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- (73) Patenthaver: **NB Health Laboratory Co. Ltd., 12-2, Kita 21-jou Nishi, Kita-ku, Sapporo-shi, Hokkaido 001-0021, Japan**
- (72) Opfinder: **TAKAYAMA, Kiyoshi, c/o NB Health Laboratory Co. Ltd., 12-2, Kita 21-jou Nishi, Kita-ku, Sapporo-shi, Hokkaido 001-0021, Japan**
SHIMIZU, Tomoko, c/o NB Health Laboratory Co. Ltd., 12-2, Kita 21-jou Nishi, Kita-ku, Sapporo-shi, Hokkaido 001-0021, Japan
URUSHIBATA, Yuji, c/o NB Health Laboratory Co. Ltd., 12-2, Kita 21-jou Nishi, Kita-ku, Sapporo-shi, Hokkaido 001-0021, Japan
SUGIMOTO, Yukihiro, c/o National University Corporation, Kumamoto University, 5-1, Oehonmachi, Chuo-ku, Kumamoto-shi, Kumamoto 862-0973, Japan
- (74) Fuldmægtig i Danmark: **PATRADE A/S, Fredens Torv 3A, 8000 Århus C, Danmark**
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DESCRIPTION

Technical Field

[0001] The present invention relates to a monoclonal antibody against a human prostaglandin E₂ receptor subtype EP4.

Background Art

[0002] Prostaglandin (PG), as well as thromboxane, is a physiologically active substance known as "prostanoid," and it is a lipid having a prostanoid acid skeleton. Prostanoid such as prostaglandin is biosynthesized from arachidonic acid that is released from a membrane phospholipid by the action of phospholipase A₂. Prostaglandin is classified into groups A to J, based on differences in the types of an oxygen atom attached to the 5-membered ring thereof and a double bond. In addition, prostaglandin is classified into groups 1 to 3, based on the number of double bonds on the side chain of the prostanoid acid skeleton. For instance, prostaglandin E (PGE) includes PGE₁, PGE₂ and PGE₃, which are different from one another in terms of the number of double bonds on the prostanoid acid skeleton side chain.

[0003] Regarding PG, PGH₂ is generated from PGG₂ that is biosynthesized from arachidonic acid by the action of cyclooxygenase I (COX-1) or cyclooxygenase II (COX-II), and then, PGD₂, PGE₂, PGF_{2α} and the like are generated based on a difference in the cleavage of the bond between oxygen atoms. Thereafter, PGA₂, PGC₂ and the like are generated from PGE₂. Each PG generation reaction occurs by the action of a specific enzyme, and it is considered that such enzyme has tissue specificity and generates PG suitable for the function of each tissue.

[0004] Among various PGs, it is considered that PGE plays various important biological activities and that, through the mediation of its specific receptor, PGE is associated with regulation of the immune system, as well as vasodilatation, a decrease in blood pressure and uterine contraction. The PGE₂ receptor is a seven transmembrane G-protein-coupled receptor, as with other PG receptors. The PGE₂ receptor is abbreviated as EP, and it was revealed that EP has 4 types of subtypes (EP1, EP2, EP3 and EP4). Each subtype is associated with various phenomena *in vivo*. That is, EP1 is associated with an increase in intracellular Ca²⁺ concentration; EP2 and EP4 are associated with an increase in cAMP level; and EP3 is associated with a decrease in cAMP level (Non Patent Literature 1). The 4 types of subtypes have high homology to one another in terms of protein structure.

[0005] It has been reported that when a low-molecular-weight compound antagonist having high selectivity to EP4 is administered to mice that had been induced to have experimental autoallergic encephalomyelitis or contact hypersensitivity, accumulation of both TH1 and TH17 cells in the regional lymph node is reduced, and the progression of the disease is suppressed (Non Patent Literature 2). It has been demonstrated that PGE₂ promotes production of IL-23 in dendritic cells, as a result of an increase in cAMP level mediated by the activation of EP4. In addition, it has also been demonstrated that, in TH 17 cells, PGE₂ is involved in proliferation of the TH17 cells in coordination with IL-23. Thus, it has been demonstrated that an increase in cAMP level mediated by the activation of EP4 plays an important role for intracellular signaling in TH17 cells (Non Patent Literature 3). These reports suggest that the PGE₂ receptor antagonist, in particular, an EP4-selective antagonist be effective for the treatment of diseases caused by immunological abnormality, with which TH1 or TH17 is associated, such as multiple sclerosis, rheumatoid arthritis, inflammatory bowel disease and contact dermatitis (Non Patent Literature 2).

[0006] It has been reported that many types of cancer cells overexpress COX-11 when compared with normal cells. Moreover, it has also been reported that PGE₂ acts on cancer tissues or tissues around the cancer tissues and is involved in the progression of cancer. For example, it has been described that PGE₂ is involved in infiltration of refractory inflammatory breast cancer cells or lung cancer cells into a metastatic tissue (Non Patent Literatures 4 and 5). Furthermore, it has been known that PGE₂ is associated with proliferation of non-small cell lung cancer cells, colon cancer cells, inflammatory breast cancer cells, B lymphocytes, prostatic cancer cells and melanoma, via EP4.

[0007] PGE₂ has been known to inhibit the function of NK cells which have an action to directly attack cancer cells. One of the mechanisms of PGE₂ to inhibit the activity of NK cells is an increase in intracellular cAMP level mediated by the activation of EP4 (Non Patent Literature 6). It has also been known that Treg cells that possibly suppress immunity to cancer are activated via EP4, and the possibility of decreasing the immune system to cancer cells *in vivo* has been suggested (Non Patent Literature 7).

According to these reports, it is apparent that PGE₂ is important for the progression of cancer. Hence, clinical studies have been conducted using non-selective inhibitors to COX involved in generation of PGE₂. However, sufficient therapeutic results could not be obtained due to the side effects of the inhibitors. The PGE₂ receptor antagonist, in particular, an EP4-selective antagonist directly suppresses proliferation of cancer cells and boosts the host immune system to cancer. Accordingly, it is anticipated that an antibody that selectively binds to the EP4 receptor will be effective for the treatment of various types of cancers such as breast cancer, colon cancer, lung cancer, prostatic cancer, skin cancer and B-lymphoma.

[0008] Conventionally, non-specific COX inhibitors have been applied for the relief of pain. However, it has been known that such non-specific inhibitors cause side effects such as heartburn, indigestion, nausea, abdominal distension, diarrhea, gastralgia, peptic ulcer or gastrointestinal bleeding. In recent years, COX-II selective inhibitors (e.g. celecoxib and rofecoxib) have been developed for the purpose of treating pain. However, it has been suggested that such COX-II selective inhibitors develop severe cardiovascular disorder in specific patients, and thus it has been desired to develop a drug for relieving pain based on a different mode of action. Among PGs generated by COX, PGE₂ is known to enhance the hypersensitivity of pain sense. It has been demonstrated by multiple animal experiments that, among PGE₂ receptors, EP4 is particularly associated with the enhancement of the hypersensitivity of pain sense. For example, it has been known that the expression of EP4 is enhanced in the dorsal root ganglion (GRG) in a rat model of inflammatory pain, and that a comparatively selective EP4 antagonist (AH23848) relieves the sensitivity of pain in the aforementioned model (Non Patent Literature 8). Moreover, in an analysis using EP4 knock-out mice as well, the same results could be obtained (Non Patent Literature 9). These reports suggest that a pharmaceutical product for selectively blocking the function of EP4 be effective for the treatment of diseases associated with immunological abnormality, cancer and pain, while having fewer side effects.

[0009] As methods for selectively blocking the function of EP4, several low-molecular-weight compound antagonists have been reported. However, none of such compound antagonists have been successful as pharmaceutical products. Such low-molecular-weight compound antagonists would be improved in terms of binding selectivity to PGE₂ receptor subtypes (EP1-4) or alleviation of binding affinity for thromboxane or other prostanoid receptors. It is concerned that the same side effects as those of COX inhibitors are generated unless sufficient receptor selectivity is secured.

[0010] An antibody selectively binding to the EP4 receptor is expected to have higher selectivity than low-molecular-weight compounds. Furthermore, since an antibody drug generally has a longer half-life in blood than low-molecular-weight compounds, it is expected to have drug effects for a long period of time by a single administration. Such antibody drug is effective for chronic diseases (e.g. rheumatoid arthritis, colitis, cancer, etc.).

[0011] In general, as a main action mechanism of an antibody drug directed at a membrane protein (receptor), the antibody has recognized cells expressing the protein, and has then removed the cells based on complement-dependent cytotoxicity (CDC) and antibody-dependent cell-mediated cytotoxicity (ADCC). However, since CDC or ADCC is associated with activation of inflammatory cells such as macrophage, such antibody drug is not necessarily suitable for the treatment of diseases caused by immunological abnormality or pain. Accordingly, when a monoclonal antibody capable of selectively inhibiting EP4 is applied for the treatment of diseases caused by immunological abnormality or pain, it is desirable a functional antibody that depends on neither CDC nor ADCC. That is to say, an antibody for selectively blocking EP4-dependent intracellular signaling is desirable.

[0012] To date, Japanese Patent No. 3118460 (Patent Literature 1) discloses a method for obtaining an antibody against EP4. However, there have not yet been any reports regarding a specific antibody that EP4-specifically suppresses the function of EP4 at a low dose and binds to neither EP1, EP2 nor EP3. In addition, it has been known that it is difficult to obtain a functional antibody against a seven-transmembrane receptor by the general method for obtaining a monoclonal antibody described in Japanese Patent No. 3118460.

Citation List

Patent Literature

[0013] Patent Literature 1: Japanese Patent No. 3118460

Non Patent Literature

[0014]

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Non Patent Literature 9: Popp L. et al., European Journal of Pain. 2009, 13: 7 (691-703)

[0015] WO2004/073589 teaches that inhibitory antibodies (both monoclonal and polyclonal) may be raised against human PGE₂-receptor EP4 and may be screened for inhibitory function. The document does not actually carry out said method and does not report successful isolation of an inhibitory antibody.

[0016] KASHIWAGI B ET AL: "Positive effect of prostaglandin on regulation of prostatic blood flow", UROLOGY, BELLE MEAD, NJ, US, vol. 68, no. 3, 1 September 2006 (2006-09-01), pages 682 - 686 disclose the use of an inhibitory anti-PGE₂ receptor antibody. The subtype and source of the antibody are not mentioned.

[0017] WO 2003/099857 A1 discloses peptide-based inhibitors of PEG₂ receptor EP4.

Summary of Invention**Technical Problem**

[0018] It is an object of the present invention to provide an antibody against a human PGE₂ receptor subtype EP4, which is useful as a therapeutic agent for diseases caused by immunological abnormality, tumor and pain, a pharmaceutical composition comprising the aforementioned anti-human EP4 antibody, and the like.

Solution to Problem

[0019] The present inventors have attempted to produce a monoclonal antibody against a human PGE₂ receptor subtype EP4. As a result, the inventors have succeeded in obtaining an antibody that specifically binds to the extracellular domain of the subtype EP4 and suppresses the function of PGE₂ receptor EP4 (e.g. the function to increase intracellular cAMP level), thereby completing the present invention.

[0020] Specifically, the present invention includes the following (1) to (13).

1. [1] A monoclonal antibody or a functional fragment thereof, each of which binds to the extracellular domain of a PGE₂ receptor subtype EP4 and inhibits the function of PGE₂-receptor EP4 to increase the intracellular cAMP level.
2. [2] The antibody or a functional fragment thereof according to embodiment 1, wherein the antibody is produced from hybridomas with the international depositary accession Nos. FERM BP-11402 (NBG016-mAb14) and FERM BP-11403 (NBG016-mAb21).
3. [3] The antibody or a functional fragment thereof according to any one of embodiments 1 or 2, wherein the antibody

specifically binds to the extracellular domain of EP4, and comprises any one of the following (A), (B), or (C), with regard to the amino acid sequences of its complementarity determining regions 1-3 (CDR1-3):

1. (A) the antibody has
 - heavy chain CDR1 comprising the amino acid sequence shown in SEQ ID NO: 5,
 - heavy chain CDR2 comprising the amino acid sequence shown in SEQ ID NO: 6,
 - heavy chain CDR3 comprising the amino acid sequence shown in SEQ ID NO: 7,
 - light chain CDR1 comprising the amino acid sequence shown in SEQ ID NO: 8,
 - light chain CDR2 comprising the amino acid sequence shown in SEQ ID NO: 9, and
 - light chain CDR3 comprising the amino acid sequence shown in SEQ ID NO: 10;
2. (B) the antibody has
 - heavy chain CDR1 comprising the amino acid sequence shown in SEQ ID NO: 15,
 - heavy chain CDR2 comprising the amino acid sequence shown in SEQ ID NO: 16,
 - heavy chain CDR3 comprising the amino acid sequence shown in SEQ ID NO: 17,
 - light chain CDR1 comprising the amino acid sequence shown in SEQ ID NO: 18,
 - light chain CDR2 comprising the amino acid sequence shown in SEQ ID NO: 19, and
 - light chain CDR3 comprising the amino acid sequence shown in SEQ ID NO: 20; or
3. (C) the antibody has
 - heavy chain CDR1 comprising the amino acid sequence shown in SEQ ID NO: 45,
 - heavy chain CDR2 comprising the amino acid sequence shown in SEQ ID NO: 46,
 - heavy chain CDR3 comprising the amino acid sequence shown in SEQ ID NO: 47,
 - light chain CDR1 comprising the amino acid sequence shown in SEQ ID NO: 48,
 - light chain CDR2 comprising the amino acid sequence shown in SEQ ID NO: 49, and
 - light chain CDR3 comprising the amino acid sequence shown in SEQ ID NO: 50.
4. [4] The antibody or a functional fragment thereof according to any one of embodiments 1 to 3, wherein the antibody specifically binds to the extracellular domain of EP4, and comprises any one of the following (a), (b), or (c), with regard to the amino acid sequences of its heavy chain variable region and light chain variable region:
 1. (a) the antibody has a heavy chain variable region comprising the amino acid sequence shown in SEQ ID NO: 2, and a light chain variable region comprising the amino acid sequence shown in SEQ ID NO: 4;
 2. (b) the antibody has a heavy chain variable region comprising the amino acid sequence shown in SEQ ID NO: 12, and a light chain variable region comprising the amino acid sequence shown in SEQ ID NO: 14; or
 3. (c) the antibody has a heavy chain variable region comprising the amino acid sequence shown in SEQ ID NO: 43, and a light chain variable region comprising the amino acid sequence shown in SEQ ID NO: 44.
5. [5] The antibody or a functional fragment thereof according to any one of embodiments 1 to 4, wherein the antibody is a humanized antibody or a chimeric antibody.
6. [6] The antibody or a functional fragment thereof according to any one of embodiments 3 or 4, wherein the heavy chain variable region or light chain variable region of said antibody or fragment thereof is encoded by a nucleic acid as shown in SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 41, or SEQ ID NO: 42.
7. [7] A pharmaceutical composition comprising the antibody or a functional fragment thereof according to any one of embodiments 1 to 5.
8. [8] The pharmaceutical composition according to embodiment 7, for use in a method of treating an immunological disease.
9. [9] The pharmaceutical composition according to embodiment 7, for use in a method of treating a tumor.
10. [10] The pharmaceutical composition according to embodiment 7, for use in a method of treating pain.
11. [11] A carrier-immobilized antibody, wherein the anti-EP4 antibody or a functional fragment thereof according to any one of embodiments 1 to 5 is immobilized on a carrier.
12. [12] A method for the removal of PGE₂-receptor EP4-expressing cells from blood wherein a carrier-immobilized antibody according to claim 11 is contacted *ex vivo* with blood containing EP4 expressing cells and subsequent removal of said EP4-expressing cells from said blood.
13. [13] A kit for measuring the expression level of PGE₂-receptor EP4 on a cell surface, which comprises the anti-EP4 antibody according to any one of embodiments 1 to 5.

Advantageous Effects of Invention

[0021] According to the present invention, an antibody that EP4-specifically suppresses the function of EP4 has been provided for the first time.

[0022] According to the present invention, the EP4-related medicament of the present invention is able to treat or prevent EP4-related immunological diseases, tumor and pain. In particular, using the antibody of the present invention having higher binding selectivity to a subtype EP4 than low-molecular-weight compounds, therapeutic effects with fewer side effects can be provided.

[0023] Using the carrier with the antibody-immobilized of the present invention upon, EP4-expressing cells can be selectively removed from the blood of a patient affected with cancer, autoimmune disease or the like.

[0024] Using the kit for measuring the expression level of EP4 of the present invention, EP4-expressing cells can be detected in the blood of a patient affected with cancer, autoimmune disease or the like, and then, using the detected cells, the condition of the disease can be evaluated.

Brief Description of Drawings

[0025]

[Figure 1] Figure 1 shows the results of flow cytometry, which analyzed the binding of a mouse isotype control antibody, NBG016-mAb14 and NBG016-mAb21 to the parent Flp-In-CHO cell line and the CHO cell line stably expressing human EP4.

[Figure 2] Figure 2 shows the results of flow cytometry, which analyzed the binding of a mouse isotype control antibody and NBG016-mAb9 to the parent Flp-In-CHO cell line and the CHO cell line stably expressing human EP4.

[Figure 3] Figure 3 shows the results obtained by analyzing the suppressive effects of a mouse isotype control antibody, NBG016-mAb14 and NBG016-mAb21 on PGE₂-induced increase in cAMP level.

[Figure 4] Figure 4 shows the results obtained by analyzing the suppressive effects of a mouse isotype control antibody and NBG016-mAb9 on PGE₂-induced increase in cAMP level.

[Figure 5] Figure 5 shows the results of flow cytometry, which analyzed the binding of NBG016-mAb14 to 293FT cells, into which each of human EP1-4 and mouse EP1-4 genes had been introduced.

[Figure 6] Figure 6 shows the results of flow cytometry, which analyzed the binding of NBG016-mAb9 to 293FT cells, into which each of human EP1-4 and mouse EP1-4 genes had been introduced.

[Figure 7] Figure 7 shows the results of flow cytometry, which analyzed the binding of a mouse isotype control antibody, NBG016-mAb14 and NBG016-mAb21 to lymphocyte subsets in human peripheral blood.

[Figure 8] Figure 8 shows the results of flow cytometry, which analyzed the binding of a mouse isotype control antibody and NBG016-mAb9 to lymphocyte subsets in human peripheral blood.

[Figure 9] Figure 9 shows the results of immunostaining the human monocytic THP1 cell line treated with PMA, using an anti-EP4 antibody.

[Figure 10] Figure 10 shows the results of flow cytometry, which analyzed the binding of a culture supernatant of antibody gene-non-introduced cells and a culture supernatant of recombinant antibody NBG016-mAb9 gene-expressing cells to the parent Flp-In-CHO cell line and the CHO cell line stably expressing human EP4.

[Figure 11] Figure 11 shows the results of flow cytometry, which analyzed the binding of a mouse isotype control antibody, the recombinant antibody NBG016-mAb14 and the recombinant antibody NBG016-mAb21 to the parent Flp-In-CHO cell line and CHO cell line stably expressing human EP4.

[Figure 12] Figure 12(A) shows the results of flow cytometry, which analyzed the binding of a mouse isotype control antibody and the mouse IgG1 antibody NBG016-mAb21 to the parent Flp-In-CHO cell line and the CHO cell line stably expressing human EP4. Figure 12(B) shows the results obtained by analyzing the suppressive effects of a mouse isotype control antibody and the mouse IgG1 antibody NBG016-mAb21 on PGE₂-induced increase in cAMP level.

[Figure 13] Figure 13 shows the results of flow cytometry, which analyzed the binding of a culture supernatant of antibody gene-non-introduced cells, a culture supernatant of human chimeric antibody NBG016-mAb14 gene-expressing cells, and a culture supernatant of human chimeric antibody NBG016-mAb21 gene-expressing cells, to the parent Flp-In-CHO cell line and the CHO cell line stably expressing human EP4.

Description of Embodiments

[0026] The present invention relates to an antibody that binds to the extracellular domain of a human PGE₂ receptor subtype EP4 and suppresses the function of EP4, or a functional fragment thereof, and a medicament comprising the antibody or a functional fragment thereof.

Definition of EP4 protein

[0027] As an EP4 protein serving as an antigen in the present invention, a recombinant protein prepared from cDNA encoding the EP4 protein or the like can be used. Alternatively, a suitable cell that expresses EP4 on the surface thereof may be used as an antigen. A nucleic acid sequence encoding a human EP4 protein can be searched in published database such as GenBank (e.g. Accession No.: NM_000958). Using a probe, a primer pair for PCR amplification, or the like produced based on the aforementioned gene sequence or the like, DNA (e.g. cDNA) encoding EP4 can be prepared from a suitable DNA library. Alternatively, total cDNA can be prepared by an artificial DNA synthesis method. As an example, an amino acid sequence corresponding to human EP4 is shown in SEQ ID NO: 21. Human EP4 has been known to have various types of variants such as amino acid substituted variants, as well as that shown in SEQ ID NO: 21. The term "human EP4" is used in the present invention to include the aforementioned variants, as long as it has the function of EP4.

[0028] The intracellular and extracellular domains of human EP4 are considered to correspond to the below-mentioned portions in the amino acid sequence shown in SEQ ID NO: 21. The left term indicates amino acid numbers, and the right term indicates the relevant domain. It is to be noted that the boundary between individual domains may include some range (1 to 5 amino acid residues, preferably 1 to 3 amino acid residues, and more preferably 1 or 2 amino acid residues).

1 to 19: N-terminal domain

44 to 54: Intracellular first loop domain

80 to 96: Extracellular first loop domain

116 to 135: Intracellular second loop domain

161 to 184: Extracellular second loop domain

212 to 267: Intracellular third loop domain

296 to 312: Extracellular third loop domain

333 to 488: C-terminal domain

Definition of antibody or functional antibody

[0029] The antibody of the present invention that suppresses the function of EP4 is a monoclonal antibody. The functional fragments of the present antibody include antibody fragments such as Fab or F(ab')₂, and single-chain antibodies. As far as it is a polypeptide (or a polypeptide complex) that constitutes a part of an antibody and suppresses the function of EP4, all types of polypeptides are included in the scope of the present invention.

Definition of functional antibody specific to EP4 and evaluation method therefor

[0030] Examples of the function of EP4 include an increase in intracellular cAMP level and activation of Phosphoinositide 3-kinase (PI3K). It has been known that these intracellular changes regulate proliferation of cancer cells, proliferation of T lymphocytes, and generation of cytokines. The specific binding of the antibody of the present invention to the extracellular domain

of a human PGE₂ receptor subtype EP4 can be proved as follows. A nucleic acid sequence encoding a human EP4 protein is inserted into an expression vector, and the vector is then introduced into suitable host cells (e.g. mammalian cells such as CHO cells, yeast cells, insect cells, etc.). Nondestructive, EP4-expressing host cells or EP4-non-expressing host cells, which do not comprise an insertion, deletion, substitution or the like of amino acids, are allowed to come into contact with the antibody of the present invention, and they are allowed to react with each other for a certain period of time. After excessive antibody has been washed off, the cells are subjected to ELISA, RIA or flow cytometry, so that the amount of antibody binding to the cells is measured. If a larger amount of the antibody of the present invention binds to the EP4-expressing host cells than to the non-expressing host cells, the results can show the specific binding of the antibody of the present invention to the extracellular domain of EP4. Moreover, there is constructed an expression vector into which a nucleic acid sequence encoding a human- or mouse-derived EP1, EP2, EP3 or EP4 protein has been inserted. Then, receptor-expressing host cells are analyzed in the same manner as described above. Thus, it can be demonstrated that the antibody of the present invention binds to human EP4-expressing host cells more strongly than to other receptor-expressing cells, and preferably that the binding of the antibody of the present invention, to cells that express receptors other than human EP4 cannot be found.

[0031] The fact that the antibody of the present invention is an antibody that inhibits the function of EP4 can be explained as follows. A nucleic acid sequence encoding a human EP4 protein is inserted into an expression vector, and the vector is then introduced into suitable host cells (e.g. mammalian cells such as CHO cells, yeast cells, insect cells, etc.). The human EP4-expressing host cells are allowed to come into contact with the antibody with a concentration of 0.01 to 30 µg/mL, and then, the cells are further allowed to come into contact with PGE₂ with a concentration of 10⁻¹² to 10⁻⁶ M. Thereafter, an increase in intracellular cAMP level is measured by a suitable method. When the antibody of the present invention is added to the cells, it is able to suppress a PGE₂-induced increase in cAMP level in a dose-dependent manner.

[0032] Moreover, the present antibody with a concentration of 0.01 to 10 µg/mL is allowed to come into contact with a cell line that naturally expresses human EP4 (e.g. human macrophage cells), and PGE₂ with a concentration of 10⁻¹² to 10⁻⁶ M is further allowed to come into contact with the cells. Thereafter, the generation of cytokines or chemokines by inflammatory stimulus (e.g. lipopolysaccharide (LPS)) is examined. It has been known that PGE₂ suppresses the generation of cytokines by LPS stimulus through the mediation of EP4 or EP2. The activity of the antibody of the present invention to inhibit the function of EP4 can be evaluated using, as an indicator, the fact that the present antibody recovers the suppression of cytokine generation by PGE₂, through the mediation of EP4. Likewise, the activity of the present antibody to inhibit the function of EP4 can also be evaluated using, as an indicator, the effect of the present antibody to inhibit the generation of IL-23 enhanced by PGE₂ from human peripheral blood dendritic cells.

[0033] Furthermore, when a cancer cell line derived from human bladder cancer, breast cancer, cervical cancer, colorectal cancer, esophageal cancer, cancer of the head and neck, skin cancer, lung cancer, oral cancer, prostatic cancer or multiple myeloma (e.g. MDA-MB-231 cells, HCA-7 cells, HT-29 cells, etc.) is allowed to come into contact with PGE₂, the proliferative activity of the cells is enhanced. After the antibody of the present invention has previously been allowed to come into contact with these cells, the activity of the present antibody to inhibit the function of PGE₂ can be evaluated using, as an indicator, the fact that an increase in the proliferative activity of the cells caused by PGE₂ is reduced.

[0034] The antibody of the present invention binds only to human EP4 and does not react with mouse EP4. Accordingly, it is difficult to evaluate by animal tests the drug effects of the antibody of the present invention regarding immunological abnormality or pain. On the other hand, regarding the antitumor effects of the present antibody, cells highly expressing EP4, which have been established from the above-mentioned human cancer tissues, are grafted into immunodeficient mice in an amount of 10⁶ to 10⁷ cells per mouse. Immediately after the graft of the cells, the antibody of the present invention is intraperitoneally or subcutaneously administered to the mice at a dose of 0.1 to 0.5 mg/mouse. When compared with an isotype control antibody administration group, tumor formation or metastasis frequency can be significantly reduced in the administration group, to which the antibody of the present invention has been administered. Thus, it can be demonstrated that the antibody of the present invention has an antitumor effect.

Detailed definition of the antibody of the present invention

[0035] Examples of the antibody of the present invention and a functional fragment thereof include: monoclonal antibodies produced from hybridomas having international depositary accession numbers FERM BP-11402 (NBG016-mAb14) and FERM BP-11403 (NBG016-mAb21); and monoclonal antibodies prepared by the methods described in the after-mentioned Examples.

[0036] Moreover, other examples of the antibody of the present invention and a functional fragment thereof include: an antibody which have a heavy chain variable region comprising the amino acid sequence shown in SEQ ID NO: 2 and a light chain variable region comprising the amino acid sequence shown in SEQ ID NO: 4; an antibody which have a heavy chain variable region comprising the amino acid sequence shown in SEQ ID NO: 12 and a light chain variable region comprising the amino acid sequence shown in SEQ ID NO: 14; an antibody which have a heavy chain variable region comprising the amino acid sequence shown in SEQ ID NO: 43 and a light chain variable region comprising the amino acid sequence shown in SEQ ID NO: 44; an antibody which have a heavy chain comprising the amino acid sequence shown in SEQ ID NO: 23 and a light chain comprising the amino acid sequence shown in SEQ ID NO: 25; an antibody which have a heavy chain comprising the amino acid sequence shown in SEQ ID NO: 27 and a light chain comprising the amino acid sequence shown in SEQ ID NO: 29; an antibody which have a heavy chain comprising the amino acid sequence shown in SEQ ID NO: 56 and a light chain comprising the amino acid sequence shown in SEQ ID NO: 57; functional fragments of the aforementioned antibodies; an antibody consisting of a heavy chain and/or a light chain having an amino acid sequence(s) comprising a deletion, substitution or addition of one or several amino acids, with respect to the amino acid sequence(s) of a heavy chain and/or a light chain that constitute(s) the aforementioned antibodies; and functional fragments thereof that suppress the function of EP4.

Definition of epitope identical to that of the antibody of the present invention

[0037] Further, a particularly preferred example of the antibody of the present invention and a functional fragment thereof is an antibody having an epitope overlapped with (or identical to) the epitope of any one of the monoclonal antibodies isolated in Examples. In the present invention, such an antibody is referred to as an antibody binding to substantially the same site. Whether or not two antibodies bind to substantially the same site can be determined, for example, by performing a competition experiment. Specifically, when the binding of the anti-EP4 antibody to EP4 described in Examples is competitively inhibited by a secondary anti-EP4 antibody, it is determined that the primary antibody and the secondary antibody bind to substantially the same antigenic site. Thus, an antibody binding to substantially the same site as the EP4 binding site of the antibody isolated in Examples, which has an action to inhibit the function of EP4, is included in the present invention.

Method for obtaining the antibody of the present invention

[0038] The anti-EP4 antibody of the present invention may be a monoclonal antibody, or a functional fragment thereof. The monoclonal antibody can stably produce an antibody that is homogenous as a pharmaceutical composition. The term "monoclonal" suggests the properties of an antibody obtained from a group of substantially homogenous antibodies. Thus, this term is not used to mean that the antibody is produced by a specific method. For instance, the monoclonal antibody used in the present invention may be produced, for example, by a hybridoma method (Kohler and Milstein, Nature 256: 495 (1975)) or a recombination method (U.S. Patent No. 4,816,567). The monoclonal antibody used in the present invention may also be isolated from a phage antibody library (Clackson et al., Nature 352: 624-628 (1991); Marks et al., J. Mol. Biol. 222: 581-597 (1991)). Particular examples of the monoclonal antibody used in the present invention include: a "chimeric" antibody (immunoglobulin), in which a portion of the heavy chain and/or light chain of the monoclonal antibody used in the present invention is derived from specific species or a specific antibody class or subclass, and a remaining portion of the chain(s) is derived from another antibody class or subclass; an antibody variant; and a functional fragment thereof (U.S. Patent No. 4,816,567; Morrison et al., Proc. Natl. Acad. Sci. USA 81: 6851-6855 (1984)).

[0039] The monoclonal antibody of the present invention can be prepared, for example, by a hybridoma method.

[0040] This method includes the following 4 steps of: (i) immunizing a host animal or host animal-derived cells with a human EP4 protein; (ii) recovering monoclonal antibody-secreting (or potentially secreting) lymphocytes; (iii) fusing the lymphocytes with immortalized cells; and (iv) selecting cells that secrete a desired monoclonal antibody. A mouse, a rat, a guinea pig, a hamster, or another suitable host animal is selected as an animal to be immunized, and then, an immunogen is injected into the selected animal.

[0041] After completion of the immunization, lymphocytes obtained from the host animal are fused with an immortalized cell line using a fusion agent such as polyethylene glycol, so as to establish hybridoma cells. As fusion cells, a rat or mouse myeloma cell line is used, for example. After completion of the cell fusion, the cells are allowed to grow in a suitable medium that contains one or more substrates that inhibit the growth or survival of unfused lymphocytes and immortalized cell line. According to an ordinary technique, parent cells that lack the enzyme, hypoxanthine-guanine phosphoribosyl transferase (HGPRT or HPRT), are used. In

this case, hypoxanthine, aminopterin and thymidine are added to a medium that inhibits the growth of the HGPRT-deficient cells and allows the growth of hybridomas (HAT medium). From the thus obtained hybridomas, those producing desired antibodies can be selected, and then, a monoclonal antibody of interest can be obtained from a medium in which the hybridomas grow according to an ordinary method.

[0042] The thus prepared hybridomas are cultured *in vitro*, or are cultured *in vivo* in the ascites of a mouse, a rat, a guinea pig, a hamster, etc., so that an antibody of interest can be prepared from a culture supernatant or ascites.

[0043] The nucleic acid of the present invention encodes the heavy chain variable region or light chain variable region of the antibody of the present invention. The nucleic acid of the present invention that encodes the heavy chain variable region or light chain variable region may be inserted into a vector, and the vector may be then expressed in cells.

[0044] The type of the vector is not particularly limited, and it may be selected, as appropriate, depending on the type of a host cell into which the vector is to be introduced, and the like. Also, the vector may be introduced into host cells suitable for the expression of an antibody (e.g. mammalian cells such as CHO cells, yeast cells, insect cells, etc.), so that a recombinant antibody can be prepared.

