn Pro Asp Asp Leu Leu Leu Asn Asn Ala Ile Pro Tyr
275 280 285

cag ttt gcc aca tat tta aaa tat gca cgt tcc ttg aag ttc gac gaa 912
Gln Phe Ala Thr Tyr Leu Lys Tyr Ala Arg Ser Leu Lys Phe Asp Glu
290 295 300

gat ccg gat tat gac tat tta atc tcg tta atg gat gac gct ttg aga 960
Asp Pro Asp Tyr Asp Tyr Leu Ile Ser Leu Met Asp Asp Ala Leu Arg
305 310 315 320

tta aac gac tta aag gat gat gga cac tat gac tgg atg gat ttg aat 1008
Leu Asn Asp Leu Lys Asp Asp Gly His Tyr Asp Trp Met Asp Leu Asn
325 330 335

ggt ggt aaa ggc tgg aat atc aag att aat aga aga gct aac ttg cat 1056
Gly Gly Lys Gly Trp Asn Ile Lys Ile Asn Arg Arg Ala Asn Leu His
340 345 350

ggt tac gga aat cca aat cca aga gtc aat ggc aat act gca aga aac 1104

Gly Tyr Gly Asn Pro Asn Pro Arg Val Asn Gly Asn Thr Ala Arg Asn
355 360 365

aat gtg aat acg aat tca aag aca cga aat aca acg cca gtt gcg aca 1152
Asn Val Asn Thr Asn Ser Lys Thr Arg Asn Thr Thr Pro Val Ala Thr
370 375 380

cct aag caa caa gct caa aac agt tat aac aag gac aat tcg aaa tcc 1200
Pro Lys Gln Gln Ala Gln Asn Ser Tyr Asn Lys Asp Asn Ser Lys Ser
385 390 395 400

aga att tct tcg aac ccg cag agc ttt act aaa caa caa cac gtc ttg 1248
Arg Ile Ser Ser Asn Pro Gln Ser Phe Thr Lys Gln Gln His Val Leu
405 410 415

aaa aaa atc gaa ccc aat agt aaa tat att cct gaa aca cat tca aat 1296
Lys Lys Ile Glu Pro Asn Ser Lys Tyr Ile Pro Glu Thr His Ser Asn
420 425 430

ctt caa cgg cca att aaa agt caa agt caa acg tac gac tcc atc agt 1344
Leu Gln Arg Pro Ile Lys Ser Gln Ser Gln Thr Tyr Asp Ser Ile Ser
435 440 445

cat aca caa aat tca cca ttt gta cca tat tca agt tct aaa gct aac 1392
His Thr Gln Asn Ser Pro Phe Val Pro Tyr Ser Ser Ser Lys Ala Asn
450 455 460

cct aaa aga agt aat aat gag cac aac tta cca aac cac tac aca aac 1440
Pro Lys Arg Ser Asn Asn Glu His Asn Leu Pro Asn His Tyr Thr Asn
465 470 475 480

ctt gca aat aag aat atc aat tat caa agt caa cga aat tac gaa caa 1488
Leu Ala Asn Lys Asn Ile Asn Tyr Gln Ser Gln Arg Asn Tyr Glu Gln
485 490 495

gaa aat gat gct tat tct gat gac gag aat gat aca ttt tgt tct aaa 1536
Glu Asn Asp Ala Tyr Ser Asp Asp Glu Asn Asp Thr Phe Cys Ser Lys
500 505 510

ata tac aaa tat tgt tgt tgc tgt ttt tgt tgc tgt tga 1575
Ile Tyr Lys Tyr Cys Cys Cys Cys Phe Cys Cys Cys
515 520

<210> 45

<211> 524
<212> PRT
<213> Saccharomyces cerevisiae

<400> 45

Met Ser Gln Arg Ser Ser Gln His Ile Val Gly Ile His Tyr Ala Val
1 5 10 15

Gly Pro Lys Ile Gly Glu Gly Ser Phe Gly Val Ile Phe Glu Gly Glu
20 25 30

Asn Ile Leu His Ser Cys Gln Ala Gln Thr Gly Ser Lys Arg Asp Ser
35 40 45

Ser Ile Ile Met Ala Asn Glu Pro Val Ala Ile Lys Phe Glu Pro Arg
50 55 60

His Ser Asp Ala Pro Gln Leu Arg Asp Glu Phe Arg Ala Tyr Arg Ile
65 70 75 80

Leu Asn Gly Cys Val Gly Ile Pro His Ala Tyr Tyr Phe Gly Gln Glu
85 90 95

Gly Met His Asn Ile Leu Ile Ile Asp Leu Leu Gly Pro Ser Leu Glu
100 105 110

Asp Leu Phe Glu Trp Cys Gly Arg Lys Phe Ser Val Lys Thr Thr Cys
115 120 125

Met Val Ala Lys Gln Met Ile Asp Arg Val Arg Ala Ile His Asp His
130 135 140

Asp Leu Ile Tyr Arg Asp Ile Lys Pro Asp Asn Phe Leu Ile Ser Gln
145 150 155 160

Tyr Gln Arg Ile Ser Pro Glu Gly Lys Val Ile Lys Ser Cys Ala Ser
165 170 175

Ser Ser Asn Asn Asp Pro Asn Leu Ile Tyr Met Val Asp Phe Gly Met
180 185 190

Ala Lys Gln Tyr Arg Asp Pro Arg Thr Lys Gln His Ile Pro Tyr Arg
195 200 205

Glu Arg Lys Ser Leu Ser Gly Thr Ala Arg Tyr Met Ser Ile Asn Thr
210 215 220

His Phe Gly Arg Glu Gln Ser Arg Arg Asp Asp Leu Glu Ser Leu Gly
225 230 235 240

His Val Phe Phe Tyr Phe Leu Arg Gly Ser Leu Pro Trp Gln Gly Leu
245 250 255

Lys Ala Pro Asn Asn Lys Leu Lys Tyr Glu Lys Ile Gly Met Thr Lys
260 265 270

Gln Lys Leu Asn Pro Asp Asp Leu Leu Leu Asn Asn Ala Ile Pro Tyr
275 280 285

Gln Phe Ala Thr Tyr Leu Lys Tyr Ala Arg Ser Leu Lys Phe Asp Glu

290 295 300

Asp Pro Asp Tyr Asp Tyr Leu Ile Ser Leu Met Asp Asp Ala Leu Arg
305 310 315 320

Leu Asn Asp Leu Lys Asp Asp Gly His Tyr Asp Trp Met Asp Leu Asn
325 330 335

Gly Gly Lys Gly Trp Asn Ile Lys Ile Asn Arg Arg Ala Asn Leu His
340 345 350

Gly Tyr Gly Asn Pro Asn Pro Arg Val Asn Gly Asn Thr Ala Arg Asn
355 360 365

Asn Val Asn Thr Asn Ser Lys Thr Arg Asn Thr Thr Pro Val Ala Thr
370 375 380

Pro Lys Gln Gln Ala Gln Asn Ser Tyr Asn Lys Asp Asn Ser Lys Ser
385 390 395 400

Arg Ile Ser Ser Asn Pro Gln Ser Phe Thr Lys Gln Gln His Val Leu
405 410 415

Lys Lys Ile Glu Pro Asn Ser Lys Tyr Ile Pro Glu Thr His Ser Asn
420 425 430

Leu Gln Arg Pro Ile Lys Ser Gln Ser Gln Thr Tyr Asp Ser Ile Ser
435 440 445

His Thr Gln Asn Ser Pro Phe Val Pro Tyr Ser Ser Ser Lys Ala Asn
450 455 460

Pro Lys Arg Ser Asn Asn Glu His Asn Leu Pro Asn His Tyr Thr Asn
465 470 475 480

Leu Ala Asn Lys Asn Ile Asn Tyr Gln Ser Gln Arg Asn Tyr Glu Gln
485 490 495

Glu Asn Asp Ala Tyr Ser Asp Asp Glu Asn Asp Thr Phe Cys Ser Lys
500 505 510

Ile Tyr Lys Tyr Cys Cys Cys Cys Phe Cys Cys Cys
515 520

<210> 46
<211> 1125
<212> DNA
<213> Saccharomyces cerevisiae

<220>

<221> CDS
<222> (1)..(1125)

<400> 46
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Met Arg Ile Gln Ser Leu Phe Val Leu Phe Asn Val Ala Ile Ile Ala
1 5 10 15

tgg tca tat cca tat gag cct tta agg gtt tta caa gta gga gag aat 96
Trp Ser Tyr Pro Tyr Glu Pro Leu Arg Val Leu Gln Val Gly Glu Asn
20 25 30

gag gta atg gag gtt ccc gaa tca gaa aag cta aac tta cga aga aga 144
Glu Val Met Glu Val Pro Glu Ser Glu Lys Leu Asn Leu Arg Arg Arg
35 40 45

ggt gtc aaa ttc ttt gat gtg acc aaa cac act tct ttc tta cct ttc 192

Gly Val Lys Phe Phe Asp Val Thr Lys His Thr Ser Phe Leu Pro Phe
50 55 60

ttt aac aag gag gaa gag cca aca gta cca acg tat aac tat cct cct 240
Phe Asn Lys Glu Glu Glu Pro Thr Val Pro Thr Tyr Asn Tyr Pro Pro
65 70 75 80

gag ata tcg aac aaa gaa gta gtg gat gat tcg att aag aat ata gac 288
Glu Ile Ser Asn Lys Glu Val Val Asp Asp Ser Ile Lys Asn Ile Asp
85 90 95

aag ggc tct atg cac aag aac ttg gca aag ttt aca agt ttt tac acc 336
Lys Gly Ser Met His Lys Asn Leu Ala Lys Phe Thr Ser Phe Tyr Thr
100 105 110

cgt tac tac aag tcc gat cac ggc ttt gaa tct gcc gag tgg tta gct 384
Arg Tyr Tyr Lys Ser Asp His Gly Phe Glu Ser Ala Glu Trp Leu Ala
115 120 125

gca act atc gct aat att aca aaa gat att ccg caa gat acg ttg act 432
Ala Thr Ile Ala Asn Ile Thr Lys Asp Ile Pro Gln Asp Thr Leu Thr
130 135 140

att gaa cat ttt gat cac aaa gaa tgg aag caa tat tca att ata gtc 480
Ile Glu His Phe Asp His Lys Glu Trp Lys Gln Tyr Ser Ile Ile Val
145 150 155 160

cgt gtc acg gga tct act acg cca gaa gat att ata ata att ggt tct 528
Arg Val Thr Gly Ser Thr Thr Pro Glu Asp Ile Ile Ile Ile Gly Ser
165 170 175

cat caa gat tct atc aat ctg cta ctg cca tcc ata atg gca gct cca 576
His Gln Asp Ser Ile Asn Leu Leu Leu Pro Ser Ile Met Ala Ala Pro
180 185 190

ggt gcg gac gac aat ggg tca ggc acg gtg act aat atg gag gct ctc 624
Gly Ala Asp Asp Asn Gly Ser Gly Thr Val Thr Asn Met Glu Ala Leu
195 200 205

aga tta tat acg gaa aat ttt ttg aag aga gga ttt aga cct aac aac 672
Arg Leu Tyr Thr Glu Asn Phe Leu Lys Arg Gly Phe Arg Pro Asn Asn
210 215 220

act gtg gaa ttt cac ttt tat tcc gcc gaa gag ggg gga ttg ttg ggt 720
Thr Val Glu Phe His Phe Tyr Ser Ala Glu Glu Gly Gly Leu Leu Gly
225 230 235 240

tct ctt gat gtt ttt aca gct tat gcc aaa cag aaa aag cat gtg aga 768
Ser Leu Asp Val Phe Thr Ala Tyr Ala Lys Gln Lys Lys His Val Arg
245 250 255

gcg atg ctt cag caa gac atg acg gga tat gtt tct gat cca gaa gat 816
Ala Met Leu Gln Gln Asp Met Thr Gly Tyr Val Ser Asp Pro Glu Asp
260 265 270

gaa cat gtg ggg att gtc acc gac tac act act ccc gca tta act gat 864
Glu His Val Gly Ile Val Thr Asp Tyr Thr Thr Pro Ala Leu Thr Asp
275 280 285

ttt ata aaa cta att atc aac tct tat cta tcc att cct tac agg gat 912
Phe Ile Lys Leu Ile Ile Asn Ser Tyr Leu Ser Ile Pro Tyr Arg Asp
290 295 300

aca caa tgt ggc tat gct tgt agc gat cat ggg agt gcc acc aga aac 960
Thr Gln Cys Gly Tyr Ala Cys Ser Asp His Gly Ser Ala Thr Arg Asn
305 310 315 320

gga ttt cca ggc tcc ttc gtg att gaa agt gag ttc aaa aag act aac 1008
Gly Phe Pro Gly Ser Phe Val Ile Glu Ser Glu Phe Lys Lys Thr Asn
325 330 335

aag tat att cac agc acc atg gat act ttg gac aga tta agt ctc gct 1056
Lys Tyr Ile His Ser Thr Met Asp Thr Leu Asp Arg Leu Ser Leu Ala
340 345 350

cat atg gcg gaa cac aca aaa att gta tta ggg gta atc att gaa ctc 1104
His Met Ala Glu His Thr Lys Ile Val Leu Gly Val Ile Ile Glu Leu
355 360 365

ggg tca tgg tcc gct tgg taa 1125
Gly Ser Trp Ser Ala Trp
370

<210> 47

<211> 374

<212> PRT

<213> Saccharomyces cerevisiae

<400> 47

Met Arg Ile Gln Ser Leu Phe Val Leu Phe Asn Val Ala Ile Ile Ala
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Trp Ser Tyr Pro Tyr Glu Pro Leu Arg Val Leu Gln Val Gly Glu Asn
20 25 30

Glu Val Met Glu Val Pro Glu Ser Glu Lys Leu Asn Leu Arg Arg Arg
35 40 45

Gly Val Lys Phe Phe Asp Val Thr Lys His Thr Ser Phe Leu Pro Phe
50 55 60

Phe Asn Lys Glu Glu Glu Pro Thr Val Pro Thr Tyr Asn Tyr Pro Pro
65 70 75 80

Glu Ile Ser Asn Lys Glu Val Val Asp Asp Ser Ile Lys Asn Ile Asp
85 90 95

Lys Gly Ser Met His Lys Asn Leu Ala Lys Phe Thr Ser Phe Tyr Thr
100 105 110

Arg Tyr Tyr Lys Ser Asp His Gly Phe Glu Ser Ala Glu Trp Leu Ala
115 120 125

Ala Thr Ile Ala Asn Ile Thr Lys Asp Ile Pro Gln Asp Thr Leu Thr
130 135 140

Ile Glu His Phe Asp His Lys Glu Trp Lys Gln Tyr Ser Ile Ile Val
145 150 155 160

Arg Val Thr Gly Ser Thr Thr Pro Glu Asp Ile Ile Ile Ile Gly Ser
165 170 175

His Gln Asp Ser Ile Asn Leu Leu Leu Pro Ser Ile Met Ala Ala Pro
180 185 190

Gly Ala Asp Asp Asn Gly Ser Gly Thr Val Thr Asn Met Glu Ala Leu
195 200 205

Arg Leu Tyr Thr Glu Asn Phe Leu Lys Arg Gly Phe Arg Pro Asn Asn
210 215 220

Thr Val Glu Phe His Phe Tyr Ser Ala Glu Glu Gly Gly Leu Leu Gly
225 230 235 240

Ser Leu Asp Val Phe Thr Ala Tyr Ala Lys Gln Lys Lys His Val Arg
245 250 255

Ala Met Leu Gln Gln Asp Met Thr Gly Tyr Val Ser Asp Pro Glu Asp
260 265 270

Glu His Val Gly Ile Val Thr Asp Tyr Thr Thr Pro Ala Leu Thr Asp
275 280 285

Phe Ile Lys Leu Ile Ile Asn Ser Tyr Leu Ser Ile Pro Tyr Arg Asp
290 295 300

Thr Gln Cys Gly Tyr Ala Cys Ser Asp His Gly Ser Ala Thr Arg Asn
305 310 315 320

Gly Phe Pro Gly Ser Phe Val Ile Glu Ser Glu Phe Lys Lys Thr Asn
325 330 335

Lys Tyr Ile His Ser Thr Met Asp Thr Leu Asp Arg Leu Ser Leu Ala
340 345 350

His Met Ala Glu His Thr Lys Ile Val Leu Gly Val Ile Ile Glu Leu
355 360 365

Gly Ser Trp Ser Ala Trp
370

<210> 48
<211> 1530
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(1530)