Definition of the chimeric antibody of the present invention and production method thereof

[0045] The embodiment of the anti-EP4 antibody of the present invention includes a genetically recombinant antibody. The type of such a genetically recombinant antibody is not particularly limited. Examples of the genetically recombinant antibody include a chimeric antibody, a humanized antibody and a human antibody. The term "chimeric antibody" is used herein to mean an antibody in which an animal-derived variable region is ligated to a different animal-derived constant region, and particularly, an antibody in which a mouse-derived antibody variable region is ligated to a human-derived antibody constant region (see Proc. Natl. Acad. Sci. U.S.A., 81, 6851-6855, (1984), etc.). When a chimeric antibody is produced, an antibody comprising such a ligation of a variable region to a constant region can be easily constructed according to a genetic recombination technique well known to a person skilled in the art. Herein, with regard to mouse-derived antibody variable regions, the heavy chain variable region preferably consists of the amino acid sequence shown in, for example, SEQ ID NO: 2 or SEQ ID NO: 12, and the light chain variable region preferably consists of the amino acid sequence shown in, for example, SEQ ID NO: 4 or SEQ ID NO: 14. The chimeric heavy chain or chimeric light chain of the present invention is inserted into a vector. The type of a vector is not particularly limited. The vector may be selected, as appropriate, depending on the type of a host cell into which it is to be introduced, and the like. Also, the vector may be introduced into host cells suitable for the expression of an antibody (e.g. mammalian cells such as CHO cells, yeast cells, insect cells, etc.), so that a recombinant antibody can be prepared.

Definition of the humanized antibody of the present invention and production method thereof

[0046] The chimeric antibody of the present invention includes a human(ized) antibody. The humanized antibody is an antibody in which a framework region is derived from a human and CDR is a mouse-derived region. The humanized antibody can be produced by first grafting CDR from the variable region of a mouse antibody into a human variable region to reconstitute heavy chain and light chain variable regions, and then ligating the thus humanized, reconstituted human variable region to a human constant region. Such a method for producing a humanized antibody is well known in the present technical field (see, for example, Nature, 321, 522-525 (1986); J. Mol. Biol., 196, 901-917 (1987); Queen C et al., Proc. Natl. Acad. Sci. USA, 86: 10029-10033 (1989)). Herein, the type of a mouse-derived CDR sequence used for the anti-EP4 antibody of the present invention is not limited. For instance, examples of the heavy chain CDR1 to 3 include the amino acid sequences shown in SEQ ID NOS: 5 to 7, and examples of the light chain CDR1 to 3 include the amino acid sequences shown in SEQ ID NOS: 8 to 10 and the amino acid sequences shown in SEQ ID NOS: 18 to 20.

[0047] In order to allow a humanized antibody heavy chain or a humanized antibody light chain to express in host cells, the humanized antibody heavy chain or the humanized antibody light chain may be inserted into a vector. The type of such a vector is not particularly limited, and it can be selected, as appropriate, depending on the type of a host cell into which it is to be introduced, and the like. Also, the vector may be introduced into host cells suitable for the expression of an antibody (e.g. mammalian cells such as CHO cells, yeast cells, insect cells, etc.), and an antibody is reconstituted in the host cells, so that a recombinant antibody can be prepared.

Definition of the human antibody of the present invention and production method thereof

[0048] The human antibody (complete human antibody) is an antibody in which a hyper variable region that is an antigen-binding site of a variable region, a remaining region of the variable region, and a constant region have the same structures as those of a human antibody. However, the hyper variable region may also be derived from another animal. Such a human antibody can be easily produced by a person skilled in the art according to a known technique. The human antibody can be obtained, for example, by a method using a human antibody-producing mouse having a human chromosomal fragment comprising the heavy chain and light chain genes of a human antibody (see Tomizuka, K. et al., *Nature Genetics*, (1997) 16, 133-143; Kuroiwa, Y. et. al., *Nuc. Acids Res.*, (1998) 26, 3447-3448; Yoshida, H. et. al., *Animal Cell Technology: Basic and Applied Aspects*, (1999) 10, 69-73 (Kitagawa, Y., Matsuda, T. and Iijima, S. eds.), Kluwer Academic Publishers; Tomizuka, K. et. al., *Proc. Natl. Acad. Sci. USA*, (2000) 97, 722-727, etc.), or by a method of obtaining a phage display-derived human antibody selected from a human antibody library (Wormstone, I. M. et. al, *Investigative Ophthalmology & Visual Science.*, (2002) 43(7), 2301-8; Carmen, S. et. al., *Briefings in Functional Genomics and Proteomics*, (2002) 1(2), 189-203; Siriwardena, D. et. al., *Ophthalmology*, (2002) 109(3), 427-431, etc.).

Functional fragment of the antibody of the present invention

[0049] The functional fragment of the antibody of the present invention means a partial region of the anti-EP4 antibody. Examples of such a functional fragment include Fab, Fab', F(ab')₂, Fv (a variable fragment of antibody), a single-chain antibody (a heavy chain, a light chain, a heavy chain variable region, a light chain variable region, etc.), scFv, a diabody (a scFv dimer), dsFv (a disulfide-stabilized variable region), and a peptide comprising CDR as at least a portion thereof. Fab is an antibody fragment having antigen-binding activity obtained by digesting an antibody molecule with the protease papain, wherein about an N-terminal half of the heavy chain binds to the light chain as a whole via a disulfide bond.

[0050] Fab can be produced by digesting an antibody molecule with papain to obtain a fragment thereof. Fab can also be produced by, for example, constituting a suitable expression vector into which DNA encoding the Fab has been inserted, then introducing the vector into suitable host cells (e.g. mammalian cells such as CHO cells, yeast cells, insect cells, etc.), and then allowing it to express in the cells.

[0051] F(ab')₂ is an antibody fragment having antigen-binding activity obtained by digesting an antibody molecule with the protease pepsin, which is slightly greater than Fab that binds to another Fab via a disulfide bond at hinge region. F(ab')₂ can be obtained by digesting an antibody molecule with the protease pepsin, or it can also be produced by binding the after-mentioned Fab to another Fab via a thioether bond or a disulfide bond. Alternatively, F(ab')₂ can also be produced according to a genetic engineering method, as with Fab.

[0052] Fab' is an antibody fragment having antigen-binding activity obtained by cleaving the disulfide bond at hinge region of the above-described F(ab')₂. Fab' can also be produced according to a genetic engineering method, as in the case of Fab and the like.

[0053] scFv is an antibody fragment having antigen-binding activity that is a VH-linker-VL or VL-linker-VH polypeptide, wherein a single heavy chain variable region (VH) is ligated to a single light chain variable region (VL) using a suitable peptide linker. Such scFv can be produced by obtaining cDNAs encoding the heavy chain variable region and light chain variable region of an antibody and then treating them according to a genetic engineering method.

[0054] Diabody is an antibody fragment having divalent antigen-binding activity, in which scFv is dimerized. Regarding the divalent antigen-binding activity, this activity may be an activity of binding to either two identical antigens, or two different antigens. The diabody can be produced by obtaining cDNAs encoding the heavy chain variable region and light chain variable region of an antibody, then constructing cDNA expressing scFV, in which the heavy chain variable region is ligated to the light chain variable region using a peptide linker, and then treating the cDNA according to a genetic engineering method.

[0055] dsFv is a polypeptide which comprises a heavy chain variable region and a light chain variable region each including a substitution of one amino acid residue with a cysteine residue, in which VH binds to VL via a disulfide bond between the cysteine residues. The amino acid residue to be substituted with the cysteine residue can be selected based on antibody structure prediction according to the method of Reiter et al. or the like. Such dsFv can be produced by obtaining cDNAs encoding the heavy chain variable region and light chain variable region of the antibody and then constructing DNA encoding the dsFv

according to a genetic engineering method.

[0056] A peptide comprising CDR is constituted such that it comprises at least one region of CDR (CDR1-3) of the heavy chain or light chain. A peptide, which comprises multiple CDR regions, is able to bind to another peptide directly or via a suitable peptide linker. In the case of a peptide comprising CDR, DNA encoding the CDR of the heavy chain or light chain of the antibody is constructed, and it is then inserted into an expression vector. The type of the vector is not particularly limited, and it may be selected, as appropriate, depending on the type of a host cells into which the vector is to be introduced, and the like. The vector is introduced into host cells suitable for the expression of an antibody (e.g. mammalian cells such as CHO cells, yeast cells, insect cells, etc.), so that the peptide can be produced. Alternatively, such a peptide comprising CDR can also be produced by chemical synthesis methods such as an Fmoc method (fluorenylmethyloxycarbonyl method) and a tBoc method (t-butyloxycarbonyl method).

Purification of the antibody of the present invention

[0057] A method for purifying the antibody of the present invention is not particularly limited, and a known method can be adopted. For example, a culture supernatant of the above-described hybridoma cells or recombinant cells is recovered, and then, the antibody of the present invention can be purified from the culture supernatant by the combined use of known methods such as various types of chromatography, salting-out, dialysis and membrane separation. When the isotype of an antibody is IgG, the antibody can be simply purified by affinity chromatography using protein A.

Medicament comprising the antibody of the present invention

[0058] The antibody of the present invention or a functional fragment thereof can be used in a medicament comprising, as an active ingredient, the antibody or a functional fragment thereof. The medicament of the present invention can be used to treat or prevent EP4-related immunological diseases, tumor, and pain.

[0059] Examples of the EP4-related immunological diseases include: psoriasis; multiple sclerosis; rheumatoid arthritis; systemic lupus erythematosus; inflammatory bowel diseases such as Crohn's disease; type I diabetes and complications thereof (e.g. diabetic retinopathy, diabetic microangiopathy, diabetic nephropathy, macular degeneration, etc.); polymyositis; Sjogren's syndrome; asthma; atopic dermatitis and contact dermatitis; immunodeficiency disorder; and organ transplantation.

[0060] The medicament of the present invention can be used to treat or prevent pain, namely, nociceptive pain and neuropathic pain. Examples of the nociceptive pain include: pain caused by activation of somatic and visceral nociceptors, such as pathologic deformation of articulations and chronic arthralgia (e.g. arthritis including rheumatoid arthritis, osteoarthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis, and juvenile arthritis) (including the alleviation of disease and the maintenance of articular structure); lumbago and neck pain; musculoskeletal pain; myositis; bone fracture; distortion, bruise; pain attended with fibromyalgia syndrome; pain associated with tumor and the treatment thereof; pain attended with influenza or other viral infectious diseases (common cold, etc.); rheumatic fever; visceral pain; pain attended with functional intestinal diseases (e.g. irritable bowel syndrome, non-cardiac chest pain, non-ulcer dyspepsia, etc.); pain attended with myocardial ischemia; dental pain; post-surgical and post-dental-treatment pain; postpartum pain; primary headache disorder (e.g. migraine headache, tension headache, cluster headache, and other primary headache disorders); secondary headache disorder (e.g. headache caused by the head and neck injury, headache caused by vascular disorder of the head and neck, headache caused by non-vascular intracranial diseases, headache caused by substance abuse or substance withdrawal, headache caused by infectious diseases, headache caused by homeostatic disorders, headache or prosopalgia caused by the disorders of the cranium, neck, eye, ear, nose, sinus, tooth, mouth or other face and cranium constitutional tissues, drug induced headache, and pain attended with migraine headache).

[0061] Examples of the neuropathic pain include: physical injury or ablation; phantom limb pain; pain caused by chronic inflammatory symptom; postherpetic neuralgia; diabetic neuropathy; nonspecific lumbago; backache; sciatica; neuropathy associated with tumor and the treatment thereof; HIV-related neuropathy; carpal tunnel syndrome; chronic alcoholism; hypothyroidism; trigeminal neuralgia; trigeminal/autonomic headache; uraemia; avitaminosis; multiple sclerosis; fibromyalgia syndrome; and pain attended with toxin.

[0062] The medicament of the present invention is effective for the treatment or prevention of tumor. The meaning of the treatment of tumor includes not only the entire or partial inhibition of the growth, diffusion or metastasis of tumor, or the entire or partial elimination of tumor cells, but it also includes the partial or entire resolution of symptoms attended with the tumor (pain,

anorexia, weight reduction, etc.).

[0063] The treatment or prevention of tumor is directed at the overgrowth of benign tumor and polyp, the overgrowth of malignant tumor and polyp, and neoplasm.

[0064] Examples of the overgrowth of benign tumor and polyp include: squamous cell papilloma; basal cell carcinoma; transitional cell papilloma; adenocarcinoma; gastrinoma; cholangiocellular adenoma; hepatocellular adenoma; nephridial adenoma; oncocytoma; glomus tumor; melanocytic nevus; fibroma; myxoma; leiomyoma; rhabdomyoma; benign teratoma; angioma; osteoma; chondroma; and meningioma.

[0065] Examples of the overgrowth of malignant tumor and polyp include: hepatic cell carcinoma; cholangiocarcinoma; renal cell carcinoma; squamous-cell carcinoma; basal cell carcinoma; transitional cell carcinoma; adenocarcinoma; malignant gastrinoma; malignant melanoma; fibrosarcoma; myxosarcoma; liposarcoma; leiomyosarcoma; rhabdomyosarcoma; malignant teratoma; angiosarcoma; Kaposi's sarcoma; osteosarcoma; chondrosarcoma; lymphangiosarcoma; malignant meningioma; non Hodgkin's lymphoma; Hodgkin's lymphoma; leukemia; and encephaloma.

[0066] Examples of the neoplasm include: epithelial cell-derived neoplasm (epithelial carcinoma), basal cell carcinoma, and adenocarcinoma; labial cancer, oral cancer, esophageal cancer, gastrointestinal cancer such as small intestinal cancer and stomach cancer, colon cancer, rectal cancer, liver cancer, bladder cancer, pancreatic cancer, ovarian cancer, cervical cancer, lung cancer, and breast cancer; skin cancer such as squamous-cell carcinoma and basal cell carcinoma, prostatic cancer, and renal cell carcinoma; and known other cancers that affect systemic epithelial, mesenchymal or blood cells.

[0067] There can be provided an antibody-drug conjugate which comprises the antibody of the present invention and a compound having antitumor activity and/or cytotoxicity. According to a genetic recombination technique, the protein toxin used as a compound having antitumor activity and/or cytotoxicity is fused with an antibody gene on the gene, so that it can be expressed as a single protein. The thus obtained protein is generally referred to as immunotoxin. Examples of the compound having antitumor activity include doxorubicin and mitomycin C. A method for producing an antibody-drug conjugate is not particularly limited. An example of the method is a method of coupling an antibody with a drug via a disulfide bond or a hydrazone bond.

Pharmaceutical composition comprising the antibody of the present invention

[0068] The present invention includes a medicament or a pharmaceutical composition. In addition to the above-described antibody of the present invention or a functional fragment thereof, a physiologically acceptable salt thereof may also be used as an active ingredient of the medicament of the present invention. When an acidic group is present, examples of such a salt include: alkaline metal and alkaline earth-metal salts such as lithium, sodium, potassium, magnesium or calcium; amine salts such as ammonia, methylamine, dimethylamine, trimethylamine, dicyclohexylamine, tris(hydroxymethyl)aminomethane, N,N-bis(hydroxyethyl)piperazine, 2-amino-2-methyl-1-propanol; ethanolamine, N-methylglucamine or L-glucamine; and salts formed with basic amino acids such as lysine, δ hydroxylysine or arginine. When a basic group is present, examples of such a salt include: salts formed with mineral acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid or phosphoric acid; salts formed with organic acids such as methanesulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid, acetic acid, propionic acid, tartaric acid, fumaric acid, maleic acid, malic acid, oxalic acid, succinic acid, citric acid, benzoic acid, mandelic acid, cinnamic acid, lactic acid, glycolic acid, glucuronic acid, ascorbic acid, nicotinic acid or salicylic acid; and salts formed with acidic amino acids such as aspartic acid or glutamic acid.

[0069] As the medicament of the present invention, the antibody of the present invention or a functional fragment thereof, which is an active ingredient of the medicament, may directly be administered. In general, however, the medicament of the present invention is desirably administered in the form of a pharmaceutical composition comprising one or two or more pharmaceutical additives, as well as the antibody of the present invention or a functional fragment thereof used as an active ingredient. As an active ingredient of the medicament of the present invention, a combination of two or more types of the antibodies of the present invention or functional fragments thereof may be used. Known other agents may also be added to the above-mentioned pharmaceutical composition.

[0070] The type of the pharmaceutical composition is not particularly limited. Examples of the dosage form include a tablet, a capsule, a granule, a powder medicine, syrup, a suspension, a suppository, an ointment, a cream, a gel, a patch, an inhalant, and an injection. These pharmaceutical preparations are prepared according to an ordinary method. In the case of a liquid agent, it may adopt a form in which the agent is dissolved or suspended in water or another suitable medium before use. Moreover, in the

case of a tablet or a granule, it may be coated according to a well-known method. In the case of an injection, it is prepared by dissolving the compound of the present invention in water. The present compound may also be dissolved in a normal saline or a dextrose solution, as necessary, and a buffer or a preservative may also be added to such a solution. The pharmaceutical composition may be provided in any given pharmaceutical form used for oral or parenteral administration. For example, the pharmaceutical composition may be prepared in the form of a pharmaceutical composition used for oral administration, such as a granule, a parvule, a powder medicine, a hard capsule, a soft capsule, syrup, an emulsion, a suspension or a liquid agent, or it may be prepared in the form of a pharmaceutical composition used for parenteral administration (intravenous administration, intramuscular administration or subcutaneous administration), such as an injection, a drop, a percutaneous absorption agent, a transmucosal absorption agent, a transnasal agent, an inhalant or a suppository. In the case of an injection or a drop, it may be prepared in a powdery form such as a freeze-dried form, and it may be then dissolved in a suitable aqueous medium such as a normal saline before use. Also, a sustained-release preparation coated with a polymer or the like can be directly administered into the brain.

[0071] The types of pharmaceutical additives used in the production of the pharmaceutical composition, the ratio of the pharmaceutical additives to the active ingredient, and a method for producing the pharmaceutical composition may be appropriately determined by a person skilled in the art, depending on the form of the pharmaceutical composition to be produced. As such pharmaceutical additives, inorganic or organic substances, or solid or liquid substances can be used. In general, such pharmaceutical additives can be added at a weight percentage of 1% to 90% based on the weight of the active ingredient. Specific examples of such substances used as pharmaceutical additives include lactose, glucose, mannitol, dextrin, cyclodextrin, starch, sucrose, magnesium aluminometasilicate, synthetic aluminum silicate, carboxymethylcellulose sodium, hydroxypropyl starch, carboxymethylcellulose calcium, ion-exchange resin, methyl cellulose, gelatin, gum Arabic, hydroxypropyl cellulose, hydroxypropylmethyl cellulose, polyvinylpyrrolidone, polyvinyl alcohol, light anhydrous silicic acid, magnesium stearate, talc, tragacanth, bentonite, Veegum, titanium oxide, sorbitan fatty acid ester, sodium lauryl sulfate, glycerin, fatty acid glycerin ester, purified lanolin, glycerinated gelatin, polysorbate, macrogol, vegetable oil, wax, liquid paraffin, white petrolatum, fluorocarbon, nonionic surfactant, propylene glycol, and water.

[0072] In order to produce a solid preparation used for oral administration, the active ingredient is mixed with an excipient ingredient such as lactose, starch, crystalline cellulose, calcium lactate or silicic acid anhydride to prepare a powder medicine. Otherwise, a binder such as saccharose, hydroxypropyl cellulose or polyvinylpyrrolidone, a disintegrator such as carboxymethyl cellulose or carboxymethylcellulose calcium, or other additives are further added to the above obtained mixture, as necessary, and the obtained mixture is then subjected to wet granulation or dry granulation, so as to prepare a granule. In order to produce a tablet, such a powder medicine or a granule may be subjected to a tablet-making operation, directly or with addition of a lubricant such as magnesium stearate or talc. The prepared granule or tablet may be coated with an enteric coating base such as hydroxypropylmethylcellulose phthalate or a methacrylic acid-methyl methacrylate polymer, so as to prepare an enteric coated drug. Otherwise, it may be coated with ethyl cellulose, carnauba wax or hydrogenated oil, so as to prepare a long-acting preparation. Moreover, in order to produce a capsule, a powder medicine or a granule is filled into a hard capsule, or the active ingredient is coated with a gelatin film, directly or after being dissolved in glycerin, polyethylene glycol, sesame oil, olive oil or the like, thereby producing a soft capsule.

[0073] In order to produce an injection, the active ingredient, together with a pH adjuster such as hydrochloric acid, sodium hydroxide, lactose, lactic acid, sodium, sodium monohydrogen phosphate or sodium dihydrogen phosphate, and an isotonicizing agent such as sodium chloride or glucose, as necessary, is dissolved in a distilled water for injection, and the obtained solution is subjected to aseptic filtration and is then filled into an ampule. Otherwise, mannitol, dextrin, cyclodextrin, gelatin or the like may be further added to the above obtained solution, and the obtained mixture may be then subjected to vacuum freeze-drying, so as to prepare an injection which is dissolved before use. Furthermore, lecithin, polysorbate 80, polyoxyethylene hydrogenated castor oil or the like is added to the active ingredient, and it is emulsified in water, so as to prepare an emulsion for injection.

[0074] In order to produce a rectal administration agent, the active ingredient, together with a suppository base such as cacao butter, tri-, di- and mono-glyceride of fatty acid, or polyethylene glycol, is moisturized and melted, and the resultant is then poured into a mold, followed by cooling. Otherwise, the active ingredient may be dissolved in polyethylene glycol or soybean oil or the like, and it may be then coated with a gelatin film or the like.

[0075] The dose and administration frequency of the medicament of the present invention are not particularly limited. These factors can be appropriately selected by a doctor's judgment, depending on conditions such as the purpose of preventing and/or treating deterioration and/or progression of a disease to be treated, the type of the disease, the body weight and age of a patient, and the severity of the disease. In general, the dose of the present medicament is approximately 0.01 to 1000 mg (the weight of the active ingredient) per adult per day via oral administration. The medicament can be applied once or divided over several administrations per day, or every several days. When the medicament is used as an injection, it is desirable that the medicament

be continuously or intermittently administered at a dose of 0.001 to 400 mg (the weight of the active ingredient) per adult per day.

[0076] The medicament of the present invention can be prepared as a sustained-release preparation such as an implantable tablet and a delivery system encapsulated into a microcapsule, using a carrier capable of preventing the sustained-release preparation from immediately being removed from the body. Examples of the carrier that can be used herein include biodegradable and biocompatible polymers, such as ethylene vinyl acetate, polyanhydride, polyglycolic acid, collagen, polyorthoester, and polylactic acid. Such materials can be easily prepared by a person skilled in the art. In addition, a liposome suspension can also be used as a pharmaceutically acceptable carrier. The type of useful liposome is not limited. Such liposome is prepared as a lipid composition comprising phosphatidyl choline, cholesterol and PEG-induced phosphatidylethanol (PEG-PE) by being passed through a filter with a suitable pore size, such that it has a size suitable for use, and it is then purified by a reverse phase evaporation method.

[0077] The medicament of the present invention can be prepared as a pharmaceutical composition in the form of a kit, and it can be included in a container or package, together with an instruction manual for administration. When the pharmaceutical composition of the present invention is provided in the form of a kit, different constituents in the composition are wrapped with different containers, and they are then mixed immediately before use. Thus, different constituents are wrapped, separately, because it makes possible to preserve active constituents for a long period of time without losing the functions of the active constituents.

[0078] A reagent contained in the kit is supplied into a container made of a material that effectively keeps the activity of the constituents for a long period of time, does not adsorb the constituents on the inner surface thereof, and does not alter the quality of the constituents. For example, a sealed glass ampule may comprise a buffer enclosed in the presence of neutral nonreactive gas such as nitrogen gas. The ampule is constituted with glass, an organic polymer such as polycarbonate or polystyrene, ceramic, metal, or any other suitable materials that are commonly used to retain the reagent.

[0079] Moreover, the kit may also comprise an instruction manual. The instruction manual for the present kit may be printed on a paper and/or may be recorded on an electrically or electromagnetically readable medium, such as a floppy (registered trademark) disk, CD-ROM, DVD-ROM, a Zip disk, a videotape or an audiotape, and it may be then provided to a user in such a form. A detailed instruction manual may be actually included with the kit, or it may be published on the website that is designated by a kit manufacturer or distributor or noticed through an e-mail or the like.

[0080] Furthermore, the present invention includes a method for preventing or treating EP4-related immunological diseases, tumor and pain, which comprises administering to a patient and the like the medicament or pharmaceutical composition of the present invention.

[0081] The term "treat" is used herein to mean inhibition or alleviation of the progression and deterioration of the pathological condition of a mammal affected with a disease that develops due to abnormality in the function of EP4 (e.g. abnormal increase in the function, etc.). Thus, this is a treatment carried out for the purpose of inhibiting or alleviating the progression and deterioration of the above-mentioned disease.

[0082] On the other hand, the term "prevent" is used herein to mean previous inhibition of the development of, or affecting with a disease that develops due to abnormality in the function of EP4 (e.g. abnormal increase in the function, etc.) in a mammal that is likely to be affected with the aforementioned disease. Thus, this is a treatment carried out for the purpose of previously inhibiting the development of various symptoms of the disease.

[0083] The "mammal" to be treated means any given animal belonging to Mammalia, and the type of the mammal is not particularly limited. Examples of the mammal used herein include humans, pet animals such as a dog, a cat or a rabbit, and livestock animals such as a bovine, a swine, sheep or a horse. The particularly preferred "mammal" is a human.

The antibody-immobilized carrier of the present invention

[0084] The present invention includes an antibody-immobilized carrier. The antibody-immobilized carrier of the present invention is formed by immobilizing the anti-human EP4 antibody of the present invention on a carrier. In a preferred embodiment, the antibody-immobilized carrier of the present invention is allowed to come into contact with blood containing EP4-expressing cells, so that it can be used to remove the EP4-expressing cells from the body fluid. The anti-human EP4 antibody immobilized on a carrier may be of only one type, or of two or more types.

[0085] A specific form of the antibody-immobilized carrier of the present invention is, for example, the antibody of the present invention immobilized on a water-insoluble carrier, which is then filled into a container. Herein, all types of materials can be used as such water-insoluble carriers. In terms of moldability, sterilization and low cytotoxicity, preferred materials include: synthetic polymers such as polyethylene, polypropylene, polystyrene, acrylic resin, nylon, polyester, polycarbonate, polyacrylamide or polyurethane; natural polymers such as agarose, cellulose, cellulose acetate, chitin, chitosan or alginate; inorganic materials such as hydroxyapatite, glass, alumina or titania; and metallic materials such as stainless steel or titanium.

[0086] Examples of the form of a carrier include a granular form, a flocculent form, a woven fabric, a non-woven fabric, a spongy porous form, and a platy form. From the viewpoint of a large surface area per volume, a granular form, a flocculent form, a woven fabric, a non-woven fabric, and a spongy porous form are preferable. For example, peripheral blood is supplied through a porous filter in which a container has previously been filled with an antibody-immobilized water-insoluble carrier, so that disease-associated EP4-expressing cells can be efficiently removed.

[0087] The antibody-immobilized carrier of the present invention can be combined with other components, so as to produce a kit for removing EP4-expressing cells. Examples of other components include an anticoagulant and an extracorporeal circulation circuit.

Diagnostic kit comprising the anti-EP4 antibody of the present invention

[0088] The anti-EP4 antibody of the present invention can be provided in the form of a diagnostic kit. The diagnostic kit of the present invention comprises an antibody, and may also comprise a labeling substance, or a secondary antibody or a labeled substance thereof. The labeled substance of antibody means an antibody labeled with an enzyme, a radioisotope, a fluorescent compound, a chemiluminescent compound, etc. In addition to the aforementioned components, the diagnostic kit of the present invention may comprise other reagents used for carrying out the detection of the present invention, for example, if the labeled substance is an enzyme-labeled substance, the diagnostic kit may also comprise an enzyme substrate (a coloring substrate, etc.), an enzyme substrate solution, an enzyme reaction termination solution, an analyte diluent, and the like. Furthermore, the present diagnostic kit may also comprise various types of buffers, sterilized water, various types of cell culture vessels, various types of reactors (e.g. Eppendorf tube, etc.), a blocking agent (Bovine Serum Albumin (BSA), Skim milk, and serum components such as Goat serum), a washing agent, a surfactant, various types of plates, an antiseptic agent such as sodium azide, an experimental operation manual (instruction manual), and the like. Examples of the measurement method applied herein include ELISA, EI, RIA, fluorescence immunoassay (FIA), luminescence immunoassay, and flow cytometry. Among these methods, flow cytometry is particularly preferable in terms of simplicity and high sensitivity. In addition, the diagnostic kit of the present invention can be used in combination with another antibody kit comprising an antibody that recognizes a cell surface antigen.

[0089] The diagnostic kit of the present invention is allowed to react with the blood cells of a patient affected with cancer, autoimmune disease or the like, so that the ratio of EP4-expressing cells in the blood can be detected. By combining the present diagnostic kit with another cell surface antigen antibody, the ratio of EP4-expressing cells in a specific cell population (e.g. dendritic cells, TH17 cells, or Treg cells) can be detected. By evaluating an increase or decrease in the ratio of the EP4-expressing cells, the condition of the disease can be evaluated.

[0090] Hereinafter, the present invention will be described more in detail in the following examples.

Examples

(1) Production of human EP4 expression vector pcDNA-DEST40-hEP4

[0091] The sequence 5'-GGGGACAAGTTTGTACAAAAAGCAGGCTTCGAAGGAGATAGAACC ATGGAGACAGACACTCCTGCTATGGGTACTGCTGCTCTGGGTTCC AGGTTCCACTGGTGAC-3' (SEQ ID NO: 30) was added to the 5'-terminus of a sequence, which had been prepared by removing a stop codon from the ORF sequence of the human EP4 gene registered in Genbank (Accession No. NM_000958), and the sequence 5'-GACCCAGCTTTCTTGTACAAAGTGGTCCCC-3' (SEQ ID NO: 31) was added to the 3'-terminus thereof, thereby synthesizing DNA. Using Gateway System (Invitrogen), the thus synthesized DNA was incorporated into a pDONR221 vector (manufactured by Invitrogen), so as to prepare pDONR-hEP4. The nucleotide sequence of the insert was determined according to an ordinary

method, and it was confirmed that the sequence included no errors. Subsequently, using Gateway System, the sequence containing the human EP4 gene was incorporated into the pcDNA-DEST40 vector (manufactured by Invitrogen) to obtain pcDNA-DEST40-hEP4. Human EP4 expressed from this plasmid is a fusion protein in which V5 and 6 × HIS tags were added to the C-terminus. The plasmid DNA of pcDNA-DEST40-hEP4 was prepared by transforming *Escherichia coli* (DH5α) according to an ordinary method and then amplifying it, and then using PureLink HiPure Plasmid Filter Maxiprep Kit (manufactured by Invitrogen) in accordance with an instruction manual included therewith.

(2) Preparation of human EP4-expressing 293FT cells

[0092] 10 µg of the above-described plasmid DNA of pcDNA-DEST40-hEP4 was introduced into 293FT cells (manufactured by Invitrogen) plated on a 100-mm collagen I coated cell culture dish, using 25 µL of Lipofectamin 2000 (manufactured by Invitrogen) in accordance with an instruction manual included therewith. Twenty-four hours after the gene introduction, the cells were washed with HBSS (Hanks' Balanced Salt Solutions, manufactured by Invitrogen), were then removed from the cell culture dish using an enzyme-free cell dissociation buffer (manufactured by Invitrogen), and were then recovered by centrifugation. The EP4 gene-introduced 293FT cells and the gene-non-introduced 293FT cells were subjected to a cell membrane permeabilization using Cytofix/Cytoperm Kit (manufactured by BD). The resulting cells were mixed with an anti-V5 tag antibody (manufactured by Invitrogen), and the mixture was then incubated (4°C, 1 hour). Thereafter, the resultant was washed with a washing buffer (0.1 % fetal bovine serum-containing PBS (Phosphate Buffered Saline, manufactured by Invitrogen)) three times, and was then stained with an Alexa488-labeled anti-mouse IgG antibody (manufactured by Invitrogen) used as a secondary antibody (4°C, 1 hour). Then, the resultant was again washed with a washing buffer three times, and was then analyzed with the flow cytometer Quanta SC MPL (manufactured by BECKMAN COULTER). As a result, since Alexa488 fluorescence positive signal was detected in only the gene-introduced 293FT cells, it could be confirmed that human EP4 was expressed in the cells.

[0093] Thus, this human EP4-expressing 293FT cell was used as a sensitizing antigen.

(3) Immunization

[0094] Antigen immunization was performed on 7-week-old female 129/Ola background mice. The human EP4-expressing 293FT cells described in (2) above were suspended in a normal saline, and thereafter, the suspension were intraperitoneally administered to the above-mentioned mice 5 times at administration intervals of 10 to 14 days.

(4) Production of hybridoma

[0095] Three days after the 5th immunization, the spleen was removed from each mouse, and splenic cells were prepared. The splenic cells and mouse myeloma P3X63Ag8.653 cells (obtained from ECACC) were subjected to cell fusion according to an ordinary method using Polyethylene Glycol 4000 (manufactured by Merck). The fused cells were suspended in GIT Medium (manufactured by Wako Pure Chemical Industries, Ltd.) that contained 100 units/mL penicillin, 100 µg/mL streptomycin; non-essential amino acid, 2 mM L-glutamine, and NCTC-109 medium (all of which were manufactured by Invitrogen). The obtained suspension was then plated at a density of 100 µL/well on a 96-well plate, and it was then cultured at 37°C in 5% CO₂. From the day following the cell fusion, the medium was exchanged with a medium formed by adding HAT Supplement (manufactured by Invitrogen) to the above-mentioned medium, and the culture was continued for 13 days after completion of the cell fusion. As a result, a colony of hybridomas (approximately 700 clones) was obtained.

(5) Construction of NS0 cell line stably expressing human EP4

[0096] Using Gateway System, the recombination reaction between the pDONR-hEP4 described in (1) above and the pEF-DEST51 vector (manufactured by Invitrogen) was performed to obtain a plasmid pEF-DEST51-hEP4. Human EP4 expressed by this plasmid is a fusion protein in which V5 and 6 × HIS tags were added to the C-terminus.

[0097] Using 35µL of Lipofectamin LTX (manufactured by Invitrogen) and 14 µL of PlusReagent (manufactured by Invitrogen) in accordance with an instruction manual included therewith, 14 µg of the plasmid pEF-DEST51-hEP4 was introduced into 1×10^7

mouse myeloma NS0 cells (obtained from Cell Bank, RIKEN BioResource Center) that had been cultured in RPMI medium containing 10% fetal bovine serum, 100 units/mL penicillin, and 100 µg/mL streptomycin (manufactured by Invitrogen). From the day following the gene introduction, while the medium was exchanged with RPMI medium supplemented with 2.5 µg/mL antibiotic blasticidin (manufactured by Invitrogen) every 3 days, the culture was continuously carried out for 2 weeks. Blasticidin-resistant NS0 cells were cloned from the formed colonies according to a penicillin cup method.

[0098] The obtained blasticidin-resistant NS0 cells were blocked with FcBlock (manufactured by Becton, Dickinson and Company) at 4°C for 15 minutes, and thereafter, the expression of an EP4 fusion protein was confirmed with the flow cytometer by the same method as described in (2) above. As a result, it could be confirmed that the obtained blasticidin-resistant NS0 cells stably expressed human EP4.

(6) Screening for anti-EP4 antibody-producing hybridoma

[0099] The NS0 cell line stably expressing human EP4 (2×10^5 cells) produced in (5) above was stained by the same method as described in (2) above, and was then analyzed with a flow cytometer. A cell membrane permeabilization was not performed, and 50 µL of culture supernatant of the hybridoma obtained in (4) above was used as a primary antibody. As a result, an Alexa488 fluorescence positive reaction was found in supernatants in 21 wells. The cells in the positive well were cloned by limiting dilution. A culture supernatant after completion of the culture for 2 weeks was also subjected to a binding test with the NS0 cell line stably expressing human EP4 with a flow cytometer. The same cloning and binding test were repeated again, and 2 clones of anti-EP4 antibody-producing hybridomas were finally obtained. These hybridomas were named as NBG016-mAb14 and NBG016-mAb21.

[0100] The obtained hybridoma cells NBG016-mAb14 and NBG016-mAb21 were deposited with the International Patent Organism Depositary, the National Institute of Advanced Industrial Science and Technology, an Independent Administrative Institution under the Ministry of Economy, Trade and Industry, at the AIST Tsukuba Central 6, Higashi 1-1-1, Tsukuba, Ibaraki, Japan (postal code: 305-8566), under accession Nos. FERM P-21978 and FERM P-21979, respectively, on June 29, 2010 (the original deposition date). Thereafter, the original deposition was then transferred to an international deposition under the provisions of the Budapest Treaty (the notification date of "Certificate of Receipt of Original Deposition" and "Viability Certification": September 5, 2011). Accession Nos. are FERM BP-11402 and FERM BP-11403, respectively.

(7) Purification of anti-EP4 antibody

[0101] The hybridoma cells NBG016-mAb14 and NBG016-mAb21 were each continuously cultured in a serum-free CD-Hybridoma Medium (manufactured by Invitrogen), until approximately 90% of cells died, so as to produce antibodies. The cells were removed from 100 mL of the culture supernatant by centrifugation (1,500 rpm, 15 minutes), and the residue was then passed through HiTrap Protein G HP Column (manufactured by GE Healthcare Japan) to purify and concentrate IgG. To determine the subtype of an IgG and the type of a light chain, the thus purified IgG was examined using Iso Strip mouse monoclonal antibody isotyping kit (manufactured by Roche Diagnostics). As a result, they were both (IgG2a, κ). Hereinafter, the terms "NBG016-mAb14" and "NBG016-mAb21" indicate these purified antibodies. When the term "hybridoma" or "cell" is used, such term indicates a hybridoma that produces these antibodies.

[0102] As in the case of (2), (3), (4) and (6) above, hybridoma cells producing an anti-EP4 antibody with a different subtype were obtained. From a culture supernatant of this hybridoma, purified IgG, the subtype and light chain type of which were (IgG1, κ), was obtained in the same manner as described in (7) above. This purified antibody was referred to as NBG016-mAb9.

(8) Production of the CHO cell line stably expressing human EP4

[0103] Using Gateway System, a human EP4 gene from pDONR-hEP4 was incorporated into the pEF5/FRT/V5-DEST vector (manufactured by Invitrogen) to obtain pEF-FRT-hEP4. Human EP4 expressed by this plasmid is a fusion protein in which V5 and 6 x HIS tags were added to the C-terminus.

[0104] Using Lipofectamin 2000, the plasmids pEF-FRT-hEP4 and pOG44 (manufactured by Invitrogen) were simultaneously introduced into Flp-In-CHO cells (manufactured by Invitrogen) that had been cultured in Ham's F-12 medium (manufactured by Invitrogen) containing 10% fetal bovine serum, 100 units/mL penicillin and 100 µg/mL streptomycin. From the day following the

gene introduction, the medium was exchanged with Ham's F-12 medium supplemented with 500 µg/mL antibiotic hygromycin (manufactured by Invitrogen), and while exchanging the medium with a fresh one every 3 days, the cells were cultured for 2 weeks. From the formed colonies, hygromycin-resistant cells were cloned according to a penicillin cup method.

[0105] A phycoerythrin (PE)-labeled anti-mouse IgG antibody (BECKMAN COULTER) was used as a secondary antibody, and the binding of the obtained hygromycin-resistant cells to an anti-V5 tag antibody was analyzed with a flow cytometer by the method described in (2) above. As a result, the obtained hygromycin-resistant Flp-In-CHO cells showed the positive signal of PE, and thus, it could be confirmed that the cells stably expressed human EP4. Hereinafter, this cell is referred to as a CHO cell line stably expressing human EP4.

(9) Binding test of anti-human EP4 antibody and human EP4-expressing cells

[0106] The binding test of an anti-human EP4 antibody and a CHO cell line stably expressing human EP4 was carried out with flow cytometry by the method described in (6) above. The CHO cell line stably expressing human EP4 or the parent Flp-In-CHO cell line (5×10^5 cells) was used. As a primary antibody, 1 µg of NBG016-mAb14, NBG016-mAb21, or a mouse isotype control antibody (manufactured by BioRegend) was used. As a secondary antibody, a PE-labeled anti-mouse IgG antibody was used.

[0107] The results are shown in Figure 1. The parent Flp-In-CHO cell line is indicated with the histogram filled with grey color, whereas the cells stably expressing human EP4 are indicated with the black solid line. Both NBG016-mAb14 and NBG016-mAb21 bind only to the CHO cell line stably expressing human EP4. Thus, the results demonstrated that these antibodies specifically bind to human EP4.

[0108] Likewise, NBG016-mAb9 was also subjected to a binding test with the CHO cell line stably expressing human EP4. The results are shown in Figure 2. The results demonstrated that NBG016-mAb9 also specifically binds to human EP4.

(10) Inhibition test regarding PGE₂-induced cAMP production by antibodies

[0109] The CHO cell line stably expressing human EP4 or the parent Flp-In-CHO cell line was cultured in a medium containing 1 mM acetylsalicylic acid for 18 hours, and was then recovered from the cell culture dish using a cell dissociation buffer. The recovered cells were then dispensed into CulturPlate-96 (manufactured by PerkinElmer) at a density of 2,500 cells per well. NBG016-mAb14, NBG016-mAb21, or a mouse isotype control antibody was added to each well to a concentration of 0.05 to 30 µg/mL, and it was then left at room temperature for 15 minutes. Subsequently, PGE₂ (manufactured by Cayman) was added to each well to a concentration of 5×10^{-11} M, and the obtained mixture was further left at room temperature for 30 minutes. Using LANCE Ultra cAMP Kit (manufactured by PerkinElmer), a reaction was carried out in accordance with an instruction manual included with the kit. Then, the level of cAMP produced in the cells was measured using the plate reader ARVO 1420 HTS (manufactured by PerkinElmer).

[0110] The results are shown in Figure 3. When the mouse isotype control antibody was added, it did not provide a significant inhibitory effect on PGE₂-induced cAMP production level. In contrast, when NBG016-mAb14 or NBG016-mAb21 was added, an inhibitory effect on cAMP production was observed in an antibody concentration-dependent manner. Using the data analysis software OriginPro 8.1 (manufactured by OriginLab), analysis was carried out with logistic function. As a result, the IC₅₀ value of NBG016-mAb14 was found to be 0.15 µg/mL (approximately 1.0 nM), and the IC₅₀ value of NBG016-mAb21 was found to be 0.24 µg/mL (approximately 1.6 nM). From these results, it was demonstrated that NBG016-mAb14 and NBG016-mAb21 were functional antibodies having antagonist activity on human EP4, and that these antibodies have receptor function-inhibiting activity that is equivalent to or greater than that of existing substances (e.g. low-molecular-weight compounds) having antagonist activity on human EP4.

[0111] Likewise, NBG016-mAb9 was also subjected to a test involving addition of 1.5×10^{-10} M PGE₂. The results are shown in Figure 4. As a result of the above-described analysis, the IC₅₀ value of NBG016-mAb9 was found to be 4.6 µg/mL (approximately 28.8 nM). These results demonstrate that NBG016-mAb9 is also a functional antibody having antagonist activity on human EP4.

(11) Production of expression vectors for human EP1-4 and mouse EP1-4

[0112] To the 5'-terminus of a sequence, which had been formed by removing a stop codon from the ORF sequence of each of human EP1 (GenBank Accession No. NM_000955), human EP2 (GenBank Accession No. NM_000956), human EP3a1 (GenBank Accession No. X83857), mouse EP1 (GenBank Accession No. NM_013641), mouse EP2 (GenBank Accession No. NM_008964), mouse EP3 (GenBank Accession No. NM_011196) and mouse EP4 (GenBank Accession No. NM_008965), the sequence CACCATGGAGACAGACACACTCCTGCTATGGGTACTGCTGCTCTGGG TTCCAGGTTCCACTGGTGAC (SEQ ID NO: 32) was added, so as to prepare a DNA fragment. This DNA fragment was amplified by PCR using KOD FX (manufactured Toyobo Co., Ltd.) according to an ordinary method. The amplified DNA was incorporated into the pENTR/D-TOPO vector (manufactured by Invitrogen), so as to prepare pENTR-hEP1, pENTR-hEP2, pENTR-hEP3, pENTR-mEP1, pENTR-mEP2, pENTR-mEP3, and pENTR-mEP4. The nucleotide sequence of each insert was determined according to an ordinary method, and it was confirmed that the sequences included no errors. Using these 7 types of plasmids and the plasmid pDONR-hEP4 produced in (1) above, individual inserts were incorporated into the pcDNA-DEST47 vector (manufactured by Invitrogen) by Gateway System. As a result, the following plasmids were obtained: pcDNA-DEST47-hEP1, pcDNA-DEST47-hEP2, pcDNA-DEST47-hEP3, pcDNA-DEST47-hEP4, pcDNA-DEST47-mEP1, pcDNA-DEST47-mEP2, pcDNA-DEST47-mEP3, and pcDNA-DEST47-mEP4. These plasmids express a fusion protein in which Cycle 3 Green Fluorescent Protein (GFP) has been added to the C-terminus of each PGE₂ receptor.

(12) Binding specificity test of anti-EP4 antibody

[0113] The pcDNA-DEST47-hEP1, pcDNA-DEST47-hEP2, pcDNA-DEST47-hEP3, pcDNA-DEST47-hEP4, pcDNA-DEST47-mEP1, pcDNA-DEST47-mEP2, pcDNA-DEST47-mEP3, and pcDNA-DEST47-mEP4 produced in (11) above (10 µg each) were each introduced into 293FT cells, using Lipofectamin 2000. On the following day, the cells were washed with HBSS, and were then removed from the cell culture dish using an enzyme-free cell dissociation buffer. The cells were then recovered by centrifugation. The thus recovered cells are referred to as 293FT cells transiently expressing EP.

[0114] The binding test of the anti-EP4 antibody of the present invention and the 293FT transiently expressing EP cells was carried out with a flow cytometer according to the method described in (6) above. 293FT cells (5×10^5 cells) that transiently expressed each of 8 types of PGE₂ receptor subtypes were used. As a primary antibody, 1 µg of the anti-EP4 antibody NBG016-mAb14 or NBG016-mAb21, or a mouse isotype control antibody (manufactured by BioRegend) was used. As a secondary antibody, a PE-labeled anti-mouse IgG antibody was used.

[0115] As an example, the results of NBG016-mAb14 are shown in Figure 5. Cells showing the positive signal of GFP-derived fluorescence were present, and thus, it could be confirmed that each PGE₂ receptor was expressed on 293FT cells. However, among the 8 types of cells, those showing positive signal of PE fluorescence were only human EP4-expressing cells. The same results were obtained from NBG016-mAb21. Thus, it was found that the anti-EP4 antibody of the present invention has strong specificity to human EP4. It was demonstrated that the present anti-EP4 antibody has PGE₂ receptor subtype-binding specificity that is higher than that of existing substances having antagonist activity on human EP4.

[0116] Likewise, the binding specificity of NBG016-mAb9 was examined. The results are shown in Figure 6. Among the 8 types of cells each expressing any one of the 8 types of PGE₂ receptor subtypes, those showing positive signal of PE fluorescence were only human EP4-expressing cells. From these results, it was found that NBG016-mAb9 also has strong specificity to human EP4.

(13) Binding test of human lymphocytes and anti-EP4 antibody

[0117] Frozen human peripheral blood mononuclear cells (manufactured by Cellular Technology Ltd.) were thawed using CTL-Anti-Aggregate-Wash Supplement (manufactured by Cellular Technology Ltd.) in accordance with an instruction manual included therewith.

[0118] The binding test of the anti-EP4 antibody of the present invention to human lymphocytes was carried out with a flow cytometer according to the method described in (6) above. The prepared human peripheral blood mononuclear cells (9×10^5 cells) were mixed with 1.5 µg of NBG016-mAb14, NBG016-mAb21 or a mouse isotype control antibody, respectively as a primary antibody, and then mixed with an Alexa488-labeled anti-mouse IgG antibody as a second antibody. When an analysis was carried out using a flow cytometer, a cell population is divided into a lymphocyte subset and a monocyte/macrophage subset based on the dot plots of forward-scattered light and side scattered light, and the Alexa488 fluorescence intensity of the lymphocyte subset

was then examined.

[0119] The analysis results with a flow cytometer are shown in Figure 7. The results of the mouse isotype control antibody are shown with the histogram filled with grey color, whereas the results of the anti-EP4 antibody are shown with the black solid line. Since a majority of the human lymphocyte subset showed a positive signal of Alexa488 fluorescence only in the case of the reaction of the human lymphocytes with the anti-EP4 antibody, it was found that the human lymphocytes bound to the anti-EP4 antibody. From these results, it became clear that the anti-EP4 antibody of the present invention has an ability to bind to human endogenous EP4.

[0120] Likewise, NBG016-mAb9 was also subjected to a binding confirmation experiment with human lymphocytes. Human peripheral blood mononuclear cells were isolated from human fresh peripheral blood using Lymphoprep (manufactured by AXIS SHIELD) in accordance with an instruction manual included therewith, and thereafter, a CD 14-negative cellular fraction was separated using Anti-Human CD14 Microbeads (manufactured by Miltenyi Biotec) and was used as a human lymphocyte subset. The subsequent binding confirmation experiment was carried out as described above, using a fluorescein isothiocyanate (FITC)-labeled anti-mouse IgG antibody (manufactured by BECKMAN COULTER) as a secondary antibody. As shown in Figure 8, a majority of the human lymphocytes bound to NBG016-mAb9, and thus, it was found that NBG016-mAb9 could also bind to human endogenous EP4.

(14) Immunostaining of PMA-stimulated THP1 with anti-EP4 antibody

[0121] The human monocytic THP1 cell line was plated on a 4-well culture slide (manufactured by Becton, Dickinson and Company) at a density of 1.5×10^5 cells per well with RPMI medium containing 100 nM PMA (Phorbol 12-myristate 13-acetate, manufactured by Sigma-Aldrich), and it was then cultured for 3 days, so that the cells were differentiated into macrophage-like cells. After the removal of the medium, the cells were washed with PBS three times, and were then immobilized with 200 μ L of 1% paraformaldehyde solution (wherein the cells were left at 4°C for 30 minutes). The cells were washed with PBS three times again. Thereafter, 300 μ L of 1% BSA (Bovine Serum Albumin, manufactured by Wako Pure Chemical Industries, Ltd.) that contained 1 mg/mL human gamma globulin (manufactured by Wako Pure Chemical Industries, Ltd.) was added to the resulting cells to block them (wherein the cells were left at rest at room temperature for 20 minutes). Subsequently, the resulting cells were washed with 0.1% Tween 20 (manufactured by MP Bio)-containing PBS (hereinafter referred to as a washing buffer for immunostaining) three times. Thereafter, 200 μ L of NBG016-mAb14, NBG016-mAb21 or a mouse isotype control antibody, which had been adjusted to 1 mg/mL, was added to the cells, and the obtained mixture was then incubated at 4°C for 1 hour. Thereafter, the resultant was washed with a washing buffer for immunostaining three times, and it was then stained with an FITC-labeled anti-mouse IgG antibody used as a secondary antibody (4°C, 1 hour). The slide was washed with a washing buffer for immunostaining three times, and was finally sealed with Propidium Iodide (PI)-containing VECTASHIELD Mounting Medium (manufactured by Vector Laboratories). The prepared slide was observed under a fluorescence microscope.

[0122] The fluorescence microscopic images of the immunostained THP1 cells are shown in Figure 9. The left view is a stained image of the mouse isotype control antibody, wherein only the cell nucleus (grey) stained with PI can be observed in the center. The right view is a stained image of the anti-EP4 antibody, wherein FITC fluorescence (white) is observed in a granular state surrounding the cell nucleus. From these results, it was found that the antibody of the present invention binds to native EP4 on the surface of the cell membrane of the macrophage-like cells that have been differentiated from the THP1 cell line by PMA.

(15) Inhibition of cytokine suppressive effect of PGE₂ by anti-EP4 antibody

[0123] PGE₂ has been known to suppress, via EP4 or EP2, the production of cytokine in microphage by LPS stimulation. Whether or not the antibody of the present invention would be able to recover the suppression of cytokine production by PGE₂ via EP4 was examined using PMA-differentiated THP1 that expressed an EP4 receptor. The THP1 cell line was plated on a 48-well cell culture plate at a density of 2.5×10^5 cells per well with 100 nM PMA-containing RPMI medium. After completion of the culture for 3 days, the medium was exchanged with an RPMI medium containing 3.0 μ g/mL NBG016-mAb14 NBG016-mAb21 or a mouse isotype control antibody, and the obtained mixture was then incubated for 30 minutes. Subsequently, PGE₂ was added to the resultant at a concentration of 20 nM, and the obtained mixture was further incubated for 30 minutes. Then, LPS was added to the resultant at a concentration of 100 ng/mL, and the obtained mixture was further cultured for 18 hours. Thereafter, a culture supernatant was recovered, and the amount of TNF α in the culture supernatant was measured using TNF α Human DuoSet Kit (manufactured by R & D Systems) in accordance with an instruction manual included therewith.

[0124] Meanwhile, 0.5 mL of AlamarBlue (manufactured by MorphoSys) diluted to 10 times its volume with RPMI medium was added to the cells after the recovery of the culture supernatant. The obtained mixture was incubated for 4 hours, and thereafter, fluorescence intensity was measured using Plate Reader ARVO 1420 HTS under conditions consisting of an excitation wavelength of 535 nm and a detection wavelength of 595 nm. Based on the measurement results with this AlamarBlue, the ratio of relative surviving cell counts among individual wells was obtained, and the amount of TNF α produced per surviving cell count ratio was calculated. The degree at which the antibody of the present invention would be able to recover the suppression of cytokine production by PGE₂ was calculated based on the following standard. Specifically, the amount of TNF α in a well to which only LPS stimulation was given was defined as a recovery percentage of 100%, and the amount of TNF α in a well to which LPS stimulation and PGE₂ were given was defined as a recovery percentage of 0%. Under such conditions, the recovery percentage in a case in which LPS stimulation, PGE₂ and the present antibody were given was obtained.

[0125] The test results are shown in Table 1. Even if the mouse isotype control antibody was added, no significant change was found in the suppression of TNF α production by PGE₂. However, it was found that when NBG016-mAb14 or NBG016-mAb21 was added, TNF α production suppressed by PGE₂ was recovered up to approximately 50%. The same results were obtained from two independent tests. From these results, it became clear that NBG016-mAb14 and NBG016-mAb21 are functional antibodies having antagonist activity on human endogenous EP4.

[Table 1]

Test 1				
LPS	PGE ₂	Antibody (3.0 μ g/mL)	TNF α level $\pm$ SD (pg/mL)	Recovery rate $\pm$ SD (%)
-	-	-	177.1	
+	-	-	550.0 $\pm$ 21.8	
+	+	-	286.1 $\pm$ 16.7	
+	+	NBG016-mAb14	423.4 $\pm$ 33.95	2.0 $\pm$ 12.9
+	+	NBG016-mAb	211 $\pm$ 48.1	69.3 $\pm$ 18.2
+	+	Isotype control	275.9 $\pm$ 11.1	-3.9 $\pm$ 4.2
Test2				
LPS	PGE ₂	Antibody (3.0 μ g/mL)	TNF α level $\pm$ SD (pg/mL)	Recovery rate $\pm$ SD (%)
	-	-	68.2 $\pm$ 8.5	
+	-	-	403.5 $\pm$ 37.1	
+	-	-	166.8 $\pm$ 15.7	
+	+	NBG016-mAb1	4281.5 $\pm$ 10.7	48.5 $\pm$ 4.5
+	+	NBG016-mAb21	286.1 $\pm$ 19.5	50.4 $\pm$ 8.3
+	+	Isotype control	148.9 $\pm$ 15.4	-7.6 $\pm$ 6.5

(16) Isolation and analysis of cDNA encoding variable region of anti-EP4 antibody

[0126] Total RNA was extracted from approximately 1×10^7 hybridoma cells producing anti-EP4 antibodies (NBG016-mAb14 and NBG016-mAb21) using Rneasy Mini Kit (manufactured by QIAGEN) in accordance with an instruction manual included with the kit. PCR was carried out according to a 5'-RACE (rapid amplification of cDNA ends) method using a 5'/3' RACE kit, 2nd Generation (manufactured by Roche Diagnostics), so as to amplify the variable region of a heavy chain or a light chain. Primers corresponding to mouse constant regions γ 1 and κ were used as 3' primers. That is, the 3' primers used for amplifying the heavy chain variable region were 5'-AGGGGCCAGTGGATAGACCGATG-3' (SEQ ID NO: 33) and 5'-GGCTGTTGTTTTGGCTGCAGAGAC-3' (SEQ ID NO: 34). On the other hand, the 3' primers used for amplifying the light chain variable region were 5'-ACTGGATGGTGGGAAGATGGATAC-3' (SEQ ID NO: 35) and 5'-TGGATACAGTTGGTGCAGCATCAG-3' (SEQ ID NO: 36). Subsequently, each of the obtained amplified fragments was electrophoresed on agarose gel, and a band was then excised. DNA was purified by melting the gel. The purified DNA was incorporated into T-Vector pMD20 (manufactured by Takara Bio Inc.). Thereafter, the nucleotide sequence was analyzed, and its amino acid sequence was then determined. The

sequence reaction was carried out using ABI Prism BigDye Terminator Cycle Sequencing Ready Reaction Kits Version 3.1 (Applied Biosystems), and the nucleotide sequence was determined using Applied Biosystems 3130x1 Genetic Analyzer (Applied Biosystems). As a result of the analysis of the nucleotide sequence, the nucleic acid sequence encoding the heavy chain variable region of NBG016-mAb14 was as shown in SEQ ID NO: 1, and the nucleic acid sequence encoding the light chain variable region thereof was as shown in SEQ ID NO: 3. Moreover, the amino acid sequence of the heavy chain variable region thereof was as shown in SEQ ID NO: 2, and the amino acid sequence of the light chain variable region thereof was as shown in SEQ ID NO: 4.

[0127] Furthermore, the nucleic acid sequence encoding the heavy chain variable region of NBG016-mAb21 was as shown in SEQ ID NO: 11, and the nucleic acid sequence encoding the light chain variable region thereof was as shown in SEQ ID NO: 13. Moreover, the amino acid sequence of the heavy chain variable region thereof was as shown in SEQ ID NO: 12, and the amino acid sequence of the light chain variable region thereof was as shown in SEQ ID NO: 14.

[0128] From the above-described results, the amino acid sequences of CDR regions defined by Kabat et al. ((1991) Sequences of Proteins of Immunological Interest, Fifth edition, U. S. Department of Health and Human Services, U.S. Government Printing Office) were clarified.

[0129] The heavy chain CDR1-3 sequences of NBG016-mAb14 were SEQ ID NOS: 5 to 7, respectively. The light chain CDR1-3 sequences thereof were SEQ ID NOS: 8 to 10, respectively. In addition, the heavy chain CDR1-3 sequences of NBG016-mAb21 were SEQ ID NOS: 15 to 17, respectively. The light chain CDR1-3 sequences thereof were SEQ ID NOS: 18 to 20, respectively. The heavy chain CDR sequences of both clones were completely identical to each other.

[0130] Regarding NBG016-mAb9 as well, according to the above-described method, the heavy chain variable region was amplified using the primers shown in SEQ ID NO: 33 and SEQ ID NO: 34, and the light chain variable region was amplified using the primers shown in SEQ ID NO: 35 and SEQ ID NO: 36. Then, the sequences of variable regions were determined. The nucleic acid sequence encoding the heavy chain variable region of NBG016-mAb9 was as shown in SEQ ID NO: 41, and the nucleic acid sequence encoding the light chain variable region thereof was as shown in SEQ ID NO: 42. In addition, the amino acid sequence of the heavy chain variable region was as shown in SEQ ID NO: 43, and the amino acid sequence of the light chain variable region thereof was as shown in SEQ ID NO: 44.

[0131] The heavy chain CDR1-3 sequences of NBG016-mAb9 were SEQ ID NOS: 45 to 47, respectively. The light chain CDR1-3 sequences thereof were SEQ ID NOS: 48 to 50, respectively.

(17) Cloning of anti-EP4 antibody gene

[0132] Using Oligo-dT Primer included with First Strand cDNA Synthesis Kit For RT-PCR (AMV) (manufactured by Roche Diagnostics), cDNA was synthesized in accordance with an instruction manual included therewith. Using the synthesized cDNA as a template, the full-length heavy chain and light chain genes of the anti-EP4 antibody of the present invention were amplified by PCR. The 5'-terminal sides of the heavy chain and light chain were designed using the nucleotide sequence determined by 5'-RACE as a reference, whereas the 3'-terminal sides thereof were designed using a constant region-specific sequence as a reference. The 5' primer used for amplifying the heavy chain gene was 5'-CACTGACCCTACGCGTATGGAATGGAGATGGATCTTTCTCTTC-3' (SEQ ID NO: 37), and the 3' primer therefor was 5'-ATAAGAATGCGGCCGCTCATTTACCAGGAGAGTGGGAGAG-3' (SEQ ID NO: 38). The 5' primers used for amplifying the light chain variable region were 5'-TTGCAGCCAGGAACGCGTATGGACATGAGGACCCCTGCT-3' (SEQ ID NO: 39) and 5'-ATAAGAATGCGGCCGCTTAACACTCATTCTGTTGAAGCT-3' (SEQ ID NO: 40). The obtained heavy chain and light chain amplification fragments were cleaved with the restriction enzymes MluI and NotI. Then, the heavy chain was inserted into pEHX1.1 (manufactured by Toyobo Co., Ltd.), and the light chain was inserted into the MluI-NotI site of pELX2.1 (manufactured by Toyobo Co., Ltd.). Thereafter, their nucleotide sequences were analyzed, and the amino acid sequences thereof were then determined.

[0133] As a result of the analysis of the nucleotide sequences, the nucleic acid sequence encoding the heavy chain of NBG016-mAb14 was as shown in SEQ ID NO: 22, and the nucleic acid sequence encoding the light chain thereof was as shown in SEQ ID NO: 24. Moreover, the amino acid sequence of the heavy chain thereof was as shown in SEQ ID NO: 23, and the amino acid sequence of the light chain thereof was as shown in SEQ ID NO: 25.

[0134] Furthermore, the nucleic acid sequence encoding the heavy chain of NBG016-mAb21 was as shown in SEQ ID NO: 26, and the nucleic acid sequence encoding the light chain thereof was as shown in SEQ ID NO: 28. Moreover, the amino acid sequence of the heavy chain thereof was as shown in SEQ ID NO: 27, and the amino acid sequence of the light chain thereof was

as shown in SEQ ID NO: 29.

[0135] The amino acid sequences of the heavy chain and light chain variable regions were identical to the amino acid sequences analyzed by the above-described 5'-RACE method.

[0136] Regarding NBG016-mAb9 as well, cDNA was synthesized according to the above-described method, and using the synthesized cDNA as a template, the full-length heavy chain and light chain genes of NBG016-mAb9 were amplified by PCR. The 5' primer used for amplifying the heavy chain gene was 5'-CACTAGAGCCCCCATACGCGTATGGCTGTCCTGGTGTTC-3' (SEQ ID NO: 51), and the 3' primer therefor was 5'-ATAAGAATGCGGCCGCTCATTTACCCGGAGAGTGGGAGAG-3' (SEQ ID NO: 52). The 5' primers used for amplifying the light chain gene were 5'-TCCTCAGGTTGCCTCACGCGTATGAAGTTCCTGTTAG-3' (SEQ ID NO: 53) and 5'-ATAAGAATGCGGCCGCTTAACACTCATTCCTGTTGAAGCT-3' (SEQ ID NO: 40). The obtained heavy chain and light chain amplification fragments were cleaved with the restriction enzymes MluI and NotI. Then, the heavy chain was inserted into pEHX1.1 (manufactured by Toyobo Co., Ltd.), and the light chain was inserted into the MluI-NotI site of pELX2.1 (manufactured by Toyobo Co., Ltd.). Thereafter, their nucleotide sequences were analyzed, and the amino acid sequences thereof were then determined.

[0137] The nucleic acid sequence encoding the heavy chain of NBG016-mAb9 was as shown in SEQ ID NO: 54, and the nucleic acid sequence encoding the light chain thereof was as shown in SEQ ID NO: 55. In addition, the amino acid sequence of the heavy chain thereof was as shown in SEQ ID NO: 56, and the amino acid sequence of the light chain thereof was as shown in SEQ ID NO: 57.

(18) Confirmation of whether the obtained antibody gene sequences would encode anti-EP4 antibody

[0138] Recombinant antibodies of NBG016-mAb14 and NBG016-mAb21 were produced using Mammalian PowerExpress System (manufactured by Toyobo Co., Ltd.). That is, pELX2.1 into which the light chain gene had been inserted was cleaved with the restriction enzymes EcoRI and BglII, and was then electrophoresed on agarose gel to purify a fragment comprising the light chain gene. The purified light chain gene fragment was inserted into the EcoRI-BglII site of pEHX1.1 into which the heavy chain gene had been inserted, so as to produce a plasmid having the genes of both the light chain and the heavy chain. This plasmid was introduced into 293FT cells using Lipofectamin 2000, so that the cells transiently expressed the antibody.

[0139] Seventy-two hours after completion of the transduction, a cell culture supernatant was collected, and it was then subjected to a binding test with the CHO cell line stably expressing human EP4 with flow cytometry according to the method described in (6) above. As a control, a culture supernatant of antibody gene-non-introduced 293FT cells was used. As a result, the recombinant antibodies NBG016-mAb14 and NBG016-mAb21 secreted into such a culture supernatant maintained an ability to bind to human EP4. From these results, it could be confirmed that the antibody gene sequences obtained in (17) above encode the anti-EP4 antibody.

[0140] A recombinant antibody of NBG016-mAb9 was also produced by the above-described method. That is, pELX2.1 into which the light chain gene had been inserted was cleaved with the restriction enzymes Sall and SpeI, and was then electrophoresed on agarose gel to purify a fragment comprising the light chain gene. The purified light chain gene fragment was inserted into the Sall-SpeI site of pEHX1.1 into which the heavy chain gene had been inserted, so as to produce a plasmid having the genes of both the light chain and the heavy chain. This plasmid was introduced into 293FT cells, so that the cells transiently expressed the antibody.

[0141] Seventy-two hours after completion of the transduction, a cell culture supernatant was collected, and it was then subjected to a binding test with the CHO cell line stably expressing human EP4 with flow cytometry according to the method described in (6) above. As a control, a culture supernatant of antibody gene-non-introduced 293FT cells was used. The results are shown in Figure 10. In Figure 10, the parent Flp-In-CHO cell line is indicated with the histogram filled with grey color, whereas the CHO cell line stably expressing human EP4 is indicated with the black solid line. Since the recombinant antibody NBG016-mAb9 secreted into the culture supernatant maintained an ability to bind to human EP4, it could be confirmed that the antibody gene sequences of NBG016-mAb9 obtained in (17) above encode the anti-EP4 antibody.