<400> 48
atg atc gct ttg aag ccc aat gct gtt cga acc ttc cga caa gtg cag 48
Met Ile Ala Leu Lys Pro Asn Ala Val Arg Thr Phe Arg Gln Val Gln
1 5 10 15

cat tgc agc ttt cgc att tgt cgg tat caa tct acg aag tca aat aag 96
His Cys Ser Phe Arg Ile Cys Arg Tyr Gln Ser Thr Lys Ser Asn Lys
20 25 30

tgt ctg acg ccc ttg caa gag tac gac aga ctg gtg aag ttg ggg aag 144
Cys Leu Thr Pro Leu Gln Glu Tyr Asp Arg Leu Val Lys Leu Gly Lys
35 40 45

cta cgg gat gat aca tat cag cgt ggt atc atc tct tcc tta ggg gat 192
Leu Arg Asp Asp Thr Tyr Gln Arg Gly Ile Ile Ser Ser Leu Gly Asp
50 55 60

ttg tat gat tca ctg gtt aaa tat gta cct ccg gtt gtc aag aca ccc 240
Leu Tyr Asp Ser Leu Val Lys Tyr Val Pro Pro Val Val Lys Thr Pro
65 70 75 80

aat gct gtc gac caa gtt ggc ggt tgg ttg aat ggt ctt aaa tcc gta 288
Asn Ala Val Asp Gln Val Gly Gly Trp Leu Asn Gly Leu Lys Ser Val
85 90 95

ttt agc cgt ggc aaa cct aag aac att ggg gcg tat gtg gat gta tcc 336
Phe Ser Arg Gly Lys Pro Lys Asn Ile Gly Ala Tyr Val Asp Val Ser
100 105 110

aaa att ggt aac tcg ata cct cga gga gtt tac cta tat gga gat gtt 384
Lys Ile Gly Asn Ser Ile Pro Arg Gly Val Tyr Leu Tyr Gly Asp Val
115 120 125

ggc tgc gga aag aca atg ttg atg gac ctt ttt tat act aca att ccc 432
Gly Cys Gly Lys Thr Met Leu Met Asp Leu Phe Tyr Thr Thr Ile Pro
130 135 140

aat cat tta aca aaa aag aga ata cat ttt cac cag ttt atg caa tat 480
Asn His Leu Thr Lys Lys Arg Ile His Phe His Gln Phe Met Gln Tyr
145 150 155 160

gtt cac aaa agg tcg cat gaa att gtt aga gag caa aat ttg aaa gaa 528
Val His Lys Arg Ser His Glu Ile Val Arg Glu Gln Asn Leu Lys Glu
165 170 175

cta ggt gat gca aaa gga aaa gag atc gat acg gtt cca ttt ttg gcc 576
Leu Gly Asp Ala Lys Gly Lys Glu Ile Asp Thr Val Pro Phe Leu Ala
180 185 190

gca gag att gca aat aat tcg cat gtt ctt tgt ttt gac gag ttt caa 624
Ala Glu Ile Ala Asn Asn Ser His Val Leu Cys Phe Asp Glu Phe Gln
195 200 205

gtc act gac gtg gca gat gca atg ata ttg aga agg ctg atg act gcc 672

Val Thr Asp Val Ala Asp Ala Met Ile Leu Arg Arg Leu Met Thr Ala
210 215 220

tta cta tcc gat gat tat ggt gtc gta ctt ttc gca acc tcg aat aga 720
Leu Leu Ser Asp Asp Tyr Gly Val Val Leu Phe Ala Thr Ser Asn Arg
225 230 235 240

cat cca gat gag ttg tat atc aac ggt gtt caa aga caa tca ttt att 768
His Pro Asp Glu Leu Tyr Ile Asn Gly Val Gln Arg Gln Ser Phe Ile
245 250 255

cct tgt att gaa ctg ata aag cat aga act aag gtt atc ttc ttg aat 816
Pro Cys Ile Glu Leu Ile Lys His Arg Thr Lys Val Ile Phe Leu Asn
260 265 270

tcg cca aca gat tac cgt aag att cca aga cct gtg tcc tca gtt tac 864
Ser Pro Thr Asp Tyr Arg Lys Ile Pro Arg Pro Val Ser Ser Val Tyr
275 280 285

tat ttc cca tcc gat acg agc ata aaa tac gca tca aag gaa tgt aaa 912
Tyr Phe Pro Ser Asp Thr Ser Ile Lys Tyr Ala Ser Lys Glu Cys Lys
290 295 300

acc cgt cga gaa act cat att aag gaa tgg tat aac tat ttc gca cag 960
Thr Arg Arg Glu Thr His Ile Lys Glu Trp Tyr Asn Tyr Phe Ala Gln
305 310 315 320

gct tcc cac acc gat gat tcc act gat tca cac acg gtg cat aag aca 1008
Ala Ser His Thr Asp Asp Ser Thr Asp Ser His Thr Val His Lys Thr
325 330 335

ttt tat gat tat cca tta act att tgg ggg aga gag ttc aaa gtc cct 1056
Phe Tyr Asp Tyr Pro Leu Thr Ile Trp Gly Arg Glu Phe Lys Val Pro
340 345 350

aag tgt acc cca cct cga gtc gcg cag ttt act ttc aag cag ttg tgt 1104
Lys Cys Thr Pro Pro Arg Val Ala Gln Phe Thr Phe Lys Gln Leu Cys
355 360 365

ggt gag cct ttg gcc gca gga gat tac ttg acg ttg gca aaa aat ttt 1152
Gly Glu Pro Leu Ala Ala Gly Asp Tyr Leu Thr Leu Ala Lys Asn Phe
370 375 380

gaa gcc ttt ata gtg acc gat att cca tat ttg tcc att tac gtt cgt 1200
Glu Ala Phe Ile Val Thr Asp Ile Pro Tyr Leu Ser Ile Tyr Val Arg
385 390 395 400

gat gaa gtg aga aga ttt att aca ttt tta gat gct gta tat gac agt 1248
Asp Glu Val Arg Arg Phe Ile Thr Phe Leu Asp Ala Val Tyr Asp Ser
405 410 415

ggc ggg aaa ctg gcc act acg ggt gca gcg gat ttt tct tcc ttg ttt 1296
Gly Gly Lys Leu Ala Thr Thr Gly Ala Ala Asp Phe Ser Ser Leu Phe
420 425 430

gtg gaa cct gaa cag ata ctt aat gat ttt gag tta cgc cca aca acc 1344
Val Glu Pro Glu Gln Ile Leu Asn Asp Phe Glu Leu Arg Pro Thr Thr
435 440 445

aaa gaa cct gat agc gtc gat act ggt atg gta gat gag atg gtt gag 1392
Lys Glu Pro Asp Ser Val Asp Thr Gly Met Val Asp Glu Met Val Glu
450 455 460

aaa cac ggt ttt tcg aaa gag att gcc aag aaa tcg cag atg ttt gct 1440
Lys His Gly Phe Ser Lys Glu Ile Ala Lys Lys Ser Gln Met Phe Ala
465 470 475 480

ctt gat gaa gaa aga ttt gcc ttt gcc cgt gcc tta agc agg ctg tca 1488
Leu Asp Glu Glu Arg Phe Ala Phe Ala Arg Ala Leu Ser Arg Leu Ser
485 490 495

cag atg agc tcc acc gat tgg gtt act aag cct aca tac taa 1530
Gln Met Ser Ser Thr Asp Trp Val Thr Lys Pro Thr Tyr
500 505

<210> 49
<211> 509
<212> PRT
<213> Saccharomyces cerevisiae

<400> 49

Met Ile Ala Leu Lys Pro Asn Ala Val Arg Thr Phe Arg Gln Val Gln

1 5 10 15

His Cys Ser Phe Arg Ile Cys Arg Tyr Gln Ser Thr Lys Ser Asn Lys
20 25 30

Cys Leu Thr Pro Leu Gln Glu Tyr Asp Arg Leu Val Lys Leu Gly Lys
35 40 45

Leu Arg Asp Asp Thr Tyr Gln Arg Gly Ile Ile Ser Ser Leu Gly Asp
50 55 60

Leu Tyr Asp Ser Leu Val Lys Tyr Val Pro Pro Val Val Lys Thr Pro
65 70 75 80

Asn Ala Val Asp Gln Val Gly Gly Trp Leu Asn Gly Leu Lys Ser Val
85 90 95

Phe Ser Arg Gly Lys Pro Lys Asn Ile Gly Ala Tyr Val Asp Val Ser
100 105 110

Lys Ile Gly Asn Ser Ile Pro Arg Gly Val Tyr Leu Tyr Gly Asp Val
115 120 125

Gly Cys Gly Lys Thr Met Leu Met Asp Leu Phe Tyr Thr Thr Ile Pro
130 135 140

Asn His Leu Thr Lys Lys Arg Ile His Phe His Gln Phe Met Gln Tyr
145 150 155 160

Val His Lys Arg Ser His Glu Ile Val Arg Glu Gln Asn Leu Lys Glu
165 170 175

Leu Gly Asp Ala Lys Gly Lys Glu Ile Asp Thr Val Pro Phe Leu Ala
180 185 190

Ala Glu Ile Ala Asn Asn Ser His Val Leu Cys Phe Asp Glu Phe Gln
195 200 205

Val Thr Asp Val Ala Asp Ala Met Ile Leu Arg Arg Leu Met Thr Ala
210 215 220

Leu Leu Ser Asp Asp Tyr Gly Val Val Leu Phe Ala Thr Ser Asn Arg
225 230 235 240

His Pro Asp Glu Leu Tyr Ile Asn Gly Val Gln Arg Gln Ser Phe Ile
245 250 255

Pro Cys Ile Glu Leu Ile Lys His Arg Thr Lys Val Ile Phe Leu Asn
260 265 270

Ser Pro Thr Asp Tyr Arg Lys Ile Pro Arg Pro Val Ser Ser Val Tyr
275 280 285

Tyr Phe Pro Ser Asp Thr Ser Ile Lys Tyr Ala Ser Lys Glu Cys Lys
290 295 300

Thr Arg Arg Glu Thr His Ile Lys Glu Trp Tyr Asn Tyr Phe Ala Gln
305 310 315 320

Ala Ser His Thr Asp Asp Ser Thr Asp Ser His Thr Val His Lys Thr
325 330 335

Phe Tyr Asp Tyr Pro Leu Thr Ile Trp Gly Arg Glu Phe Lys Val Pro
340 345 350

Lys Cys Thr Pro Pro Arg Val Ala Gln Phe Thr Phe Lys Gln Leu Cys
355 360 365

Gly Glu Pro Leu Ala Ala Gly Asp Tyr Leu Thr Leu Ala Lys Asn Phe
370 375 380

Glu Ala Phe Ile Val Thr Asp Ile Pro Tyr Leu Ser Ile Tyr Val Arg
385 390 395 400

Asp Glu Val Arg Arg Phe Ile Thr Phe Leu Asp Ala Val Tyr Asp Ser
405 410 415

Gly Gly Lys Leu Ala Thr Thr Gly Ala Ala Asp Phe Ser Ser Leu Phe
420 425 430

Val Glu Pro Glu Gln Ile Leu Asn Asp Phe Glu Leu Arg Pro Thr Thr
435 440 445

Lys Glu Pro Asp Ser Val Asp Thr Gly Met Val Asp Glu Met Val Glu
450 455 460

Lys His Gly Phe Ser Lys Glu Ile Ala Lys Lys Ser Gln Met Phe Ala
465 470 475 480

Leu Asp Glu Glu Arg Phe Ala Phe Ala Arg Ala Leu Ser Arg Leu Ser
485 490 495

Gln Met Ser Ser Thr Asp Trp Val Thr Lys Pro Thr Tyr
500 505

<210> 50
<211> 1710
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(1710)

<400> 50

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atg aag gat tta aaa tta tcg aat ttc aaa ggc aaa ttt ata agc aga        48
Met Lys Asp Leu Lys Leu Ser Asn Phe Lys Gly Lys Phe Ile Ser Arg
1               5                   10                  15

acc agt cac tgg gga ctt acg ggt aag aag ttg cgg tat ttc atc act        96
Thr Ser His Trp Gly Leu Thr Gly Lys Lys Leu Arg Tyr Phe Ile Thr
            20                  25                  30

atc gca tct atg acg ggc ttc tcc ctg ttt gga tac gac caa ggg ttg       144
Ile Ala Ser Met Thr Gly Phe Ser Leu Phe Gly Tyr Asp Gln Gly Leu
        35                  40                  45

atg gca agt cta att act ggt aaa cag ttc aac tat gaa ttt cca gca       192
Met Ala Ser Leu Ile Thr Gly Lys Gln Phe Asn Tyr Glu Phe Pro Ala
    50                  55                  60

acc aaa gaa aat ggc gat cat gac aga cac gca act gta gtg cag ggc       240
Thr Lys Glu Asn Gly Asp His Asp Arg His Ala Thr Val Val Gln Gly
65                  70                  75                  80

gct aca acc tcc tgt tat gaa tta ggt tgt ttc gca ggt tct cta ttc       288
Ala Thr Thr Ser Cys Tyr Glu Leu Gly Cys Phe Ala Gly Ser Leu Phe
                85                  90                  95

gtt atg ttc tgc ggt gaa aga att ggt aga aaa cca tta atc ctg atg       336
Val Met Phe Cys Gly Glu Arg Ile Gly Arg Lys Pro Leu Ile Leu Met
            100                 105                 110

ggt tcc gta ata acc atc att ggt gcc gtt att tct aca tgc gca ttt       384
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Gly Ser Val Ile Thr Ile Ile Gly Ala Val Ile Ser Thr Cys Ala Phe
115 120 125

cgt ggt tac tgg gca tta ggc cag ttt atc atc gga aga gtc gtc acc 432
Arg Gly Tyr Trp Ala Leu Gly Gln Phe Ile Ile Gly Arg Val Val Thr
130 135 140

ggt gtt gga aca ggg ttg aat aca tct act att ccc gtt tgg caa tca 480
Gly Val Gly Thr Gly Leu Asn Thr Ser Thr Ile Pro Val Trp Gln Ser
145 150 155 160

gaa atg tca aaa gct gaa aat aga ggg ttg ctg gtc aat tta gaa ggt 528
Glu Met Ser Lys Ala Glu Asn Arg Gly Leu Leu Val Asn Leu Glu Gly
165 170 175

tcc aca att gct ttt ggt act atg att gct tat tgg att gat ttt ggg 576
Ser Thr Ile Ala Phe Gly Thr Met Ile Ala Tyr Trp Ile Asp Phe Gly
180 185 190

ttg tct tat acc aac agt tct gtt cag tgg aga ttc ccc gtg tca atg 624
Leu Ser Tyr Thr Asn Ser Ser Val Gln Trp Arg Phe Pro Val Ser Met
195 200 205

caa atc gtt ttt gct ctc ttc ctg ctt gct ttc atg att aaa cta cct 672
Gln Ile Val Phe Ala Leu Phe Leu Leu Ala Phe Met Ile Lys Leu Pro
210 215 220

gaa tcg cca cgt tgg ctg att tct caa agt cga aca gaa gaa gct cgc 720
Glu Ser Pro Arg Trp Leu Ile Ser Gln Ser Arg Thr Glu Glu Ala Arg
225 230 235 240

tac ttg gta gga aca cta gac gac gcg gat cca aat gat gag gaa gtt 768
Tyr Leu Val Gly Thr Leu Asp Asp Ala Asp Pro Asn Asp Glu Glu Val
245 250 255

ata aca gaa gtt gct atg ctt cac gat gct gtt aac agg acc aaa cac 816
Ile Thr Glu Val Ala Met Leu His Asp Ala Val Asn Arg Thr Lys His
260 265 270

gag aaa cat tca ctg tca agt ttg ttc tcc aga ggc agg tcc caa aat 864
Glu Lys His Ser Leu Ser Ser Leu Phe Ser Arg Gly Arg Ser Gln Asn
275 280 285

ctt cag agg gct ttg att gca gct tca acg caa ttt ttc cag caa ttt 912
Leu Gln Arg Ala Leu Ile Ala Ala Ser Thr Gln Phe Phe Gln Gln Phe
290 295 300

act ggt tgt aac gct gcc ata tac tac tct act gta tta ttc aac aaa 960
Thr Gly Cys Asn Ala Ala Ile Tyr Tyr Ser Thr Val Leu Phe Asn Lys
305 310 315 320

aca att aaa tta gac tat aga tta tca atg atc ata ggt ggg gtc ttc 1008
Thr Ile Lys Leu Asp Tyr Arg Leu Ser Met Ile Ile Gly Gly Val Phe
325 330 335

gca aca atc tac gcc tta tct act att ggt tca ttt ttt cta att gaa 1056
Ala Thr Ile Tyr Ala Leu Ser Thr Ile Gly Ser Phe Phe Leu Ile Glu
340 345 350

aag cta ggt aga cgt aag ctg ttt tta tta ggt gcc aca ggt caa gca 1104
Lys Leu Gly Arg Arg Lys Leu Phe Leu Leu Gly Ala Thr Gly Gln Ala
355 360 365

gtt tca ttc aca att aca ttt gca tgc ttg gtc aaa gaa aat aaa gaa 1152
Val Ser Phe Thr Ile Thr Phe Ala Cys Leu Val Lys Glu Asn Lys Glu
370 375 380

aac gca aga ggt gct gcc gtc ggc tta ttt ttg ttc att aca ttc ttt 1200
Asn Ala Arg Gly Ala Ala Val Gly Leu Phe Leu Phe Ile Thr Phe Phe
385 390 395 400

ggt ttg tct ttg cta tca tta cca tgg ata tac cca cca gaa att gca 1248
Gly Leu Ser Leu Leu Ser Leu Pro Trp Ile Tyr Pro Pro Glu Ile Ala
405 410 415

tca atg aaa gtt cgt gca tca aca aac gct ttc tcc aca tgt act aat 1296
Ser Met Lys Val Arg Ala Ser Thr Asn Ala Phe Ser Thr Cys Thr Asn
420 425 430

tgg ttg tgt aac ttt gcg gtt gtc atg ttc acc cca ata ttt att gga 1344
Trp Leu Cys Asn Phe Ala Val Val Met Phe Thr Pro Ile Phe Ile Gly
435 440 445

cag tcc ggt tgg ggt tgc tac tta ttt ttt gct gtt atg aat tat tta 1392

Gln Ser Gly Trp Gly Cys Tyr Leu Phe Phe Ala Val Met Asn Tyr Leu
450 455 460

tac att cca gtt atc ttc ttt ttc tac cct gaa acc gcc gga aga agt 1440
Tyr Ile Pro Val Ile Phe Phe Phe Tyr Pro Glu Thr Ala Gly Arg Ser
465 470 475 480

ttg gag gaa atc gac atc atc ttt gct aaa gca tac gag gat ggc act 1488
Leu Glu Glu Ile Asp Ile Ile Phe Ala Lys Ala Tyr Glu Asp Gly Thr
485 490 495

caa cca tgg aga gtt gct aac cat ttg ccc aag tta tcc cta caa gaa 1536
Gln Pro Trp Arg Val Ala Asn His Leu Pro Lys Leu Ser Leu Gln Glu
500 505 510

gtc gaa gat cat gcc aat gca ttg ggc tct tat gac gac gaa atg gaa 1584
Val Glu Asp His Ala Asn Ala Leu Gly Ser Tyr Asp Asp Glu Met Glu
515 520 525

aaa gag gac ttt ggt gaa gat aga gta gaa gac acc tat aac caa att 1632
Lys Glu Asp Phe Gly Glu Asp Arg Val Glu Asp Thr Tyr Asn Gln Ile
530 535 540

aac ggc gat aat tcg tct agt tct tca aac atc aaa aat gaa gat aca 1680
Asn Gly Asp Asn Ser Ser Ser Ser Ser Asn Ile Lys Asn Glu Asp Thr
545 550 555 560

gtg aac gat aaa gca aat ttt gag ggt tga 1710
Val Asn Asp Lys Ala Asn Phe Glu Gly
565

<210> 51
<211> 569
<212> PRT
<213> Saccharomyces cerevisiae

<400> 51

Met Lys Asp Leu Lys Leu Ser Asn Phe Lys Gly Lys Phe Ile Ser Arg
1 5 10 15

Thr Ser His Trp Gly Leu Thr Gly Lys Lys Leu Arg Tyr Phe Ile Thr
20 25 30

Ile Ala Ser Met Thr Gly Phe Ser Leu Phe Gly Tyr Asp Gln Gly Leu
35 40 45

Met Ala Ser Leu Ile Thr Gly Lys Gln Phe Asn Tyr Glu Phe Pro Ala
50 55 60

Thr Lys Glu Asn Gly Asp His Asp Arg His Ala Thr Val Val Gln Gly
65 70 75 80

Ala Thr Thr Ser Cys Tyr Glu Leu Gly Cys Phe Ala Gly Ser Leu Phe
85 90 95

Val Met Phe Cys Gly Glu Arg Ile Gly Arg Lys Pro Leu Ile Leu Met
100 105 110

Gly Ser Val Ile Thr Ile Ile Gly Ala Val Ile Ser Thr Cys Ala Phe
115 120 125

Arg Gly Tyr Trp Ala Leu Gly Gln Phe Ile Ile Gly Arg Val Val Thr
130 135 140

Gly Val Gly Thr Gly Leu Asn Thr Ser Thr Ile Pro Val Trp Gln Ser
145 150 155 160

Glu Met Ser Lys Ala Glu Asn Arg Gly Leu Leu Val Asn Leu Glu Gly
165 170 175

Ser Thr Ile Ala Phe Gly Thr Met Ile Ala Tyr Trp Ile Asp Phe Gly

180 185 190

Leu Ser Tyr Thr Asn Ser Ser Val Gln Trp Arg Phe Pro Val Ser Met
195 200 205

Gln Ile Val Phe Ala Leu Phe Leu Leu Ala Phe Met Ile Lys Leu Pro
210 215 220

Glu Ser Pro Arg Trp Leu Ile Ser Gln Ser Arg Thr Glu Glu Ala Arg
225 230 235 240

Tyr Leu Val Gly Thr Leu Asp Asp Ala Asp Pro Asn Asp Glu Glu Val
245 250 255

Ile Thr Glu Val Ala Met Leu His Asp Ala Val Asn Arg Thr Lys His
260 265 270

Glu Lys His Ser Leu Ser Ser Leu Phe Ser Arg Gly Arg Ser Gln Asn
275 280 285

Leu Gln Arg Ala Leu Ile Ala Ala Ser Thr Gln Phe Phe Gln Gln Phe
290 295 300

Thr Gly Cys Asn Ala Ala Ile Tyr Tyr Ser Thr Val Leu Phe Asn Lys
305 310 315 320

Thr Ile Lys Leu Asp Tyr Arg Leu Ser Met Ile Ile Gly Gly Val Phe
325 330 335

Ala Thr Ile Tyr Ala Leu Ser Thr Ile Gly Ser Phe Phe Leu Ile Glu
340 345 350

Lys Leu Gly Arg Arg Lys Leu Phe Leu Leu Gly Ala Thr Gly Gln Ala
355 360 365

Val Ser Phe Thr Ile Thr Phe Ala Cys Leu Val Lys Glu Asn Lys Glu
370 375 380

Asn Ala Arg Gly Ala Ala Val Gly Leu Phe Leu Phe Ile Thr Phe Phe
385 390 395 400

Gly Leu Ser Leu Leu Ser Leu Pro Trp Ile Tyr Pro Pro Glu Ile Ala
405 410 415

Ser Met Lys Val Arg Ala Ser Thr Asn Ala Phe Ser Thr Cys Thr Asn
420 425 430

Trp Leu Cys Asn Phe Ala Val Val Met Phe Thr Pro Ile Phe Ile Gly
435 440 445

Gln Ser Gly Trp Gly Cys Tyr Leu Phe Phe Ala Val Met Asn Tyr Leu
450 455 460

Tyr Ile Pro Val Ile Phe Phe Phe Tyr Pro Glu Thr Ala Gly Arg Ser
465 470 475 480

Leu Glu Glu Ile Asp Ile Ile Phe Ala Lys Ala Tyr Glu Asp Gly Thr
485 490 495

Gln Pro Trp Arg Val Ala Asn His Leu Pro Lys Leu Ser Leu Gln Glu
500 505 510

Val Glu Asp His Ala Asn Ala Leu Gly Ser Tyr Asp Asp Glu Met Glu
515 520 525

Lys Glu Asp Phe Gly Glu Asp Arg Val Glu Asp Thr Tyr Asn Gln Ile
530 535 540

Asn Gly Asp Asn Ser Ser Ser Ser Ser Asn Ile Lys Asn Glu Asp Thr
545 550 555 560

Val Asn Asp Lys Ala Asn Phe Glu Gly
565

<210> 52
<211> 432
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(432)

<400> 52
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Met Glu Thr Asn Phe Ser Phe Asp Ser Asn Leu Ile Val Ile Ile Ile
1 5 10 15

atc acg ttg ttt gcc aca aga att att gct aaa aga ttt tta tct act 96
Ile Thr Leu Phe Ala Thr Arg Ile Ile Ala Lys Arg Phe Leu Ser Thr
20 25 30

cca aaa atg gta tcc cag gaa aca gtt gct cac gta aag gat ctg att 144
Pro Lys Met Val Ser Gln Glu Thr Val Ala His Val Lys Asp Leu Ile
35 40 45

ggc caa aag gaa gtg ttt gtt gca gca aag aca tac tgc cct tac tgt 192
Gly Gln Lys Glu Val Phe Val Ala Ala Lys Thr Tyr Cys Pro Tyr Cys
50 55 60

aaa gct act ttg tct acc ctc ttc caa gaa ttg aac gtt ccc aaa tcc 240
Lys Ala Thr Leu Ser Thr Leu Phe Gln Glu Leu Asn Val Pro Lys Ser
65 70 75 80

aag gcc ctt gtg ttg gaa tta gat gaa atg agc aat ggc tca gag att 288
Lys Ala Leu Val Leu Glu Leu Asp Glu Met Ser Asn Gly Ser Glu Ile
85 90 95

caa gac gct tta gaa gaa atc tcg ggc caa aaa act gta cct aac gta 336
Gln Asp Ala Leu Glu Glu Ile Ser Gly Gln Lys Thr Val Pro Asn Val
100 105 110

tac atc aat ggc aag cac att ggt ggt aac agc gat ttg gaa act ttg 384
Tyr Ile Asn Gly Lys His Ile Gly Gly Asn Ser Asp Leu Glu Thr Leu
115 120 125

aag aaa aat ggc aag tta gct gaa ata ttg aag ccg gta ttt caa tag 432
Lys Lys Asn Gly Lys Leu Ala Glu Ile Leu Lys Pro Val Phe Gln
130 135 140

<210> 53
<211> 143
<212> PRT
<213> Saccharomyces cerevisiae

<400> 53

Met Glu Thr Asn Phe Ser Phe Asp Ser Asn Leu Ile Val Ile Ile Ile
1 5 10 15

Ile Thr Leu Phe Ala Thr Arg Ile Ile Ala Lys Arg Phe Leu Ser Thr
20 25 30

Pro Lys Met Val Ser Gln Glu Thr Val Ala His Val Lys Asp Leu Ile
35 40 45

Gly Gln Lys Glu Val Phe Val Ala Ala Lys Thr Tyr Cys Pro Tyr Cys

50 55 60

Lys Ala Thr Leu Ser Thr Leu Phe Gln Glu Leu Asn Val Pro Lys Ser
65 70 75 80

Lys Ala Leu Val Leu Glu Leu Asp Glu Met Ser Asn Gly Ser Glu Ile
85 90 95

Gln Asp Ala Leu Glu Glu Ile Ser Gly Gln Lys Thr Val Pro Asn Val
100 105 110

Tyr Ile Asn Gly Lys His Ile Gly Gly Asn Ser Asp Leu Glu Thr Leu
115 120 125

Lys Lys Asn Gly Lys Leu Ala Glu Ile Leu Lys Pro Val Phe Gln
130 135 140

<210> 54
<211> 426
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(426)

<400> 54
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Met Lys Cys His Ala Lys Arg Thr Leu Ala Phe Leu Ala Thr Ala Leu
1 5 10 15

ccc cta tct gga aaa agc cga gca tgc acc cgt acc cca caa agc ttc 96
Pro Leu Ser Gly Lys Ser Arg Ala Cys Thr Arg Thr Pro Gln Ser Phe
20 25 30

gct tcc ggt ttc cgg gca gca gcg ccg ttt ctt ttt tcc cgc tgc ttc 144
Ala Ser Gly Phe Arg Ala Ala Ala Pro Phe Leu Phe Ser Arg Cys Phe
35 40 45

gcc ctt tgt att act cat tgc gca ctt ttt cac ttg cca tat tcg ttc 192
Ala Leu Cys Ile Thr His Cys Ala Leu Phe His Leu Pro Tyr Ser Phe
50 55 60

acc ggt ttt tct ttt tat ttc ttc gtc ttt ttt cgt ctt ttt ctt cac 240
Thr Gly Phe Ser Phe Tyr Phe Phe Val Phe Phe Arg Leu Phe Leu His
65 70 75 80

tgg ata tac gct ttt tgc att tgc aat agc aca tat gtg tat ata tat 288
Trp Ile Tyr Ala Phe Cys Ile Cys Asn Ser Thr Tyr Val Tyr Ile Tyr
85 90 95

aag caa gtg ttg agc ttg cct gtc aaa tcc tcc atg tgt cct tct cgt 336
Lys Gln Val Leu Ser Leu Pro Val Lys Ser Ser Met Cys Pro Ser Arg
100 105 110

cta tct tgt tct gtc tgg tat aga gta ata ctt aca tac ata tac gta 384
Leu Ser Cys Ser Val Trp Tyr Arg Val Ile Leu Thr Tyr Ile Tyr Val
115 120 125

cat tgt ttc cgc tgg cta gtt cgt aac cac ctc ctt tcc tag 426
His Cys Phe Arg Trp Leu Val Arg Asn His Leu Leu Ser
130 135 140

<210> 55
<211> 141
<212> PRT
<213> Saccharomyces cerevisiae

<400> 55

Met Lys Cys His Ala Lys Arg Thr Leu Ala Phe Leu Ala Thr Ala Leu
1 5 10 15

Pro Leu Ser Gly Lys Ser Arg Ala Cys Thr Arg Thr Pro Gln Ser Phe
20 25 30

Ala Ser Gly Phe Arg Ala Ala Ala Pro Phe Leu Phe Ser Arg Cys Phe
35 40 45

Ala Leu Cys Ile Thr His Cys Ala Leu Phe His Leu Pro Tyr Ser Phe
50 55 60

Thr Gly Phe Ser Phe Tyr Phe Phe Val Phe Phe Arg Leu Phe Leu His
65 70 75 80

Trp Ile Tyr Ala Phe Cys Ile Cys Asn Ser Thr Tyr Val Tyr Ile Tyr
85 90 95

Lys Gln Val Leu Ser Leu Pro Val Lys Ser Ser Met Cys Pro Ser Arg
100 105 110

Leu Ser Cys Ser Val Trp Tyr Arg Val Ile Leu Thr Tyr Ile Tyr Val
115 120 125

His Cys Phe Arg Trp Leu Val Arg Asn His Leu Leu Ser
130 135 140

<210> 56
<211> 1488
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(1488)

<400> 56

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atg aaa act gat aga tta ctg att aac gct tcc ccg gag aca tgt acc        48
Met Lys Thr Asp Arg Leu Leu Ile Asn Ala Ser Pro Glu Thr Cys Thr
1               5                  10                  15

aag gga gat gct gag atg gat act atg gat act att gac aga atg aca        96
Lys Gly Asp Ala Glu Met Asp Thr Met Asp Thr Ile Asp Arg Met Thr
            20                  25                  30

tca gtt aaa gtt tta gcg gaa ggc aag gta tta agc aac ttc gaa gaa       144
Ser Val Lys Val Leu Ala Glu Gly Lys Val Leu Ser Asn Phe Glu Glu
        35                  40                  45

ccg ggc tta atg agg tgc ggt tat cat gat gca aaa aac tgg gtc aga       192
Pro Gly Leu Met Arg Cys Gly Tyr His Asp Ala Lys Asn Trp Val Arg
    50                  55                  60

aga tta tcg agc gaa aca att gtc ggt gag gac acg agt aat tta tac       240
Arg Leu Ser Ser Glu Thr Ile Val Gly Glu Asp Thr Ser Asn Leu Tyr
65                  70                  75                  80

cca ttt tat gtt gat act gca tac gat gta agg cgt ttg aga aag gat       288
Pro Phe Tyr Val Asp Thr Ala Tyr Asp Val Arg Arg Leu Arg Lys Asp
                85                  90                  95

ctt ata aat gct aag gtt gac ttg cag gtt gaa aac ctg ata ata atc       336
Leu Ile Asn Ala Lys Val Asp Leu Gln Val Glu Asn Leu Ile Ile Ile
            100                 105                 110

tgc aat att aat gat att tcc act gta ttt ctc atg aga gaa gtg gtg       384
Cys Asn Ile Asn Asp Ile Ser Thr Val Phe Leu Met Arg Glu Val Val
        115                 120                 125

gaa tgg atc tta cgc aat ttc cat tca ata act gta tat gta caa gat       432
Glu Trp Ile Leu Arg Asn Phe His Ser Ile Thr Val Tyr Val Gln Asp
    130                 135                 140

att ttt aaa aag tca act cag ttt gct gtt ggt gac ctc tgc aaa gac       480
Ile Phe Lys Lys Ser Thr Gln Phe Ala Val Gly Asp Leu Cys Lys Asp
145                 150                 155                 160

agc aat tgc agt aaa aac aga gta aag tat tgg tca aaa gaa ttt gtt       528
Ser Asn Cys Ser Lys Asn Arg Val Lys Tyr Trp Ser Lys Glu Phe Val
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165 170 175

aaa aaa cac gat tca ttc ttt gac ttg atg att aca cta ggg ggt gat 576
Lys Lys His Asp Ser Phe Phe Asp Leu Met Ile Thr Leu Gly Gly Asp
180 185 190

gga act gtc ctt ttt gct tca tct ata ttc acg aaa gat gtt ccg ccg 624
Gly Thr Val Leu Phe Ala Ser Ser Ile Phe Thr Lys Asp Val Pro Pro
195 200 205

att gtt cca ttt gcc ctt gga tca tta gga ttt cta aca aat ttt gaa 672
Ile Val Pro Phe Ala Leu Gly Ser Leu Gly Phe Leu Thr Asn Phe Glu
210 215 220

ttt caa aat ttc aaa gaa acg ttg aaa cat atc tta aca gat gag gtt 720
Phe Gln Asn Phe Lys Glu Thr Leu Lys His Ile Leu Thr Asp Glu Val
225 230 235 240

cgt att aat tta cga atg agg ttg caa tgc aaa ctc tac cgt aga aat 768
Arg Ile Asn Leu Arg Met Arg Leu Gln Cys Lys Leu Tyr Arg Arg Asn
245 250 255

aaa cca gaa att gat gcc gca act ggg aga aaa ata tgt tac atc gat 816
Lys Pro Glu Ile Asp Ala Ala Thr Gly Arg Lys Ile Cys Tyr Ile Asp
260 265 270

ttc atc tcc gaa cat cac gta ttg aac gaa gta acc ata gat aga ggt 864
Phe Ile Ser Glu His His Val Leu Asn Glu Val Thr Ile Asp Arg Gly
275 280 285

cca gct cct tgt tta tcc cta tta gaa ctc tat gga aac gac tca cta 912
Pro Ala Pro Cys Leu Ser Leu Leu Glu Leu Tyr Gly Asn Asp Ser Leu
290 295 300

atg act aag gtt cag gga gat gga ttg att gtt gcc acg cct acg gga 960
Met Thr Lys Val Gln Gly Asp Gly Leu Ile Val Ala Thr Pro Thr Gly
305 310 315 320

tcc acg gca tac tca ttg agt gca gga ggc tct tta ata tcg cca agc 1008
Ser Thr Ala Tyr Ser Leu Ser Ala Gly Gly Ser Leu Ile Ser Pro Ser
325 330 335

gta aat gcc ata gcg gtg acg cct ata tgt cct cat act ttg agc ttt 1056
Val Asn Ala Ile Ala Val Thr Pro Ile Cys Pro His Thr Leu Ser Phe
340 345 350

agg cct ata att tta cca gat agc atg gaa tta aaa gtt aga gta gat 1104
Arg Pro Ile Ile Leu Pro Asp Ser Met Glu Leu Lys Val Arg Val Asp
355 360 365

atg aac tca aga ggg acg tcg tgg gtg aat ttt gac gga aaa gat aga 1152
Met Asn Ser Arg Gly Thr Ser Trp Val Asn Phe Asp Gly Lys Asp Arg
370 375 380

gtt gaa ttg aaa cag ggt gac tat gtt gtg ata act gca agc ccc tat 1200
Val Glu Leu Lys Gln Gly Asp Tyr Val Val Ile Thr Ala Ser Pro Tyr
385 390 395 400

tcg gta ccg act atc gag tca tct gcc agt gaa ttt ttt gaa agt atc 1248
Ser Val Pro Thr Ile Glu Ser Ser Ala Ser Glu Phe Phe Glu Ser Ile
405 410 415

agt aaa aat ctt aat tgg aat gac cgc gaa gag cag aag cca ttt gca 1296
Ser Lys Asn Leu Asn Trp Asn Asp Arg Glu Glu Gln Lys Pro Phe Ala
420 425 430

cat att ctc tcg cca aaa aat caa gaa aaa tat aga tta gac tca tcg 1344
His Ile Leu Ser Pro Lys Asn Gln Glu Lys Tyr Arg Leu Asp Ser Ser
435 440 445

aaa aat gga aac gac acc ata agt aat ccc ctc gag agt tca tgc ata 1392
Lys Asn Gly Asn Asp Thr Ile Ser Asn Pro Leu Glu Ser Ser Cys Ile
450 455 460

agc tca gat gca caa gat gag gag agg aaa tcc gta acg gaa aca gaa 1440
Ser Ser Asp Ala Gln Asp Glu Glu Arg Lys Ser Val Thr Glu Thr Glu
465 470 475 480

aca gaa ata gtt gtt gaa cgg act cgt cag gct cat ttt gca atc taa 1488
Thr Glu Ile Val Val Glu Arg Thr Arg Gln Ala His Phe Ala Ile
485 490 495