(19) Production of recombinant anti-EP4 antibody stably expressing CHO cells

[0142] A vector comprising the light chain and heavy chain genes of each of NBG016-mAb14 and NBG016-mAb21 produced in

(18) above was cleaved with the restriction enzyme SspI, and was then purified by ethanol precipitation. Using Lipofectamin 2000, the resultant was transduced into CHO-K1 cells (Cell Bank, RIKEN BioResource Center), and the obtained cells were then cultured in Ham's F12 medium containing 10% fetal bovine serum for 24 hours. Twenty-four hours later, the aforementioned medium was exchanged with another Ham's F12 medium containing 10% fetal bovine serum and 10 µg/mL puromycin, and then, the cells were cultured for 12 days, while exchanging the medium with a fresh one every 3 days. Twelve days later, a colony was separated by a penicillin cup method.

[0143] The separated CHO-K1 cells were plated on a 24-well plate, and were then cultured in Ham's F12 medium containing 10 µg/mL puromycin for 3 days. Three days later, the medium was exchanged with another Ham's F12 medium containing 10 µg/mL puromycin (to which fetal bovine serum had not been added), and the culture was further carried out for 72 hours. Thereafter, a culture supernatant was recovered.

[0144] Mouse IgG in the culture supernatant was detected by ELISA. A series of culture supernatant dilutions were prepared using PBS, were then dispensed into Maxisorp 96-well plate (manufactured by Nunc), and were then left at 4°C overnight. On the following day, 3% BSA (manufactured by Sigma)-containing PBS was added to the culture, and the obtained mixture was then left at room temperature for 1 hour for blocking. The resultant was washed with 0.1% Tween 20-containing PBS, and a horse radish peroxidase (HRP)-labeled anti-mouse IgG antibody (manufactured by Millipore) diluted to 4,000 times with 1% BSA-containing PBS was then added to the resultant. The obtained mixture was left at room temperature for 1 hour. Thereafter, the reaction product was washed with 0.1% Tween 20-containing PBS, and 100 µL of coloring reagent (Sureblue TMB microwell peroxidase substrate, manufactured by Kirkegaard & Perry Laboratories) was then added thereto. The obtained mixture was left at room temperature for 5 minutes, and 100 µL of 1 N sulfuric acid was added to the mixture to terminate the reaction. Then, the absorbance at 450 nm was measured. As a result, the expression of IgG was confirmed in a culture supernatant of CHO-K1 cells established by introduction of a vector comprising the light chain and heavy chain genes.

(20) Binding test of recombinant anti-EP4 antibodies and CHO cell line stably expressing human EP4

[0145] The recombinant antibody NBG016-mAb14 and the recombinant antibody NBG016-mAb21 were purified from a culture supernatant of the cell line established in (19) above in the same manner as in (7) above. A binding test of each of the obtained purified recombinant anti-EP4 antibodies and the CHO cell line stably expressing human EP4 was carried out with a flow cytometer by the method described in (6) above. The purified recombinant anti-EP4 antibody or mouse isotype control antibody was used in an amount of 1 µg per 5×10^5 cells. As a secondary antibody, a PE-labeled anti-mouse IgG antibody was used.

[0146] The results are shown in Figure 11. The parent Flp-In-CHO cell line is indicated with the histogram filled with grey color, whereas the CHO cell line stably expressing EP4 is indicated with the black solid line. Both the recombinant antibody NBG016-mAb14 and the recombinant antibody NBG016-mAb21 bound only to the CHO cell line stably expressing human EP4 stably expressing. As a result, it was confirmed that the purified recombinant anti-EP4 antibodies maintained an ability to bind to human EP4.

(21) Expression vector for mouse IgG1 antibody NBG016-mAb21

[0147] The subclass of the NBG016-mAb21 purified in (7) above was IgG2a. Thus, the subclass of the NBG016-mAb21 was modified to be IgG1 so as to produce the mouse IgG1 antibody NBG016-mAb21. The mouse IgG1 antibody NBG016-mAb21 gene was produced as follows by Overlapping PCR. Using the heavy chain gene of NBG016-mAb21 as a template, and also using 5'-CACTGACCCTACGCGTATGGAATGGAGATGGATCTTTCTCTTC-3' (SEQ ID NO: 37) and 5'-GACAGATGGGGGTGTCGTTTATAGCGCTAGAGACAGTGACCAGAGTC CC-3' (SEQ ID NO: 58), the variable region gene of NBG016-mAb21 was amplified by PCR. At the same time, using cDNA synthesized from the total RNA of a hybridoma producing mouse IgG1 as a template, and also using 5'-GGGACTCTGGTCACTGTCTCTAGCGCTAAAACGACACCCCATCTGT C-3' (SEQ ID NO: 59) and 5'-ATAAGAATGCGGCCGCTCATTACCAGGAGAGTGGGAGAG-3' (SEQ ID NO: 38), a mouse IgG1 portion ranging from CH1 to the constant region gene was amplified by PCR. The thus amplified heavy chain variable region gene was mixed with the amplified CH1-constant region gene fragment, and the obtained mixture was then amplified by PCR using the primers of SEQ ID NO: 37 and SEQ ID NO: 38. The thus amplified DNA fragment was cleaved with the restriction enzymes MluI and NotI, and the cleaved fragment was then inserted into the MluI-NotI site of the expression vector pEHX1.1. The obtained expression vector was cleaved with the restriction enzymes EcoRI and BglII, and a light chain gene fragment (EcoRI-BglII fragment) of NBG016-mAb21 was then inserted therein, so as to produce an expression vector for the mouse IgG1 antibody NBG016-mAb2.

(22) Method for producing cell line stably expressing mouse IgG1 antibody NBG016-mAb21

[0148] Floating CHO-K1 cells (manufactured by Toyobo Co., Ltd.) (2.5×10^5 cells/ml) cultured in 8 mM glutamine-containing EX-CELL CD CHO medium (manufactured by SAFC Bioscience) were dispensed in an amount of 1 ml into each of two wells of a 24-well plate. Thereafter, 136 μ l of Opti-MEM, 15 μ l of Lipofectamin 2000, and 4 μ g of expression vector for mouse IgG1 antibody NBG016-mAb21 cleaved with the restriction enzyme SspI were blended, and the obtained mixture was left at room temperature for 20 minutes. Subsequently, the reaction product was added in an amount of 68 μ l each to the wells containing CHO-K1, and the obtained mixture was then incubated in a CO₂ incubator for 24 hours. Twenty-hour hours later, the cells were suspended in 8 ml of EX-CELL CD CHO medium containing 8 mM glutamine, and the obtained suspension was dispensed in an amount of 4 ml into each of two wells of a 6-well plate. Then, 3 μ l of 10 mg/ml puromycin was added to one well, and 4 μ l of 10 mg/ml puromycin was added to the other well. While exchanging the medium with a fresh one every 3 or 4 days, the cells were cultured for 18 days. Thereafter, proliferating cells were recovered from the well, and the recovered cells were then suspended in Conditioned medium (a medium containing per ml: 700 ml of EX-CELL CD CHO medium, 300 ml of culture supernatant of floating CHO-K1 cells, and 1 ml or 0.75 ml of 10mg/ml puromycin). The obtained suspension was dispensed in an amount of 200 μ l into each well of a 96-well plate. One week later, 100 μ l of Conditioned medium was added, and the obtained mixture was further culture for 1 week. Thereafter, the cells were subcultured several times, and 500 μ l of drug-resistant cells (4×10^4 cells/ml) were then added to a 24-well plate, followed by culture for 5 days. Five days later, the amount of the antibody in the culture supernatant was quantified using Mouse IgG EIA Kit (manufactured by Takara Bio Inc.), and antibody-producing cells were then screened. The thus obtained cells were defined as a CHO cell line stably expressing mouse IgG1 antibody NBG016-mAb21.

(23) Purification of mouse IgG1 antibody NBG016-mAb21

[0149] The CHO cell line stably expressing mouse IgG1 antibody NBG016-mAb21 was cultured in EX-CELL CD CHO medium containing 8 mM glutamine and 7.5 μ g/ml puromycin for 10 days, so as to allow it to produce antibody. From 200 mL of this culture supernatant, purified IgG was obtained in the same manner as described in (7) above. Hereinafter, the obtained purified IgG was referred to as mouse IgG1 antibody NBG016-mAb21.

(24) Binding test of mouse IgG1 antibody NBG016-mAb21 and human EP4

[0150] A binding test of the mouse IgG1 antibody NBG016-mAb21 to the CHO cell line stably expressing human EP4 was carried out in the same manner as described in (9) above. The results are shown in Figure 12(A). The parent Flp-In-CHO cell line is indicated with the histogram filled with grey color, whereas the CHO cell line stably expressing human EP4 is indicated with the black solid line. The mouse IgG1 antibody NBG016-mAb21 bound only to the human EP4 stably expressing CHO cell line stably expressing human EP4. As a result, it was confirmed that the produced mouse IgG1 antibody NBG016-mAb21 maintained an ability to bind to human EP4.

(25) Inhibitory test regarding PGE₂-induced cAMP production by mouse IgG1 antibody NBG016-mAb21

[0151] Whether or not PGE₂-induced cAMP production would be inhibited by the mouse IgG1 antibody NBG016-mAb21 was examined in the same manner as described in (10) above. The cells were allowed to react with the antibody at room temperature for 15 minutes, and PGE₂ was then added to the reaction mixture at a concentration of 1.5×10^{-10} M. The thus obtained mixture was further left at room temperature for 30 minutes. Using LANCE Ultra cAMP Kit (manufactured by PerkinElmer), and a reaction was carried out in accordance with an instruction manual included with the kit, so as to measure the level of cAMP.

[0152] The results are shown in Figure 12(B). When a mouse isotype control antibody was added, it did not provide a significant inhibitory effect on PGE₂-induced cAMP production level. In contrast, when the mouse IgG1 antibody NBG016-mAb21 was added, a cAMP production inhibitory effect was observed in an antibody concentration-dependent manner. The IC₅₀ value was found to be 1.1 μ g/mL (approximately 6.9 nM). From these results, it was demonstrated that even if NBG016-mAb21 is modified to a mouse IgG1 antibody, it could maintain antagonist activity on EP4.

(26) Production of human chimeric antibodies NBG016-mAb14 and NBG016-mAb21

[0153] Using Mammalian PowerExpress System (manufactured by Toyobo Co., Ltd.), human chimeric antibodies in which the CH1 region and constant region of NBG016-mAb14 or NBG016-mAb21 were substituted with those of a human antibody gene. The heavy chain variable region gene of each of NBG016-mAb14 and NBG016-mAb21 was amplified by PCR using 5'-CACTGACCCTAAGCTTATGGAATGGAGATGGATCTTTCTCTTC-3' (SEQ ID NO: 60) and 5'-GGCTGTTGTGCTAGCTGCAGAGACAGTGACCAGAGT-3' (SEQ ID NO: 61). The obtained heavy chain gene fragment was cleaved with the restriction enzymes HindIII and NheI, and the cleaved fragment was then inserted into the HindIII-NheI site of the expression vector pEHyX1.1. At the same time, the light chain variable region gene of each of NBG016-mAb14 and NBG016-mAb21 was amplified by PCR using 5'-ATTGCAGCCAGGAGAATTCATGGACATGAGGACCCCTGCT-3' (SEQ ID NO: 62) and 5'-GGTGCAGCATCCGTACGTTTTATTCCAACCTTTGTCCCC-3' (SEQ ID NO: 63). The obtained light chain gene fragment was cleaved with the restriction enzymes BsiWI and EcoRI, and the cleaved fragment was then inserted into the BsiWI-EcoRI site of the expression vector pELkX2.1.

[0154] The light chain gene-inserted pELk2.1 was cleaved with the restriction enzymes BglII, NotI and Scal, and the cleaved fragment was then electrophoresed on agarose gel, so as to purify a fragment containing the light chain gene. The purified light chain gene fragment was incorporated into the BglII-NotI site of pEHyX1.1, into which the heavy chain gene had been inserted, thereby producing a plasmid that maintained the genes of both the light chain and the heavy chain. Using Lipofectamin 2000, this plasmid was introduced into 293FT cells, so that the cells transiently expressed the antibody.

[0155] Seventy-two hours after completion of the introduction, a cell culture supernatant was collected, and it was then subjected to a binding test with the CHO cell line stably expressing human EP4 with flow cytometry according to the method described in (6) above. As a control, a culture supernatant of antibody gene-non-introduced 293FT cells was used. As a secondary antibody, a PE-labeled anti-human IgG antibody (manufactured by Abcam) was used. The results are shown in Figure 13. In Figure 13, the parent Flp-In-CHO cell line is indicated with the histogram filled with grey color, whereas the CHO cell line stably expressing human EP4 is indicated with the black solid line. From the results shown in the figure, it could be confirmed that the human chimeric antibodies NBG016-mAb14 and NBG016-mAb21 secreted into the culture supernatant each maintained an ability to bind to human EP4.

[0156] These results demonstrated that the nucleic acid sequence encoding the antibody provided by the present invention can be used to produce a recombinant antibody (e.g. a chimeric antibody, a humanized antibody, a human antibody, etc.) that maintains the function of the antibody of the present invention.

Industrial Applicability

[0157] Since the antibody provided by the present invention specifically suppresses the function of a human PGE₂ receptor subtype EP4, the present antibody is anticipated to play an important role in providing a method for preventing or treating EP4-related diseases or in the development of a preventive or therapeutic agent for the aforementioned diseases.

SEQUENCE LISTING

[0158]

<110> E. I. DU PONT DE NEMOURS AND COMPANY Pioneer Hi-Bred International, Inc. Allen, Stephen M Brugiere, Norbert Kumria, Ratna Luck, Stanley Mohanty, Amitabh Mullen, Jeffrey Raja, Rupa Sakai, Hajime Tingey, Scott V Williams, Robert W

<120> DROUGHT TOLERANT PLANTS AND RELATED CONSTRUCTS AND METHODS INVOLVING GENES ENCODING MATE-EFFLUX POLYPEPTIDES

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<210> 17

<211> 1457

<212> DNA

<213> Arabidopsis thaliana

<400> 17

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cgccatgggc caccgtgaca gtgtctcaat atctattgcc cgtgatctcg gtcattggtcg    180
ccggccactg cgggtgaactc cagctgtctg gtgtcactct tgccactgct ttcgcaaacg    240
tctccggctt cggcatcatg tatggtttag tgggtgcact tgaaactcta tgtggccaag    300
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<210> 18

<211> 483

<212> PRT

<213> Arabidopsis thaliana

<400> 18

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20      25      30
Asn Val Ser Ser Met Ala Ala Pro Met Ala Thr Val Thr Val Ser Gln
35      40      45
Tyr Leu Leu Pro Val Ile Ser Val Met Val Ala Gly His Cys Gly Glu
50      55      60
Leu Gln Leu Ser Gly Val Thr Leu Ala Thr Ala Phe Ala Asn Val Ser
65      70      75      80
Gly Phe Gly Ile Met Tyr Gly Leu Val Gly Ala Leu Glu Thr Leu Cys
85      90      95
Gly Gln Ala Tyr Gly Ala Lys Gln Tyr Thr Lys Ile Gly Thr Tyr Thr
100     105     110
Phe Ser Ala Ile Val Ser Asn Val Pro Ile Val Val Leu Ile Ser Ile

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115      120      125
Leu Trp Phe Tyr Met Asp Lys Leu Phe Val Ser Leu Gly Gln Asp Pro
130      135      140
Asp Ile Ser Lys Val Ala Gly Ser Tyr Ala Val Cys Leu Ile Pro Ala
145      150      155      160
Leu Leu Ala Gln Ala Val Gln Gln Pro Leu Thr Arg Phe Leu Gln Thr
165      170      175
Gln Gly Leu Val Leu Pro Leu Leu Tyr Cys Ala Ile Thr Thr Leu Leu
180      185      190
Phe His Ile Pro Val Cys Leu Ile Leu Val Tyr Ala Phe Gly Leu Gly
195      200      205
Ser Asn Gly Ala Ala Leu Ala Ile Gly Leu Ser Tyr Trp Phe Asn Val
210      215      220
Leu Ile Leu Ala Leu Tyr Val Arg Phe Ser Ser Ala Cys Glu Lys Thr
225      230      235      240
Arg Gly Phe Val Ser Asp Asp Phe Val Leu Ser Val Lys Gln Phe Phe
245      250      255
Gln Tyr Gly Ile Pro Ser Ala Ala Met Thr Thr Ile Glu Trp Ser Leu
260      265      270
Phe Glu Leu Leu Ile Leu Ser Ser Gly Leu Leu Pro Asn Pro Lys Leu
275      280      285
Glu Thr Ser Val Leu Ser Ile Cys Leu Thr Thr Ser Ser Leu His Cys
290      295      300
Val Ile Pro Met Gly Ile Gly Ala Ala Gly Ser Thr Arg Ile Ser Asn
305      310      315      320
Glu Leu Gly Ala Gly Asn Pro Glu Val Ala Arg Leu Ala Val Phe Ala
325      330      335
Gly Ile Phe Leu Trp Phe Leu Glu Ala Thr Ile Cys Ser Thr Leu Leu
340      345      350
Phe Thr Cys Lys Asn Ile Phe Gly Tyr Ala Phe Ser Asn Ser Lys Glu
355      360      365
Val Val Asp Tyr Val Thr Glu Leu Ser Ser Leu Leu Cys Leu Ser Phe
370      375      380
Met Val Asp Gly Phe Ser Ser Val Leu Asp Gly Val Ala Arg Gly Ser
385      390      395      400
Gly Trp Gln Asn Ile Gly Ala Trp Ala Asn Val Val Ala Tyr Tyr Leu
405      410      415
Leu Gly Ala Pro Val Gly Phe Phe Leu Gly Phe Trp Gly His Met Asn
420      425      430
Gly Lys Gly Leu Trp Ile Gly Val Ile Val Gly Ser Thr Ala Gln Gly
435      440      445
Ile Ile Leu Ala Ile Val Thr Ala Cys Leu Ser Trp Glu Glu Gln Val
450      455      460
Asn Ser Asn Leu Lys Tyr Ile Phe Gly His Leu Met Asn Leu Phe Phe
465      470      475      480
Thr Pro Tyr

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<210> 19

<211> 1896

<212> DNA

<213> zea mays

<400> 19

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aggggtggccg agccccagat ggccgcgcgc agggaggagg acgaggcgcc acggcccgctg      180
cttctgtctgc cgcggacggc gcaggaggac cagaagtggg ggaggcggtg ggcgcgcgag      240
gcgggggtggg tggggtacct ggccctgcc atgggtggtg tgaacctgtc gcagtaacgc      300
gtccagggtgt cgtccaacat gatggtgggg caccctcccc gcgtgctccc gctctcctcc      360
gcggccatcg ccacctccct cgccaacgtc tccgggttca gcctcctgat cggaatggca      420
agtgcactgg agacgctatg cggccaggcc tacggtgcga agcagtacca taagctaggg      480
ctagacacct acagagcggt cgtcaccctc ctggtggtct gcgtccctc ctcgtcctc      540
tgggtgttca tggacaagat cctggtcctc ataggccagg accctctcat ctcgcaaggc      600
gccgggaggt acatggtctg gctgatcccg gggctcttcg ccaacgcggt gatccagccg      660

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ctcaccaagt tccctgcagc gcagagcctc atctaccgcg tgctgctgtc gtcggcgggc      720
acggcgggcg tccacgtccc cctgtgttac gtgatggtgt tcaagaccgg gctcgggtac      780
acggcgcccg ccttgacctt aagcatatcg tactggctga acgtggccat gctcgtcgga      840
tacatcgccct tctccagctc ttgcaaggag acgcgcgcgc gcccgacggt cgagggtctc      900
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tggtggtcgt ttgagctcct tactctcatg tcagggtctc taaccaaccc agagctgcag      1020
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<210> 20

<211> 487

<212> PRT

<213> zea mays

<400> 20

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

      290      295      300
Val Thr Leu Leu Phe Thr Ile Pro Phe Gly Leu Gly Ala Ala Gly Ser
305      310      315      320
Thr Arg Val Ala Asn Glu Leu Gly Ala Gly Asn Pro Asp Gly Ala Arg
325      330      335
Ser Ala Val Arg Val Val Leu Ser Met Ala Gly Ile Asp Ala Val Val
340      345      350
Val Ser Gly Ser Leu Leu Ala Ala Arg Arg Leu Val Gly Ile Ala Tyr
355      360      365
Ser Ser Glu Glu Glu Val Ile Ser Ala Val Ala Ala Met Val Pro Leu
370      375      380
Val Cys Ile Thr Ala Ile Thr Asp Cys Leu Gln Gly Ile Leu Ser Gly
385      390      395      400
Val Ala Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr Val Asn Leu
405      410      415
Gly Ser Phe Tyr Leu Leu Gly Ile Pro Met Ala Ile Leu Leu Gly Phe
420      425      430
Val Leu Arg Met Gly Ser Arg Gly Leu Trp Met Gly Ile Val Cys Gly
435      440      445
Ser Leu Ser Gln Thr Thr Leu Met Ser Ala Ile Thr Phe Phe Thr Asp
450      455      460
Trp Asn Lys Met Ala Glu Lys Ala Arg Glu Arg Val Phe Ser Asp Lys
465      470      475      480
Gln Pro Gln Glu Pro Gly Pro
485

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<210> 21

<211> 2002

<212> DNA

<213> zea mays

<400> 21

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tgctcgtcgc tcacccgagc cgggggaagg aggacctggg agatcagcgc cgcctccgct 180
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aaaaaaaaaa aaaaaaaaaa aa

2002

<210> 22

<211> 496

<212> PRT

<213> Zea mays

<400> 22

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20      25      30
Val Ser Ser Glu Gly Arg Trp Ala Glu Ala Thr Ala Glu Ala Gly Arg
35      40      45
Leu Ala Ala Leu Ala Ala Pro Met Ile Ala Val Ala Leu Leu Gln Leu
50      55      60
Met Met Gln Val Ile Ser Thr Ile Met Val Gly His Leu Gly Glu Val
65      70      75      80
Pro Leu Ala Gly Ala Ala Ile Ala Gly Ser Leu Thr Asn Val Ser Gly
85      90      95
Phe Ser Val Leu Met Gly Leu Ala Cys Gly Leu Glu Thr Ile Cys Gly
100     105     110
Gln Ala Phe Gly Ala Glu Gln Tyr His Lys Val Ala Leu Tyr Thr Tyr
115     120     125
Arg Ser Ile Val Val Leu Leu Ile Ala Ser Val Pro Met Ala Ile Leu
130     135     140
Trp Val Phe Leu Pro Asp Val Leu Pro Leu Ile Gly Gln Asp Pro Gln
145     150     155     160
Ile Ala Ile Glu Ala Gly Arg Tyr Ala Leu Trp Leu Ile Pro Gly Leu
165     170     175
Phe Ala Phe Ser Val Ala Gln Cys Leu Ser Lys Phe Leu Gln Ser Gln
180     185     190
Ser Leu Ile Phe Pro Leu Val Leu Ser Ser Leu Thr Thr Leu Ala Val
195     200     205
Phe Ile Pro Leu Cys Trp Phe Met Val Tyr Lys Val Gly Met Gly Asn
210     215     220
Ala Gly Ala Ala Phe Ala Val Ser Ile Cys Asp Trp Val Glu Val Thr
225     230     235     240
Val Leu Gly Leu Tyr Ile Lys Phe Ser Pro Ser Cys Glu Lys Thr Arg
245     250     255
Ala Pro Phe Thr Trp Glu Ala Phe Gln Gly Ile Gly Ser Phe Met Arg
260     265     270
Leu Ala Val Pro Ser Ala Leu Met Val Cys Leu Glu Trp Trp Ser Tyr
275     280     285
Glu Leu Leu Val Leu Leu Ser Gly Met Leu Pro Asn Ala Ala Leu Glu
290     295     300
Thr Ser Val Leu Ser Ile Cys Ile Ser Thr Val Ile Leu Val Tyr Asn
305     310     315     320
Leu Pro Tyr Gly Ile Gly Thr Ala Ala Ser Val Arg Val Ser Asn Glu
325     330     335
Leu Gly Ala Gly Asn Pro Asp Ser Ala Arg Leu Val Val Val Val Ala
340     345     350
Leu Ser Ile Ile Ile Phe Thr Ala Val Leu Val Ser Val Thr Leu Leu
355     360     365
Ser Leu Arg His Phe Ile Gly Ile Ala Phe Ser Asn Glu Glu Glu Val
370     375     380
Val Asn Tyr Val Thr Arg Met Val Pro Leu Leu Ser Ile Ser Val Ile
385     390     395     400
Thr Asp Asn Leu Gln Gly Val Leu Ser Gly Ile Ser Arg Gly Cys Gly
405     410     415
Trp Gln His Leu Gly Ala Tyr Val Asn Leu Gly Ala Phe Tyr Leu Val
420     425     430
Gly Ile Pro Val Ala Leu Val Ala Gly Phe Ala Leu His Leu Gly Gly
435     440     445
Ala Gly Phe Trp Ile Gly Met Ile Ala Gly Gly Ala Thr Gln Val Thr
450     455     460
Leu Leu Thr Ile Ile Thr Ala Met Thr Asn Trp Arg Lys Met Ala Asp
465     470     475     480
Lys Ala Arg Asp Arg Val Tyr Glu Gly Ser Leu Pro Ile Gln Ala Asn
485     490     495

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<210> 23

<211> 1914

<212> DNA

<213> zea may

<400> 23

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ttgtgcagca actgggagaa agaagctttg aaggcaaagg acagagtatt tagtacatcc    1500
gtaccagctg acatgatgac atgatatttc tgaagatatt ttttgaagga aatgcccatg    1560
aaactttgcc aaggaacata ctaagaattg gttgttcaga ttcaaggcct ttctccatgc    1620
catcagaatg atgcttgggt ctagttaatg ctctgagca gtctgtttt tacttttggg    1680
caatactcaa tacatggaag atgtttggtt tgaagaacca cgccatccta gatgaggtg    1740
tatattataa gttgatataa cggctccata ctagtattg aggaatgaga cgatgattat    1800
ctcatgtaat aataatgctt tccccctct agttattgat gtaagacaat tgaggcaa    1860
gaacaaaatg tcacatttga ttaaataaaa aaaaaaaaaa aaaaaaaaaa aaaa    1914

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<210> 24

<211> 475

<212> PRT

<213> zea mays

<400> 24

```

Met Asp Glu Pro Leu Leu Gly Asn Gly Leu Lys Thr Ser Gly Lys Arg
1      5      10      15
Glu Ser Leu Val Val Ala Glu Val Arg Lys Gln Met Tyr Leu Ala Gly
20     25     30
Pro Leu Ile Ala Ala Trp Ile Leu Gln Asn Ile Val Gln Met Ile Ser
35     40     45
Ile Met Phe Val Gly His Leu Gly Glu Leu Ala Leu Ser Ser Ala Ser
50     55     60
Ile Ala Thr Ser Phe Ala Gly Val Thr Gly Phe Ser Leu Leu Ser Gly
65     70     75     80
Met Ala Ser Ser Leu Asp Thr Leu Cys Gly Gln Ser Phe Gly Ala Lys
85     90     95
Gln Tyr Tyr Leu Leu Gly Ile Tyr Lys Gln Arg Ala Ile Leu Val Leu
100    105    110

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Thr Leu Val Ser Leu Val Val Ala Ile Ile Trp Ser Tyr Thr Gly Gln
 115 120 125
 Ile Leu Leu Leu Phe Gly Gln Asp Pro Glu Ile Ala Ala Gly Ala Gly
 130 135 140
 Ser Tyr Ile Arg Trp Met Ile Pro Ala Leu Phe Val Tyr Gly Pro Leu
 145 150 155 160
 Gln Cys His Val Arg Phe Leu Gln Thr Gln Asn Ile Val Leu Pro Val
 165 170 175
 Met Leu Ser Ser Gly Ala Thr Ala Leu Asn His Leu Leu Val Cys Trp
 180 185 190
 Leu Leu Val Tyr Lys Ile Gly Met Gly Asn Lys Gly Ala Ala Leu Ala
 195 200 205
 Asn Ala Ile Ser Tyr Phe Thr Asn Val Ser Ile Leu Ala Ile Tyr Val
 210 215 220
 Arg Leu Ala Pro Ala Cys Arg Asn Thr Trp Arg Gly Phe Ser Lys Glu
 225 230 235 240
 Ala Phe His Asp Ile Thr Ser Phe Leu Arg Leu Gly Ile Pro Ser Ala
 245 250 255
 Leu Met Val Cys Leu Glu Trp Trp Ser Phe Glu Leu Leu Val Leu Leu
 260 265 270
 Ser Gly Leu Leu Pro Asn Pro Lys Leu Glu Thr Ser Val Leu Ser Ile
 275 280 285
 Ser Leu Asn Thr Gly Ser Leu Ala Phe Met Ile Pro Phe Gly Leu Ser
 290 295 300
 Ala Ala Ile Ser Thr Arg Val Ser Asn Glu Leu Gly Ala Gly Arg Pro
 305 310 315 320
 His Ala Ala His Leu Ala Thr Arg Val Val Met Val Leu Ala Ile Val
 325 330 335
 Val Gly Val Leu Ile Gly Leu Ala Met Ile Leu Val Arg Asn Ile Trp
 340 345 350
 Gly Tyr Ala Tyr Ser Asn Glu Lys Glu Val Val Lys Tyr Ile Ser Lys
 355 360 365
 Met Met Pro Ile Leu Ala Val Ser Phe Leu Phe Asp Cys Val Gln Cys
 370 375 380
 Val Leu Ser Gly Val Ala Arg Gly Cys Gly Trp Gln Lys Ile Gly Ala
 385 390 395 400
 Cys Val Asn Leu Gly Ala Tyr Tyr Leu Ile Gly Ile Pro Ala Ala Phe
 405 410 415
 Cys Phe Ala Phe Met Tyr His Leu Gly Gly Met Gly Leu Trp Leu Gly
 420 425 430
 Ile Ile Cys Ala Leu Val Ile Gln Met Leu Leu Leu Leu Thr Ile Thr
 435 440 445
 Leu Cys Ser Asn Trp Glu Lys Glu Ala Leu Lys Ala Lys Asp Arg Val
 450 455 460
 Phe Ser Thr Ser Val Pro Ala Asp Met Met Thr
 465 470 475

<210> 25

<211> 1778

<212> DNA

<213> zea mays

<400> 25

gacgggttcg ttcagtgtct ggccggcgcat agatagatag ccatggcgaa gaagccagtg 60
 gaggaagcgc tcctcgcagc ggcagacgag caggagagcc tgagcgtgcy cgaggagctg 120
 aagaagcagc tatggctggc tgggcccacg atcgccggcg cgcctcctgca gaacgtgatc 180
 cagatgatct ccgtcatgta cgtgggacac ctgggagagc tgcccctcgc tggcgcatcc 240
 atggccaact ccttcgccac cgtcaccggc ctacgctgc tgctaggcat ggcaagcgct 300
 ctagacacac tgtcgggcca agcgttcggc ggcaggcagt actatctcct gggcatctac 360
 aagcagcgcg ccatgttccct cctgaccctg gtgagcgtcc ctctgtcagt ggtgtggttc 420
 tacaccggcg agatcctcct cctgttcggc caggaccggg acatcgccgc agaggccggc 480
 acctacgccc ggtggatgat ccgctgctg ttcgcgtacg gcctgctgca gtgccacgtc 540
 cggttctccc agacgcagaa catcgtggtg cccgtgatgg cgagcgccgg cgccgcccgg 600
 gcctgccacg tctcgtctg ctggggcgctg gtgtacgcgc tcgggatggg cagcaagggc 660
 cggcgctca gcaactccat ctccactagg gtcaacgtgg ccgtgctggc cgtgtacgtg 720

aggggtgtcca ggcgctgcaa ggagacgtgg acgggcttct ccacggaggc cttccgcgac 780
 gcgctcggct tcttcaggct tgccgtcccg tccgctctca tggctctgct ggagatgtgg 840
 tcggtttgaa tcattgtgct ccttcggggc cttcttccca acccaaaact ggagacctcc 900
 gtgctgtgca tcagccttaa cactgtcgcg ttcgtgtgga tgatccctt tgggcttagc 960
 tcagctatca gcaactcgct gtccaatgag ctgggtgccg ggcgtcctcg agccgcccgc 1020
 cttgcggtgc gtgtcgttgt gttgctgtct gtcccgaaag ggctaggcgt gggcctcatc 1080
 ctggtgtgcy tgcgctacgt ctggggccat gcctacagca acgtcgagga ggtggtgacg 1140
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 gtgctttcag gtgtggctag aggtctgtga tggcagaaga tcggtgcctg catcaacctt 1260
 ggcgctact acatcgtcgg catccctct gottacctca tagcgttcgt cctgcgtgctc 1320
 ggtgggacgg gactctggtt gggcatcata tgtgggctca tcgtacagct ccttctgctc 1380
 gcgatcatca ctctctgcac caactgggat agcgaggcaa cgaaggcaaa gaacagagtg 1440
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 gcaaacacgg aaactatagg agttatgct gtatgttttg aaacttcagc acctctgatc 1560
 ctctccgatt ttctggctcc cacattaaact ctaatggtta gcattgacac ttgcagtctg 1620
 gattttgaaa cataaatgcy ttccttgaac agagttagaa gggaccaatg gaaaacttat 1680
 acaatagtgt tagatcgcgt gcaacattgt cctccaaagt gacctcatca cacaacaaaa 1740
 cgtgggttaat tccaaaaaaa aaaaaaaaaa aaaaaaaa 1778

<210> 26

<211> 476

<212> PRT

<213> zea mays

<400> 26