<210> 57

<211> 495

<212> PRT

<213> Saccharomyces cerevisiae

<400> 57

Met Lys Thr Asp Arg Leu Leu Ile Asn Ala Ser Pro Glu Thr Cys Thr
1 5 10 15

Lys Gly Asp Ala Glu Met Asp Thr Met Asp Thr Ile Asp Arg Met Thr
20 25 30

Ser Val Lys Val Leu Ala Glu Gly Lys Val Leu Ser Asn Phe Glu Glu
35 40 45

Pro Gly Leu Met Arg Cys Gly Tyr His Asp Ala Lys Asn Trp Val Arg
50 55 60

Arg Leu Ser Ser Glu Thr Ile Val Gly Glu Asp Thr Ser Asn Leu Tyr
65 70 75 80

Pro Phe Tyr Val Asp Thr Ala Tyr Asp Val Arg Arg Leu Arg Lys Asp
85 90 95

Leu Ile Asn Ala Lys Val Asp Leu Gln Val Glu Asn Leu Ile Ile Ile
100 105 110

Cys Asn Ile Asn Asp Ile Ser Thr Val Phe Leu Met Arg Glu Val Val
115 120 125

Glu Trp Ile Leu Arg Asn Phe His Ser Ile Thr Val Tyr Val Gln Asp
130 135 140

Ile Phe Lys Lys Ser Thr Gln Phe Ala Val Gly Asp Leu Cys Lys Asp
145 150 155 160

Ser Asn Cys Ser Lys Asn Arg Val Lys Tyr Trp Ser Lys Glu Phe Val
165 170 175

Lys Lys His Asp Ser Phe Phe Asp Leu Met Ile Thr Leu Gly Gly Asp
180 185 190

Gly Thr Val Leu Phe Ala Ser Ser Ile Phe Thr Lys Asp Val Pro Pro
195 200 205

Ile Val Pro Phe Ala Leu Gly Ser Leu Gly Phe Leu Thr Asn Phe Glu
210 215 220

Phe Gln Asn Phe Lys Glu Thr Leu Lys His Ile Leu Thr Asp Glu Val
225 230 235 240

Arg Ile Asn Leu Arg Met Arg Leu Gln Cys Lys Leu Tyr Arg Arg Asn
245 250 255

Lys Pro Glu Ile Asp Ala Ala Thr Gly Arg Lys Ile Cys Tyr Ile Asp
260 265 270

Phe Ile Ser Glu His His Val Leu Asn Glu Val Thr Ile Asp Arg Gly
275 280 285

Pro Ala Pro Cys Leu Ser Leu Leu Glu Leu Tyr Gly Asn Asp Ser Leu
290 295 300

Met Thr Lys Val Gln Gly Asp Gly Leu Ile Val Ala Thr Pro Thr Gly
305 310 315 320

Ser Thr Ala Tyr Ser Leu Ser Ala Gly Gly Ser Leu Ile Ser Pro Ser
325 330 335

Val Asn Ala Ile Ala Val Thr Pro Ile Cys Pro His Thr Leu Ser Phe
340 345 350

Arg Pro Ile Ile Leu Pro Asp Ser Met Glu Leu Lys Val Arg Val Asp
355 360 365

Met Asn Ser Arg Gly Thr Ser Trp Val Asn Phe Asp Gly Lys Asp Arg
370 375 380

Val Glu Leu Lys Gln Gly Asp Tyr Val Val Ile Thr Ala Ser Pro Tyr
385 390 395 400

Ser Val Pro Thr Ile Glu Ser Ser Ala Ser Glu Phe Phe Glu Ser Ile
405 410 415

Ser Lys Asn Leu Asn Trp Asn Asp Arg Glu Glu Gln Lys Pro Phe Ala
420 425 430

His Ile Leu Ser Pro Lys Asn Gln Glu Lys Tyr Arg Leu Asp Ser Ser
435 440 445

Lys Asn Gly Asn Asp Thr Ile Ser Asn Pro Leu Glu Ser Ser Cys Ile
450 455 460

Ser Ser Asp Ala Gln Asp Glu Glu Arg Lys Ser Val Thr Glu Thr Glu
465 470 475 480

Thr Glu Ile Val Val Glu Arg Thr Arg Gln Ala His Phe Ala Ile
485 490 495

<210> 58
<211> 1125
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(1125)

<400> 58
atg agg ata cag tcg ctt ttt gtt tta ttt aat gtt gcc atc atc gca 48
Met Arg Ile Gln Ser Leu Phe Val Leu Phe Asn Val Ala Ile Ile Ala
1 5 10 15

tgg tca tat cca tat gag cct tta agg gtt tta caa gta gga gag aat 96
Trp Ser Tyr Pro Tyr Glu Pro Leu Arg Val Leu Gln Val Gly Glu Asn
20 25 30

gag gta atg gag gtt ccc gaa tca gaa aag cta aac tta cga aga aga 144
Glu Val Met Glu Val Pro Glu Ser Glu Lys Leu Asn Leu Arg Arg Arg
35 40 45

ggt gtc aaa ttc ttt gat gtg acc aaa cac act tct ttc tta cct ttc 192
Gly Val Lys Phe Phe Asp Val Thr Lys His Thr Ser Phe Leu Pro Phe
50 55 60

ttt aac aag gag gaa gag cca aca gta cca acg tat aac tat cct cct 240
Phe Asn Lys Glu Glu Glu Pro Thr Val Pro Thr Tyr Asn Tyr Pro Pro
65 70 75 80

gag ata tcg aac aaa gaa gta gtg gat gat tcg att aag aat ata gac 288
Glu Ile Ser Asn Lys Glu Val Val Asp Asp Ser Ile Lys Asn Ile Asp
85 90 95

aag ggc tct atg cac aag aac ttg gca aag ttt aca agt ttt tac acc 336
Lys Gly Ser Met His Lys Asn Leu Ala Lys Phe Thr Ser Phe Tyr Thr

100 105 110

cgt tac tac aag tcc gat cac ggc ttt gaa tct gcc gag tgg tta gct 384
Arg Tyr Tyr Lys Ser Asp His Gly Phe Glu Ser Ala Glu Trp Leu Ala
115 120 125

gca act atc gct aat att aca aaa gat att ccg caa gat acg ttg act 432
Ala Thr Ile Ala Asn Ile Thr Lys Asp Ile Pro Gln Asp Thr Leu Thr
130 135 140

att gaa cat ttt gat cac aaa gaa tgg aag caa tat tca att ata gtc 480
Ile Glu His Phe Asp His Lys Glu Trp Lys Gln Tyr Ser Ile Ile Val
145 150 155 160

cgt gtc acg gga tct act acg cca gaa gat att ata ata att ggt tct 528
Arg Val Thr Gly Ser Thr Thr Pro Glu Asp Ile Ile Ile Ile Gly Ser
165 170 175

cat caa gat tct atc aat ctg cta ctg cca tcc ata atg gca gct cca 576
His Gln Asp Ser Ile Asn Leu Leu Leu Pro Ser Ile Met Ala Ala Pro
180 185 190

ggt gcg gac gac aat ggg tca ggc acg gtg act aat atg gag gct ctc 624
Gly Ala Asp Asp Asn Gly Ser Gly Thr Val Thr Asn Met Glu Ala Leu
195 200 205

aga tta tat acg gaa aat ttt ttg aag aga gga ttt aga cct aac aac 672
Arg Leu Tyr Thr Glu Asn Phe Leu Lys Arg Gly Phe Arg Pro Asn Asn
210 215 220

act gtg gaa ttt cac ttt tat tcc gcc gaa gag ggg gga ttg ttg ggt 720
Thr Val Glu Phe His Phe Tyr Ser Ala Glu Glu Gly Gly Leu Leu Gly
225 230 235 240

tct ctt gat gtt ttt aca gct tat gcc aaa cag aaa aag cat gtg aga 768
Ser Leu Asp Val Phe Thr Ala Tyr Ala Lys Gln Lys Lys His Val Arg
245 250 255

gcg atg ctt cag caa gac atg acg gga tat gtt tct gat cca gaa gat 816
Ala Met Leu Gln Gln Asp Met Thr Gly Tyr Val Ser Asp Pro Glu Asp
260 265 270

gaa cat gtg ggg att gtc acc gac tac act act ccc gca tta act gat 864
Glu His Val Gly Ile Val Thr Asp Tyr Thr Thr Pro Ala Leu Thr Asp
275 280 285

ttt ata aaa cta att atc aac tct tat cta tcc att cct tac agg gat 912
Phe Ile Lys Leu Ile Ile Asn Ser Tyr Leu Ser Ile Pro Tyr Arg Asp
290 295 300

aca caa tgt ggc tat gct tgt agc gat cat ggg agt gcc acc aga aac 960
Thr Gln Cys Gly Tyr Ala Cys Ser Asp His Gly Ser Ala Thr Arg Asn
305 310 315 320

gga ttt cca ggc tcc ttc gtg att gaa agt gag ttc aaa aag act aac 1008
Gly Phe Pro Gly Ser Phe Val Ile Glu Ser Glu Phe Lys Lys Thr Asn
325 330 335

aag tat att cac agc acc atg gat act ttg gac aga tta agt ctc gct 1056
Lys Tyr Ile His Ser Thr Met Asp Thr Leu Asp Arg Leu Ser Leu Ala
340 345 350

cat atg gcg gaa cac aca aaa att gta tta ggg gta atc att gaa ctc 1104
His Met Ala Glu His Thr Lys Ile Val Leu Gly Val Ile Ile Glu Leu
355 360 365

ggg tca tgg tcc gct tgg taa 1125
Gly Ser Trp Ser Ala Trp
370

<210> 59
<211> 374
<212> PRT
<213> Saccharomyces cerevisiae

<400> 59

Met Arg Ile Gln Ser Leu Phe Val Leu Phe Asn Val Ala Ile Ile Ala
1 5 10 15

Trp Ser Tyr Pro Tyr Glu Pro Leu Arg Val Leu Gln Val Gly Glu Asn
20 25 30

Glu Val Met Glu Val Pro Glu Ser Glu Lys Leu Asn Leu Arg Arg Arg
35 40 45

Gly Val Lys Phe Phe Asp Val Thr Lys His Thr Ser Phe Leu Pro Phe
50 55 60

Phe Asn Lys Glu Glu Glu Pro Thr Val Pro Thr Tyr Asn Tyr Pro Pro
65 70 75 80

Glu Ile Ser Asn Lys Glu Val Val Asp Asp Ser Ile Lys Asn Ile Asp
85 90 95

Lys Gly Ser Met His Lys Asn Leu Ala Lys Phe Thr Ser Phe Tyr Thr
100 105 110

Arg Tyr Tyr Lys Ser Asp His Gly Phe Glu Ser Ala Glu Trp Leu Ala
115 120 125

Ala Thr Ile Ala Asn Ile Thr Lys Asp Ile Pro Gln Asp Thr Leu Thr
130 135 140

Ile Glu His Phe Asp His Lys Glu Trp Lys Gln Tyr Ser Ile Ile Val
145 150 155 160

Arg Val Thr Gly Ser Thr Thr Pro Glu Asp Ile Ile Ile Ile Gly Ser
165 170 175

His Gln Asp Ser Ile Asn Leu Leu Leu Pro Ser Ile Met Ala Ala Pro
180 185 190

Gly Ala Asp Asp Asn Gly Ser Gly Thr Val Thr Asn Met Glu Ala Leu
195 200 205

Arg Leu Tyr Thr Glu Asn Phe Leu Lys Arg Gly Phe Arg Pro Asn Asn
210 215 220

Thr Val Glu Phe His Phe Tyr Ser Ala Glu Glu Gly Gly Leu Leu Gly
225 230 235 240

Ser Leu Asp Val Phe Thr Ala Tyr Ala Lys Gln Lys Lys His Val Arg
245 250 255

Ala Met Leu Gln Gln Asp Met Thr Gly Tyr Val Ser Asp Pro Glu Asp
260 265 270

Glu His Val Gly Ile Val Thr Asp Tyr Thr Thr Pro Ala Leu Thr Asp
275 280 285

Phe Ile Lys Leu Ile Ile Asn Ser Tyr Leu Ser Ile Pro Tyr Arg Asp
290 295 300

Thr Gln Cys Gly Tyr Ala Cys Ser Asp His Gly Ser Ala Thr Arg Asn
305 310 315 320

Gly Phe Pro Gly Ser Phe Val Ile Glu Ser Glu Phe Lys Lys Thr Asn
325 330 335

Lys Tyr Ile His Ser Thr Met Asp Thr Leu Asp Arg Leu Ser Leu Ala
340 345 350

His Met Ala Glu His Thr Lys Ile Val Leu Gly Val Ile Ile Glu Leu

355 360 365

Gly Ser Trp Ser Ala Trp
370

<210> 60
<211> 1470
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(1470)

<400> 60
atg aca aaa agt gat tta tta ttt gat aaa ttc aac gac aaa cat gga 48
Met Thr Lys Ser Asp Leu Leu Phe Asp Lys Phe Asn Asp Lys His Gly
1 5 10 15

aag ttt cta gtt ttt ttt ggt acc ttt gta gat acc cct aaa tta gga 96
Lys Phe Leu Val Phe Phe Gly Thr Phe Val Asp Thr Pro Lys Leu Gly
20 25 30

gag ctg aga atc aga gag aaa aca tct gtt gga gtt ctc aac gga atc 144
Glu Leu Arg Ile Arg Glu Lys Thr Ser Val Gly Val Leu Asn Gly Ile
35 40 45

atc agg ttt gtg aac aga aat tca ctc gat cct gtc aaa gat tgt tta 192
Ile Arg Phe Val Asn Arg Asn Ser Leu Asp Pro Val Lys Asp Cys Leu
50 55 60

gat cac gat agt agc tta tca cca gag gat gtc acg gtg gtt gac ata 240
Asp His Asp Ser Ser Leu Ser Pro Glu Asp Val Thr Val Val Asp Ile
65 70 75 80

att gga aaa gac aag act cga aat aac agc ttt tat ttt cca ggt ttt 288
Ile Gly Lys Asp Lys Thr Arg Asn Asn Ser Phe Tyr Phe Pro Gly Phe
85 90 95

```
gtt gac acg cat aac cat gtc tcg caa tat cca aat gtc ggc gta ttt      336
Val Asp Thr His Asn His Val Ser Gln Tyr Pro Asn Val Gly Val Phe
            100                 105                 110

ggg aat tct acc ctg ctg gat tgg cta gag aag tat acc ttc ccc ata      384
Gly Asn Ser Thr Leu Leu Asp Trp Leu Glu Lys Tyr Thr Phe Pro Ile
        115                 120                 125

gaa gcc gca cta gca aac gaa aat att gcg aga gaa gtt tac aat aag      432
Glu Ala Ala Leu Ala Asn Glu Asn Ile Ala Arg Glu Val Tyr Asn Lys
    130                 135                 140

gta ata agt aag acg ctt tct cac ggt aca acg act gtg gct tac tat      480
Val Ile Ser Lys Thr Leu Ser His Gly Thr Thr Thr Val Ala Tyr Tyr
145                 150                 155                 160

aat acc att gat ctc aag tcc act aag ctc ttg gct caa cta agc tcc      528
Asn Thr Ile Asp Leu Lys Ser Thr Lys Leu Leu Ala Gln Leu Ser Ser
                165                 170                 175

tta ttg ggg cag cgt gtt ctt gtt gga aaa gtg tgc atg gat acc aat      576
Leu Leu Gly Gln Arg Val Leu Val Gly Lys Val Cys Met Asp Thr Asn
            180                 185                 190

ggt ccc gag tat tat att gaa gat act aaa act tcc ttt gaa agc act      624
Gly Pro Glu Tyr Tyr Ile Glu Asp Thr Lys Thr Ser Phe Glu Ser Thr
        195                 200                 205

gtg aaa gtt gtt aag tac ata cgg gaa acc att tgt gat ccc ctc gta      672
Val Lys Val Val Lys Tyr Ile Arg Glu Thr Ile Cys Asp Pro Leu Val
    210                 215                 220

aat cct ata gtg aca cca agg ttc gcg ccc tct tgt tct aga gaa cta      720
Asn Pro Ile Val Thr Pro Arg Phe Ala Pro Ser Cys Ser Arg Glu Leu
225                 230                 235                 240

atg caa cag ttg tcc aag cta gtc aag gat gaa aac ata cac gtt caa      768
Met Gln Gln Leu Ser Lys Leu Val Lys Asp Glu Asn Ile His Val Gln
                245                 250                 255

acc cac ttg tcg gaa aat aag gag gag ata cag tgg gtt caa gat tta      816
Thr His Leu Ser Glu Asn Lys Glu Glu Ile Gln Trp Val Gln Asp Leu
```

260 265 270

ttt ccc gaa tgt gag agc tat act gat gta tac gac aaa tat ggg ctg 864
Phe Pro Glu Cys Glu Ser Tyr Thr Asp Val Tyr Asp Lys Tyr Gly Leu
275 280 285

ctc aca gaa aaa aca gta ttg gca cat tgt att cat cta aca gat gcc 912
Leu Thr Glu Lys Thr Val Leu Ala His Cys Ile His Leu Thr Asp Ala
290 295 300

gaa gcg cgt gtg att aaa cag cgt cgc tgt ggt ata tct cat tgt ccc 960
Glu Ala Arg Val Ile Lys Gln Arg Arg Cys Gly Ile Ser His Cys Pro
305 310 315 320

att tcc aac tcc tct ctg act tct gga gag tgt agg gtt cga tgg ttg 1008
Ile Ser Asn Ser Ser Leu Thr Ser Gly Glu Cys Arg Val Arg Trp Leu
325 330 335

ctg gac cag ggc ata aag gtt ggt cta ggc acc gac gtt tca gcc ggt 1056
Leu Asp Gln Gly Ile Lys Val Gly Leu Gly Thr Asp Val Ser Ala Gly
340 345 350

cat tct tgt agc ata ctc acc acc gga agg cag gcc ttt gca gtt tca 1104
His Ser Cys Ser Ile Leu Thr Thr Gly Arg Gln Ala Phe Ala Val Ser
355 360 365

agg cat ttg gca atg aga gaa act gat cat gca aaa ctt tca gtc tcc 1152
Arg His Leu Ala Met Arg Glu Thr Asp His Ala Lys Leu Ser Val Ser
370 375 380

gag tgc cta ttt ctt gct aca atg ggc gga gca caa gtc ttg cgt atg 1200
Glu Cys Leu Phe Leu Ala Thr Met Gly Gly Ala Gln Val Leu Arg Met
385 390 395 400

gat gag acc ttg ggg act ttt gac gtc ggt aag cag ttt gac gct caa 1248
Asp Glu Thr Leu Gly Thr Phe Asp Val Gly Lys Gln Phe Asp Ala Gln
405 410 415

atg atc gat acc aat gct ccc ggc tca aac gtg gat atg ttt cat tgg 1296
Met Ile Asp Thr Asn Ala Pro Gly Ser Asn Val Asp Met Phe His Trp
420 425 430

cag cta aag gag aag gat caa atg caa gag caa gag caa gag caa ggg 1344
Gln Leu Lys Glu Lys Asp Gln Met Gln Glu Gln Glu Gln Glu Gln Gly
435 440 445

caa gac cct tat aag aac cca ccg ctg ctt act aat gaa gac ata atc 1392
Gln Asp Pro Tyr Lys Asn Pro Pro Leu Leu Thr Asn Glu Asp Ile Ile
450 455 460

gca aaa tgg ttc ttt aac ggt gat gat cgc aac acc act aaa gtt tgg 1440
Ala Lys Trp Phe Phe Asn Gly Asp Asp Arg Asn Thr Thr Lys Val Trp
465 470 475 480

gta gcc ggc cag caa gtc tac cag att tag 1470
Val Ala Gly Gln Gln Val Tyr Gln Ile
485

<210> 61
<211> 489
<212> PRT
<213> Saccharomyces cerevisiae

<400> 61

Met Thr Lys Ser Asp Leu Leu Phe Asp Lys Phe Asn Asp Lys His Gly
1 5 10 15

Lys Phe Leu Val Phe Phe Gly Thr Phe Val Asp Thr Pro Lys Leu Gly
20 25 30

Glu Leu Arg Ile Arg Glu Lys Thr Ser Val Gly Val Leu Asn Gly Ile
35 40 45

Ile Arg Phe Val Asn Arg Asn Ser Leu Asp Pro Val Lys Asp Cys Leu
50 55 60

Asp His Asp Ser Ser Leu Ser Pro Glu Asp Val Thr Val Val Asp Ile
65 70 75 80

Ile Gly Lys Asp Lys Thr Arg Asn Asn Ser Phe Tyr Phe Pro Gly Phe
85 90 95

Val Asp Thr His Asn His Val Ser Gln Tyr Pro Asn Val Gly Val Phe
100 105 110

Gly Asn Ser Thr Leu Leu Asp Trp Leu Glu Lys Tyr Thr Phe Pro Ile
115 120 125

Glu Ala Ala Leu Ala Asn Glu Asn Ile Ala Arg Glu Val Tyr Asn Lys
130 135 140

Val Ile Ser Lys Thr Leu Ser His Gly Thr Thr Thr Val Ala Tyr Tyr
145 150 155 160

Asn Thr Ile Asp Leu Lys Ser Thr Lys Leu Leu Ala Gln Leu Ser Ser
165 170 175

Leu Leu Gly Gln Arg Val Leu Val Gly Lys Val Cys Met Asp Thr Asn
180 185 190

Gly Pro Glu Tyr Tyr Ile Glu Asp Thr Lys Thr Ser Phe Glu Ser Thr
195 200 205

Val Lys Val Val Lys Tyr Ile Arg Glu Thr Ile Cys Asp Pro Leu Val
210 215 220

Asn Pro Ile Val Thr Pro Arg Phe Ala Pro Ser Cys Ser Arg Glu Leu
225 230 235 240

Met Gln Gln Leu Ser Lys Leu Val Lys Asp Glu Asn Ile His Val Gln
245 250 255

Thr His Leu Ser Glu Asn Lys Glu Glu Ile Gln Trp Val Gln Asp Leu
260 265 270

Phe Pro Glu Cys Glu Ser Tyr Thr Asp Val Tyr Asp Lys Tyr Gly Leu
275 280 285

Leu Thr Glu Lys Thr Val Leu Ala His Cys Ile His Leu Thr Asp Ala
290 295 300

Glu Ala Arg Val Ile Lys Gln Arg Arg Cys Gly Ile Ser His Cys Pro
305 310 315 320

Ile Ser Asn Ser Ser Leu Thr Ser Gly Glu Cys Arg Val Arg Trp Leu
325 330 335

Leu Asp Gln Gly Ile Lys Val Gly Leu Gly Thr Asp Val Ser Ala Gly
340 345 350

His Ser Cys Ser Ile Leu Thr Thr Gly Arg Gln Ala Phe Ala Val Ser
355 360 365

Arg His Leu Ala Met Arg Glu Thr Asp His Ala Lys Leu Ser Val Ser
370 375 380

Glu Cys Leu Phe Leu Ala Thr Met Gly Gly Ala Gln Val Leu Arg Met
385 390 395 400

Asp Glu Thr Leu Gly Thr Phe Asp Val Gly Lys Gln Phe Asp Ala Gln

405 410 415

Met Ile Asp Thr Asn Ala Pro Gly Ser Asn Val Asp Met Phe His Trp
420 425 430

Gln Leu Lys Glu Lys Asp Gln Met Gln Glu Gln Glu Gln Glu Gln Gly
435 440 445

Gln Asp Pro Tyr Lys Asn Pro Pro Leu Leu Thr Asn Glu Asp Ile Ile
450 455 460

Ala Lys Trp Phe Phe Asn Gly Asp Asp Arg Asn Thr Thr Lys Val Trp
465 470 475 480

Val Ala Gly Gln Gln Val Tyr Gln Ile
485

<210> 62
<211> 441
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(441)

<400> 62
atg aaa ggc tca ccc att tct caa ttt agt aag acc tct att aat gct 48
Met Lys Gly Ser Pro Ile Ser Gln Phe Ser Lys Thr Ser Ile Asn Ala
1 5 10 15