```

Met Ala Lys Lys Pro Val Glu Glu Ala Leu Leu Ala Ala Ala Asp Glu
1      5      10      15
Gln Glu Ser Leu Ser Val Arg Glu Glu Leu Lys Lys Gln Leu Trp Leu
20      25      30
Ala Gly Pro Met Ile Ala Gly Ala Leu Leu Gln Asn Val Ile Gln Met
35      40      45
Ile Ser Val Met Tyr Val Gly His Leu Gly Glu Leu Pro Leu Ala Gly
50      55      60
Ala Ser Met Ala Asn Ser Phe Ala Thr Val Thr Gly Leu Ser Leu Leu
65      70      75      80
Leu Gly Met Ala Ser Ala Leu Asp Thr Leu Cys Gly Gln Ala Phe Gly
85      90      95
Ala Arg Gln Tyr Tyr Leu Leu Gly Ile Tyr Lys Gln Arg Ala Met Phe
100     105     110
Leu Leu Thr Leu Val Ser Val Pro Leu Ser Val Val Trp Phe Tyr Thr
115     120     125
Gly Glu Ile Leu Leu Leu Phe Gly Gln Asp Pro Asp Ile Ala Ala Glu
130     135     140
Ala Gly Thr Tyr Ala Arg Trp Met Ile Pro Leu Leu Phe Ala Tyr Gly
145     150     155     160
Leu Leu Gln Cys His Val Arg Phe Leu Gln Thr Gln Asn Ile Val Val
165     170     175
Pro Val Met Ala Ser Ala Gly Ala Ala Ala Cys His Val Val Val
180     185     190
Cys Trp Ala Leu Val Tyr Ala Leu Gly Met Gly Ser Lys Gly Ala Ala
195     200     205
Leu Ser Asn Ser Ile Ser Tyr Trp Val Asn Val Ala Val Leu Ala Val
210     215     220
Tyr Val Arg Val Ser Ser Ala Cys Lys Glu Thr Trp Thr Gly Phe Ser
225     230     235     240
Thr Glu Ala Phe Arg Asp Ala Leu Gly Phe Phe Arg Leu Ala Val Pro
245     250     255
Ser Ala Leu Met Val Cys Leu Glu Met Trp Ser Phe Glu Leu Ile Val
260     265     270
Leu Leu Ser Gly Leu Leu Pro Asn Pro Lys Leu Glu Thr Ser Val Leu
275     280     285
Ser Ile Ser Leu Asn Thr Ala Ala Phe Val Trp Met Ile Pro Phe Gly
290     295     300
Leu Ser Ser Ala Ile Ser Thr Arg Val Ser Asn Glu Leu Gly Ala Gly
305     310     315     320

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

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<210> 27

<211> 483

<212> PRT

<213> Arabidopsis thaliana

<400> 27

```

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

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

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<210> 28

<211> 487

<212> PRT

<213> zea mays

<400> 28

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

Leu Glu Trp Trp Ser Phe Glu Leu Leu Thr Leu Met Ser Gly Leu Leu
275     280     285
Pro Asn Pro Glu Leu Gln Thr Ser Val Leu Ser Ile Cys Leu Thr Ser
290     295     300
Val Thr Leu Leu Phe Thr Ile Pro Phe Gly Leu Gly Ala Ala Gly Ser
305     310     315     320
Thr Arg Val Ala Asn Glu Leu Gly Ala Gly Asn Pro Asp Gly Ala Arg
325     330     335
Ser Ala Val Arg Val Val Leu Ser Met Ala Gly Ile Asp Ala Val Val
340     345     350
Val Ser Gly Ser Leu Leu Ala Ala Arg Arg Leu Val Gly Ile Ala Tyr
355     360     365
Ser Ser Glu Glu Glu Val Ile Ser Ala Val Ala Met Val Pro Leu
370     375     380
Val Cys Ile Thr Ala Ile Thr Asp Cys Leu Gln Gly Ile Leu Ser Gly
385     390     395     400
Val Ala Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr Val Asn Leu
405     410     415
Gly Ser Phe Tyr Leu Leu Gly Ile Pro Met Ala Ile Leu Leu Gly Phe
420     425     430
Val Leu Arg Met Gly Ser Arg Gly Leu Trp Met Gly Ile Val Cys Gly
435     440     445
Ser Leu Ser Gln Thr Thr Leu Met Ser Ala Ile Thr Phe Phe Thr Asp
450     455     460
Trp Asn Lys Met Ala Glu Lys Ala Arg Glu Arg Val Phe Ser Asp Lys
465     470     475     480
Gln Pro Gln Glu Pro Gly Pro
485

```

<210> 29

<211> 487

<212> PRT

<213> zea may

<400> 29

```

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

Ser Cys Lys Glu Thr Arg Ala Arg Pro Thr Val Glu Val Phe Arg Gly
245     250     255
Val Asp Ala Phe Leu Arg Leu Ala Leu Pro Ser Ala Leu Met Met Cys
260     265     270
Leu Glu Trp Trp Ser Phe Glu Leu Leu Thr Leu Met Ser Gly Leu Leu
275     280     285
Pro Asn Pro Glu Leu Gln Thr Ser Val Leu Ser Ile Cys Leu Thr Ser
290     295     300
Val Thr Leu Leu Phe Thr Ile Pro Phe Gly Leu Gly Ala Ala Gly Ser
305     310     315     320
Thr Arg Val Ala Asn Glu Leu Gly Ala Gly Asn Pro Asp Gly Ala Arg
325     330     335
Ser Ala Val Arg Val Val Leu Ser Met Ala Gly Ile Asp Ala Val Val
340     345     350
Val Ser Gly Ser Leu Leu Ala Ala Arg Arg Leu Val Gly Ile Ala Tyr
355     360     365
Ser Ser Glu Glu Glu Val Ile Ser Ala Val Ala Ala Met Val Pro Leu
370     375     380
Val Cys Ile Thr Ala Ile Thr Asp Cys Leu Gln Gly Ile Leu Ser Gly
385     390     395     400
Val Ala Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr Val Asn Leu
405     410     415
Gly Ser Phe Tyr Leu Leu Gly Ile Pro Met Ala Ile Leu Leu Gly Phe
420     425     430
Val Leu Arg Met Gly Ser Arg Gly Leu Trp Met Gly Ile Val Cys Gly
435     440     445
Ser Leu Ser Gln Thr Thr Leu Met Ser Ala Ile Thr Phe Phe Thr Asp
450     455     460
Trp Asn Lys Met Ala Glu Lys Ala Arg Glu Arg Val Phe Ser Asp Lys
465     470     475     480
Gln Pro Gln Glu Pro Gly Pro
485

```

<210> 30

<211> 505

<212> PRT

<213> sorghum bicolor

<400> 30

```

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

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```

Leu Ser Ser Phe Thr Thr Leu Ala Val Phe Ile Pro Leu Cys Trp Phe
210      215      220
Met Val Tyr Lys Val Gly Met Gly Asn Ala Gly Ala Ala Phe Ala Val
225      230      235      240
Ser Ile Cys Asp Trp Val Glu Val Thr Val Leu Gly Leu Tyr Ile Lys
245      250      255
Phe Ser Pro Ser Cys Glu Lys Thr Arg Ala Pro Phe Thr Trp Glu Ala
260      265      270
Phe Arg Gly Ile Gly Asn Phe Met Arg Leu Ala Val Pro Ser Ala Leu
275      280      285
Met Ile Cys Leu Glu Trp Trp Ser Tyr Glu Leu Leu Val Leu Leu Cys
290      295      300
Gly Val Leu Pro Asn Ala Ala Leu Glu Thr Ser Val Leu Ser Ile Cys
305      310      315      320
Ile Ser Thr Val Val Leu Val Tyr Asn Leu Pro Tyr Gly Ile Gly Thr
325      330      335
Ala Ala Ser Val Arg Val Ser Asn Glu Leu Gly Ala Gly Asn Pro Asp
340      345      350
Gly Ala Arg Leu Val Val Val Val Ala Leu Ser Ile Ile Ile Cys Thr
355      360      365
Ala Val Leu Leu Ser Ile Thr Leu Leu Ser Phe Arg His Phe Val Gly
370      375      380
Ile Ala Phe Ser Asn Glu Glu Glu Val Val Asn His Val Thr Arg Met
385      390      395      400
Val Pro Leu Leu Ser Ile Ser Val Leu Thr Asp Asn Leu Gln Gly Val
405      410      415
Leu Ser Gly Ile Ser Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr
420      425      430
Val Asn Leu Gly Ala Phe Tyr Leu Ile Gly Ile Pro Val Gly Leu Val
435      440      445
Ala Gly Phe Ala Leu His Leu Gly Gly Ala Gly Phe Trp Ile Gly Met
450      455      460
Ile Ala Gly Gly Ala Thr Gln Val Thr Leu Leu Ser Val Ile Thr Ala
465      470      475      480
Met Thr Asn Trp Gln Lys Met Ala Asp Lys Ala Arg Asp Arg Val Tyr
485      490      495
Glu Gly Ser Leu Pro Thr Gln Ala Asp
500      505

```

<210> 31

<211> 496

<212> PRT

<213> zea mays

<400> 31

```

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

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```

Ile Ala Ile Glu Ala Gly Arg Tyr Ala Leu Trp Leu Ile Pro Gly Leu
165 170 175
Phe Ala Phe Ser Val Ala Gln Cys Leu Ser Lys Phe Leu Gln Ser Gln
180 185 190
Ser Leu Ile Phe Pro Leu Val Leu Ser Ser Leu Thr Thr Leu Ala Val
195 200 205
Phe Ile Pro Leu Cys Trp Phe Met Val Tyr Lys Val Gly Met Gly Asn
210 215 220
Ala Gly Ala Ala Phe Ala Val Ser Ile Cys Asp Trp Val Glu Val Thr
225 230 235 240
Val Leu Gly Leu Tyr Ile Lys Phe Ser Pro Ser Cys Glu Lys Thr Arg
245 250 255
Ala Pro Phe Thr Trp Glu Ala Phe Gln Gly Ile Gly Ser Phe Met Arg
260 265 270
Leu Ala Val Pro Ser Ala Leu Met Val Cys Leu Glu Trp Trp Ser Tyr
275 280 285
Glu Leu Leu Val Leu Leu Ser Gly Met Leu Pro Asn Ala Ala Leu Glu
290 295 300
Thr Ser Val Leu Ser Ile Cys Ile Ser Thr Val Ile Leu Val Tyr Asn
305 310 315 320
Leu Pro Tyr Gly Ile Gly Thr Ala Ala Ser Val Arg Val Ser Asn Glu
325 330 335
Leu Gly Ala Gly Asn Pro Asp Ser Ala Arg Leu Val Val Val Ala
340 345 350
Leu Ser Ile Ile Phe Thr Ala Val Leu Val Ser Val Thr Leu Leu
355 360 365
Ser Leu Arg His Phe Ile Gly Ile Ala Phe Ser Asn Glu Glu Glu Val
370 375 380
Val Asn Tyr Val Thr Arg Met Val Pro Leu Leu Ser Ile Ser Val Ile
385 390 395 400
Thr Asp Asn Leu Gln Gly Val Leu Ser Gly Ile Ser Arg Gly Cys Gly
405 410 415
Trp Gln His Leu Gly Ala Tyr Val Asn Leu Gly Ala Phe Tyr Leu Val
420 425 430
Gly Ile Pro Val Ala Leu Val Ala Gly Phe Ala Leu His Leu Gly Gly
435 440 445
Ala Gly Phe Trp Ile Gly Met Ile Ala Gly Gly Ala Thr Gln Val Thr
450 455 460
Leu Leu Thr Ile Ile Thr Ala Met Thr Asn Trp Arg Lys Met Ala Asp
465 470 475 480
Lys Ala Arg Asp Arg Val Tyr Glu Gly Ser Leu Pro Ile Gln Ala Asn
485 490 495

```

<210> 32

<211> 479

<212> PRT

<213> zea mays

<400> 32

```

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

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```

Tyr Thr Gly Gln Ile Leu Leu Leu Phe Gly Gln Asp Pro Glu Ile Ala
130      135      140
Ala Gly Ala Gly Ser Tyr Ile Arg Trp Met Ile Pro Ala Leu Phe Val
145      150      155      160
Tyr Gly Pro Leu Gln Cys His Val Arg Phe Leu Gln Thr Gln Asn Ile
165      170      175
Val Leu Pro Val Met Leu Ser Ser Gly Ala Thr Ala Leu Asn His Leu
180      185      190
Leu Val Cys Trp Leu Leu Val Tyr Lys Ile Gly Met Gly Asn Lys Gly
195      200      205
Ala Ala Leu Ala Asn Ala Ile Ser Tyr Phe Thr Asn Val Ser Ile Leu
210      215      220
Ala Ile Tyr Val Arg Leu Ala Pro Ala Cys Arg Asn Thr Trp Arg Gly
225      230      235      240
Phe Ser Lys Glu Ala Phe His Asp Ile Thr Ser Phe Leu Arg Leu Gly
245      250      255
Ile Pro Ser Ala Leu Met Val Cys Leu Glu Trp Trp Ser Phe Glu Leu
260      265      270
Leu Val Leu Leu Ser Gly Leu Leu Pro Asn Pro Lys Leu Glu Thr Ser
275      280      285
Val Leu Ser Ile Ser Leu Asn Thr Gly Ser Leu Ala Phe Met Ile Pro
290      295      300
Phe Gly Leu Ser Ala Ala Ile Ser Thr Arg Val Ser Asn Glu Leu Gly
305      310      315      320
Ala Gly Arg Pro His Ala Ala His Leu Ala Thr Arg Val Val Met Val
325      330      335
Leu Ala Ile Val Val Gly Val Leu Ile Gly Leu Ala Met Ile Leu Val
340      345      350
Arg Asn Ile Trp Gly Tyr Ala Tyr Ser Asn Glu Lys Glu Val Val Lys
355      360      365
Tyr Ile Ser Lys Met Met Pro Ile Leu Ala Val Ser Phe Leu Phe Asp
370      375      380
Cys Val Gln Cys Val Leu Ser Gly Val Ala Arg Gly Cys Gly Trp Gln
385      390      395      400
Lys Ile Gly Ala Cys Val Asn Leu Gly Ala Tyr Tyr Leu Ile Gly Ile
405      410      415
Pro Ala Ala Phe Cys Phe Ala Phe Met Tyr His Leu Gly Gly Met Gly
420      425      430
Leu Trp Leu Gly Ile Ile Cys Ala Leu Val Ile Gln Met Leu Leu Leu
435      440      445
Leu Thr Ile Thr Leu Cys Ser Asn Trp Glu Lys Glu Ala Leu Lys Ala
450      455      460
Lys Asp Arg Val Phe Ser Thr Ser Val Pro Ala Asp Met Met Thr
465      470      475

```

<210> 33

<211> 475

<212> PRT

<213> zea may

<400> 33

```

Met Asp Glu Pro Leu Leu Gly Asn Gly Leu Lys Thr Ser Gly Lys Arg
1      5      10      15
Glu Ser Leu Val Val Ala Glu Val Arg Lys Gln Met Tyr Leu Ala Gly
20      25      30
Pro Leu Ile Ala Ala Trp Ile Leu Gln Asn Ile Val Gln Met Ile Ser
35      40      45
Ile Met Phe Val Gly His Leu Gly Glu Leu Ala Leu Ser Ser Ala Ser
50      55      60
Ile Ala Thr Ser Phe Ala Gly Val Thr Gly Phe Ser Leu Leu Ser Gly
65      70      75      80
Met Ala Ser Ser Leu Asp Thr Leu Cys Gly Gln Ser Phe Gly Ala Lys
85      90      95
Gln Tyr Tyr Leu Leu Gly Ile Tyr Lys Gln Arg Ala Ile Leu Val Leu
100      105      110

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```

Thr Leu Val Ser Leu Val Val Ala Ile Ile Trp Ser Tyr Thr Gly Gln
115 120 125
Ile Leu Leu Leu Phe Gly Gln Asp Pro Glu Ile Ala Ala Gly Ala Gly
130 135 140
Ser Tyr Ile Arg Trp Met Ile Pro Ala Leu Phe Val Tyr Gly Pro Leu
145 150 155 160
Gln Cys His Val Arg Phe Leu Gln Thr Gln Asn Ile Val Leu Pro Val
165 170 175
Met Leu Ser Ser Gly Ala Thr Ala Leu Asn His Leu Leu Val Cys Trp
180 185 190
Leu Leu Val Tyr Lys Ile Gly Met Gly Asn Lys Gly Ala Ala Leu Ala
195 200 205
Asn Ala Ile Ser Tyr Phe Thr Asn Val Ser Ile Leu Ala Ile Tyr Val
210 215 220
Arg Leu Ala Pro Ala Cys Arg Asn Thr Trp Arg Gly Phe Ser Lys Glu
225 230 235 240
Ala Phe His Asp Ile Thr Ser Phe Leu Arg Leu Gly Ile Pro Ser Ala
245 250 255
Leu Met Val Cys Leu Glu Trp Trp Ser Phe Glu Leu Leu Val Leu Leu
260 265 270
Ser Gly Leu Leu Pro Asn Pro Lys Leu Glu Thr Ser Val Leu Ser Ile
275 280 285
Ser Leu Asn Thr Gly Ser Leu Ala Phe Met Ile Pro Phe Gly Leu Ser
290 295 300
Ala Ala Ile Ser Thr Arg Val Ser Asn Glu Leu Gly Ala Gly Arg Pro
305 310 315 320
His Ala Ala His Leu Ala Thr Arg Val Val Met Val Leu Ala Ile Val
325 330 335
Val Gly Val Leu Ile Gly Leu Ala Met Ile Leu Val Arg Asn Ile Trp
340 345 350
Gly Tyr Ala Tyr Ser Asn Glu Lys Glu Val Val Lys Tyr Ile Ser Lys
355 360 365
Met Met Pro Ile Leu Ala Val Ser Phe Leu Phe Asp Cys Val Gln Cys
370 375 380
Val Leu Ser Gly Val Ala Arg Gly Cys Gly Trp Gln Lys Ile Gly Ala
385 390 395 400
Cys Val Asn Leu Gly Ala Tyr Tyr Leu Ile Gly Ile Pro Ala Ala Phe
405 410 415
Cys Phe Ala Phe Met Tyr His Leu Gly Gly Met Gly Leu Trp Leu Gly
420 425 430
Ile Ile Cys Ala Leu Val Ile Gln Met Leu Leu Leu Leu Thr Ile Thr
435 440 445
Leu Cys Ser Asn Trp Glu Lys Glu Ala Leu Lys Ala Lys Asp Arg Val
450 455 460
Phe Ser Thr Ser Val Pro Ala Asp Met Met Thr
465 470 475

```

<210> 34

<211> 476

<212> PRT

<213> zea may

<400> 34

```

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

```

```

Ala Arg Gln Tyr Tyr Leu Leu Gly Ile Tyr Lys Gln Arg Ala Met Phe
100 105 110
Leu Leu Thr Leu Val Ser Val Pro Leu Ser Val Val Trp Phe Tyr Thr
115 120 125
Gly Glu Ile Leu Leu Phe Gly Gln Asp Pro Asp Ile Ala Ala Glu
130 135 140
Ala Gly Thr Tyr Ala Arg Trp Met Ile Pro Leu Leu Phe Ala Tyr Gly
145 150 155 160
Leu Leu Gln Cys His Val Arg Phe Leu Gln Thr Gln Asn Ile Val Val
165 170 175
Pro Val Met Ala Ser Ala Gly Ala Ala Ala Ala Cys His Val Val Val
180 185 190
Cys Trp Ala Leu Val Tyr Ala Leu Gly Met Gly Ser Lys Gly Ala Ala
195 200 205
Leu Ser Asn Ser Ile Ser Tyr Trp Val Asn Val Ala Val Leu Ala Val
210 215 220
Tyr Val Arg Val Ser Ser Ala Cys Lys Glu Thr Trp Thr Gly Phe Ser
225 230 235 240
Thr Glu Ala Phe Arg Asp Ala Leu Gly Phe Phe Arg Leu Ala Val Pro
245 250 255
Ser Ala Leu Met Val Cys Leu Glu Met Trp Ser Phe Glu Leu Ile Val
260 265 270
Leu Leu Ser Gly Leu Leu Pro Asn Pro Lys Leu Glu Thr Ser Val Leu
275 280 285
Ser Ile Ser Leu Asn Thr Ala Ala Phe Val Trp Met Ile Pro Phe Gly
290 295 300
Leu Ser Ser Ala Ile Ser Thr Arg Val Ser Asn Glu Leu Gly Ala Gly
305 310 315 320
Arg Pro Arg Ala Ala Arg Leu Ala Val Arg Val Val Val Leu Leu Ser
325 330 335
Val Ala Glu Gly Leu Gly Val Gly Leu Ile Leu Val Cys Val Arg Tyr
340 345 350
Val Trp Gly His Ala Tyr Ser Asn Val Glu Glu Val Val Thr Tyr Val
355 360 365
Ala Asn Met Met Leu Val Ile Ala Val Ser Asn Phe Phe Asp Gly Ile
370 375 380
Gln Cys Val Leu Ser Gly Val Ala Arg Gly Cys Gly Trp Gln Lys Ile
385 390 395 400
Gly Ala Cys Ile Asn Leu Gly Ala Tyr Tyr Ile Val Gly Ile Pro Ser
405 410 415
Ala Tyr Leu Ile Ala Phe Val Leu Arg Val Gly Gly Thr Gly Leu Trp
420 425 430
Leu Gly Ile Ile Cys Gly Leu Ile Val Gln Leu Leu Leu Ala Ile
435 440 445
Ile Thr Leu Cys Thr Asn Trp Asp Ser Glu Ala Thr Lys Ala Lys Asn
450 455 460
Arg Val Phe Asn Ser Ser Ser Pro Ala Ser Gly Thr
465 470 475

```

<210> 35

<211> 431

<212> PRT

<213> zea may

<400> 35

```

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

```

Leu Leu Leu Gly Met Ala Ser Ala Leu Asp Thr Leu Cys Gly Gln Ala
 85 90 95
 Phe Gly Ala Arg Gln Tyr Tyr Leu Leu Gly Ile Tyr Lys Gln Arg Ala
 100 105 110
 Met Phe Leu Leu Thr Leu Cys His Val Arg Phe Leu Gln Thr Gln Asn
 115 120 125
 Ile Val Val Pro Val Met Ala Ser Ala Gly Ala Ala Ala Cys His
 130 135 140
 Val Val Val Cys Trp Ala Leu Val Tyr Ala Leu Gly Met Gly Ser Lys
 145 150 155 160
 Gly Ala Ala Leu Ser Asn Ala Ile Ser Tyr Trp Val Asn Val Ala Val
 165 170 175
 Leu Ala Val Tyr Val Arg Val Ser Ser Ala Cys Lys Glu Thr Trp Thr
 180 185 190
 Gly Phe Ser Thr Glu Ala Phe Arg Asp Ala Leu Gly Phe Phe Arg Leu
 195 200 205
 Ala Val Pro Ser Ala Leu Met Val Cys Leu Glu Met Trp Ser Phe Glu
 210 215 220
 Leu Ile Val Leu Leu Ser Gly Leu Leu Pro Asn Pro Lys Leu Glu Thr
 225 230 235 240
 Ser Val Leu Ser Ile Ser Leu Asn Thr Ala Ala Phe Val Trp Met Ile
 245 250 255
 Pro Phe Gly Leu Ser Ser Ala Ile Ser Thr Arg Val Ser Asn Glu Leu
 260 265 270
 Gly Ala Gly Arg Pro Arg Ala Ala Arg Leu Ala Val Arg Val Val Val
 275 280 285
 Leu Leu Ser Val Ala Glu Gly Leu Gly Val Gly Leu Ile Leu Val Cys
 290 295 300
 Val Arg Tyr Val Trp Gly His Ala Tyr Ser Asn Val Glu Glu Val Val
 305 310 315 320
 Thr Tyr Val Ala Asn Met Met Leu Val Ile Ala Val Ser Asn Phe Phe
 325 330 335
 Asp Gly Ile Gln Cys Val Leu Ser Gly Val Ala Arg Gly Cys Gly Trp
 340 345 350
 Gln Lys Ile Gly Ala Cys Ile Asn Leu Gly Ala Tyr Tyr Ile Val Gly
 355 360 365
 Ile Pro Ser Ala Tyr Leu Ile Ala Phe Val Leu Arg Val Gly Gly Thr
 370 375 380
 Gly Leu Trp Leu Gly Ile Ile Cys Gly Leu Ile Val Gln Leu Leu Leu
 385 390 395 400
 Leu Ala Ile Ile Thr Leu Cys Thr Asn Trp Asp Ser Glu Ala Thr Lys
 405 410 415
 Ala Lys Asn Arg Val Phe Asn Ser Ser Ser Pro Ala Ser Gly Thr
 420 425 430

<210> 36

<211> 1803

<212> DNA

<213> Zea mays

<400> 36

ggcgggagag agaagagtcg acgacgacgg taaccggccg ccatggaggt gaggggtccg 60
 cttcttcgcg agcacatatt gcggaacggc gacggacggg agaagaagtg cggcgtgagg 120
 cggtggaggg agctgctagc gcgggaggcc gggaaggtcg gctgcgtggc cctgccgatg 180
 gcggccgtga cgtgtctgca gtacgcggtg caggtggcgt ccaacatgat ggtcggcccc 240
 ctccccggcg tctctccgct ctccgcctcc gccatcgcca cctccctcac caccgtatcc 300
 ggtttcagcc tctctcattg tatggcaagt ggactggaaa ctctatgcgg tcaagcctat 360
 ggagcaaaac agtatgataa actggggatg cacacctaca gagctatagt cacactcatt 420
 gctgtgagca ttccaatctc acttctgtgg gcattcatag gcaaaactct gatcctcata 480
 ggtcaggacc ccttgatctc aagggaagct gggagataca tagtctgggt gattccaggt 540
 ctctatgcat atgccatcag ccagcctctc acaaaatttc tacagtctca gagcctgata 600
 attcctatgc tttggtcctc cattgcaact ctgctcttgc acattcctct ttgttggtta 660
 ctagtgttca agaccagtat ggggtacatt ggagcttctt tggcaataag cttgtcgtat 720
 tgggtaaacg tgatgatgct tgccgcttac atcagatact cggattcctg taaggagacc 780
 cgctcacctc caaccgttga ggccttcaaa ggagtcagtg tgtttctacg cctggctctg 840

ccgtctgcac tgatgtttgt tttcgaatgg tggctctttg agatccttat tcttgtctca 900
 ggrattttac caaatccaga gctgcamact tcagttcttt caatctgttt gacgactatc 960
 acatthaatg atactatacc ttatgggctt ggagcggctg caagcaactag ggtagcaaat 1020
 gagttgggtg atggtataccc tgaaggagct cgatcatctg ttcgtgccat catgtgtatt 1080
 gcagtgatgg aagcagctat gatcacagtc atattgttag cgtcacagca catcttggtt 1140
 tacgcataata gcagcgacaa ggatgtcgtc gcgtatgtca atgcaatggt tcccctgtg 1200
 tgcgctcccg ttgctgctga cagcctacaa ggtgttctat caggtgttgc ccgaggatgc 1260
 ggggtggcagc acttggggcg ctacgtcaac ctgggctcgt tctacctcgt cgggattcca 1320
 acagcactct tctctggctt cgttctgaag atggaagcga aagggtcttt gatgggcatt 1380
 tctcgccgtt ccatagtcca gttcttgctt cttgccgtca taacgttctt cagcaactgg 1440
 gagaagatgt ctgagaaggc aagggagaga gttttcagcg atgatgagcc gtcagataag 1500
 ggaacttcgg attccgatgg accgagtttt gttctagttt tggcacgagc catctgaatc 1560
 tgaatccccct tgtgaagacg cagcgggacaa gatctttagt acaaaagagc coactctgga 1620
 atgggggttta tgatgccttg ctttctgttc tctgaactga atgtacaggg aacttgttga 1680
 actctgacca ctgttctgtg ctccgtgctc gtgcttgcgt ttgtttgtta aaacaacggg 1740
 acaattgtag cagaacatg actacatgag gctctctgat ctatggtaga aatagtaacc 1800
 aca 1803

<210> 37

<211> 504

<212> PRT

<213> Zea mays

<220>

<221> misc_feature

<222> (295)..(295)

<223> Xaa can be any naturally occurring amino acid

<400> 37

```

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

```

```

290      295      300
Thr Ile Thr Leu Met Tyr Thr Ile Pro Tyr Gly Leu Gly Ala Ala Ala
305      310      315      320
Ser Thr Arg Val Ala Asn Glu Leu Gly Gly Gly Asn Pro Glu Gly Ala
325      330      335
Arg Ser Ser Val Arg Ala Ile Met Cys Ile Ala Val Met Glu Ala Ala
340      345      350
Met Ile Thr Val Ile Leu Leu Ala Ser Gln His Ile Leu Gly Tyr Ala
355      360      365
Tyr Ser Ser Asp Lys Asp Val Val Ala Tyr Val Asn Ala Met Val Pro
370      375      380
Leu Val Cys Val Ser Val Ala Ala Asp Ser Leu Gln Gly Val Leu Ser
385      390      395      400
Gly Val Ala Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr Val Asn
405      410      415
Leu Gly Ser Phe Tyr Leu Val Gly Ile Pro Thr Ala Leu Phe Leu Gly
420      425      430
Phe Val Leu Lys Met Glu Ala Lys Gly Leu Trp Met Gly Ile Ser Cys
435      440      445
Gly Ser Ile Val Gln Phe Leu Leu Leu Ala Val Ile Thr Phe Phe Ser
450      455      460
Asn Trp Glu Lys Met Ser Glu Lys Ala Arg Glu Arg Val Phe Ser Asp
465      470      475      480
Asp Glu Pro Ser Asp Lys Gly Thr Ser Asp Ser Asp Gly Pro Ser Phe
485      490      495
Val Leu Val Leu Ala Arg Ala Ile
500

```

<210> 38

<211> 514

<212> PRT

<213> Sorghum bicolor

<400> 38

```

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

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```

245      250      255
Glu Ala Phe Lys Gly Val Gly Val Phe Leu Arg Leu Ala Leu Pro Ser
260      265      270
Ala Leu Met Leu Trp Phe His Ile Gly Leu Met Asn Ser Ile Pro Gln
275      280      285
Phe Tyr Ser Phe Glu Trp Trp Ser Phe Glu Ile Leu Ile Leu Val Ser
290      295      300
Gly Ile Leu Pro Asn Pro Glu Leu Gln Thr Ser Val Leu Ser Ile Cys
305      310      315      320
Leu Thr Thr Ile Thr Leu Met Tyr Thr Ile Pro Tyr Gly Leu Gly Ala
325      330      335
Ala Ala Ser Thr Arg Val Ala Asn Glu Leu Gly Gly Gly Asn Pro Glu
340      345      350
Gly Ala Arg Ser Ser Val Gln Val Val Met Cys Ile Ala Val Met Glu
355      360      365
Ala Val Ile Ile Thr Ile Ile Leu Leu Ala Ser Gln His Ile Leu Gly
370      375      380
Tyr Ala Tyr Ser Ser Asp Lys Asp Val Val Ala Tyr Val Asn Ala Met
385      390      395      400
Val Pro Phe Val Cys Val Ser Val Ala Ala Asp Ser Leu Gln Gly Val
405      410      415
Leu Ser Gly Ile Ala Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr
420      425      430
Val Asn Leu Gly Ser Phe Tyr Leu Val Gly Ile Pro Thr Ala Leu Phe
435      440      445
Leu Gly Phe Val Leu Lys Met Glu Ala Lys Gly Leu Trp Met Gly Ile
450      455      460
Ser Cys Gly Ser Ile Val Gln Phe Leu Leu Leu Ala Ile Ile Thr Phe
465      470      475      480
Phe Ser Asn Trp Gln Lys Met Ser Glu Lys Ala Arg Glu Arg Val Phe
485      490      495
Ser Asp Glu Pro Ser Asp Lys Glu Pro Leu Glu Ser Asp Gly Ser Asn
500      505      510
Leu Phe

```

<210> 39

<211> 490

<212> PRT

<213> Triticum aestivum

<400> 39

```

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

```

```

180      185      190
Leu His Ile Pro Val Cys Trp Leu Leu Val Phe Lys Thr Ser Leu Gly
195     200     205
Tyr Ile Gly Ala Ala Leu Ala Ile Ser Val Ser Tyr Trp Leu Asn Val
210     215     220
Phe Met Leu Val Ala Tyr Ile Gly Cys Ser Asn Ser Cys Lys Glu Thr
225     230     235     240
Phe Ser Pro Pro Thr Leu Asp Ala Phe Ser Gly Val Gly Val Phe Met
245     250     255
Arg Leu Ala Leu Pro Ser Ala Leu Met Leu Cys Phe Glu Trp Trp Ser
260     265     270
Phe Glu Val Ile Ile Leu Leu Ser Gly Leu Leu Pro Asn Pro Glu Leu
275     280     285
Gln Thr Ser Val Leu Ser Thr Cys Met Thr Thr Ile Thr Leu Met Tyr
290     295     300
Thr Ile Ala Tyr Gly Ile Gly Ala Ala Gly Ser Thr Arg Val Ser Asn
305     310     315     320
Glu Leu Gly Ala Gly Asn Pro Glu Gly Ala Arg Leu Ala Val Arg Val
325     330     335
Val Met Ser Ile Ala Val Thr Glu Ala Val Leu Ile Thr Gly Ala Leu
340     345     350
Leu Ala Ser Gln His Ile Leu Gly Tyr Ala Tyr Ser Ser Asp Lys Glu
355     360     365
Val Val Asp Tyr Val Asn Ala Met Val Pro Phe Ile Cys Ile Ser Val
370     375     380
Ala Ala Asp Ser Leu Gln Gly Val Leu Ser Gly Ile Ala Arg Gly Cys
385     390     395     400
Gly Ser Gln His Leu Gly Ala Tyr Val Asn Leu Gly Ser Phe Tyr Leu
405     410     415
Phe Gly Ile Pro Met Ser Leu Leu Leu Gly Phe Val Leu Lys Met Gly
420     425     430
Gly Lys Gly Leu Trp Met Gly Ile Ser Cys Gly Ser Ile Val Gln Phe
435     440     445
Leu Leu Leu Ser Gly Ile Val Phe Phe Ser Asn Trp Gln Lys Met Ser
450     455     460
Asp Asn Ala Arg Glu Arg Val Phe Gly Gly Thr Pro Ala Glu Lys Glu
465     470     475     480
Pro Leu Met Ser Asp Val Thr Gly Ala Ala
485     490