ctt acc agg cct tgg aag aaa tac aga gat ggt gaa tta ttt tat ggg 96
Leu Thr Arg Pro Trp Lys Lys Tyr Arg Asp Gly Glu Leu Phe Tyr Gly
20 25 30

```
tta tca aaa gtt ggg aat aaa aga gtg ccg ttg acc acg aag caa ggt      144
Leu Ser Lys Val Gly Asn Lys Arg Val Pro Leu Thr Thr Lys Gln Gly
        35                  40                  45

aac aag acg atg tac aaa ggg aca aga gct tca ggg att ggt aga cat      192
Asn Lys Thr Met Tyr Lys Gly Thr Arg Ala Ser Gly Ile Gly Arg His
    50                  55                  60

aca aaa ttc ggt ggt tat gtg ata aac tgg aag aaa gtc aga acc tat      240
Thr Lys Phe Gly Gly Tyr Val Ile Asn Trp Lys Lys Val Arg Thr Tyr
65                  70                  75                  80

gtt acc cca gat atg gtt aat ttc gaa tta aag ccc tac gtt aac gca      288
Val Thr Pro Asp Met Val Asn Phe Glu Leu Lys Pro Tyr Val Asn Ala
                85                  90                  95

aat gta cca cct cta aaa cac gaa ttt aaa gga ttt agc ggc ggc cca      336
Asn Val Pro Pro Leu Lys His Glu Phe Lys Gly Phe Ser Gly Gly Pro
            100                 105                 110

tta gat cct cgt tta cag tta tta aag ata aaa gaa tac ata gta aac      384
Leu Asp Pro Arg Leu Gln Leu Leu Lys Ile Lys Glu Tyr Ile Val Asn
        115                 120                 125

ggg agg gta caa agc gaa ggg gcc acc gac act tca tgt tat aag gag      432
Gly Arg Val Gln Ser Glu Gly Ala Thr Asp Thr Ser Cys Tyr Lys Glu
    130                 135                 140

cgt gga taa                                                         441
Arg Gly
145
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<210> 63
<211> 146
<212> PRT
<213> Saccharomyces cerevisiae

<400> 63

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Met Lys Gly Ser Pro Ile Ser Gln Phe Ser Lys Thr Ser Ile Asn Ala
1               5                   10                  15
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Leu Thr Arg Pro Trp Lys Lys Tyr Arg Asp Gly Glu Leu Phe Tyr Gly
20 25 30

Leu Ser Lys Val Gly Asn Lys Arg Val Pro Leu Thr Thr Lys Gln Gly
35 40 45

Asn Lys Thr Met Tyr Lys Gly Thr Arg Ala Ser Gly Ile Gly Arg His
50 55 60

Thr Lys Phe Gly Gly Tyr Val Ile Asn Trp Lys Lys Val Arg Thr Tyr
65 70 75 80

Val Thr Pro Asp Met Val Asn Phe Glu Leu Lys Pro Tyr Val Asn Ala
85 90 95

Asn Val Pro Pro Leu Lys His Glu Phe Lys Gly Phe Ser Gly Gly Pro
100 105 110

Leu Asp Pro Arg Leu Gln Leu Leu Lys Ile Lys Glu Tyr Ile Val Asn
115 120 125

Gly Arg Val Gln Ser Glu Gly Ala Thr Asp Thr Ser Cys Tyr Lys Glu
130 135 140

Arg Gly
145

<210> 64
<211> 429
<212> DNA
<213> Saccharomyces cerevisiae

<220>

<221> CDS

<222> (1)..(429)

<400> 64

atg gcg tat aat caa gaa gat agt aaa aga cta tca gac aag tat aag 48
Met Ala Tyr Asn Gln Glu Asp Ser Lys Arg Leu Ser Asp Lys Tyr Lys
1 5 10 15

aag gag gga cat ttt gac aag ttg aaa aga gaa ata ttg tct aac cca 96
Lys Glu Gly His Phe Asp Lys Leu Lys Arg Glu Ile Leu Ser Asn Pro
20 25 30

tgg aat aat aca gaa gag aat agt gaa tct ttt gaa caa gcg ctt cgg 144
Trp Asn Asn Thr Glu Glu Asn Ser Glu Ser Phe Glu Gln Ala Leu Arg
35 40 45

aaa aga gtt gcc agt act gtt aaa gaa atg gtt aac gaa gat gaa gaa 192
Lys Arg Val Ala Ser Thr Val Lys Glu Met Val Asn Glu Asp Glu Glu
50 55 60

tta ata ttt aaa aac aga ggg cta acc agt gca ttg att gaa tca caa 240
Leu Ile Phe Lys Asn Arg Gly Leu Thr Ser Ala Leu Ile Glu Ser Gln
65 70 75 80

ttg gtc aag gac aac tac cta aag ctg ggt agt aaa atg gag ggg gat 288
Leu Val Lys Asp Asn Tyr Leu Lys Leu Gly Ser Lys Met Glu Gly Asp
85 90 95

aat ggt gat ggt gag aag aaa ttt gac ttg gat gtc tat gta cgg tct 336
Asn Gly Asp Gly Glu Lys Lys Phe Asp Leu Asp Val Tyr Val Arg Ser
100 105 110

aag tta cag gat ccc aaa cta ttg gaa atg ata aag gga caa ctt cag 384
Lys Leu Gln Asp Pro Lys Leu Leu Glu Met Ile Lys Gly Gln Leu Gln
115 120 125

gaa aca ctg aac tct tat gaa gag gaa gca aat gga agt acg taa 429
Glu Thr Leu Asn Ser Tyr Glu Glu Glu Ala Asn Gly Ser Thr
130 135 140

<210> 65
<211> 142
<212> PRT
<213> Saccharomyces cerevisiae

<400> 65

Met Ala Tyr Asn Gln Glu Asp Ser Lys Arg Leu Ser Asp Lys Tyr Lys
1 5 10 15

Lys Glu Gly His Phe Asp Lys Leu Lys Arg Glu Ile Leu Ser Asn Pro
20 25 30

Trp Asn Asn Thr Glu Glu Asn Ser Glu Ser Phe Glu Gln Ala Leu Arg
35 40 45

Lys Arg Val Ala Ser Thr Val Lys Glu Met Val Asn Glu Asp Glu Glu
50 55 60

Leu Ile Phe Lys Asn Arg Gly Leu Thr Ser Ala Leu Ile Glu Ser Gln
65 70 75 80

Leu Val Lys Asp Asn Tyr Leu Lys Leu Gly Ser Lys Met Glu Gly Asp
85 90 95

Asn Gly Asp Gly Glu Lys Lys Phe Asp Leu Asp Val Tyr Val Arg Ser
100 105 110

Lys Leu Gln Asp Pro Lys Leu Leu Glu Met Ile Lys Gly Gln Leu Gln
115 120 125

Glu Thr Leu Asn Ser Tyr Glu Glu Glu Ala Asn Gly Ser Thr

130 135 140

<210> 66
<211> 462
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(462)

<400> 66

atg acc ttt tta caa ttt atc aat aat aat aga caa gaa gga caa ggt 48
Met Thr Phe Leu Gln Phe Ile Asn Asn Asn Arg Gln Glu Gly Gln Gly
1 5 10 15

tat att tca gaa aaa tta ttc aaa act aag aag aat gag atg ata aga 96
Tyr Ile Ser Glu Lys Leu Phe Lys Thr Lys Lys Asn Glu Met Ile Arg
20 25 30

aaa aca gtt acc aat tta gta gct gta aga tta aaa aac tta tcc cac 144
Lys Thr Val Thr Asn Leu Val Ala Val Arg Leu Lys Asn Leu Ser His
35 40 45

gaa ttt gat gta ata gag aat tat ctg cgc tat ata gct agc acc agt 192
Glu Phe Asp Val Ile Glu Asn Tyr Leu Arg Tyr Ile Ala Ser Thr Ser
50 55 60

gaa cat cta ttt act gct att aag cgc cac ttt aac aaa tgt gcc aga 240
Glu His Leu Phe Thr Ala Ile Lys Arg His Phe Asn Lys Cys Ala Arg
65 70 75 80

aaa ctt ttg aaa gaa gca atc gac tcc aaa tca aac tca gaa act gct 288
Lys Leu Leu Lys Glu Ala Ile Asp Ser Lys Ser Asn Ser Glu Thr Ala
85 90 95

acg gtg gtt ctg caa gaa gga ttt tct ggc att tgc tta ttg aaa gcg 336
Thr Val Val Leu Gln Glu Gly Phe Ser Gly Ile Cys Leu Leu Lys Ala
100 105 110

tct tca att ata tta aaa cta aaa ttg aag ttt cca aaa aag aaa gat 384
Ser Ser Ile Ile Leu Lys Leu Lys Leu Lys Phe Pro Lys Lys Lys Asp
115 120 125

aga act gat att agc aaa ttg tgt gac aag aaa gaa cgg atg aca cag 432
Arg Thr Asp Ile Ser Lys Leu Cys Asp Lys Lys Glu Arg Met Thr Gln
130 135 140

tgg tta gaa att tca att ttg atg aac tga 462
Trp Leu Glu Ile Ser Ile Leu Met Asn
145 150

<210> 67
<211> 153
<212> PRT
<213> Saccharomyces cerevisiae

<400> 67

Met Thr Phe Leu Gln Phe Ile Asn Asn Asn Arg Gln Glu Gly Gln Gly
1 5 10 15

Tyr Ile Ser Glu Lys Leu Phe Lys Thr Lys Lys Asn Glu Met Ile Arg
20 25 30

Lys Thr Val Thr Asn Leu Val Ala Val Arg Leu Lys Asn Leu Ser His
35 40 45

Glu Phe Asp Val Ile Glu Asn Tyr Leu Arg Tyr Ile Ala Ser Thr Ser
50 55 60

Glu His Leu Phe Thr Ala Ile Lys Arg His Phe Asn Lys Cys Ala Arg
65 70 75 80

Lys Leu Leu Lys Glu Ala Ile Asp Ser Lys Ser Asn Ser Glu Thr Ala

85 90 95

Thr Val Val Leu Gln Glu Gly Phe Ser Gly Ile Cys Leu Leu Lys Ala
100 105 110

Ser Ser Ile Ile Leu Lys Leu Lys Leu Lys Phe Pro Lys Lys Lys Asp
115 120 125

Arg Thr Asp Ile Ser Lys Leu Cys Asp Lys Lys Glu Arg Met Thr Gln
130 135 140

Trp Leu Glu Ile Ser Ile Leu Met Asn
145 150

<210> 68
<211> 1584
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(1584)

<400> 68
atg agt ctc tcg cag gtg tca cct tta ccc cat atc aag gat gtt gtt 48
Met Ser Leu Ser Gln Val Ser Pro Leu Pro His Ile Lys Asp Val Val
1 5 10 15

tta gga gat aca gta ggc caa ggc gca ttc gcc tgc gtt aaa aat gct 96
Leu Gly Asp Thr Val Gly Gln Gly Ala Phe Ala Cys Val Lys Asn Ala
20 25 30

cat ctt caa atg gat ccc tcc att att cta gct gtt aaa ttc att cat 144
His Leu Gln Met Asp Pro Ser Ile Ile Leu Ala Val Lys Phe Ile His
35 40 45

gtt ccc act tgc aaa aaa atg gga ctc agt gac aag gat atc aca aaa 192
Val Pro Thr Cys Lys Lys Met Gly Leu Ser Asp Lys Asp Ile Thr Lys
50 55 60

gag gtt gtt ttg caa tcg aag tgt tct aag cat cct aat gtt ttg aga 240
Glu Val Val Leu Gln Ser Lys Cys Ser Lys His Pro Asn Val Leu Arg
65 70 75 80

ctt atc gat tgt aat gtc tct aaa gaa tat atg tgg ata att ctg gag 288
Leu Ile Asp Cys Asn Val Ser Lys Glu Tyr Met Trp Ile Ile Leu Glu
85 90 95

atg gca gat ggt ggt gat cta ttt gat aag att gag cct gac gtt gga 336
Met Ala Asp Gly Gly Asp Leu Phe Asp Lys Ile Glu Pro Asp Val Gly
100 105 110

gtt gat tcc gac gtg gcc caa ttt tac ttt caa cag ctc gtt agt gct 384
Val Asp Ser Asp Val Ala Gln Phe Tyr Phe Gln Gln Leu Val Ser Ala
115 120 125

att aat tat ctg cat gta gaa tgt gga gtt gct cac aga gac atc aag 432
Ile Asn Tyr Leu His Val Glu Cys Gly Val Ala His Arg Asp Ile Lys
130 135 140

cct gaa aac atc tta ctc gat aag aac gga aat ctg aag cta gct gat 480
Pro Glu Asn Ile Leu Leu Asp Lys Asn Gly Asn Leu Lys Leu Ala Asp
145 150 155 160

ttt ggg ctc gcc tct caa ttt agg agg aaa gat ggt aca tta cgt gta 528
Phe Gly Leu Ala Ser Gln Phe Arg Arg Lys Asp Gly Thr Leu Arg Val
165 170 175

tcc atg gat caa agg ggt tct cca ccc tac atg gct cct gaa gta tta 576
Ser Met Asp Gln Arg Gly Ser Pro Pro Tyr Met Ala Pro Glu Val Leu
180 185 190

tat tct gaa gag ggt tat tac gca gat cga aca gat ata tgg tct att 624
Tyr Ser Glu Glu Gly Tyr Tyr Ala Asp Arg Thr Asp Ile Trp Ser Ile
195 200 205

ggc atc ctc ttg ttc gta ttg ttg act ggt caa acg cct tgg gaa tta 672
Gly Ile Leu Leu Phe Val Leu Leu Thr Gly Gln Thr Pro Trp Glu Leu

210 215 220

cct tca tta gag aac gaa gat ttc gtc ttt ttt att gaa aat gat gga 720
Pro Ser Leu Glu Asn Glu Asp Phe Val Phe Phe Ile Glu Asn Asp Gly
225 230 235 240

aat tta aac tgg gga ccc tgg tca aag ata gaa ttt act cac ttg aac 768
Asn Leu Asn Trp Gly Pro Trp Ser Lys Ile Glu Phe Thr His Leu Asn
245 250 255

cta ctc cga aaa att tta caa cct gac cca aat aag agg gtg aca ttg 816
Leu Leu Arg Lys Ile Leu Gln Pro Asp Pro Asn Lys Arg Val Thr Leu
260 265 270

aag gct tta aag tta cat cct tgg gta tta cgt cga gct tca ttt tct 864
Lys Ala Leu Lys Leu His Pro Trp Val Leu Arg Arg Ala Ser Phe Ser
275 280 285

ggg gat gat ggt ctc tgt aat gac cct gaa ctc ttg gct aag aaa ctg 912
Gly Asp Asp Gly Leu Cys Asn Asp Pro Glu Leu Leu Ala Lys Lys Leu
290 295 300

ttt tct cac tta aaa gtc tca ctg agt aac gaa aat tat ttg aaa ttc 960
Phe Ser His Leu Lys Val Ser Leu Ser Asn Glu Asn Tyr Leu Lys Phe
305 310 315 320

act caa gat aca aac tct aat aat agg tac att tct act cag cca att 1008
Thr Gln Asp Thr Asn Ser Asn Asn Arg Tyr Ile Ser Thr Gln Pro Ile
325 330 335

ggt aac gaa ttg gct gag ctt gaa cac gac tca atg cat ttc cag aca 1056
Gly Asn Glu Leu Ala Glu Leu Glu His Asp Ser Met His Phe Gln Thr
340 345 350

gtt tcg aat aca caa cgt gca ttt acc tcg tat gat tca aat acg aac 1104
Val Ser Asn Thr Gln Arg Ala Phe Thr Ser Tyr Asp Ser Asn Thr Asn
355 360 365

tat aat agc gga aca ggt atg aca caa gag gct aag tgg acg caa ttc 1152
Tyr Asn Ser Gly Thr Gly Met Thr Gln Glu Ala Lys Trp Thr Gln Phe
370 375 380

ata agc tat gat atc gct gcc tta cag ttt cat tct gat gaa aat gat 1200
Ile Ser Tyr Asp Ile Ala Ala Leu Gln Phe His Ser Asp Glu Asn Asp
385 390 395 400

tgt aat gaa tta gta aaa cga cat tta caa ttt aat ccg aat aaa ctt 1248
Cys Asn Glu Leu Val Lys Arg His Leu Gln Phe Asn Pro Asn Lys Leu
405 410 415

acc aag ttc tac acg ttg caa cct atg gat gtt ttg tta ccg att ttg 1296
Thr Lys Phe Tyr Thr Leu Gln Pro Met Asp Val Leu Leu Pro Ile Leu
420 425 430

gag aaa gcc ttg aat tta tca caa att aga gta aaa ccc gac ctt ttt 1344
Glu Lys Ala Leu Asn Leu Ser Gln Ile Arg Val Lys Pro Asp Leu Phe
435 440 445

gcg aat ttt gaa aga ttg tgc gaa tta ttg ggt tat gat aac gtt ttc 1392
Ala Asn Phe Glu Arg Leu Cys Glu Leu Leu Gly Tyr Asp Asn Val Phe
450 455 460

cca ctt att ata aat att aaa acc aaa agt aat ggg ggt tat caa tta 1440
Pro Leu Ile Ile Asn Ile Lys Thr Lys Ser Asn Gly Gly Tyr Gln Leu
465 470 475 480

tgc ggt agc att tcc atc ata aag att gaa gaa gag ttg aaa agt gtc 1488
Cys Gly Ser Ile Ser Ile Ile Lys Ile Glu Glu Glu Leu Lys Ser Val
485 490 495

gga ttt gaa aga aaa act ggt gat cct tta gaa tgg aga aga ttg ttc 1536
Gly Phe Glu Arg Lys Thr Gly Asp Pro Leu Glu Trp Arg Arg Leu Phe
500 505 510

aag aaa att tca act atc tgt agg gat att atc cta att ccc aac tga 1584
Lys Lys Ile Ser Thr Ile Cys Arg Asp Ile Ile Leu Ile Pro Asn
515 520 525

<210> 69
<211> 527
<212> PRT
<213> Saccharomyces cerevisiae

<400> 69

Met Ser Leu Ser Gln Val Ser Pro Leu Pro His Ile Lys Asp Val Val
1 5 10 15

Leu Gly Asp Thr Val Gly Gln Gly Ala Phe Ala Cys Val Lys Asn Ala
20 25 30

His Leu Gln Met Asp Pro Ser Ile Ile Leu Ala Val Lys Phe Ile His
35 40 45

Val Pro Thr Cys Lys Lys Met Gly Leu Ser Asp Lys Asp Ile Thr Lys
50 55 60

Glu Val Val Leu Gln Ser Lys Cys Ser Lys His Pro Asn Val Leu Arg
65 70 75 80

Leu Ile Asp Cys Asn Val Ser Lys Glu Tyr Met Trp Ile Ile Leu Glu
85 90 95

Met Ala Asp Gly Gly Asp Leu Phe Asp Lys Ile Glu Pro Asp Val Gly
100 105 110

Val Asp Ser Asp Val Ala Gln Phe Tyr Phe Gln Gln Leu Val Ser Ala
115 120 125

Ile Asn Tyr Leu His Val Glu Cys Gly Val Ala His Arg Asp Ile Lys
130 135 140

Pro Glu Asn Ile Leu Leu Asp Lys Asn Gly Asn Leu Lys Leu Ala Asp
145 150 155 160

Phe Gly Leu Ala Ser Gln Phe Arg Arg Lys Asp Gly Thr Leu Arg Val
165 170 175

Ser Met Asp Gln Arg Gly Ser Pro Pro Tyr Met Ala Pro Glu Val Leu
180 185 190

Tyr Ser Glu Glu Gly Tyr Tyr Ala Asp Arg Thr Asp Ile Trp Ser Ile
195 200 205

Gly Ile Leu Leu Phe Val Leu Leu Thr Gly Gln Thr Pro Trp Glu Leu
210 215 220

Pro Ser Leu Glu Asn Glu Asp Phe Val Phe Phe Ile Glu Asn Asp Gly
225 230 235 240

Asn Leu Asn Trp Gly Pro Trp Ser Lys Ile Glu Phe Thr His Leu Asn
245 250 255

Leu Leu Arg Lys Ile Leu Gln Pro Asp Pro Asn Lys Arg Val Thr Leu
260 265 270

Lys Ala Leu Lys Leu His Pro Trp Val Leu Arg Arg Ala Ser Phe Ser
275 280 285

Gly Asp Asp Gly Leu Cys Asn Asp Pro Glu Leu Leu Ala Lys Lys Leu
290 295 300

Phe Ser His Leu Lys Val Ser Leu Ser Asn Glu Asn Tyr Leu Lys Phe
305 310 315 320

Thr Gln Asp Thr Asn Ser Asn Asn Arg Tyr Ile Ser Thr Gln Pro Ile

325 330 335

Gly Asn Glu Leu Ala Glu Leu Glu His Asp Ser Met His Phe Gln Thr
340 345 350

Val Ser Asn Thr Gln Arg Ala Phe Thr Ser Tyr Asp Ser Asn Thr Asn
355 360 365

Tyr Asn Ser Gly Thr Gly Met Thr Gln Glu Ala Lys Trp Thr Gln Phe
370 375 380

Ile Ser Tyr Asp Ile Ala Ala Leu Gln Phe His Ser Asp Glu Asn Asp
385 390 395 400

Cys Asn Glu Leu Val Lys Arg His Leu Gln Phe Asn Pro Asn Lys Leu
405 410 415

Thr Lys Phe Tyr Thr Leu Gln Pro Met Asp Val Leu Leu Pro Ile Leu
420 425 430

Glu Lys Ala Leu Asn Leu Ser Gln Ile Arg Val Lys Pro Asp Leu Phe
435 440 445

Ala Asn Phe Glu Arg Leu Cys Glu Leu Leu Gly Tyr Asp Asn Val Phe
450 455 460

Pro Leu Ile Ile Asn Ile Lys Thr Lys Ser Asn Gly Gly Tyr Gln Leu
465 470 475 480

Cys Gly Ser Ile Ser Ile Ile Lys Ile Glu Glu Glu Leu Lys Ser Val
485 490 495

Gly Phe Glu Arg Lys Thr Gly Asp Pro Leu Glu Trp Arg Arg Leu Phe
500 505 510

Lys Lys Ile Ser Thr Ile Cys Arg Asp Ile Ile Leu Ile Pro Asn
515 520 525

<210> 70
<211> 849
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(849)

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Met Asp Pro Ser Leu Val Leu Glu Gln Thr Ile Gln Asp Val Ser Asn
1 5 10 15

ctc cca tca gaa ttt cgt tac ctc tta gag gag atc ggt tca aat gat 96
Leu Pro Ser Glu Phe Arg Tyr Leu Leu Glu Glu Ile Gly Ser Asn Asp
20 25 30

ttg aag ctc atc gaa gaa aaa aag aaa tac gag caa aaa gaa tca caa 144
Leu Lys Leu Ile Glu Glu Lys Lys Lys Tyr Glu Gln Lys Glu Ser Gln
35 40 45

ata cac aaa ttt ata aga cag caa ggc tca ata ccg aaa cat cca cag 192
Ile His Lys Phe Ile Arg Gln Gln Gly Ser Ile Pro Lys His Pro Gln
50 55 60

gaa gat ggg ctt gac aaa gaa ata aaa gaa tca ctt ttg aaa tgt cag 240
Glu Asp Gly Leu Asp Lys Glu Ile Lys Glu Ser Leu Leu Lys Cys Gln
65 70 75 80

tct ttg caa aga gaa aaa tgc gtt ctg gcg aac act gcc ttg ttt cta 288
Ser Leu Gln Arg Glu Lys Cys Val Leu Ala Asn Thr Ala Leu Phe Leu

85 90 95

att gct aga cac ttg aat aag ttg gaa aaa aac atc gct tta ttg gag 336
Ile Ala Arg His Leu Asn Lys Leu Glu Lys Asn Ile Ala Leu Leu Glu
100 105 110

gaa gat ggt gtt cta gcc ccc gtg gaa gaa gat gga gac atg gat agc 384
Glu Asp Gly Val Leu Ala Pro Val Glu Glu Asp Gly Asp Met Asp Ser
115 120 125

gct gct gaa gcc tct aga gaa agt tca gtt gtg agt aac agt agc gtg 432
Ala Ala Glu Ala Ser Arg Glu Ser Ser Val Val Ser Asn Ser Ser Val
130 135 140

aaa aag aga aga gct gca tca agc tca gga tcc gtt cca ccc act ttg 480
Lys Lys Arg Arg Ala Ala Ser Ser Ser Gly Ser Val Pro Pro Thr Leu
145 150 155 160

aaa aag aaa aaa act agt cga aca tct aaa ctg caa aat gaa att gac 528
Lys Lys Lys Lys Thr Ser Arg Thr Ser Lys Leu Gln Asn Glu Ile Asp
165 170 175

gtt tct tca aga gaa aag tct gtt act cca gtg agc cca agc att gaa 576
Val Ser Ser Arg Glu Lys Ser Val Thr Pro Val Ser Pro Ser Ile Glu
180 185 190

aag aag att gca aga aca aaa gaa ttc aaa aac agt aga aat ggt aaa 624
Lys Lys Ile Ala Arg Thr Lys Glu Phe Lys Asn Ser Arg Asn Gly Lys
195 200 205

ggc caa aac ggt tcc cct gaa aac gag gaa gag gac aaa act tta tac 672
Gly Gln Asn Gly Ser Pro Glu Asn Glu Glu Glu Asp Lys Thr Leu Tyr
210 215 220

tgc ttc tgt caa aga gtt tcg ttt gga gaa atg gtt gca tgt gat gga 720
Cys Phe Cys Gln Arg Val Ser Phe Gly Glu Met Val Ala Cys Asp Gly
225 230 235 240

ccc aac tgt aaa tat gaa tgg ttt cat tat gat tgt gta aat tta aaa 768
Pro Asn Cys Lys Tyr Glu Trp Phe His Tyr Asp Cys Val Asn Leu Lys
245 250 255

gaa cct ccg aaa gga aca tgg tac tgt ccc gaa tgt aaa att gag atg 816
Glu Pro Pro Lys Gly Thr Trp Tyr Cys Pro Glu Cys Lys Ile Glu Met
260 265 270

gaa aaa aac aaa ctg aaa aga aaa cgt aac tga 849
Glu Lys Asn Lys Leu Lys Arg Lys Arg Asn
275 280

<210> 71
<211> 282
<212> PRT
<213> Saccharomyces cerevisiae

<400> 71

Met Asp Pro Ser Leu Val Leu Glu Gln Thr Ile Gln Asp Val Ser Asn
1 5 10 15