```

<210> 40

<211> 483

<212> PRT

<213> Arabidopsis thaliana

<400> 40

```

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

```

```

145          150          155          160
Leu Leu Ala Gln Ala Val Gln Gln Pro Leu Thr Arg Phe Leu Gln Thr
165          170          175
Gln Gly Leu Val Leu Pro Leu Leu Tyr Cys Ala Ile Thr Thr Leu Leu
180          185          190
Phe His Ile Pro Val Cys Leu Ile Leu Val Tyr Ala Phe Gly Leu Gly
195          200          205
Ser Asn Gly Ala Ala Leu Ala Ile Gly Leu Ser Tyr Trp Phe Asn Val
210          215          220
Leu Ile Leu Ala Leu Tyr Val Arg Phe Ser Ser Cys Glu Lys Thr
225          230          235          240
Arg Gly Phe Val Ser Asp Asp Phe Val Leu Ser Val Lys Gln Phe Phe
245          250          255
Gln Tyr Gly Ile Pro Ser Ala Ala Met Thr Thr Ile Glu Trp Ser Leu
260          265          270
Phe Glu Phe Leu Ile Leu Ser Ser Gly Leu Leu Pro Asn Pro Lys Leu
275          280          285
Glu Thr Ser Val Leu Ser Ile Cys Leu Thr Thr Ser Ser Leu His Tyr
290          295          300
Val Ile Pro Met Gly Ile Gly Ala Ala Gly Ser Ile Arg Val Ser Asn
305          310          315          320
Glu Leu Gly Ala Gly Asn Pro Glu Val Ala Arg Leu Ala Val Phe Ala
325          330          335
Gly Ile Phe Leu Trp Phe Leu Glu Ala Thr Ile Cys Ser Thr Leu Leu
340          345          350
Phe Ile Cys Arg Asp Ile Phe Gly Tyr Ala Phe Ser Asn Ser Lys Glu
355          360          365
Val Val Asp Tyr Val Thr Glu Leu Ser Pro Leu Leu Cys Ile Ser Phe
370          375          380
Leu Val Asp Gly Phe Ser Ala Val Leu Gly Gly Val Ala Arg Gly Ser
385          390          395          400
Gly Trp Gln His Ile Gly Ala Trp Ala Asn Val Val Ala Tyr Tyr Leu
405          410          415
Leu Gly Ala Pro Val Gly Leu Phe Leu Gly Phe Trp Cys His Met Asn
420          425          430
Gly Lys Gly Leu Trp Ile Gly Val Val Val Gly Ser Thr Ala Gln Gly
435          440          445
Ile Ile Leu Ala Ile Val Thr Ala Cys Met Ser Trp Asn Glu Gln Ala
450          455          460
Ala Lys Ala Arg Gln Arg Ile Val Val Arg Thr Ser Ser Phe Gly Asn
465          470          475          480
Gly Leu Ala

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<210> 41

<211> 476

<212> PRT

<213> *Arabidopsis thaliana*

<400> 41

```

Met Glu Glu Pro Phe Leu Leu Gln Asp Glu His Leu Val Pro Cys Lys
1      5      10      15
Asp Thr Trp Lys Ser Gly Gln Val Thr Val Glu Leu Lys Lys Val Ser
20     25     30
Ser Leu Ala Ala Pro Met Ala Ala Val Thr Ile Ala Gln Tyr Leu Leu
35     40     45
Pro Val Ile Ser Val Met Val Ala Gly His Asn Gly Glu Leu Gln Leu
50     55     60
Ser Gly Val Ala Leu Ala Thr Ser Phe Thr Asn Val Ser Gly Phe Ser
65     70     75     80
Ile Leu Phe Gly Leu Ala Gly Ala Leu Glu Thr Leu Cys Gly Gln Ala
85     90     95
Tyr Gly Ala Lys Gln Tyr Glu Lys Ile Gly Thr Tyr Thr Tyr Ser Ala
100    105    110
Thr Ala Ser Asn Ile Pro Ile Cys Val Leu Ile Ser Val Leu Trp Ile

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      115      120      125
Tyr Ile Glu Lys Leu Leu Ile Ser Leu Gly Gln Asp Pro Asp Ile Ser
130      135      140
Arg Val Ala Gly Ser Tyr Ala Leu Trp Leu Ile Pro Ala Leu Phe Ala
145      150      155      160
His Ala Phe Phe Ile Pro Leu Thr Arg Phe Leu Leu Ala Gln Gly Leu
165      170      175
Val Leu Pro Leu Leu Tyr Cys Thr Leu Thr Thr Leu Leu Phe His Ile
180      185      190
Pro Val Cys Trp Ala Phe Val Tyr Ala Phe Gly Leu Gly Ser Asn Gly
195      200      205
Ala Ala Met Ala Ile Ser Val Ser Phe Trp Phe Tyr Val Val Ile Leu
210      215      220
Ser Cys Tyr Val Arg Tyr Ser Ser Ser Cys Asp Lys Thr Arg Val Phe
225      230      235      240
Val Ser Ser Asp Phe Val Ser Cys Ile Lys Gln Phe Phe His Phe Gly
245      250      255
Val Pro Ser Ala Ala Met Val Cys Leu Glu Trp Trp Leu Phe Glu Leu
260      265      270
Leu Ile Leu Cys Ser Gly Leu Leu Pro Asn Pro Lys Leu Glu Thr Ser
275      280      285
Val Leu Ser Ile Cys Leu Thr Thr Ala Ser Leu His Tyr Val Ile Pro
290      295      300
Gly Gly Val Ala Ala Ala Val Ser Thr Arg Val Ser Asn Lys Leu Gly
305      310      315      320
Ala Gly Ile Pro Gln Val Ala Arg Val Ser Val Leu Ala Gly Leu Cys
325      330      335
Leu Trp Leu Val Glu Ser Ala Phe Phe Ser Thr Leu Leu Phe Thr Cys
340      345      350
Arg Asn Ile Ile Gly Tyr Ala Phe Ser Asn Ser Lys Glu Val Val Asp
355      360      365
Tyr Val Ala Asn Leu Thr Pro Leu Leu Cys Leu Ser Phe Ile Leu Asp
370      375      380
Gly Phe Thr Ala Val Leu Asn Gly Val Ala Arg Gly Ser Gly Trp Gln
385      390      395      400
His Ile Gly Ala Leu Asn Asn Val Val Ala Tyr Tyr Leu Val Gly Ala
405      410      415
Pro Val Gly Val Tyr Leu Ala Phe Asn Arg Glu Leu Asn Gly Lys Gly
420      425      430
Leu Trp Cys Gly Val Val Val Gly Ser Ala Val Gln Ala Ile Ile Leu
435      440      445
Ala Phe Val Thr Ala Ser Ile Asn Trp Lys Glu Gln Ala Glu Lys Ala
450      455      460
Arg Lys Arg Met Val Ser Ser Glu Asn Arg Leu Ala
465      470      475

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<210> 42

<211> 476

<212> PRT

<213> Arabidopsis thaliana

<400> 42

```

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

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```

100      105      110
Ile Ser Ser Asn Ile Pro Ile Cys Val Leu Ile Ser Ile Leu Trp Ile
115      120      125
Tyr Met Glu Lys Leu Leu Ile Ser Leu Gly Gln Asp Pro Asp Ile Ser
130      135      140
Arg Val Ala Gly Ser Tyr Ala Leu Arg Leu Ile Pro Thr Leu Phe Ala
145      150      155      160
His Ala Ile Val Leu Pro Leu Thr Arg Phe Leu Leu Ala Gln Gly Leu
165      170      175
Val Leu Pro Leu Leu Tyr Phe Ala Leu Thr Thr Leu Leu Phe His Ile
180      185      190
Ala Val Cys Trp Thr Leu Val Ser Ala Leu Gly Leu Gly Ser Asn Gly
195      200      205
Ala Ala Leu Ala Ile Ser Val Ser Phe Trp Phe Phe Ala Met Thr Leu
210      215      220
Ser Cys Tyr Val Arg Phe Ser Ser Ser Cys Glu Lys Thr Arg Arg Phe
225      230      235      240
Val Ser Gln Asp Phe Leu Ser Ser Val Lys Gln Phe Phe Arg Tyr Gly
245      250      255
Val Pro Ser Ala Ala Met Leu Cys Leu Glu Trp Trp Leu Phe Glu Leu
260      265      270
Leu Ile Leu Cys Ser Gly Leu Leu Gln Asn Pro Lys Leu Glu Thr Ser
275      280      285
Val Leu Ser Ile Cys Leu Thr Thr Ala Thr Leu His Tyr Val Ile Pro
290      295      300
Val Gly Val Ala Ala Ala Val Ser Thr Arg Val Ser Asn Lys Leu Gly
305      310      315      320
Ala Gly Ile Pro Gln Val Ala Arg Val Ser Val Leu Ala Gly Leu Cys
325      330      335
Leu Trp Leu Val Glu Ser Ser Phe Phe Ser Ile Leu Leu Phe Ala Phe
340      345      350
Arg Asn Ile Ile Gly Tyr Ala Phe Ser Asn Ser Lys Glu Val Val Asp
355      360      365
Tyr Val Ala Asp Leu Ser Pro Leu Leu Cys Leu Ser Phe Val Leu Asp
370      375      380
Gly Phe Thr Ala Val Leu Asn Gly Val Ala Arg Gly Cys Gly Trp Gln
385      390      395      400
His Ile Gly Ala Leu Asn Asn Val Val Ala Tyr Tyr Leu Val Gly Ala
405      410      415
Pro Val Gly Ile Tyr Leu Ala Phe Ser Cys Glu Leu Asn Gly Lys Gly
420      425      430
Leu Trp Cys Gly Val Val Val Gly Ser Ala Val Gln Ala Ile Ile Leu
435      440      445
Ala Ile Val Thr Ala Ser Met Asn Trp Lys Glu Gln Ala Lys Lys Ala
450      455      460
Arg Lys Arg Leu Ile Ser Ser Glu Asn Gly Leu Ala
465      470      475

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<210> 43

<211> 476

<212> PRT

<213> Arabidopsis thaliana

<400> 43

```

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

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```

      85              90              95
Tyr Gly Ala Glu Gln Tyr Glu Lys Ile Gly Thr Tyr Thr Tyr Ser Ala
      100              105              110
Met Ala Ser Asn Ile Pro Ile Cys Phe Ile Ile Ser Ile Leu Trp Ile
      115              120              125
Tyr Ile Glu Lys Leu Leu Ile Thr Leu Gly Gln Glu Pro Asp Ile Ser
      130              135              140
Arg Val Ala Gly Ser Tyr Ser Leu Trp Leu Val Pro Ala Leu Phe Ala
      145              150              155              160
His Ala Ile Phe Leu Pro Leu Thr Arg Phe Leu Leu Ala Gln Gly Leu
      165              170              175
Val Ile Ser Leu Leu Tyr Ser Ala Met Thr Thr Leu Leu Phe His Ile
      180              185              190
Ala Val Cys Trp Thr Leu Val Phe Ala Leu Gly Leu Gly Ser Asn Gly
      195              200              205
Ala Ala Ile Ala Ile Ser Leu Ser Phe Trp Phe Tyr Ala Val Ile Leu
      210              215              220
Ser Cys His Val Arg Phe Phe Ser Ser Cys Glu Lys Thr Arg Gly Phe
      225              230              235              240
Val Ser Asn Asp Phe Met Ser Ser Ile Lys Gln Tyr Phe Gln Tyr Gly
      245              250              255
Val Pro Ser Ala Gly Leu Ile Cys Leu Glu Trp Trp Leu Phe Glu Leu
      260              265              270
Leu Ile Leu Cys Ser Gly Leu Leu Pro Asn Pro Lys Leu Glu Thr Ser
      275              280              285
Val Leu Ser Ile Cys Leu Thr Ile Gly Thr Leu His Tyr Val Ile Pro
      290              295              300
Ser Gly Val Ala Ala Ala Val Ser Thr Arg Val Ser Asn Lys Leu Gly
      305              310              315              320
Ala Gly Asn Pro Gln Val Ala Arg Val Ser Val Leu Ala Gly Leu Cys
      325              330              335
Leu Trp Leu Val Glu Ser Ala Phe Phe Ser Thr Leu Leu Phe Thr Cys
      340              345              350
Arg Asn Ile Ile Gly Tyr Thr Phe Ser Asn Ser Lys Glu Val Val Asp
      355              360              365
Tyr Val Ala Asp Ile Ser Pro Leu Leu Cys Leu Ser Phe Ile Leu Asp
      370              375              380
Gly Leu Thr Ala Val Leu Asn Gly Val Ala Arg Gly Cys Gly Trp Gln
      385              390              395              400
His Ile Gly Ala Leu Ile Asn Val Val Ala Tyr Tyr Leu Val Gly Ala
      405              410              415
Pro Val Gly Val Tyr Leu Ala Phe Ser Arg Glu Trp Asn Gly Lys Gly
      420              425              430
Leu Trp Cys Gly Val Met Val Gly Ser Ala Val Gln Ala Thr Leu Leu
      435              440              445
Ala Ile Val Thr Ala Ser Met Asn Trp Lys Glu Gln Ala Glu Lys Ala
      450              455              460
Arg Lys Arg Ile Ile Ser Thr Glu Asn Gly Leu Val
      465              470              475

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<210> 44

<211> 476

<212> PRT

<213> Arabidopsis thaliana

<400> 44

```

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

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```

65          70          75          80
Ile Met Cys Gly Leu Val Gly Ala Leu Glu Thr Leu Cys Gly Gln Ala
85          90          95
Tyr Gly Ala Lys Gln Tyr Glu Lys Ile Gly Thr Tyr Ala Tyr Ser Ala
100         105         110
Ile Ala Ser Asn Ile Pro Ile Cys Phe Leu Ile Ser Ile Leu Trp Leu
115         120         125
Tyr Ile Glu Lys Ile Leu Ile Ser Leu Gly Gln Asp Pro Glu Ile Ser
130         135         140
Arg Ile Ala Gly Ser Tyr Ala Phe Trp Leu Ile Pro Ala Leu Phe Gly
145         150         155         160
Gln Ala Ile Val Ile Pro Leu Ser Arg Phe Leu Leu Thr Gln Gly Leu
165         170         175
Val Ile Pro Leu Leu Phe Thr Ala Val Thr Thr Leu Leu Phe His Val
180         185         190
Leu Val Cys Trp Thr Leu Val Phe Leu Phe Gly Leu Gly Cys Asn Gly
195         200         205
Pro Ala Met Ala Thr Ser Val Ser Phe Trp Phe Tyr Ala Val Ile Leu
210         215         220
Ser Cys Tyr Val Arg Phe Ser Ser Ser Cys Glu Lys Thr Arg Gly Phe
225         230         235         240
Val Ser Arg Asp Phe Val Ser Ser Ile Lys Gln Phe Phe Gln Tyr Gly
245         250         255
Ile Pro Ser Ala Ala Met Ile Cys Leu Glu Trp Trp Leu Phe Glu Ile
260         265         270
Leu Ile Leu Cys Ser Gly Leu Leu Pro Asn Pro Lys Leu Glu Thr Ser
275         280         285
Val Leu Ser Ile Cys Leu Thr Ile Glu Thr Leu His Tyr Val Ile Ser
290         295         300
Ala Gly Val Ala Ala Val Ser Thr Arg Val Ser Asn Asn Leu Gly
305         310         315         320
Ala Gly Asn Pro Gln Val Ala Arg Val Ser Val Leu Ala Gly Leu Cys
325         330         335
Leu Trp Ile Val Glu Ser Ala Phe Phe Ser Ile Leu Leu Phe Thr Cys
340         345         350
Arg Asn Ile Ile Gly Tyr Ala Phe Ser Asn Ser Lys Glu Val Leu Asp
355         360         365
Tyr Val Ala Asp Leu Thr Pro Leu Leu Cys Leu Ser Phe Ile Leu Asp
370         375         380
Gly Phe Thr Ala Val Leu Asn Gly Val Ala Arg Gly Ser Gly Trp Gln
385         390         395         400
His Ile Gly Ala Trp Asn Asn Thr Val Ser Tyr Tyr Leu Val Gly Ala
405         410         415
Pro Val Gly Ile Tyr Leu Ala Phe Ser Arg Glu Leu Asn Gly Lys Gly
420         425         430
Leu Trp Cys Gly Val Val Val Gly Ser Thr Val Gln Ala Thr Ile Leu
435         440         445
Ala Ile Val Thr Ala Ser Ile Asn Trp Lys Glu Gln Ala Glu Lys Ala
450         455         460
Arg Lys Arg Ile Val Ser Thr Glu Asn Arg Leu Ala
465         470         475

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<210> 45

<211> 485

<212> PRT

<213> Arabidopsis thaliana

<400> 45

```

Met Asp Ser Ala Glu Lys Gly Leu Leu Val Val Ser Asp Arg Glu Glu
1          5          10          15
Val Asn Lys Lys Asp Gly Phe Leu Arg Glu Thr Lys Lys Leu Ser Tyr
20         25         30
Ile Ala Gly Pro Met Ile Ala Val Asn Ser Ser Met Tyr Val Leu Gln
35         40         45
Val Ile Ser Ile Met Met Val Gly His Leu Gly Glu Leu Phe Leu Ser

```

```

50          55          60
Ser Thr Ala Ile Ala Val Ser Phe Cys Ser Val Thr Gly Phe Ser Val
65          70          75          80
Val Phe Gly Leu Ala Ser Ala Leu Glu Thr Leu Cys Gly Gln Ala Asn
85          90          95
Gly Ala Lys Gln Tyr Glu Lys Leu Gly Val His Thr Tyr Thr Gly Ile
100         105         110
Val Ser Leu Phe Leu Val Cys Ile Pro Leu Ser Leu Leu Trp Thr Tyr
115         120         125
Ile Gly Asp Ile Leu Ser Leu Ile Gly Gln Asp Ala Met Val Ala Gln
130         135         140
Glu Ala Gly Lys Phe Ala Thr Trp Leu Ile Pro Ala Leu Phe Gly Tyr
145         150         155         160
Ala Thr Leu Gln Pro Leu Val Arg Phe Phe Gln Ala Gln Ser Leu Ile
165         170         175
Leu Pro Leu Val Met Ser Ser Val Ser Ser Leu Cys Ile His Ile Val
180         185         190
Leu Cys Trp Ser Leu Val Phe Lys Phe Gly Leu Gly Ser Leu Gly Ala
195         200         205
Ala Ile Ala Ile Gly Val Ser Tyr Trp Leu Asn Val Thr Val Leu Gly
210         215         220
Leu Tyr Met Thr Phe Ser Ser Ser Cys Ser Lys Ser Arg Ala Thr Ile
225         230         235         240
Ser Met Ser Leu Phe Glu Gly Met Gly Glu Phe Phe Arg Phe Gly Ile
245         250         255
Pro Ser Ala Ser Met Ile Cys Leu Glu Trp Trp Ser Phe Glu Phe Leu
260         265         270
Val Leu Leu Ser Gly Ile Leu Pro Asn Pro Lys Leu Glu Ala Ser Val
275         280         285
Leu Ser Val Cys Leu Ser Thr Gln Ser Ser Leu Tyr Gln Ile Pro Glu
290         295         300
Ser Leu Gly Ala Ala Ala Ser Thr Arg Val Ala Asn Glu Leu Gly Ala
305         310         315         320
Gly Asn Pro Lys Gln Ala Arg Met Ala Val Tyr Thr Ala Met Val Ile
325         330         335
Thr Gly Val Glu Ser Ile Met Val Gly Ala Ile Val Phe Gly Ala Arg
340         345         350
Asn Val Phe Gly Tyr Leu Phe Ser Ser Glu Thr Glu Val Val Asp Tyr
355         360         365
Val Lys Ser Met Ala Pro Leu Ser Leu Ser Val Ile Phe Asp Ala
370         375         380
Leu His Ala Ala Leu Ser Gly Val Ala Arg Gly Ser Gly Arg Gln Asp
385         390         395         400
Ile Gly Ala Tyr Val Asn Leu Ala Ala Tyr Tyr Leu Phe Gly Ile Pro
405         410         415
Thr Ala Ile Leu Leu Ala Phe Gly Phe Lys Met Arg Gly Arg Gly Leu
420         425         430
Trp Ile Gly Ile Thr Val Gly Ser Cys Val Gln Ala Val Leu Leu Gly
435         440         445
Leu Ile Val Ile Leu Thr Asn Trp Lys Lys Gln Ala Arg Lys Ala Arg
450         455         460
Glu Arg Val Met Gly Asp Glu Tyr Glu Glu Lys Glu Ser Glu Glu Glu
465         470         475         480
His Glu Tyr Ile Ser
485

```

<210> 46

<211> 481

<212> PRT

<213> Arabidopsis thaliana

<400> 46

```

Met Gly Asp Ala Glu Ser Thr Lys Asp Arg Leu Leu Leu Pro Val Glu
1          5          10          15
Arg Val Glu Asn Val Thr Trp Ser Asp Leu Arg Asp Gly Ser Phe Thr

```

	20		25		30										
Val	Glu	Leu	Lys	Arg	Leu	Ile	Phe	Phe	Ala	Ala	Pro	Met	Ala	Ala	Val
	35						40					45			
Val	Ile	Ala	Gln	Phe	Met	Leu	Gln	Ile	Val	Ser	Met	Met	Met	Val	Gly
	50						55				60				
His	Leu	Gly	Asn	Leu	Ser	Leu	Ala	Ser	Ala	Ser	Leu	Ala	Ser	Ser	Phe
	65						70				75				80
Cys	Asn	Val	Thr	Gly	Phe	Ser	Phe	Ile	Ile	Gly	Leu	Ser	Cys	Ala	Leu
			85							90				95	
Asp	Thr	Leu	Ser	Gly	Gln	Ala	Tyr	Gly	Ala	Lys	Leu	Tyr	Arg	Lys	Leu
			100							105				110	
Gly	Val	Gln	Thr	Tyr	Thr	Ala	Met	Phe	Cys	Leu	Ala	Leu	Val	Cys	Leu
			115							120				125	
Pro	Leu	Ser	Leu	Ile	Trp	Phe	Asn	Met	Glu	Lys	Leu	Leu	Leu	Ile	Leu
			130							135				140	
Gly	Gln	Asp	Pro	Ser	Ile	Ala	His	Glu	Ala	Gly	Lys	Tyr	Ala	Thr	Trp
			145							150				155	160
Leu	Ile	Pro	Gly	Leu	Phe	Ala	Tyr	Ala	Val	Leu	Gln	Pro	Leu	Thr	Arg
			165							170				175	
Tyr	Phe	Gln	Asn	Gln	Ser	Leu	Ile	Thr	Pro	Leu	Leu	Ile	Thr	Ser	Tyr
			180							185				190	
Val	Val	Phe	Cys	Ile	His	Val	Pro	Leu	Cys	Trp	Phe	Leu	Val	Tyr	Asn
			195							200				205	
Ser	Gly	Leu	Gly	Asn	Leu	Gly	Gly	Ala	Leu	Ala	Ile	Ser	Leu	Ser	Asn
			210							215				220	
Trp	Leu	Tyr	Ala	Ile	Phe	Leu	Gly	Ser	Phe	Met	Tyr	Tyr	Ser	Ser	Ala
			225							230				235	240
Cys	Ser	Glu	Thr	Arg	Ala	Pro	Leu	Ser	Met	Glu	Ile	Phe	Asp	Gly	Ile
			245							250				255	
Gly	Glu	Phe	Phe	Lys	Tyr	Ala	Leu	Pro	Ser	Ala	Ala	Met	Ile	Cys	Leu
			260							265				270	
Glu	Trp	Trp	Ser	Tyr	Glu	Leu	Ile	Ile	Leu	Leu	Ser	Gly	Leu	Leu	Pro
			275							280				285	
Asn	Pro	Gln	Leu	Glu	Thr	Ser	Val	Leu	Ser	Val	Cys	Leu	Gln	Thr	Ile
			290							295				300	
Ser	Thr	Met	Tyr	Ser	Ile	Pro	Leu	Ala	Ile	Ala	Ala	Ala	Ala	Ser	Thr
			305							310				315	320
Arg	Ile	Ser	Asn	Glu	Leu	Gly	Ala	Gly	Asn	Ser	Arg	Ala	Ala	His	Ile
			325							330				335	
Val	Val	Tyr	Ala	Ala	Met	Ser	Leu	Ala	Val	Ile	Asp	Ala	Leu	Ile	Val
			340							345				350	
Ser	Met	Ser	Leu	Leu	Ile	Gly	Arg	Asn	Leu	Phe	Gly	His	Ile	Phe	Ser
			355							360				365	
Ser	Asp	Lys	Glu	Thr	Ile	Asp	Tyr	Val	Ala	Lys	Met	Ala	Pro	Leu	Val
			370							375				380	
Ser	Ile	Ser	Leu	Met	Leu	Asp	Ala	Leu	Gln	Gly	Val	Leu	Ser	Gly	Ile
			385							390				395	400
Ala	Arg	Gly	Cys	Gly	Trp	Gln	His	Ile	Gly	Ala	Tyr	Ile	Asn	Leu	Gly
			405							410				415	
Ala	Phe	Tyr	Leu	Trp	Gly	Ile	Pro	Ile	Ala	Ala	Ser	Leu	Ala	Phe	Trp
			420							425				430	
Ile	His	Leu	Lys	Gly	Val	Gly	Leu	Trp	Ile	Gly	Ile	Gln	Ala	Gly	Ala
			435							440				445	
Val	Leu	Gln	Thr	Leu	Leu	Ala	Leu	Val	Thr	Gly	Cys	Thr	Asn	Trp	
			450							455				460	
Glu	Ser	Gln	Ala	Asp	Lys	Ala	Arg	Asn	Arg	Met	Ala	Leu	Ala	Tyr	Gly
			465							470				475	480
Thr															

<210> 47

<211> 482

<212> PRT

<213> Arabidopsis thaliana

<400> 47

```

Met Gly Asp Ala Glu Ser Thr Ser Lys Thr Ser Leu Leu Leu Pro Val
1      5      10      15
Glu Arg Val Glu Asn Val Thr Trp Arg Asp Leu Arg Asp Gly Leu Phe
20      25      30
Thr Ala Glu Leu Lys Arg Leu Ile Cys Phe Ala Ala Pro Met Ala Ala
35      40      45
Val Val Ile Ala Gln Phe Met Leu Gln Ile Ile Ser Met Val Met Val
50      55      60
Gly His Leu Gly Asn Leu Ser Leu Ala Ser Ala Ser Leu Ala Ser Ser
65      70      75      80
Phe Cys Asn Val Thr Gly Phe Ser Phe Ile Val Gly Leu Ser Cys Ala
85      90      95
Leu Asp Thr Leu Ser Gly Gln Ala Tyr Gly Ala Lys Leu Tyr Arg Lys
100     105     110
Val Gly Val Gln Thr Tyr Thr Ala Met Phe Cys Leu Ala Leu Val Cys
115     120     125
Leu Pro Leu Thr Leu Ile Trp Leu Asn Met Glu Thr Leu Leu Val Phe
130     135     140
Leu Gly Gln Asp Pro Ser Ile Ala His Glu Ala Gly Arg Tyr Ala Ala
145     150     155     160
Cys Leu Ile Pro Gly Leu Phe Ala Tyr Ala Val Leu Gln Pro Leu Thr
165     170     175
Arg Tyr Phe Gln Asn Gln Ser Met Ile Thr Pro Leu Leu Ile Thr Ser
180     185     190
Cys Phe Val Phe Cys Leu His Val Pro Leu Cys Trp Leu Leu Val Tyr
195     200     205
Lys Ser Gly Leu Gly Asn Leu Gly Gly Ala Leu Ala Leu Ser Phe Ser
210     215     220
Asn Cys Leu Tyr Thr Ile Ile Leu Gly Ser Leu Met Cys Phe Ser Ser
225     230     235     240
Ala Cys Ser Glu Thr Arg Ala Pro Leu Ser Met Glu Ile Phe Asp Gly
245     250     255
Ile Gly Glu Phe Phe Arg Tyr Ala Leu Pro Ser Ala Ala Met Ile Cys
260     265     270
Leu Glu Trp Trp Ser Tyr Glu Leu Ile Ile Leu Leu Ser Gly Leu Leu
275     280     285
Pro Asn Pro Gln Leu Glu Thr Ser Val Leu Ser Val Cys Leu Gln Thr
290     295     300
Thr Ala Thr Val Tyr Ser Ile His Leu Ala Ile Ala Ala Ala Ser
305     310     315     320
Thr Arg Ile Ser Asn Glu Leu Gly Ala Gly Asn Ser Arg Ala Ala Asn
325     330     335
Ile Val Val Tyr Ala Ala Met Ser Leu Ala Val Val Glu Ile Leu Ile
340     345     350
Leu Ser Thr Ser Leu Leu Val Gly Arg Asn Val Phe Gly His Val Phe
355     360     365
Ser Ser Asp Lys Glu Thr Ile Asp Tyr Val Ala Lys Met Ala Pro Leu
370     375     380
Val Ser Ile Ser Leu Ile Leu Asp Gly Leu Gln Gly Val Leu Ser Gly
385     390     395     400
Ile Ala Arg Gly Cys Gly Trp Gln His Ile Gly Ala Tyr Ile Asn Leu
405     410     415
Gly Ala Phe Tyr Leu Trp Gly Ile Pro Ile Ala Ala Ser Leu Ala Phe
420     425     430
Trp Ile His Leu Lys Gly Val Gly Leu Trp Ile Gly Ile Gln Ala Gly
435     440     445
Ala Val Leu Gln Thr Leu Leu Leu Thr Leu Val Thr Gly Cys Thr Asn
450     455     460
Trp Glu Ser Gln Ala Asp Lys Ala Arg Asn Arg Met Ala Leu Ala Tyr
465     470     475     480
Gly Thr

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<210> 48

<211> 487

<212> PRT

<213> Arabidopsis thaliana

<400> 48

```

Met Glu Asp Ala Glu Ser Thr Thr Lys Asp Pro Val Asp Arg Val Glu
1      5      10      15
Lys Val Thr Trp Arg Asp Leu Gln Asp Gly Ser Phe Thr Ala Glu Leu
20      25      30
Lys Lys Leu Ile Cys Phe Ala Ala Pro Met Ala Ala Val Val Ile Thr
35      40      45
Gln Ser Met Leu Gln Ile Ile Thr Met Val Ile Val Gly His Leu Gly
50      55      60
Arg Leu Ser Leu Ala Ser Ala Ser Phe Ala Ile Ser Phe Cys Asn Val
65      70      75      80
Thr Gly Phe Ser Phe Ile Met Gly Leu Ser Cys Ala Leu Asp Thr Leu
85      90      95
Ser Gly Gln Ala Tyr Gly Ala Lys Leu Tyr Arg Lys Leu Gly Val Gln
100     105     110
Ala Tyr Thr Ala Met Phe Cys Leu Thr Leu Val Cys Leu Pro Leu Ser
115     120     125
Leu Leu Trp Phe Asn Met Gly Lys Leu Leu Val Ile Leu Gly Gln Asp
130     135     140
Pro Ser Ile Ala His Glu Ala Gly Arg Phe Ala Ala Trp Leu Ile Pro
145     150     155     160
Gly Leu Phe Ala Tyr Ala Val Leu Gln Pro Leu Thr Arg Tyr Phe Lys
165     170     175
Asn Gln Ser Leu Ile Thr Pro Leu Leu Ile Thr Ser Cys Val Val Phe
180     185     190
Cys Leu His Val Pro Leu Cys Trp Leu Leu Val Tyr Lys Ser Gly Leu
195     200     205
Asp His Ile Gly Gly Ala Leu Ala Leu Ser Leu Ser Tyr Trp Leu Tyr
210     215     220
Ala Ile Phe Leu Gly Ser Phe Met Tyr Phe Ser Ser Ala Cys Ser Glu
225     230     235     240
Thr Arg Ala Pro Leu Thr Met Glu Ile Phe Glu Gly Val Arg Glu Phe
245     250     255
Ile Lys Tyr Ala Leu Pro Ser Ala Ala Met Leu Cys Leu Glu Trp Trp
260     265     270
Ser Tyr Glu Leu Ile Ile Leu Leu Ser Gly Leu Leu Pro Asn Pro Gln
275     280     285
Leu Glu Thr Ser Val Leu Ser Val Cys Leu Gln Thr Leu Ser Met Thr
290     295     300
Tyr Ser Ile Pro Leu Ala Ile Ala Ala Ala Ser Thr Arg Ile Ser
305     310     315     320
Asn Glu Leu Gly Ala Gly Asn Ser Arg Ala Ala His Ile Val Val Tyr
325     330     335
Ala Ala Met Ser Leu Ala Val Val Asp Ala Leu Met Val Gly Thr Ser
340     345     350
Leu Leu Ala Gly Lys Asn Leu Leu Gly Gln Val Phe Ser Ser Asp Lys
355     360     365
Asn Thr Ile Asp Tyr Val Ala Lys Met Ala Pro Leu Val Ser Ile Ser
370     375     380
Leu Ile Leu Asp Ser Leu Gln Gly Val Leu Ser Gly Val Ala Ser Gly
385     390     395     400
Cys Gly Trp Gln His Ile Gly Ala Tyr Ile Asn Phe Gly Ala Phe Tyr
405     410     415
Leu Trp Gly Ile Pro Ile Ala Ala Ser Leu Ala Phe Trp Val His Leu
420     425     430
Lys Gly Val Gly Leu Trp Ile Gly Ile Ile Ala Gly Ala Val Leu Gln
435     440     445
Thr Leu Leu Leu Ala Leu Val Thr Gly Cys Ile Asn Trp Glu Asn Gln
450     455     460
Ala Arg Glu Ala Arg Lys Arg Met Ala Val Ala His Glu Ser Glu Leu
465     470     475     480