Leu Pro Ser Glu Phe Arg Tyr Leu Leu Glu Glu Ile Gly Ser Asn Asp
20 25 30

Leu Lys Leu Ile Glu Glu Lys Lys Lys Tyr Glu Gln Lys Glu Ser Gln
35 40 45

Ile His Lys Phe Ile Arg Gln Gln Gly Ser Ile Pro Lys His Pro Gln
50 55 60

Glu Asp Gly Leu Asp Lys Glu Ile Lys Glu Ser Leu Leu Lys Cys Gln
65 70 75 80

Ser Leu Gln Arg Glu Lys Cys Val Leu Ala Asn Thr Ala Leu Phe Leu
85 90 95

Ile Ala Arg His Leu Asn Lys Leu Glu Lys Asn Ile Ala Leu Leu Glu
100 105 110

Glu Asp Gly Val Leu Ala Pro Val Glu Glu Asp Gly Asp Met Asp Ser
115 120 125

Ala Ala Glu Ala Ser Arg Glu Ser Ser Val Val Ser Asn Ser Ser Val
130 135 140

Lys Lys Arg Arg Ala Ala Ser Ser Ser Gly Ser Val Pro Pro Thr Leu
145 150 155 160

Lys Lys Lys Lys Thr Ser Arg Thr Ser Lys Leu Gln Asn Glu Ile Asp
165 170 175

Val Ser Ser Arg Glu Lys Ser Val Thr Pro Val Ser Pro Ser Ile Glu
180 185 190

Lys Lys Ile Ala Arg Thr Lys Glu Phe Lys Asn Ser Arg Asn Gly Lys
195 200 205

Gly Gln Asn Gly Ser Pro Glu Asn Glu Glu Glu Asp Lys Thr Leu Tyr
210 215 220

Cys Phe Cys Gln Arg Val Ser Phe Gly Glu Met Val Ala Cys Asp Gly
225 230 235 240

Pro Asn Cys Lys Tyr Glu Trp Phe His Tyr Asp Cys Val Asn Leu Lys
245 250 255

Glu Pro Pro Lys Gly Thr Trp Tyr Cys Pro Glu Cys Lys Ile Glu Met
260 265 270

Glu Lys Asn Lys Leu Lys Arg Lys Arg Asn

275 280

<210> 72
<211> 1479
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(1479)

<400> 72

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atg gag agt cga act aca ggg cct tta acg act gaa acc tac gat ggc        48
Met Glu Ser Arg Thr Thr Gly Pro Leu Thr Thr Glu Thr Tyr Asp Gly
1               5                  10                  15

ccc act gtg gcc ttc atg ata tta ggt gcc gcc cta gta ttt ttt atg        96
Pro Thr Val Ala Phe Met Ile Leu Gly Ala Ala Leu Val Phe Phe Met
            20                  25                  30

gtg ccc gga ttg gga ttc ttg tac tcc gga ttg gca aga agg aag tct       144
Val Pro Gly Leu Gly Phe Leu Tyr Ser Gly Leu Ala Arg Arg Lys Ser
        35                  40                  45

gca cta gca cta atc tgg gtt gta tta atg gcg act ttg gtc ggt ata       192
Ala Leu Ala Leu Ile Trp Val Val Leu Met Ala Thr Leu Val Gly Ile
    50                  55                  60

ctg caa tgg tat ttc tgg ggt tac tct cta gct ttt tca aag tcc gct       240
Leu Gln Trp Tyr Phe Trp Gly Tyr Ser Leu Ala Phe Ser Lys Ser Ala
65                  70                  75                  80

ccg aat aat aaa ttc att ggg aat cta gat tcg ttt ggc ttt aga aac       288
Pro Asn Asn Lys Phe Ile Gly Asn Leu Asp Ser Phe Gly Phe Arg Asn
                85                  90                  95

gtg tac gga aaa aaa ttc gat gaa gat gcc tac cct gag ctc gcg tat       336
Val Tyr Gly Lys Lys Phe Asp Glu Asp Ala Tyr Pro Glu Leu Ala Tyr
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100 105 110

gca acc ttc caa atg atg ttt tcg tgc gtc aac tta agt att atc gct 384
Ala Thr Phe Gln Met Met Phe Ser Cys Val Asn Leu Ser Ile Ile Ala
115 120 125

ggc gcc act gcc gaa aga ggc agg ctg cta ccg cac atg gtt ttt ctc 432
Gly Ala Thr Ala Glu Arg Gly Arg Leu Leu Pro His Met Val Phe Leu
130 135 140

ttt att cta gct acc att gga tat tgt cca gtg acg tat tgg att tgg 480
Phe Ile Leu Ala Thr Ile Gly Tyr Cys Pro Val Thr Tyr Trp Ile Trp
145 150 155 160

tca cca ggt ggt tgg gca tac caa tgg gga gtc ctc gat tgg gca ggc 528
Ser Pro Gly Gly Trp Ala Tyr Gln Trp Gly Val Leu Asp Trp Ala Gly
165 170 175

ggc ggc aac att gaa ata tta agc gct gtt tcc ggg ttt gtt tac tct 576
Gly Gly Asn Ile Glu Ile Leu Ser Ala Val Ser Gly Phe Val Tyr Ser
180 185 190

tgg ttt ttg ggc aaa aga aat gaa aag tta ctg ata aat ttc agg cct 624
Trp Phe Leu Gly Lys Arg Asn Glu Lys Leu Leu Ile Asn Phe Arg Pro
195 200 205

cat aat gtt tca ttg gtc act cta ggc aca tcc ata ctg tgg ttt ggc 672
His Asn Val Ser Leu Val Thr Leu Gly Thr Ser Ile Leu Trp Phe Gly
210 215 220

tgg ctg cta ttt aat tct gca tcc tca tta tcc cca aat ttg agg tca 720
Trp Leu Leu Phe Asn Ser Ala Ser Ser Leu Ser Pro Asn Leu Arg Ser
225 230 235 240

gtt tat gca ttc atg aat aca tgt ctc agt gcc att act ggt ggg atg 768
Val Tyr Ala Phe Met Asn Thr Cys Leu Ser Ala Ile Thr Gly Gly Met
245 250 255

acg tgg tgt ctt ctg gat tac aga tcg gag aag aaa tgg tcg aca gtt 816
Thr Trp Cys Leu Leu Asp Tyr Arg Ser Glu Lys Lys Trp Ser Thr Val
260 265 270

ggt ctg tgc tcc ggt atc att tct ggg ctg gtg gct gca acg cca agc 864
Gly Leu Cys Ser Gly Ile Ile Ser Gly Leu Val Ala Ala Thr Pro Ser
275 280 285

tca ggc tgt ata acc ctt tac ggt tca ctt att caa ggc att gtg gcg 912
Ser Gly Cys Ile Thr Leu Tyr Gly Ser Leu Ile Gln Gly Ile Val Ala
290 295 300

ggg gta gtg tgt aac ttt gcg acg aag ttg aaa tac tac gct aaa gta 960
Gly Val Val Cys Asn Phe Ala Thr Lys Leu Lys Tyr Tyr Ala Lys Val
305 310 315 320

gat gat gcc atg gac att cta gct gag cac ggg gtt gca ggc gta ata 1008
Asp Asp Ala Met Asp Ile Leu Ala Glu His Gly Val Ala Gly Val Ile
325 330 335

gga cta att ttc aat gcc ctt ttt gga gca gac tgg gtc att ggt atg 1056
Gly Leu Ile Phe Asn Ala Leu Phe Gly Ala Asp Trp Val Ile Gly Met
340 345 350

gat ggc act aca gag cac gag ggc ggc tgg gta act cac aat tac aag 1104
Asp Gly Thr Thr Glu His Glu Gly Gly Trp Val Thr His Asn Tyr Lys
355 360 365

caa atg tat aag cag atc gct tac att gcc gca tcc att ggg tac act 1152
Gln Met Tyr Lys Gln Ile Ala Tyr Ile Ala Ala Ser Ile Gly Tyr Thr
370 375 380

gct gct gta act gca ata atc tgc ttt gtg ctc ggc tac ata ccc ggt 1200
Ala Ala Val Thr Ala Ile Ile Cys Phe Val Leu Gly Tyr Ile Pro Gly
385 390 395 400

atg agg cta aga ata tca gaa gag gca gag gag gcg ggt atg gac gaa 1248
Met Arg Leu Arg Ile Ser Glu Glu Ala Glu Glu Ala Gly Met Asp Glu
405 410 415

gat caa att ggc gaa ttt gcg tac gat tat gtg gaa gtg aga aga gat 1296
Asp Gln Ile Gly Glu Phe Ala Tyr Asp Tyr Val Glu Val Arg Arg Asp
420 425 430

tac tat cta tgg ggt gta gac gaa gat tca caa cgc tct gat gta aat 1344
Tyr Tyr Leu Trp Gly Val Asp Glu Asp Ser Gln Arg Ser Asp Val Asn

435 440 445

cac cgg gtg aac aac gct cat ttg gcc gct gaa cgt agc agt agc ggt 1392
His Arg Val Asn Asn Ala His Leu Ala Ala Glu Arg Ser Ser Ser Gly
450 455 460

act aat agt tcc tcg gat ggg aat gga gaa atg att caa tcc gaa aag 1440
Thr Asn Ser Ser Ser Asp Gly Asn Gly Glu Met Ile Gln Ser Glu Lys
465 470 475 480

atc cta cca att cat caa gaa gat cct gcc aat agg taa 1479
Ile Leu Pro Ile His Gln Glu Asp Pro Ala Asn Arg
485 490

<210> 73
<211> 492
<212> PRT
<213> Saccharomyces cerevisiae

<400> 73

Met Glu Ser Arg Thr Thr Gly Pro Leu Thr Thr Glu Thr Tyr Asp Gly
1 5 10 15

Pro Thr Val Ala Phe Met Ile Leu Gly Ala Ala Leu Val Phe Phe Met
20 25 30

Val Pro Gly Leu Gly Phe Leu Tyr Ser Gly Leu Ala Arg Arg Lys Ser
35 40 45

Ala Leu Ala Leu Ile Trp Val Val Leu Met Ala Thr Leu Val Gly Ile
50 55 60

Leu Gln Trp Tyr Phe Trp Gly Tyr Ser Leu Ala Phe Ser Lys Ser Ala
65 70 75 80

Pro Asn Asn Lys Phe Ile Gly Asn Leu Asp Ser Phe Gly Phe Arg Asn
85 90 95

Val Tyr Gly Lys Lys Phe Asp Glu Asp Ala Tyr Pro Glu Leu Ala Tyr
100 105 110

Ala Thr Phe Gln Met Met Phe Ser Cys Val Asn Leu Ser Ile Ile Ala
115 120 125

Gly Ala Thr Ala Glu Arg Gly Arg Leu Leu Pro His Met Val Phe Leu
130 135 140

Phe Ile Leu Ala Thr Ile Gly Tyr Cys Pro Val Thr Tyr Trp Ile Trp
145 150 155 160

Ser Pro Gly Gly Trp Ala Tyr Gln Trp Gly Val Leu Asp Trp Ala Gly
165 170 175

Gly Gly Asn Ile Glu Ile Leu Ser Ala Val Ser Gly Phe Val Tyr Ser
180 185 190

Trp Phe Leu Gly Lys Arg Asn Glu Lys Leu Leu Ile Asn Phe Arg Pro
195 200 205

His Asn Val Ser Leu Val Thr Leu Gly Thr Ser Ile Leu Trp Phe Gly
210 215 220

Trp Leu Leu Phe Asn Ser Ala Ser Ser Leu Ser Pro Asn Leu Arg Ser
225 230 235 240

Val Tyr Ala Phe Met Asn Thr Cys Leu Ser Ala Ile Thr Gly Gly Met
245 250 255

Thr Trp Cys Leu Leu Asp Tyr Arg Ser Glu Lys Lys Trp Ser Thr Val
260 265 270

Gly Leu Cys Ser Gly Ile Ile Ser Gly Leu Val Ala Ala Thr Pro Ser
275 280 285

Ser Gly Cys Ile Thr Leu Tyr Gly Ser Leu Ile Gln Gly Ile Val Ala
290 295 300

Gly Val Val Cys Asn Phe Ala Thr Lys Leu Lys Tyr Tyr Ala Lys Val
305 310 315 320

Asp Asp Ala Met Asp Ile Leu Ala Glu His Gly Val Ala Gly Val Ile
325 330 335

Gly Leu Ile Phe Asn Ala Leu Phe Gly Ala Asp Trp Val Ile Gly Met
340 345 350

Asp Gly Thr Thr Glu His Glu Gly Gly Trp Val Thr His Asn Tyr Lys
355 360 365

Gln Met Tyr Lys Gln Ile Ala Tyr Ile Ala Ala Ser Ile Gly Tyr Thr
370 375 380

Ala Ala Val Thr Ala Ile Ile Cys Phe Val Leu Gly Tyr Ile Pro Gly
385 390 395 400

Met Arg Leu Arg Ile Ser Glu Glu Ala Glu Glu Ala Gly Met Asp Glu
405 410 415

Asp Gln Ile Gly Glu Phe Ala Tyr Asp Tyr Val Glu Val Arg Arg Asp
420 425 430

Tyr Tyr Leu Trp Gly Val Asp Glu Asp Ser Gln Arg Ser Asp Val Asn
435 440 445

His Arg Val Asn Asn Ala His Leu Ala Ala Glu Arg Ser Ser Ser Gly
450 455 460

Thr Asn Ser Ser Ser Asp Gly Asn Gly Glu Met Ile Gln Ser Glu Lys
465 470 475 480

Ile Leu Pro Ile His Gln Glu Asp Pro Ala Asn Arg
485 490

<210> 74
<211> 939
<212> DNA
<213> Saccharomyces cerevisiae

<220>
<221> CDS
<222> (1)..(939)

<400> 74
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Met Cys Ile Leu Met Ala Thr Arg Ala His Pro Asp Tyr Glu Leu Ile
1 5 10 15

tta ata tct aac aga gac gaa ttc ttg gca aga aaa aca cat gct aca 96
Leu Ile Ser Asn Arg Asp Glu Phe Leu Ala Arg Lys Thr His Ala Thr
20 25 30

tgc tgg cat aac aat gat ttt atc ctt tca ccc tac gat ctg gcc aaa 144
Cys Trp His Asn Asn Asp Phe Ile Leu Ser Pro Tyr Asp Leu Ala Lys

35 40 45

acc tca gca gaa aaa caa ata ttt ggc act tgg tct ggc ata aat aaa 192
Thr Ser Ala Glu Lys Gln Ile Phe Gly Thr Trp Ser Gly Ile Asn Lys
50 55 60

gaa gga aaa tta gcc act att ctt aat tta aaa ctt gac aat gag caa 240
Glu Gly Lys Leu Ala Thr Ile Leu Asn Leu Lys Leu Asp Asn Glu Gln
65 70 75 80

aat aat acg aaa tca aga tcc cgt ggt ctg tta cca ttt ata ttt ttg 288
Asn Asn Thr Lys Ser Arg Ser Arg Gly Leu Leu Pro Phe Ile Phe Leu
85 90 95

tcg atc cat aaa gca gat ttt gaa gat tgg gat aat tac aaa aag ttt 336
Ser Ile His Lys Ala Asp Phe Glu Asp Trp Asp Asn Tyr Lys Lys Phe
100 105 110

gaa ggt cac tat gat ggg ttg aag tcc aca ggt gat ttt aat ttt ttt 384
Glu Gly His Tyr Asp Gly Leu Lys Ser Thr Gly Asp Phe Asn Phe Phe
115 120 125

tac ggc gac gtt atc aaa aag caa tat aaa gtt att gat tct cta gga 432
Tyr Gly Asp Val Ile Lys Lys Gln Tyr Lys Val Ile Asp Ser Leu Gly
130 135 140

aga act ttt gat gtg ttg agt tct acc tgt agg aaa gat ctt gat tct 480
Arg Thr Phe Asp Val Leu Ser Ser Thr Cys Arg Lys Asp Leu Asp Ser
145 150 155 160

tac atg gtt gtt tct aat ggt aaa ttt tat gac agc tcc agt ata cca 528
Tyr Met Val Val Ser Asn Gly Lys Phe Tyr Asp Ser Ser Ser Ile Pro
165 170 175

ggg cag gct tgg gaa aaa gta aag gta gca cgt gat agt tta gaa aat 576
Gly Gln Ala Trp Glu Lys Val Lys Val Ala Arg Asp Ser Leu Glu Asn
180 185 190

cta gtt tta gag aat att gaa tca gat gag gag aaa ata ata tca agt 624
Leu Val Leu Glu Asn Ile Glu Ser Asp Glu Glu Lys Ile Ile Ser Ser
195 200 205

tgc ttt caa ctc gcc tcg aag tct tcc ctt cca agc act att tca aac 672
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Ser Lys Asn Lys Ile Ile Thr Pro Glu Asp Val Glu Phe Lys Leu Ala
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Gln His Glu Phe Glu Ala Val Ile Lys Arg Leu Tyr Glu Gly Tyr Arg
675 680 685

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725 730 735

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755 760 765

Thr Thr Val Pro Phe Leu Lys Met Asp Gln Arg Ile Arg Ile Ala Lys
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Asp Gln Lys Phe Ala His Leu Met Val Glu Phe Phe Thr Lys Gln Gly
785 790 795 800

Lys Tyr Ser Asp Ala Ile Ala Ile Ile Leu Ser Ser Lys Asn Arg Phe
805 810 815

Asn Trp Thr Tyr Ser Met Val Arg Asn Leu His Lys Ala Leu Glu Glu
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Ile Glu Asp Arg Asn Ser Val Glu Ile Leu Leu Asp Val Val Asn Lys
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Tyr Tyr Ala Arg Cys Tyr Arg Arg Leu Ala Val Thr Pro Gly Ala Ile
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Ser Lys Val Leu Val Ser Val Cys Ser His Thr Asp Pro Cys Thr Ala
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DEMANDE OU BREVET VOLUMINEUX

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

CECI EST LE TOME	1	DE	3
CONTENANT LES PAGES	1	À	338

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	3
CONTAINING PAGES	1	TO	338

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

NOM DU FICHIER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

CLAIMS

1. A transformed plant cell with altered metabolic activity compared to a corresponding non transformed wild type plant cell, wherein the metabolic activity is altered by transformation with a Stress-Related Protein (SRP) coding nucleic acid and results in increased tolerance and/or resistance to an environmental stress as compared to a corresponding non-transformed wild type plant cell.

2. The transformed plant cell of claim 1, wherein metabolic activity is altered concerning one or more metabolites selected from the group consisting of 2,3-dimethyl-5-phytylquinol, 2-hydroxy-palmitic acid, 3,4-dihydroxyphenyl-alanine (= dopa), 3-hydroxy-palmitic acid, 5-oxoproline, alanine, alpha linolenic acid (c18:3 (c9, c12, c15)), alpha-tocopherol, aminoadipic acid, anhydroglucose, arginine, aspartic acid, beta-apo-8' carotenal, beta-carotene, beta-sitosterol, beta-tocopherol, (delta-7-cis,10-cis)-hexadecadienic acid, hexadecatrienic acid, margaric acid, delta-15-cis-tetracosenic acid, ferulic acid, campesterol, cerotic acid (c26:0), citrulline, cryptoxanthine, eicosenoic acid (20:1), fructose, fumarate, galactose, gamma-aminobutyric acid, gamma-tocopherol, gluconic acid, glucose, glutamic acid, glutamine, glycerate, glycerinaldehyd, glycerol, glycerol-3-phosphate, glycine, homoserine, inositol, isoleucine, iso-maltose, isopentenyl pyrophosphate, leucine, lignoceric acid (c24:0), linoleic acid (c18:2 (c9, c12)), luteine, lycopene, malate, mannose, methionine, methylgalactofuranoside, methylgalactopyranoside, methylgalactopyranoside, palmitic acid (c16:0), phenylalanine, phosphate, proline, putrescine, pyruvat, raffinose, ribonic acid, serine, shikimate, sinapine acid, stearic acid (c18:0), succinate, sucrose, threonine, triacontanoic acid, tryptophane, tyrosine, ubichinone, udp-glucose, valine, zeaxanthine.

3. The transgenic plant cell of claim 1 or 2, wherein the metabolic activity is altered by transformation with a Stress-Related Protein (SRP) coding nucleic acid selected from the group consisting of:

a) nucleic acid molecule encoding one of the polypeptides shown in Fig. 1a, 1b or 1c or a fragment thereof, which confers an altered metabolic activity in an organism or a part thereof;

b) nucleic acid molecule comprising one of the nucleic acid molecules shown in Fig. 1a, 1b or 1c;

c) nucleic acid molecule whose sequence can be deduced from a polypeptide sequence encoded by a nucleic acid molecule of (a) or (b) as a result of the degeneracy of the genetic code and conferring an altered metabolic activity in an organism or a part thereof;

d) nucleic acid molecule which encodes a polypeptide which has at least 50% identity with the amino acid sequence of the polypeptide encoded by the nucleic acid molecule of (a) to (c) and conferring an altered metabolic activity in an organism or a part thereof;

e) nucleic acid molecule which hybidizes with a nucleic acid molecule of (a) to (c) under under stringent hybridisation conditions and conferring an altered metabolic activity in an organism or a part thereof;

f) nucleic acid molecule which encompasses a nucleic acid molecule which is obtained by amplifying nucleic acid molecules from a cDNA library or a genomic library using the primers in table 2 and conferring an altered metabolic activity in an organism or a part thereof;

g) nucleic acid molecule encoding a polypeptide which is isolated with the aid of monoclonal antibodies against a polypeptide encoded by one of the nucleic acid molecules of (a) to (f) and conferring an altered metabolic activity in an organism or a part thereof;

h) nucleic acid molecule encoding a polypeptide comprising the consensus sequence shown in Fig 2 and conferring an altered metabolic activity in an organism or a part thereof; and

i) nucleic acid molecule which is obtainable by screening a suitable nucleic acid library under stringent hybridization conditions with a probe comprising one of the sequences of the nucleic acid molecule of (a) to (k) or with a fragment thereof having at least 15 nt, preferably 20 nt, 30 nt, 50 nt, 100 nt, 200 nt or 500 nt of the nucleic acid molecule characterized in (a) to (k) and conferring an altered metabolic activity in an organism or a part thereof.

or comprising a sequence which is complementary thereto.

4. The transgenic plant cell of claim 3, wherein the environmental stress is selected from the group consisting of salinity, drought, temperature, metal, chemical, pathogenic and oxidative stresses, or combinations thereof.

5. The transgenic plant cell of any of claims 1 – 4 derived from a monocotyledonous plant.

6. The transgenic plant cell of any of claims 1 – 5 derived from a dicotyledonous plant.

7. The transgenic plant cell of any of claims 1 – 6, wherein the plant is selected from the group consisting of maize, wheat, rye, oat, triticale, rice, barley, soybean, peanut, cotton, rapeseed, canola, manihot, pepper, sunflower, flax, borage, safflower, linseed, primrose, rapeseed, turnip rape, tagetes, solanaceous plants, potato, tobacco,

eggplant, tomato, Vicia species, pea, alfalfa, coffee, cacao, tea, Salix species, oil palm, coconut, perennial grass, forage crops and Arabidopsis thaliana.

8. The transgenic plant cell of any of claims 1 – 4, derived from a gymnosperm plant.

9. The transgenic plant cell of any of claims 1 – 4 or 6, wherein the plant is selected from the group of spruce, pine and fir.

10. A transgenic plant generated from a plant cell according to any of claims 1 – 7 and which is a monocot or dicot plant.

11. A transgenic plant of claim 10, which is selected from the group consisting of maize, wheat, rye, oat, triticale, rice, barley, soybean, peanut, cotton, rapeseed, canola, manihot, pepper, sunflower, flax, borage, safflower, linseed, primrose, rapeseed, turnip rape, tagetes, solanaceous plants, potato, tobacco, eggplant, tomato, Vicia species, pea, alfalfa, coffee, cacao, tea, Salix species, oil palm, coconut, perennial grass, forage crops and Arabidopsis thaliana.

12. A transgenic plant generated from a plant cell according to any of claims 1 – 4, 8 or 9 and which is a gymnosperm plant.

13. A transgenic plant of claim 12, which is selected from the group consisting of spruce, pine and fir.

14. A seed produced by a transgenic plant of any of claims 10 - 13, wherein the seed is genetically homozygous for a transgene conferring altered metabolic activity resulting in an increased tolerance to environmental stress as compared to a corresponding non-transformed wild type plant.

15. An isolated nucleic acid molecule comprising a nucleic acid molecule selected from the group consisting of:

a) nucleic acid molecule encoding of the polypeptide shown in Fig. 1a, 1b or 1c or a fragment thereof, which confers an altered metabolic activity in an organism or a part thereof;

b) nucleic acid molecule comprising of the nucleic acid molecule shown in Fig. 1a, 1b or 1c;

c) nucleic acid molecule whose sequence can be deduced from a polypeptide sequence encoded by a nucleic acid molecule of (a) or (b) as a result of the degeneracy of the genetic code and conferring an altered metabolic activity in an organism or a part thereof;

d) nucleic acid molecule which encodes a polypeptide which has at least 50% identity with the amino acid sequence of the polypeptide encoded by the nucleic acid molecule of (a) to (c) and conferring an altered metabolic activity in an organism or a part thereof;

e) nucleic acid molecule which hybidizes with a nucleic acid molecule of (a) to (c) under under stringent hybridisation conditions and conferring an altered metabolic activity in an organism or a part thereof;

f) nucleic acid molecule which encompasses a nucleic acid molecule which is obtained by amplifying nucleic acid molecules from a cDNA library or a genomic library using the primers in table 2 and conferring an altered metabolic activity in an organism or a part thereof;

g) nucleic acid molecule encoding a polypeptide which is isolated with the aid of monoclonal antibodies against a polypeptide encoded by one of the nucleic acid molecules of (a) to (f) and conferring an altered metabolic activity in an organism or a part thereof;

h) nucleic acid molecule encoding a polypeptide comprising the consensus sequence shown in Fig. 2 and conferring an altered metabolic activity in an organism or a part thereof; and

i) nucleic acid molecule which is obtainable by screening a suitable nucleic acid library under stringent hybridization conditions with a probe comprising one of the sequences of the nucleic acid molecule of (a) to (k) or with a fragment thereof having at least 15 nt, preferably 20 nt, 30 nt, 50 nt, 100 nt, 200 nt or 500 nt of the nucleic acid molecule characterized in (a) to (k) and conferring altered metabolic activity in an organism or a part thereof,

whereby the nucleic acid molecule distinguishes over the sequence as shown in Fig. 1a, 1b or 1c by one or more nucleotides.

16. An isolated nucleic acid molecule comprising a nucleic acid molecule selected from the group consisting of:

a) nucleic acid molecule encoding of the polypeptide shown in Fig. 1a, 1b or 1c or a fragment thereof, which confers an altered metabolic activity in an organism or a part thereof;

b) nucleic acid molecule comprising of the nucleic acid molecule shown in Fig. 1a, 1b or 1c;

c) nucleic acid molecule whose sequence can be deduced from a polypeptide sequence encoded by a nucleic acid molecule of (a) or (b) as a result of the degeneracy of the genetic code and conferring an altered metabolic activity in an organism or a part thereof;

d) nucleic acid molecule which encodes a polypeptide which has at least 50% identity with the amino acid sequence of the polypeptide encoded by the nucleic acid molecule of (a) to (c) and conferring an altered metabolic activity in an organism or a part thereof;

e) nucleic acid molecule which hybidizes with a nucleic acid molecule of (a) to (c) under under stringent hybridisation conditions and conferring an altered metabolic activity in an organism or a part thereof;

f) nucleic acid molecule which encompasses a nucleic acid molecule which is obtained by amplifying nucleic acid molecules from a cDNA library or a genomic library using the primers in table 2 and conferring an altered metabolic activity in an organism or a part thereof;

g) nucleic acid molecule encoding a polypeptide which is isolated with the aid of monoclonal antibodies against a polypeptide encoded by one of the nucleic acid molecules of (a) to (f) and conferring an altered metabolic activity in an organism or a part thereof;

h) nucleic acid molecule encoding a polypeptide comprising the consensus sequence shown in Fig. 2 and conferring an altered metabolic activity in an organism or a part thereof; and

i) nucleic acid molecule which is obtainable by screening a suitable nucleic acid library under stringent hybridization conditions with a probe comprising one of the sequences of the nucleic acid molecule of (a) to (k) or with a fragment thereof having at least 15 nt, preferably 20 nt, 30 nt, 50 nt, 100 nt, 200 nt or 500 nt of the nucleic acid molecule characterized in (a) to (k) and conferring altered metabolic activity in an organism or a part thereof.

17. A nucleic acid construct which confers the expression of the nucleic acid molecule of claim 15 or 16, comprising one or more regulatory elements, whereby expression of the SRP coding nucleic acid in a host cell results altered metabolic activity resulting in increased tolerance to environmental stress as compared to a corresponding non-transformed wild type host cell.

18. A vector comprising the nucleic acid molecule as claimed in claim 15 or 16 or the nucleic acid construct of claim 17, whereby expression of the SRP coding nucleic acid in a host cell results altered metabolic activity resulting in increased tolerance to environmental stress as compared to a corresponding non-transformed wild type host cell.

19. A host cell, which has been transformed stably or transiently with the vector as claimed in claim 18 or the nucleic acid molecule as claimed in claim 15 or 16 or the nucleic acid construct of claim 17.

20. An isolated Stress Related Protein (SRP) which is selected from the group comprising Fig. 1a, 1b or 1c and/or homologs thereof.

21. An isolated Stress Related Protein (SRP) of claim 20 which is selected from yeast, preferably *Saccharomyces cerevisiae*, or *E.coli*, *Brassica napus*, *Glycine max*, *or Oryza sativa.*

22. A method of producing a transgenic plant with altered metabolic activity compared to a corresponding non transformed wild type plant cell, wherein the metabolic activity is altered by expression of a Stress-Related Protein (SRP) coding nucleic acid and results in increased tolerance and/or resistance to an environmental stress as compared to a corresponding non-transformed wild type plant cell, comprising

a. transforming a plant cell with an expression vector according to claim 18 and

b. generating from the plant cell a transgenic plant with an increased tolerance to environmental stress as compared to a corresponding non-transformed wild type plant.

23. The method of claim 22, wherein the SRP coding nucleic acid is selected from the group comprising the nucleic acids of Fig. 1a, 1b or 1c and/or homologs of the afore mentioned sequences.

24. The method of any of claims 22 or 23, wherein the SRP coding nucleic acid is at least about 50% homologous to one of the nucleic acids of Fig. 1a, 1b or 1c.

25. A method of modifying stress tolerance of a plant comprising, modifying the level of expression of an SRP in the plant.

26. The method of claim 25, wherein the SRP encoding nucleic acid is selected from the group comprising the nucleic acids of Fig. 1a, 1b or 1c and/or homologs of the afore mentioned sequences.

27. The method of any of claims 25 or 26, wherein the SRP coding nucleic acid is at least about 50% homologous to one of the nucleic acid of Fig. 1a, 1b or 1c.

28. The method of any of claims 25 - 27, wherein an expression vector is used according to any of claims 17 or 18.

29. The method of any of claims 25 - 28, wherein the stress tolerance is decreased.

30. The method of any of claims 25 - 29, wherein the plant is transgenic.

31. The method of any of claims 25 - 30, wherein the plant is transformed with an inducible promoter that directs expression of the SRP.

32. The method of any of claims 25 - 31, wherein the promoter is tissue specific.

33. The method of any of claims 25 - 32, wherein the promoter is developmentally regulated.

34. The method of any of claims 25 - 33, wherein SRP expression is modified by administration of an targeting nucleic sequence complementary to the regulatory region

of the SRP encoding nucleic acid and/or by a transcription factor and/or by a zinc finger protein.

35. A method of detecting environmental stress in plant cells or plants comprising screening the plant cells for altered metabolic activity as compared to non-stress conditions.

36. A method of screening plant cells or plants for increased tolerance and/or resistance to environmental stress comprising screening the plant cells under stress conditions for altered metabolic activity as compared to non-stress conditions.

37. A method of breeding plant cells or plants towards increased tolerance and/or resistance to environmental stress comprising screening the plant cells under stress conditions for altered metabolic activity as compared to non-stress conditions and selecting those with increased tolerance and/or resistance to environmental stress.

38. The method of one of claims 35 - 37, wherein metabolite activity is altered concerning one or more metabolites selected from the group consisting of 2,3-dimethyl-5-phytylquinol, 2-hydroxy-palmitic acid, 3,4-dihydroxyphenylalanine (= dopa), 3-hydroxy-palmitic acid, 5-oxoproline, alanine, alpha linolenic acid (c18:3 (c9, c12, c15)), alpha-tocopherol, aminoadipic acid, anhydroglucose, arginine, aspartic acid, beta-apo-8' carotenal, beta-carotene, beta-sitosterol, beta-tocopherol, (delta-7-cis,10-cis)-hexa-decadienic acid, hexadecatrienic acid, margaric acid, delta-15-cis-tetracosenic acid, ferulic acid, campesterol, cerotic acid (c26:0), citrulline, cryptoxanthine, eicosenoic acid (20:1), fructose, fumarates, galactose, gamma-aminobutyric acid, gamma-tocopherol, gluconic acid, glucose, glutamic acid, glutamine, glycerate, glycerinaldehyd, glycerol, glycerol-3-phosphate, glycine, homoserine, inositol, isoleucine, iso-maltose, isopentenyl pyrophosphate, leucine, lignoceric acid (c24:0), linoleic acid (c18:2 (c9, c12)), luteine, lycopene, malates, mannose, methionine, methylgalactofuranoside, methylgalactopyranoside, methylgalactopyranoside, palmitic acid (c16:0), phenylalanine, phosphate, proline, putrescine, pyruvat, raffinose, ribonic acid, serine, shikimate, sinapine acid, stearic acid (c18:0), succinates, sucrose, threonine, triacontanoic acid, tryptophane, tyrosine, ubichinone, udp-glucose, valine, zeaxanthine.

39. The method of one of the claims 35 - 38, wherein the altered metabolic activity is by transformation with a Stress-Related Protein (SRP) coding nucleic acid.

40. The method of one of the claims 35 – 39, wherein metabolic activity is altered by transformation with one or more Stress-Related Protein (SRP) coding nucleic acids selected from the group comprising at least one of the nucleic acids of Fig. 1a, 1b or 1c and/or homologs of the afore mentioned sequences.

41. Use of a SRP encoding nucleic acid selected from the group comprising the nucleic acid of Fig. 1a, 1b or 1c and/or homologs of the afore mentioned sequences for preparing a plant cell with increased environmental stress tolerance.

42. Use of altered metabolic activity and/or a SRP encoding nucleic acid selected from the group comprising the nucleic acid of Fig. 1a, 1b or 1c and/or homologs of the afore mentioned sequences or parts thereof as markers for selection of plants or plant cells with increased tolerance to environmental stress.

43. Use of altered metabolic activity and/or a SRP encoding nucleic acid selected from the group comprising the nucleic acid of Fig. 1a, 1b or 1c and/or homologs of the afore mentioned sequences or parts thereof as markers for detection of stress in plants or plant cells.

44. A nucleic acid construct which confers the expression of the nucleic acid molecule of claim 15 or 16, comprising one or more regulatory elements, whereby expression of the SRP coding nucleic acid in a host cell results in increased tolerance to environmental stress as compared to a corresponding non-transformed wild type host cell.

45. A vector comprising the nucleic acid molecule as claimed in claim 15 or 16 or the nucleic acid construct of claim 44, whereby expression of the SRP coding nucleic acid in a host cell results in increased tolerance to environmental stress as compared to a corresponding non-transformed wild type host cell.

46. A plant cell comprising a nucleic acid construct of claim 44 or a vector of claim 45.

47. A plant comprising a cell of claim 46.

48. An isolated nucleic acid, comprising a polynucleotide selected from the group consisting of:

a. a nucleic acid sequence of Fig. 1c;

b. a polynucleotide encoding a polypeptide of Fig. 1c;

c. a polynucleotide having at least 70% sequence identity with a nucleic acid sequence of Fig. 1c, wherein expression of said polynculeotide confers increased tolerance to one or more abiotic stress in a plant as compared to a corresponding non-transformed plant; and

d. a polynucleotide hybridizing under stringent conditions to a nucleic acid sequence of Fig. 1c, wherein expression of said polynculeotide confers increased tolerance to one or more abiotic stress in a plant as compared to a corresponding non-transformed plant.

49. A vector comprising the isolated nucleic acid of claim 48.

50. A plant stably transformed with the isolated nucleic acid of claim 48.

51. A plant stably transformed with the vector of claim 49.

52. A seed of the plant of claim 50, wherein said seed comprises the isolated nucleic acid of claim 48.

53. A seed of the plant of claim 50, wherein said seed comprises the vector of claim 49.

54. A method of increasing tolerance of a plant to at least one abiotic stress, comprising: transforming a plant with an isolated nucleic acid of claim 48.

55. A method of increasing tolerance of a plant to at least one abiotic stress, comprising: transforming a plant with a vector of claim 49.

56. A plant transformed with a nucleic acid selected from the group consisting of:

a. a nucleic acid sequence of Fig. 1a or Fig. 1b;

b. a polynucleotide encoding a polypeptide of Fig. 1a or Fig. 1b;

c. a polynucleotide having at least 70% sequence identity with a nucleic acid sequence of Fig. 1a or Fig. 1b, wherein expression of said polynculeotide confers increased tolerance to one or more abiotic stress in a plant as compared to a corresponding non-transformed plant; and

d. a polynucleotide hybridizing under stringent conditions to a nucleic acid sequence of Fig. 1a or Fig. 1b, wherein expression of said polynculeotide confers increased tolerance to one or more abiotic stress in a plant as compared to a corresponding non-transformed plant.

57. A seed of the plant of claim 56.

58. A method of increasing tolerance of a plant to at least one abiotic stress, comprising: transforming a plant with a nucleic acid selected from the group consisting of:

a. a nucleic acid sequence of Fig. 1a or Fig. 1b;

b. a polynucleotide encoding a polypeptide of Fig. 1a or Fig. 1b;

c. a polynucleotide having at least 70% sequence identity with a nucleic acid sequence of Fig. 1a or Fig. 1b, wherein expression of said polynculeotide confers increased tolerance to one or more abiotic stress in a plant as compared to a corresponding non-transformed plant; and

d. a polynucleotide hybridizing under stringent conditions to a nucleic acid sequence of Fig. 1a or Fig. 1b, wherein expression of said polynculeotide confers increased tolerance to one or more abiotic in a plant as compared to a corresponding non-transformed plant.