```

Thr Glu Ser Glu Leu Pro Phe
485

<210> 49

<211> 487

<212> PRT

<213> Arabidopsis thaliana

<400> 49

```

Met Gln Asp Ala Glu Arg Thr Thr Asn Asp Pro Val Asp Arg Ile Glu
1      5      10      15
Lys Val Thr Trp Arg Asp Leu Gln Asp Gly Ser Phe Thr Ala Glu Leu
20      25      30
Lys Arg Leu Ile Cys Phe Ala Ala Pro Met Ala Val Val Ile Ile
35      40      45
Gln Phe Met Ile Gln Ile Ile Ser Met Val Met Val Gly His Leu Gly
50      55      60
Arg Leu Ser Leu Ala Ser Ala Ser Phe Ala Val Ser Phe Cys Asn Val
65      70      75      80
Thr Gly Phe Ser Phe Ile Ile Gly Leu Ser Cys Ala Leu Asp Thr Leu
85      90      95
Ser Gly Gln Ala Tyr Gly Ala Lys Leu Tyr Arg Lys Leu Gly Val Gln
100     105     110
Ala Tyr Thr Ala Met Phe Cys Leu Thr Leu Val Cys Leu Pro Leu Ser
115     120     125
Leu Leu Trp Phe Asn Met Gly Lys Leu Ile Val Ile Leu Gly Gln Asp
130     135     140
Pro Ala Ile Ala His Glu Ala Gly Arg Tyr Ala Ala Trp Leu Ile Pro
145     150     155     160
Gly Leu Phe Ala Tyr Ala Val Leu Gln Pro Leu Ile Arg Tyr Phe Lys
165     170     175
Asn Gln Ser Leu Ile Thr Pro Leu Leu Val Thr Ser Ser Val Val Phe
180     185     190
Cys Ile His Val Pro Leu Cys Trp Leu Leu Val Tyr Lys Ser Gly Leu
195     200     205
Gly His Ile Gly Gly Ala Leu Ala Leu Ser Leu Ser Tyr Trp Leu Tyr
210     215     220
Ala Ile Phe Leu Gly Ser Phe Met Tyr Tyr Ser Ser Ala Cys Ser Glu
225     230     235     240
Thr Arg Ala Pro Leu Thr Met Glu Ile Phe Glu Gly Val Arg Glu Phe
245     250     255
Ile Lys Tyr Ala Leu Pro Ser Ala Ala Met Leu Cys Leu Glu Trp Trp
260     265     270
Ser Tyr Glu Leu Ile Ile Leu Leu Ser Gly Leu Leu Pro Asn Pro Gln
275     280     285
Leu Glu Thr Ser Val Leu Ser Ile Cys Phe Glu Thr Leu Ser Ile Thr
290     295     300
Tyr Ser Ile Pro Leu Ala Ile Ala Ala Ala Ser Thr Arg Ile Ser
305     310     315     320
Asn Glu Leu Gly Ala Gly Asn Ser Arg Ala Ala His Ile Val Val Tyr
325     330     335
Ala Ala Met Ser Leu Ala Val Met Asp Ala Leu Met Val Ser Met Ser
340     345     350
Leu Leu Ala Gly Arg His Val Phe Gly His Val Phe Ser Ser Asp Lys
355     360     365
Lys Thr Ile Glu Tyr Val Ala Lys Met Ala Pro Leu Val Ser Ile Ser
370     375     380
Ile Ile Leu Asp Ser Leu Gln Gly Val Leu Ser Gly Val Ala Ser Gly
385     390     395     400
Cys Gly Trp Gln His Ile Gly Ala Tyr Ile Asn Phe Gly Ala Phe Tyr
405     410     415
Leu Trp Gly Ile Pro Ile Ala Ala Ser Leu Ala Phe Trp Val His Leu
420     425     430
Lys Gly Val Gly Leu Trp Ile Gly Ile Leu Ala Gly Ala Val Leu Gln
435     440     445

Thr Leu Leu Leu Ala Leu Val Thr Gly Cys Thr Asn Trp Lys Thr Gln
450     455     460
Ala Arg Glu Ala Arg Glu Arg Met Ala Val Ala His Glu Ser Glu Leu
465     470     475     480
Thr Glu Ser Glu Leu Pro Ile
485

```

<210> 50

<211> 1434

<212> DNA

<213> Arabidopsis thaliana

<400> 50

```

atggaagatc cactttttatt gggagatgat cagttaatca ctagaaacct caagtcaacg      60
ccgacatggt ggatgaattt tacggcggag ctgaagaacg tcagctctat ggcggcgccct      120
atggccacgg tgacagtgtc tcaatatcta ttgcccgta tctcggtcat ggtcgccggc      180
cactgcgggtg aactccagct gtctggtgtc actccttgcca ctgctttcgc aaacgtctcc      240
ggcttcggga tcatgtatgg tttagtgggt gcacttgaaa ctctatgtgg ccaagcttat      300
ggagcaaaac aatacactaa aatcggaact tacactttct ctgcaatagt ctcaaacgta      360
cctatagtgt ttctcatatc gattctctgg tttacatgg acaaaactct tgtttcactt      420
ggacaagatc ctgacatctc caagtagct ggttcttacg cggttgtct tataccggca      480
ttgttagctc aagcagtgca acaacctttg actcggtttc tccagactca gggtttggtt      540
cttctcttc tctactgtgc cataaccacc cttttattcc atataccagt ttgtttgatt      600
ctggtttacg cgtttggtct tgggaagcaat ggagcgcct tggctattgg tttgtcttac      660
tggtttaatg tcttgattct tgccttatat gtgagatttt caagcgcttg cgagaagact      720
cgcggtttg tatcogatga tttcgtgttg agtgtcaagc agttttttca gtatgggata      780
ccatcagcag caatgacaac catagaatgg tctgtgtttg agtccttat ctatcttca      840
ggactctctc caaaccggaa actcgagacc tctgttcttt ccatttgtct tacaacatca      900
tctctccact gtgtcattcc aatgggtatc ggggctgctg gaagcacacg gatttcaaac      960
gaattgggag cgggaaatcc ggaggttgct aggcctggcag tgtttgcggg tattttcctt      1020
tggttcctag aggcctacat ttgtagcaca cttctgttca cttgcaaaaa tatttttggc      1080
tacgcgttca gcaatagcaa agaagttgtg gactatgtca cggagctatc ttcgctgctt      1140
tgtctttcat ttatggtcga tggattttct tcagtgcttg atggggttgc taggggaagt      1200
gggtggcaaa atattggagc ttgggcaaat gtggtggctt actatctcct aggagctcct      1260
gttggatttt tcttaggatt ttggggtcat atgaacggca aagggtctatg gattgggtgtg      1320
atcgttgggt ccactgtcca agggatcata ctagctatag tcaactgcttg cctgagtttg      1380
gaggagcagg ctgccaaggc cagagaaaga atagttggaa gaacattgga gtga      1434

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<210> 51

<211> 477

<212> PRT

<213> Arabidopsis thaliana

<400> 51

```

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

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```

      165      170      175
Gln Gly Leu Val Leu Pro Leu Leu Tyr Cys Ala Ile Thr Thr Leu Leu
180      185      190
Phe His Ile Pro Val Cys Leu Ile Leu Val Tyr Ala Phe Gly Leu Gly
195      200      205
Ser Asn Gly Ala Ala Leu Ala Ile Gly Leu Ser Tyr Trp Phe Asn Val
210      215      220
Leu Ile Leu Ala Leu Tyr Val Arg Phe Ser Ser Ala Cys Glu Lys Thr
225      230      235      240
Arg Gly Phe Val Ser Asp Asp Phe Val Leu Ser Val Lys Gln Phe Phe
245      250      255
Gln Tyr Gly Ile Pro Ser Ala Ala Met Thr Thr Ile Glu Trp Ser Leu
260      265      270
Phe Glu Leu Leu Ile Leu Ser Ser Gly Leu Leu Pro Asn Pro Lys Leu
275      280      285
Glu Thr Ser Val Leu Ser Ile Cys Leu Thr Thr Ser Ser Leu His Cys
290      295      300
Val Ile Pro Met Gly Ile Gly Ala Ala Gly Ser Thr Arg Ile Ser Asn
305      310      315      320
Glu Leu Gly Ala Gly Asn Pro Glu Val Ala Arg Leu Ala Val Phe Ala
325      330      335
Gly Ile Phe Leu Trp Phe Leu Glu Ala Thr Ile Cys Ser Thr Leu Leu
340      345      350
Phe Thr Cys Lys Asn Ile Phe Gly Tyr Ala Phe Ser Asn Ser Lys Glu
355      360      365
Val Val Asp Tyr Val Thr Glu Leu Ser Ser Leu Leu Cys Leu Ser Phe
370      375      380
Met Val Asp Gly Phe Ser Ser Val Leu Asp Gly Val Ala Arg Gly Ser
385      390      395      400
Gly Trp Gln Asn Ile Gly Ala Trp Ala Asn Val Val Ala Tyr Tyr Leu
405      410      415
Leu Gly Ala Pro Val Gly Phe Phe Leu Gly Phe Trp Gly His Met Asn
420      425      430
Gly Lys Gly Leu Trp Ile Gly Val Ile Val Gly Ser Thr Ala Gln Gly
435      440      445
Ile Ile Leu Ala Ile Val Thr Ala Cys Leu Ser Trp Glu Glu Gln Ala
450      455      460
Ala Lys Ala Arg Glu Arg Ile Val Gly Arg Thr Leu Glu
465      470      475

```

<210> 52

<211> 485

<212> PRT

<213> Glycine max

<400> 52

```

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

```

```

145          150          155          160
Met Gln Pro Phe Val Arg Tyr Phe Gln Met Gln Ser Leu Leu Leu Pro
165          170          175
Met Leu Ile Ser Ser Cys Val Thr Leu Cys Ile His Ile Pro Leu Cys
180          185          190
Trp Ala Leu Val Phe Gln Thr Gly Met Asn Asn Ile Gly Gly Ala Leu
195          200          205
Ala Met Ser Ile Ser Ile Trp Leu Asn Val Thr Phe Leu Gly Leu Tyr
210          215          220
Met Arg Tyr Ser Pro Ala Cys Ala Lys Thr Arg Ala Pro Ile Ser Met
225          230          235          240
Glu Leu Phe Gln Gly Ile Trp Glu Phe Phe Arg Phe Ala Ile Pro Ser
245          250          255
Ala Val Met Ile Cys Leu Glu Trp Trp Ser Phe Glu Leu Leu Ile Leu
260          265          270
Leu Ser Gly Leu Leu Pro Asn Pro Gln Leu Glu Thr Ser Val Leu Ser
275          280          285
Ile Cys Leu Asn Thr Ile Ser Thr Leu Phe Ser Ile Pro Phe Gly Ile
290          295          300
Ala Ala Ala Ala Ser Thr Arg Ile Ser Asn Glu Leu Gly Ala Gly Asn
305          310          315          320
Pro His Ala Ala His Val Ala Val Leu Ala Ala Met Ser Phe Ala Ile
325          330          335
Met Glu Thr Ala Ile Val Ser Gly Thr Leu Phe Val Cys Arg His Asp
340          345          350
Phe Gly Tyr Ile Phe Ser Asn Glu Lys Glu Val Val Asp Tyr Val Thr
355          360          365
Val Met Ala Pro Leu Ile Cys Ile Ser Val Ile Leu Asp Ser Ile Gln
370          375          380
Gly Val Leu Ala Gly Val Ala Arg Gly Cys Gly Trp Gln His Ile Gly
385          390          395          400
Val Tyr Val Asn Leu Gly Ala Phe Tyr Leu Cys Gly Ile Pro Val Ala
405          410          415
Ala Thr Leu Ala Phe Leu Ala Lys Met Arg Gly Lys Gly Leu Trp Ile
420          425          430
Gly Val Gln Val Gly Ala Phe Val Gln Cys Ile Leu Phe Ser Thr Ile
435          440          445
Thr Ser Cys Ile Asn Trp Glu Gln Gln Cys Leu Lys Phe Phe Ser Gln
450          455          460
Ser Trp Val Trp Ser Thr Asn Met Phe His Pro Ser Ala Val Ile Ile
465          470          475          480
Lys Arg Ile Gln Ala
485

```

<210> 53

<211> 480

<212> PRT

<213> Glycine max

<400> 53

```

Met Glu Glu Asn Leu Leu Val Leu Ala Lys Gly Ser Gly Glu Glu Gln
1          5          10          15
Lys Val Ala Trp Glu Gly Leu Gly Glu Glu Met Lys Arg Met Ile Asp
20          25          30
Ile Ala Gly Pro Met Val Val Val Thr Ala Ser Gln Arg Leu Leu Gln
35          40          45
Val Val Ser Val Met Met Val Gly His Leu Asn Asp Asp Leu Phe Leu
50          55          60
Ser Ser Ala Ala Leu Ala Ile Ser Leu Thr Ala Val Thr Gly Phe Ser
65          70          75          80
Phe Leu Met Gly Met Ala Ser Gly Leu Glu Thr Ile Cys Gly Gln Ala
85          90          95
Tyr Gly Ala Gln Gln His Lys Lys Ile Gly Val Gln Thr Tyr Thr Ala
100          105          110
Ile Phe Ala Leu Thr Phe Val Cys Leu Pro Phe Thr Phe Leu Trp Ile

```

```

      115      120      125
Asn Met Glu Lys Ile Leu Val Phe Ile Gly Gln Asp Pro Leu Ile Ala
130      135      140
Lys Glu Ala Gly Lys Phe Ile Ile Trp Leu Ile Pro Ala Leu Phe Ala
145      150      155      160
Tyr Ala Ile Leu Gln Pro Leu Val Arg Tyr Phe Gln Met Gln Ser Leu
165      170      175
Leu Leu Pro Met Leu Met Thr Ser Cys Val Thr Leu Cys Val His Ile
180      185      190
Pro Leu Cys Trp Val Leu Val Phe Lys Thr Arg Leu Asn Asn Val Gly
195      200      205
Gly Ala Leu Ala Met Ser Ile Ser Thr Trp Ser Asn Val Ile Phe Leu
210      215      220
Gly Leu Tyr Met Arg Tyr Ser Pro Arg Cys Ala Lys Thr Arg Ala Pro
225      230      235      240
Ile Ser Met Glu Leu Phe Gln Gly Leu Arg Glu Phe Phe Arg Phe Ala
245      250      255
Ile Pro Ser Ala Val Met Ile Cys Leu Glu Trp Trp Ser Phe Glu Leu
260      265      270
Ile Ile Leu Leu Ser Gly Leu Leu Leu Asn Pro Gln Leu Glu Thr Ser
275      280      285
Val Leu Ser Ile Cys Leu Asn Thr Thr Ser Ile Leu Tyr Ala Ile Pro
290      295      300
Phe Gly Ile Gly Ala Ala Ala Ser Thr Arg Ile Ser Asn Glu Leu Gly
305      310      315      320
Ala Gly Asn Pro His Gly Ala Cys Val Ser Val Leu Ala Ala Ile Ser
325      330      335
Phe Ala Ile Ile Glu Thr Thr Val Val Ser Gly Thr Leu Phe Ala Cys
340      345      350
Arg His Val Phe Gly Tyr Val Phe Ser Asn Glu Lys Glu Val Val Asp
355      360      365
Tyr Val Thr Val Met Ala Pro Leu Val Cys Ile Ser Val Ile Leu Asp
370      375      380
Asn Ile Gln Gly Val Leu Ala Gly Val Ala Arg Gly Cys Gly Trp Gln
385      390      395      400
His Ile Gly Val Tyr Val Asn Ile Gly Ala Phe Tyr Leu Cys Gly Ile
405      410      415
Pro Met Ala Ile Leu Leu Ser Phe Phe Ala Lys Met Arg Gly Lys Gly
420      425      430
Leu Trp Ile Gly Val Gln Val Gly Ser Phe Ala Gln Cys Val Leu Leu
435      440      445
Ser Thr Ile Thr Ser Cys Ile Asn Trp Glu Gln Gln Thr Ile Lys Ala
450      455      460
Arg Lys Arg Leu Phe Gly Ser Glu Phe Ser Ala Asp Asp Arg Leu Ile
465      470      475      480

```

<210> 54

<211> 454

<212> PRT

<213> Glycine max

<400> 54

```

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

```

```

      100      105      110
Gln Asp Pro Leu Ile Ala His Glu Ala Gly Asn Phe Ile Ile Trp Leu
      115      120      125
Leu Pro Ala Leu Phe Ala Tyr Ala Ile Leu Gln Pro Leu Val Arg Tyr
      130      135      140
Phe Gln Met Gln Ser Leu Leu Leu Pro Met Leu Ala Thr Ser Cys Val
      145      150      155      160
Thr Leu Cys Leu His Ile Pro Leu Cys Trp Ala Leu Val Phe Lys Thr
      165      170      175
Glu Leu Ser Asn Val Gly Gly Ala Leu Ala Met Ser Ile Ser Ile Trp
      180      185      190
Leu Asn Val Ile Phe Leu Val Leu Tyr Met Arg Tyr Ser Pro Ala Cys
      195      200      205
Glu Lys Thr Arg Ala Pro Val Ser Met Glu Leu Phe Gln Gly Ile Trp
      210      215      220
Glu Phe Phe Arg Phe Ala Ile Pro Ser Ala Val Met Ile Cys Leu Glu
      225      230      235      240
Trp Trp Ser Phe Glu Leu Leu Ile Leu Leu Ser Gly Leu Leu Pro Asn
      245      250      255
Pro Gln Leu Glu Thr Ser Val Leu Ser Ile Cys Leu Asn Thr Ile Ser
      260      265      270
Thr Leu Tyr Ala Ile Ala Phe Gly Ile Ala Ala Ala Ser Thr Arg
      275      280      285
Ile Ser Asn Glu Leu Gly Ala Gly Asn Pro His Ser Ala Arg Val Ala
      290      295      300
Val Leu Ala Ser Met Ser Phe Ala Ile Met Glu Ala Thr Ile Ile Ser
      305      310      315      320
Gly Ile Leu Phe Val Cys Arg His Val Phe Gly Tyr Thr Phe Ser Asn
      325      330      335
Lys Lys Glu Val Val Asp Tyr Val Thr Val Met Ala Pro Leu Val Cys
      340      345      350
Ile Ser Val Ile Leu Asp Asn Ile Gln Gly Val Leu Ala Gly Ile Ala
      355      360      365
Arg Gly Cys Gly Trp Gln His Ile Gly Val Tyr Val Asn Leu Gly Ala
      370      375      380
Phe Tyr Leu Cys Gly Ile Pro Val Ala Ala Ser Leu Ala Phe Leu Ala
      385      390      395      400
Lys Met Ser Gly Lys Gly Leu Trp Ile Gly Leu Gln Val Gly Ala Phe
      405      410      415
Val Gln Cys Ala Leu Leu Ser Thr Val Thr Ser Cys Thr Asn Trp Glu
      420      425      430
Gln Gln Ala Met Lys Ala Arg Lys Arg Leu Phe Asp Ser Glu Ile Ser
      435      440      445
Ala Glu Asn Ile Leu Val
      450

```

<210> 55

<211> 493

<212> PRT

<213> Glycine max

<400> 55

```

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

```

```

      100      105      110
Thr Leu Leu Trp Val Tyr Leu Gly Lys Ile Leu Ile Phe Leu Gly Gln
      115      120      125
Asp Pro Leu Ile Ser Gln Glu Ala Gly Lys Phe Ala Leu Cys Met Ile
      130      135      140
Pro Ala Leu Phe Ala Tyr Ala Thr Leu Gln Ala Leu Val Arg Tyr Phe
      145      150      155      160
Leu Met Gln Ser Leu Thr Ser Pro Leu Phe Ile Ser Ser Ser Ile Thr
      165      170      175
Leu Cys Phe His Val Ala Phe Cys Trp Leu Leu Val Phe Lys Cys Gly
      180      185      190
Phe Gly Asn Leu Gly Ala Ala Phe Ser Ile Gly Thr Ser Tyr Trp Leu
      195      200      205
Asn Val Val Leu Leu Gly Leu Tyr Met Lys Phe Ser Thr Glu Cys Glu
      210      215      220
Lys Thr Arg Val Pro Ile Ser Met Glu Leu Phe His Gly Ile Gly Glu
      225      230      235      240
Phe Phe Arg Cys Ala Ile Pro Ser Ala Gly Met Ile Cys Leu Glu Trp
      245      250      255
Trp Ser Phe Glu Leu Leu Thr Leu Leu Ser Gly Leu Leu Pro Asn Pro
      260      265      270
Glu Leu Glu Thr Ser Val Leu Ser Ile Cys Leu Ser Val Thr Thr Thr
      275      280      285
Ile Tyr Thr Ile Pro Glu Ala Ile Gly Ser Ala Ala Ser Thr Arg Val
      290      295      300
Ser Asn Ala Leu Gly Ala Gly Ser Pro Gln Ser Ala Gln Leu Ser Val
      305      310      315      320
Ser Ala Ala Met Thr Leu Ala Ala Ser Ala Ala Ile Leu Val Ser Ser
      325      330      335
Ile Ile Phe Ala Cys Arg Gln Val Val Gly Tyr Val Phe Ser Ser Glu
      340      345      350
Leu Asp Val Val Asp Tyr Phe Thr Asp Met Val Pro Leu Leu Cys Leu
      355      360      365
Ser Val Ile Leu Asp Thr Leu His Gly Thr Leu Ser Gly Ile Ala Arg
      370      375      380
Gly Cys Gly Trp Gln His Leu Gly Ala Tyr Val Asn Leu Gly Ala Tyr
      385      390      395      400
Tyr Val Val Gly Ile Pro Ile Ala Ala Met Leu Gly Phe Trp Val Gln
      405      410      415
Leu Arg Gly Lys Gly Leu Trp Ile Gly Ile Leu Thr Gly Ala Phe Cys
      420      425      430
Gln Thr Val Met Leu Ser Leu Ile Thr Ser Cys Thr Asn Trp Glu Lys
      435      440      445
Gln Lys Leu Phe Phe Gln Ser Lys Lys Ser Ser Ile Leu Thr His Ala
      450      455      460
Val Leu Phe Ser Phe Glu Gln Ala Leu Leu Val Leu Val Leu Thr Glu
      465      470      475      480
Glu Tyr Ser Leu Leu Glu Cys Pro Glu Ile Ala Gly Asn
      485      490

```

<210> 56

<211> 448

<212> PRT

<213> Glycine max

<400> 56

```

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

```

```

65          70          75          80
Lys Phe Gly Gln Tyr Thr Tyr Thr Ala Val Ile Ser Leu Ser Leu Ile
85          90          95
Cys Phe Pro Ile Thr Ile Leu Trp Thr Phe Met Asp Lys Ile Leu Thr
100         105         110
Leu Leu Gly Gln Asp Pro Thr Ile Ser Leu Glu Ala Arg Lys Tyr Ala
115         120         125
Ile Trp Leu Ile Pro Ala Leu Phe Gly Ser Ala Ile Leu Lys Pro Leu
130         135         140
Thr Arg Phe Phe Gln Thr Gln Ser Leu Ile Ser Pro Met Ile Leu Thr
145         150         155
Ser Ala Ile Ala Leu Cys Phe His Gly Ala Thr Cys Trp Thr Leu Val
160         165         170
Phe Lys Leu Glu Leu Gly His Val Gly Ala Ala Ile Ser Phe Ser Leu
175         180         185
Cys Val Trp Phe Asn Val Met Leu Leu Ser Phe Val Arg Tyr Ser
190         195         200
Ser Ala Cys Glu Lys Thr Arg Ile Pro Phe Ser Lys Asn Ala Leu Val
205         210         215
Gly Val Gly Val Phe Phe Arg Phe Ala Val Pro Ala Ala Val Met Val
220         225         230
Cys Leu Lys Trp Trp Ala Cys Glu Ile Leu Val Leu Leu Ala Gly Leu
235         240         245
Phe Pro Asn Pro Lys Leu Glu Thr Ser Val Leu Ser Ile Trp Phe Val
250         255         260
Ser Gln Ser Asn Cys Met Val Ile Leu Phe Pro Leu Ala Asn Ile Ser
265         270         275
Ile Glu Ala Tyr Thr Arg Val Ser Asn Glu Leu Gly Ala Gly Asn Pro
280         285         290
Gln Ala Val Arg Val Ala Val Ser Ala Thr Met Phe Leu Ala Val Thr
295         300         305
Glu Gly Leu Ile Val Ser Ala Thr Leu Phe Gly Cys Arg His Leu Leu
310         315         320
Gly Tyr Ala Tyr Ser Asp Asp Arg Met Val Val His Tyr Val Ala Val
325         330         335
Met Thr Pro Leu Leu Cys Leu Ser Ile Phe Thr Asp Ser Leu Gln Gly
340         345         350
Val Leu Ser Gly Val Ala Arg Gly Ser Gly Trp Gln His Leu Gly Ala
355         360         365
Tyr Val Asn Leu Gly Ala Phe Tyr Leu Val Gly Ile Pro Val Gly Ile
370         375         380
Val Leu Gly Phe Val Ala His Leu Arg Ala Lys Gly Leu Trp Ile Gly
385         390         395
Ile Val Thr Gly Ser Ile Val Gln Ser Ile Leu Leu Ser Leu Val Thr
400         405         410
Ala Leu Thr Asn Trp Lys Lys Gln Lys Tyr Cys Met Phe Gly Val Asn
415         420         425
Ala Ser Gly Leu Glu Thr Ile Cys Gly Gln Ala Tyr Gly Gly Gln Gln
430         435         440         445

```

<210> 57

<211> 475

<212> PRT

<213> Glycine max

<400> 57

```

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

```

```

      85      90      95
Tyr Gln Arg Ile Gly Ile Gln Thr Tyr Thr Ala Ile Phe Ser Leu Ile
100      105      110
Leu Val Ser Ile Pro Val Ser Leu Leu Trp Ile Asn Met Glu Thr Ile
115      120      125
Leu Val Phe Ile Gly Gln Asp Pro Leu Ile Ser His Glu Ala Gly Lys
130      135      140
Phe Thr Ile Trp Leu Val Pro Ala Leu Phe Ala Tyr Ala Ile Leu Gln
145      150      155      160
Pro Leu Val Arg Tyr Phe Gln Ile Gln Ser Leu Leu Pro Met Phe
165      170      175
Ala Ser Ser Cys Val Thr Leu Ile Ile His Val Pro Leu Cys Trp Ala
180      185      190
Leu Val Phe Lys Thr Ser Leu Ser Asn Val Gly Gly Ala Leu Ala Val
195      200      205
Ser Ile Ser Ile Trp Ser Asn Val Ile Phe Leu Val Leu Tyr Met Arg
210      215      220
Tyr Ser Ser Ala Cys Ala Lys Thr Arg Ala Pro Ile Ser Met Glu Leu
225      230      235      240
Phe Lys Gly Met Trp Glu Phe Phe Arg Phe Ala Ile Pro Ser Ala Val
245      250      255
Met Val Cys Leu Glu Trp Trp Ser Tyr Glu Leu Leu Val Leu Leu Ser
260      265      270
Gly Leu Leu Pro Asn Pro Gln Leu Glu Thr Ser Val Leu Ser Val Cys
275      280      285
Leu Asn Thr Ile Ala Thr Leu Tyr Thr Ile Pro Phe Gly Ile Gly Ala
290      295      300
Ala Ala Ser Thr Arg Val Ser Asn Glu Leu Gly Ala Gly Asn Ser His
305      310      315      320
Ala Ala Arg Val Ala Val Leu Ala Ala Met Ser Leu Ala Val Ile Glu
325      330      335
Thr Ser Ile Val Ser Ala Thr Leu Phe Ala Cys Arg Asn Val Phe Gly
340      345      350
Tyr Ile Phe Ser Asn Glu Lys Glu Val Val Asp Tyr Val Thr Ala Met
355      360      365
Ala Pro Leu Val Cys Ile Ser Val Ile Leu Asp Ser Ile Gln Gly Val
370      375      380
Leu Thr Gly Ile Ala Arg Gly Cys Gly Trp Gln His Leu Gly Val Tyr
385      390      395      400
Val Asn Leu Gly Ala Phe Tyr Leu Cys Gly Ile Pro Met Ala Ala Leu
405      410      415
Leu Ala Phe Leu Val Arg Leu Gly Gly Lys Gly Leu Trp Ile Gly Ile
420      425      430
Gln Ser Gly Ala Phe Val Gln Cys Ile Leu Leu Ser Ile Ile Thr Gly
435      440      445
Cys Ile Asn Trp Glu Lys Gln Ala Ile Lys Ala Arg Lys Arg Leu Phe
450      455      460
Asp Glu Lys Ile Ser Ala Asp Asn Ile Leu Val
465      470      475

```

<210> 58

<211> 480

<212> PRT

<213> Glycine max

<400> 58

```

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

```

```

65          70          75          80
Ala Gly Gly Leu Glu Thr Leu Gly Gly Gln Ala Phe Gly Ala Gly Gln
85
Tyr Glu Lys Phe Gly Gln Tyr Thr Tyr Thr Ala Val Ile Ser Leu Ser
100
Leu Ile Cys Phe Pro Ile Thr Ile Leu Trp Thr Phe Met Asp Lys Ile
115
Leu Thr Leu Leu Gly Gln Asp Pro Thr Ile Ser Leu Glu Ala Arg Lys
130
Tyr Ala Ile Trp Leu Ile Pro Ala Leu Phe Gly Ser Ala Ile Leu Lys
145
Pro Leu Thr Arg Phe Phe Gln Thr Gln Ser Leu Ile Ser Pro Met Ile
165
Leu Thr Ser Ala Ile Ala Leu Cys Phe His Gly Ala Thr Cys Trp Thr
180
Leu Val Phe Lys Leu Glu Leu Gly His Val Gly Ala Ala Ile Ser Phe
195
Ser Leu Cys Val Trp Phe Asn Val Met Leu Leu Leu Ser Phe Val Arg
210
Tyr Ser Ser Ala Cys Glu Lys Thr Arg Ile Pro Phe Ser Lys Asn Ala
225
Leu Val Gly Val Gly Asp Phe Phe Arg Phe Ala Val Pro Ala Ala Val
245
Met Val Cys Leu Lys Trp Trp Ala Cys Glu Ile Leu Val Leu Leu Ala
260
Gly Leu Phe Pro Asn Pro Lys Leu Glu Thr Ser Val Leu Ser Ile Cys
275
Leu Thr Ile Ser Thr Leu His Phe Thr Ile Pro Tyr Gly Phe Gly Ala
290
Ala Ala Ser Thr Arg Val Ser Asn Glu Leu Gly Ala Gly Asn Pro Gln
305
Ala Val Arg Val Ala Val Ser Ala Thr Met Phe Leu Ala Val Thr Glu
325
Gly Leu Ile Val Ser Ala Thr Leu Phe Gly Cys Arg His Ile Leu Gly
340
Tyr Ala Tyr Ser Asp Asp Arg Met Val Val His Tyr Val Ala Val Met
355
Thr Pro Leu Leu Cys Leu Ser Ile Phe Thr Asp Ser Leu Gln Gly Val
370
Leu Ser Gly Val Ala Arg Gly Ser Gly Trp Gln His Leu Gly Ala Tyr
385
Val Asn Leu Gly Ala Phe Tyr Leu Val Gly Ile Pro Val Gly Ile Val
405
Leu Gly Phe Val Ala His Leu Arg Ala Lys Gly Leu Trp Ile Gly Ile
420
Val Thr Gly Ser Ile Val Gln Ser Ile Leu Leu Ser Leu Val Thr Ala
435
Leu Thr Asn Trp Lys Lys Gln Ala Met Met Ala Arg Glu Arg Ile Phe
450
Asp Val Lys Pro Pro Asp Glu Asn Glu Ser Asn His Met Thr Ser Ala
465
470
475
480

```

<210> 59

<211> 500

<212> PRT

<213> Oryza sativa

<400> 59

```

Met Glu Glu Arg Ile Pro Leu Leu Ser Lys Arg Phe Pro Ala Asp Gly
1      5      10      15
Thr Ala Gly Val Gly Gly Gly Arg Glu Glu Gly Gly Asp Arg Trp
20
Trp Ser Gly Leu Ala Arg Glu Ala Gly Lys Val Gly Ser Met Ala Leu
35
Pro Met Ala Ala Met Ser Val Ala Gln Asn Ala Val Gln Val Ala Ser
40
45

```

```

      50      55      60
Asn Met Met Val Gly His Leu Pro Gly Val Leu Pro Leu Ser Ala Ser
65      70      75      80
Ala Ile Ala Thr Ser Leu Ala Ser Val Ser Gly Phe Ser Leu Leu Val
      85      90      95
Gly Met Ala Ser Gly Leu Glu Thr Leu Cys Gly Gln Ala Tyr Gly Ala
      100      105      110
Lys Gln Tyr Asp Lys Leu Gly Val Gln Thr Tyr Arg Ala Ile Val Thr
      115      120      125
Leu Thr Val Val Thr Ile Pro Ile Ser Leu Leu Trp Val Phe Ile Gly
      130      135      140
Lys Leu Leu Thr Leu Ile Gly Gln Asp Pro Val Ile Ser His Glu Ala
      145      150      155      160
Gly Arg Tyr Ile Val Trp Leu Ile Pro Gly Leu Phe Ala Tyr Ala Val
      165      170      175
Cys Gln Pro Leu Thr Lys Phe Leu Gln Ser Gln Ser Leu Ile Phe Pro
      180      185      190
Met Leu Trp Ser Ser Ile Ala Thr Leu Leu Leu His Ile Pro Leu Ser
      195      200      205
Trp Leu Leu Val Phe Lys Thr Ser Met Gly Phe Thr Gly Ala Ala Leu
      210      215      220
Ala Ile Ser Ile Ser Tyr Trp Leu Asn Thr Phe Met Leu Ala Ala Tyr
      225      230      235      240
Ile Arg Phe Ser Cys Ser Cys Lys Val Thr Arg Ser Pro Pro Thr Ile
      245      250      255
Glu Ala Phe Arg Gly Val Gly Leu Phe Leu Arg Ile Ala Leu Pro Ser
      260      265      270
Ala Leu Met Leu Cys Phe Glu Trp Trp Ser Phe Glu Ile Leu Val Leu
      275      280      285
Leu Ser Gly Leu Leu Pro Asn Pro Glu Leu Glu Ser Ser Val Leu Ser
      290      295      300
Ile Cys Leu Thr Thr Thr Ser Leu Met Tyr Thr Ile Pro Tyr Gly Leu
      305      310      315      320
Gly Gly Ala Ala Ser Thr Arg Val Ala Asn Glu Leu Gly Ala Gly Asn
      325      330      335
Pro Glu Gly Ala Arg Ser Ala Val His Leu Val Met Ser Ile Ala Gly
      340      345      350
Thr Glu Ala Val Leu Val Thr Gly Met Leu Phe Ala Ala Gln Arg Ile
      355      360      365
Leu Gly Tyr Ala Tyr Ser Ser Asp Glu Glu Val Val Thr Tyr Phe Thr
      370      375      380
Ser Met Val Pro Phe Val Cys Ile Ser Val Ala Ala Asp Ser Leu Gln
      385      390      395      400
Gly Val Leu Ser Gly Ile Ala Arg Gly Cys Gly Trp Gln His Leu Gly
      405      410      415
Ala Tyr Val Asn Leu Gly Ser Phe Tyr Leu Val Gly Ile Pro Val Ala
      420      425      430
Leu Leu Leu Gly Phe Gly Phe Lys Met Glu Gly Lys Gly Leu Trp Leu
      435      440      445
Gly Ile Ala Cys Gly Ser Val Leu Gln Phe Leu Leu Leu Ala Val Ile
      450      455      460
Ala Phe Phe Ser Asn Trp Gln Lys Met Ala Glu Lys Ala Arg Glu Arg
      465      470      475      480
Ile Phe Gly Glu Thr Pro Ser Glu Lys Gln His Leu Val Leu Asp Ala
      485      490      495
Thr Asn Ser Val
      500

```

<210> 60

<211> 491

<212> PRT

<213> Oryza sativa

<400> 60

Met Ala Ala Ala Ala Arg Glu Glu Gln Pro Leu Leu Leu Arg Arg Glu

```

1           5           10           15
Glu Gly Glu Glu Gly Glu Glu Val Gly Trp Arg Arg Arg Trp Gly
20          25          30
Ser Glu Ala Gly Lys Leu Ala Tyr Leu Ala Leu Pro Met Val Ala Val
35          40          45
Ser Leu Thr Asn Tyr Ala Val Gln Val Phe Ser Asn Met Met Val Gly
50          55          60
His Leu Pro Gly Val Leu Pro Leu Ser Ser Ala Ala Ile Ala Thr Ser
65          70          75          80
Leu Ala Ser Val Thr Gly Phe Ser Leu Leu Ile Gly Met Ala Ser Ala
85          90          95
Leu Glu Thr Leu Cys Gly Gln Ala Tyr Gly Ala Lys Gln Tyr His Thr
100         105         110
Leu Gly Val His Thr Tyr Arg Ala Ile Leu Thr Leu Val Val Cys
115         120         125
Ile Pro Leu Ser Leu Leu Trp Val Phe Met Gly Lys Ile Leu Val Leu
130         135         140
Ile Gly Gln Asp Pro Leu Ile Ser His Gly Ala Gly Arg Tyr Ile Val
145         150         155         160
Trp Leu Ile Pro Gly Leu Phe Ala Asn Ala Leu Ile Gln Pro Ile Thr
165         170         175
Lys Phe Leu Gln Ser Gln Ser Leu Ile Met Pro Met Leu Val Ala Ser
180         185         190
Val Ala Thr Leu Val Phe His Ile Pro Leu Cys Trp Leu Met Val Phe
195         200         205
Lys Thr Gly Leu Gly Tyr Thr Gly Ala Ala Leu Ser Ile Ser Ile Ser
210         215         220
Tyr Trp Leu Asn Val Ala Met Leu Val Ala Tyr Ile Leu Leu Ser Ser
225         230         235         240
Ser Cys Lys Glu Thr Arg Thr Pro Pro Thr Ile Glu Ala Phe Lys Gly
245         250         255
Leu Asp Gly Phe Leu Arg Leu Ala Leu Pro Ser Ala Leu Met Ile Cys
260         265         270
Leu Glu Trp Trp Ser Phe Glu Leu Ile Leu Met Ser Gly Leu Leu
275         280         285
Pro Asn Pro Glu Leu Gln Thr Ser Val Leu Ser Ile Cys Leu Thr Ser
290         295         300
Ile Thr Leu Leu Phe Thr Ile Pro Tyr Gly Leu Gly Ala Gly Gly Ser
305         310         315         320
Thr Arg Val Ala Asn Glu Leu Gly Ala Gly Asn Pro Glu Gly Ala Arg
325         330         335
Ser Ala Val Tyr Val Val Leu Ser Val Ala Val Thr Glu Ala Leu Ile
340         345         350
Val Cys Gly Thr Leu Leu Ala Ser Arg Arg Leu Leu Gly Arg Ala Tyr
355         360         365
Ser Ser Glu Glu Glu Val Ile Ser Phe Val Ala Met Met Val Pro Leu
370         375         380
Val Cys Ile Thr Val Val Thr Asp Gly Leu Gln Gly Val Met Ser Gly
385         390         395         400
Ile Ala Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr Val Asn Leu
405         410         415
Gly Ser Phe Tyr Leu Leu Gly Ile Pro Met Ala Ile Leu Leu Gly Phe
420         425         430
Val Leu His Met Gly Ala Lys Gly Leu Trp Met Gly Ile Val Cys Gly
435         440         445
Ser Ile Ser Gln Ile Thr Leu Leu Ser Ala Ile Thr Phe Phe Thr Asn
450         455         460
Trp Gln Lys Met Ala Glu Asn Ala Arg Glu Arg Val Phe Ser Glu Lys
465         470         475         480
Pro Thr Glu Pro Ser Arg Tyr His Leu Val Glu
485         490

```

<210> 61

<211> 502

<212> PRT

<213> *Oryza sativa*

<400> 61

```

Met Gly Ser Ser Asp Ser Gln Ala Pro Leu Leu Leu Pro Arg Gly Ser
1      5      10      15
His Arg Lys Glu Glu Glu Glu Tyr Ala Ala Ala Gly Lys Val
20      25      30
Arg Gly Cys Cys Gly Gly Asp Gly Glu Gly Trp Trp Arg Glu Ala
35      40      45
Thr Ala Glu Ala Gly Arg Leu Ala Ser Leu Ala Ala Pro Met Ile Ala
50      55      60
Val Ala Leu Leu Gln Leu Met Met Gln Leu Ile Ser Thr Val Met Val
65      70      75      80
Gly His Leu Gly Glu Val Ala Leu Ala Gly Ala Ala Ile Ala Asn Ser
85      90      95
Leu Thr Asn Val Ser Gly Phe Ser Val Leu Met Gly Leu Ala Cys Gly
100     105     110
Leu Glu Thr Ile Cys Gly Gln Ala Tyr Gly Ala Glu Gln Tyr His Lys
115     120     125
Leu Ala Leu Tyr Met Tyr Arg Ser Ile Ile Val Leu Leu Val Val Ser
130     135     140
Val Pro Ile Ala Ile Ile Trp Val Phe Ile Pro Glu Val Leu Pro Leu
145     150     155     160
Ile Gly Gln Gln Pro Glu Ile Ala Ser Glu Val Gly Lys Tyr Ala Leu
165     170     175
Trp Leu Ile Pro Gly Leu Phe Ala Phe Thr Val Ala Gln Cys Leu Ser
180     185     190
Lys Phe Leu Gln Thr Gln Ser Leu Ile Phe Pro Met Val Leu Ser Ser
195     200     205
Ser Ile Thr Leu Ala Leu Phe Ile Pro Leu Cys Trp Phe Met Val Tyr
210     215     220
Lys Val Gly Met Gly Asn Ala Gly Ala Ala Leu Ser Val Ser Ile Cys
225     230     235     240
Asp Trp Val Glu Val Thr Val Leu Gly Leu Tyr Ile Val Leu Ser Pro
245     250     255
Ser Cys Glu Lys Thr Arg Ala Pro Leu Thr Trp Glu Ala Phe Ser Gly
260     265     270
Ile Gly Ser Phe Leu Arg Leu Ala Val Pro Ser Ala Leu Met Ile Cys
275     280     285
Leu Glu Trp Trp Ser Tyr Glu Leu Leu Val Leu Ser Gly Ile Leu
290     295     300
Pro Asn Pro Ala Leu Glu Thr Ser Val Leu Ser Ile Cys Ile Ser Thr
305     310     315     320
Val Val Leu Val Tyr Asn Leu Pro His Gly Ile Gly Thr Ala Ala Ser
325     330     335
Val Arg Val Ser Asn Glu Leu Gly Ala Gly Asn Pro Glu Gly Ala Arg
340     345     350
Leu Val Val Gly Val Ala Leu Ser Val Ile Leu Cys Ser Ala Val Leu
355     360     365
Val Ser Val Thr Leu Leu Ala Leu Arg His Phe Ile Gly Ile Ala Phe
370     375     380
Ser Asn Glu Glu Glu Val Ile Asn Tyr Val Thr Arg Met Val Pro Val
385     390     395     400
Leu Ser Ile Ser Val Ile Thr Asp Ser Leu Gln Gly Val Leu Ser Gly
405     410     415
Val Ser Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr Val Asn Leu
420     425     430
Gly Ala Phe Tyr Leu Val Gly Val Pro Val Ala Leu Phe Phe Gly Phe
435     440     445
Ala Met His Leu Gly Gly Met Gly Phe Trp Met Gly Met Val Ala Gly
450     455     460
Gly Ala Thr Gln Val Thr Leu Leu Ser Ile Ile Thr Ala Met Thr Asn
465     470     475     480
Trp Arg Lys Met Ala Glu Lys Ala Arg Asp Arg Val Phe Glu Glu Arg
485     490     495

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```

Ile Pro Thr Gln Ser Val
500

```

<210> 62

<211> 489

<212> PRT

<213> Sorghum bicolor

<400> 62

```

Met Ala Ala Ala Arg Glu Glu Asp Glu Ala Thr Gln Ala Arg Pro Leu
1      5      10      15
Leu Leu Pro Arg Arg Pro Ala Gln Glu Asp Gln Lys Trp Trp Arg Arg
20      25      30
Trp Ala Arg Glu Ala Gly Trp Val Gly Tyr Leu Ala Leu Pro Met Val
35      40      45
Val Val Asn Leu Ser Gln Tyr Ala Val Gln Val Ser Ser Asn Met Met
50      55      60
Val Gly His Leu Pro Gly Val Leu Pro Leu Ser Ser Ala Ala Ile Ala
65      70      75      80
Thr Ser Leu Ala Asn Val Ser Gly Phe Ser Leu Leu Ile Gly Leu Ala
85      90      95
Ser Ala Leu Glu Thr Leu Cys Gly Gln Ala Tyr Gly Ala Lys Gln Tyr
100     105     110
His Lys Leu Gly Leu Asp Thr Tyr Arg Ala Ile Val Thr Leu Leu Val
115     120     125
Val Cys Ile Pro Leu Ser Leu Leu Trp Val Phe Met Asp Lys Ile Leu
130     135     140
Val Leu Ile Gly Gln Asp Pro Leu Ile Ser Gln Gly Ala Gly Arg Tyr
145     150     155     160
Met Ile Trp Met Ile Pro Gly Leu Phe Ala Asn Ala Val Ile Gln Pro
165     170     175
Leu Thr Lys Phe Leu Gln Thr Gln Ser Leu Ile Tyr Pro Leu Leu Leu
180     185     190
Ser Ser Val Ala Thr Ala Ala Ile His Ile Pro Leu Cys Tyr Val Met
195     200     205
Val Phe Lys Thr Gly Leu Gly Tyr Thr Gly Ala Ala Leu Thr Ile Ser
210     215     220
Ile Ser Tyr Trp Leu Asn Val Ala Met Leu Val Gly Tyr Ile Val Phe
225     230     235     240
Ser Ser Ser Cys Lys Glu Thr Arg Ala Arg Pro Thr Ile Glu Val Phe
245     250     255
Arg Gly Val Asp Ala Phe Leu Arg Leu Ala Leu Pro Ser Ala Leu Met
260     265     270
Met Cys Phe Glu Trp Trp Ser Phe Glu Leu Leu Thr Leu Met Ser Gly
275     280     285
Leu Leu Pro Asn Pro Glu Leu Gln Thr Ser Val Leu Ser Ile Cys Leu
290     295     300
Thr Ser Val Thr Leu Leu Phe Thr Ile Pro Phe Gly Leu Gly Ala Ala
305     310     315     320
Gly Ser Thr Arg Val Ala Asn Glu Leu Gly Ala Gly Asn Pro Asp Gly
325     330     335
Ala Arg Ser Ala Val Arg Val Val Leu Ser Met Ala Gly Ile Asp Ala
340     345     350
Val Ile Val Ser Gly Thr Leu Leu Ala Ala Arg Arg Leu Val Gly Leu
355     360     365
Ala Tyr Ser Ser Glu Glu Glu Val Ile Ser Ser Val Ala Ala Met Val
370     375     380
Pro Leu Val Cys Ile Thr Val Ile Thr Asp Cys Leu Gln Gly Val Leu
385     390     395     400
Ser Gly Val Ala Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr Val
405     410     415
Asn Leu Gly Ser Phe Tyr Leu Leu Gly Ile Pro Met Ala Ile Leu Leu
420     425     430
Gly Phe Val Leu His Met Gly Ser Arg Gly Leu Trp Met Gly Ile Val
435     440     445

Cys Gly Ser Leu Ser Gln Thr Thr Leu Met Ser Ala Ile Thr Phe Phe
450     455     460
Thr Asp Trp Pro Lys Met Ala Glu Lys Ala Arg Glu Arg Val Phe Ser
465     470     475     480
Asp Lys Ala His Glu Ser Ala Gly Pro
485

```

<210> 63

<211> 514

<212> PRT

<213> Sorghum bicolor

<400> 63

```

Met Glu Glu Arg Val Pro Leu Leu Pro Gln Tyr Thr Leu Arg Asn Asp
1      5      10      15
Asp Gly Arg Glu Glu Lys Cys Gly Gly Gly Gly Val Arg Trp Trp
20      25      30
Arg Glu Leu Leu Ala Arg Glu Ala Gly Lys Val Gly Cys Val Ala Leu
35      40      45
Pro Met Ala Ala Val Ser Val Ser Gln Tyr Ala Val Gln Val Ala Ser
50      55      60
Asn Met Met Val Gly His Leu Pro Gly Val Leu Pro Leu Ser Ala Ser
65      70      75      80
Ala Ile Ala Thr Ser Leu Ala Thr Val Ser Gly Phe Ser Leu Leu Ile
85      90      95
Gly Met Ala Ser Gly Leu Glu Thr Leu Cys Gly Gln Ala Tyr Gly Ala
100     105     110
Lys Gln Tyr Asp Lys Leu Gly Met His Thr Tyr Arg Ala Ile Val Thr
115     120     125
Leu Ile Val Val Ser Ile Pro Ile Ser Leu Leu Trp Ala Phe Ile Gly
130     135     140
Lys Leu Leu Met Leu Ile Gly Gln Asp Pro Leu Ile Ser Lys Glu Ala
145     150     155     160
Gly Arg Tyr Ile Ala Trp Leu Ile Pro Gly Leu Phe Ala Tyr Ala Ile
165     170     175
Ser Gln Pro Leu Thr Lys Phe Leu Gln Ser Gln Ser Leu Ile Ile Pro
180     185     190
Met Leu Trp Ser Ser Ile Ala Thr Leu Leu Leu His Ile Pro Ile Cys
195     200     205
Trp Leu Leu Val Phe Lys Thr Ser Leu Gly Tyr Ile Gly Ala Ser Leu
210     215     220
Ala Ile Ser Leu Ser Tyr Trp Leu Asn Val Ile Met Leu Ala Ala Tyr
225     230     235     240
Ile Arg Tyr Ser Asn Ser Cys Lys Glu Thr Arg Ser Pro Pro Thr Val
245     250     255
Glu Ala Phe Lys Gly Val Gly Val Phe Leu Arg Leu Ala Leu Pro Ser
260     265     270
Ala Leu Met Leu Trp Phe His Ile Gly Leu Met Asn Ser Ile Pro Gln
275     280     285
Phe Tyr Ser Phe Glu Trp Trp Ser Phe Glu Ile Leu Ile Leu Val Ser
290     295     300
Gly Ile Leu Pro Asn Pro Glu Leu Gln Thr Ser Val Leu Ser Ile Cys
305     310     315     320
Leu Thr Thr Ile Thr Leu Met Tyr Thr Ile Pro Tyr Gly Leu Gly Ala
325     330     335
Ala Ala Ser Thr Arg Val Ala Asn Glu Leu Gly Gly Gly Asn Pro Glu
340     345     350
Gly Ala Arg Ser Ser Val Gln Val Val Met Cys Ile Ala Val Met Glu
355     360     365
Ala Val Ile Ile Thr Ile Ile Leu Leu Ala Ser Gln His Ile Leu Gly
370     375     380
Tyr Ala Tyr Ser Ser Asp Lys Asp Val Val Ala Tyr Val Asn Ala Met
385     390     395     400
Val Pro Phe Val Cys Val Ser Val Ala Ala Asp Ser Leu Gln Gly Val
405     410     415

Leu Ser Gly Ile Ala Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr
420     425     430
Val Asn Leu Gly Ser Phe Tyr Leu Val Gly Ile Pro Thr Ala Leu Phe
435     440     445
Leu Gly Phe Val Leu Lys Met Glu Ala Lys Gly Leu Trp Met Gly Ile
450     455     460
Ser Cys Gly Ser Ile Val Gln Phe Leu Leu Leu Ala Ile Ile Thr Phe
465     470     475     480
Phe Ser Asn Trp Gln Lys Met Ser Glu Lys Ala Arg Glu Arg Val Phe
485     490     495
Ser Asp Glu Pro Ser Asp Lys Glu Pro Leu Glu Ser Asp Gly Ser Asn
500     505     510
Leu Phe

```

<210> 64

<211> 505

<212> PRT

<213> Sorghum bicolor

<400> 64

```

Met Gly Ser Ser Glu Ala Pro Leu Leu Leu Ala His Pro Gly Glu Gly
1      5      10
Lys Glu Asp Pro Gly Ala Asp Val Gly Asp Arg Arg Arg Leu Arg Cys
20      25      30
Cys Trp Trp Trp Arg Arg Cys Gly Gly Ala Ser Ser Glu Gly Trp Trp
35      40      45
Ala Glu Val Thr Ala Glu Ala Gly Arg Leu Ala Ala Leu Ala Ala Pro
50      55      60
Met Ile Ala Val Ala Leu Leu Gln Leu Met Met Gln Leu Ile Ser Thr
65      70      75      80
Ile Met Val Gly His Leu Gly Glu Val Pro Leu Ala Gly Ala Ala Ile
85      90      95
Ala Asn Ser Leu Thr Asn Val Ser Gly Phe Ser Val Leu Met Gly Leu
100     105     110
Ala Ser Gly Leu Glu Thr Ile Cys Gly Gln Ala Phe Gly Ala Glu Gln
115     120     125
Tyr His Lys Val Ala Leu Tyr Thr Tyr Arg Ser Ile Ile Val Leu Leu
130     135     140
Ile Ala Ser Val Pro Met Ala Ile Thr Trp Val Phe Ile Pro Asp Val
145     150     155     160
Leu Pro Leu Ile Gly Gln Asp Pro Gln Ile Ala Ser Glu Ala Gly Arg
165     170     175
Tyr Ala Leu Trp Leu Ile Pro Gly Leu Phe Ala Phe Ser Val Ala Gln
180     185     190
Cys Leu Ser Lys Phe Leu Gln Ser Gln Ser Leu Ile Phe Pro Met Val
195     200     205
Leu Ser Ser Phe Thr Thr Leu Ala Val Phe Ile Pro Leu Cys Trp Phe
210     215     220
Met Val Tyr Lys Val Gly Met Gly Asn Ala Gly Ala Ala Phe Ala Val
225     230     235     240
Ser Ile Cys Asp Trp Val Glu Val Thr Val Leu Gly Leu Tyr Ile Lys
245     250     255
Phe Ser Pro Ser Cys Glu Lys Thr Arg Ala Pro Phe Thr Trp Glu Ala
260     265     270
Phe Arg Gly Ile Gly Asn Phe Met Arg Leu Ala Val Pro Ser Ala Leu
275     280     285
Met Ile Cys Leu Glu Trp Trp Ser Tyr Glu Leu Leu Val Leu Leu Cys
290     295     300
Gly Val Leu Pro Asn Ala Ala Leu Glu Thr Ser Val Leu Ser Ile Cys
305     310     315     320
Ile Ser Thr Val Val Leu Val Tyr Asn Leu Pro Tyr Gly Ile Gly Thr
325     330     335
Ala Ala Ser Val Arg Val Ser Asn Glu Leu Gly Ala Gly Asn Pro Asp
340     345     350

Gly Ala Arg Leu Val Val Val Val Ala Leu Ser Ile Ile Ile Cys Thr
355     360     365
Ala Val Leu Leu Ser Ile Thr Leu Leu Ser Phe Arg His Phe Val Gly
370     375     380
Ile Ala Phe Ser Asn Glu Glu Val Val Asn His Val Thr Arg Met
385     390     395     400
Val Pro Leu Leu Ser Ile Ser Val Leu Thr Asp Asn Leu Gln Gly Val
405     410     415
Leu Ser Gly Ile Ser Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr
420     425     430
Val Asn Leu Gly Ala Phe Tyr Leu Ile Gly Ile Pro Val Gly Leu Val
435     440     445
Ala Gly Phe Ala Leu His Leu Gly Gly Ala Gly Phe Trp Ile Gly Met
450     455     460
Ile Ala Gly Gly Ala Thr Gln Val Thr Leu Leu Ser Val Ile Thr Ala
465     470     475     480
Met Thr Asn Trp Gln Lys Met Ala Asp Lys Ala Arg Asp Arg Val Tyr
485     490     495
Glu Gly Ser Leu Pro Thr Gln Ala Asp
500     505

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<210> 65

<211> 488

<212> PRT

<213> Hordeum vulgare

<400> 65

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

Ile Ser Thr Val Val Leu Leu Tyr Asn Leu Pro Tyr Gly Ile Gly Thr
305     310     315     320
Ala Ala Ser Val Arg Val Ser Asn Glu Leu Gly Ala Gly Asn Pro Glu
325     330     335
Gly Ala Arg Leu Val Val Gly Val Ala Leu Ser Ile Val Val Cys Ser
340     345     350
Ala Ala Leu Val Ser Thr Thr Leu Leu Ala Ser Arg His Phe Ile Gly
355     360     365
Ile Ala Phe Ser Asn Glu Glu Glu Val Ile Asp Tyr Val Thr Arg Met
370     375     380
Val Pro Val Leu Ser Ile Ser Val Ile Thr Asp Ser Leu Gln Gly Val
385     390     395     400
Leu Ser Gly Val Ser Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr
405     410     415
Val Asn Leu Gly Ala Phe Tyr Leu Val Gly Ile Pro Val Ala Leu Phe
420     425     430
Phe Gly Phe Thr Met Gln Leu Arg Gly Met Gly Phe Trp Ile Gly Met
435     440     445
Ile Ala Gly Gly Ala Thr Gln Val Thr Leu Leu Ser Val Ile Thr Ala
450     455     460
Thr Thr Lys Trp Asp Lys Met Ala Asp Lys Ala Lys Glu Arg Val Phe
465     470     475     480
Glu Asp Arg Leu Pro Thr Gln Gln
485

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<210> 66

<211> 1627

<212> DNA

<213> Triticum aestivum

<400> 66

ttccattcc	attccacac	ccacctccct	tcgcctggtc	cggggggcggg	catccatgga	60
ctcttcctcc	gaggcgccgc	tgctgctcag	caggggggaac	gagcacaagg	aggtgcccgga	120
tgtggcggga	ggcaagcggc	cgtggtggag	ggaggcggcg	gaggagtccg	gccggctggc	180
cgcgctggct	gcgcgatga	tcgcggtggc	gctgctgcag	ctgttgatgc	agctcatctc	240
caacctcatg	gtggggcacc	tcggcgaggt	cgcgctcgct	ggcgccggcca	tcgccaaactc	300
cctcaccac	gtctccggct	tcagcgctct	cataggactg	gcatgcggat	tggaaactat	360
ttgtgggcag	gcctatggag	cagaacagta	tcataagtta	tccttgatg	cotacaggtc	420
catcattgta	cttcttattg	tgagtgtgcc	catcgccatt	gtatgggttt	tcattccgga	480
agtaacttct	ctcataggtc	agcaaccaga	aattgcaaat	gaggctggga	aatatgcatt	540
gtggcttata	cctggtttat	ttgccttcag	tgttgctcaa	tgcttttcaa	agtttctgca	600
gtgtcagagc	ctcatctttc	ctatggttct	tagctccatg	atcacactcg	ctgtatttat	660
tcctctgtgt	tggttcctgg	tttataaagt	tggatgggt	aatgttggag	ctgctttatc	720
cgtcagcatc	tgcgattggg	ttgaagtgac	tgttcttgg	ctttacatca	agttctcacc	780
ttcttgtgag	aaaacacgtg	ctccactcac	gtgggaagct	tttaaaggaa	ttggcagttt	840
catgcgtttg	gctgtacgt	cggctcttat	gatttgcctt	gaatggtggt	cttaagagct	900
gcttgttctg	ctttctggga	tcttaccaaa	tccagcaact	gaaacttctg	tgctttctat	960
atgcatactc	acagtggtgc	tgttgtacaa	tcttccttac	ggtattggaa	cagctgcaag	1020
tgtgcgcgtc	tcaaatgaac	taggtgctgg	caaccagaaa	ggtgctcgct	tggtggtagg	1080
tgttgctttg	tcgattgtag	tttgttcagc	aatcctggtg	agcacagctc	ttctagccct	1140
gcgcacttc	attggaattg	cattcagcaa	caggaggag	gttgtagatt	atgtcaccag	1200
aatggtaccc	gtactttcca	tttcagtcac	tacagacagc	ttccaaggag	tcctttcagg	1260
tgtttctcgg	ggctgtggat	ggcagcattt	aggcgcatat	gtcaacctgg	gtgcattcta	1320
tccttggtgg	atcccgttg	cactcttttt	tggttttaca	atgcaactaa	gaggaatggg	1380
attttgatt	ggcatgtag	ctggtggagc	cacacaggtc	actctcctat	ctgtgataac	1440
tgccactaca	aaatgggaca	agatggctga	caaggctaag	gagagagtat	ttgaagacag	1500
gcttccaaca	caataagact	tgaagaactg	ccatgtcaaa	attttgaaga	gctaaataat	1560
cagagaattc	taattacctt	taatttcaaa	aaaaaaaaa	aaaaaaaaa	aaaaaaaaa	1620
aaaaaaa						1627

<210> 67

<211> 486

<212> PRT

<213> Triticum aestivum

<400> 67

```

Met Gly Ser Ser Glu Ala Pro Leu Leu Leu Ala His Pro Gly Glu Gly
1      5      10      15
Lys Glu Asp Pro Gly Ala Asp Val Gly Asp Arg Arg Arg Leu Arg Cys
20      25      30
Cys Trp Trp Trp Arg Arg Cys Gly Gly Ala Ser Ser Glu Gly Trp Trp
35      40      45
Ala Glu Val Thr Ala Glu Ala Gly Arg Leu Ala Ala Leu Ala Ala Pro
50      55      60
Met Ile Ala Val Ala Leu Leu Gln Leu Met Met Gln Leu Ile Ser Thr
65      70      75      80
Ile Met Val Gly His Leu Gly Glu Val Pro Leu Ala Gly Ala Ala Ile
85      90      95
Ala Asn Ser Leu Thr Asn Val Ser Gly Phe Ser Val Leu Met Gly Leu
100     105     110
Ala Ser Gly Leu Glu Thr Ile Cys Gly Gln Ala Phe Gly Ala Glu Gln
115     120     125
Tyr His Lys Val Ala Leu Tyr Thr Tyr Arg Ser Ile Ile Val Leu Leu
130     135     140
Ile Ala Ser Val Pro Met Ala Ile Thr Trp Val Phe Ile Pro Asp Val
145     150     155     160
Leu Pro Leu Ile Gly Gln Asp Pro Gln Ile Ala Ser Glu Ala Gly Arg
165     170     175
Tyr Ala Leu Trp Leu Ile Pro Gly Leu Phe Ala Phe Ser Val Ala Gln
180     185     190
Cys Leu Ser Lys Phe Leu Gln Ser Gln Ser Leu Ile Phe Pro Met Val
195     200     205
Leu Ser Ser Phe Thr Thr Leu Ala Val Phe Ile Pro Leu Cys Trp Phe
210     215     220
Met Val Tyr Lys Val Gly Met Gly Asn Ala Gly Ala Ala Phe Ala Val
225     230     235     240
Ser Ile Cys Asp Trp Val Glu Val Thr Val Leu Gly Leu Tyr Ile Lys
245     250     255
Phe Ser Pro Ser Cys Glu Lys Thr Arg Ala Pro Phe Thr Trp Glu Ala
260     265     270
Phe Arg Gly Ile Gly Asn Phe Met Arg Leu Ala Val Pro Ser Ala Leu
275     280     285
Met Ile Cys Leu Glu Trp Trp Ser Tyr Glu Leu Leu Val Leu Leu Cys
290     295     300
Gly Val Leu Pro Asn Ala Ala Leu Glu Thr Ser Val Leu Ser Ile Cys
305     310     315     320
Ile Ser Thr Val Val Leu Val Tyr Asn Leu Pro Tyr Gly Ile Gly Thr
325     330     335
Ala Ala Ser Val Arg Val Ser Asn Glu Leu Gly Ala Gly Asn Pro Asp
340     345     350
Gly Ala Arg Leu Val Val Val Val Ala Leu Ser Ile Ile Ile Cys Thr
355     360     365
Ala Val Leu Leu Ser Ile Thr Leu Leu Ser Phe Arg His Phe Val Gly
370     375     380
Ile Ala Phe Ser Asn Glu Glu Glu Val Val Asn His Val Thr Arg Met
385     390     395     400
Val Pro Leu Leu Ser Ile Ser Val Leu Thr Asp Asn Leu Gln Gly Val
405     410     415
Leu Ser Gly Ile Ser Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr
420     425     430
Val Asn Leu Gly Ala Phe Tyr Leu Ile Gly Ile Pro Val Gly Leu Val
435     440     445
Ala Gly Phe Ala Leu His Leu Gly Gly Ala Gly Phe Trp Ile Gly Met
450     455     460
Ile Ala Gly Gly Ala Thr Gln Val Thr Leu Leu Ser Val Ile Thr Ala
465     470     475     480
Met Thr Asn Trp Gln Lys
485

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<210> 68

<211> 1633

<212> DNA

<213> *Eragrostis nindensis*

<400> 68

```

cgggcgcccat gatcgcggtg gcgctgctgc agctcacgat gcagctcatc tccaccgtca    60
tgggtgggcca cctcggcgag gtcccgcctcg cgggggcccgc catcgccaac tcgctcacca    120
acgtcgccgg attcagcgtc ctcattggac tagcaaccgg gttggaaact cttgtggac    180
aggcctacgg agggagaacag tatcataagc tatctttgta tacctaccgg tctatagttg    240
tacttcttat cgcgagtggt cccatogcca ttatgtgggt tttcatccg gaggtacttc    300
ctctaattgg tcaggatcca cagatagcca gtgaggctgg gaagtatgcc ttgtggctta    360
tccctggttt atttgccttc agtgtggcac aatgcttttc taaattcctc caatctcaga    420
gcctgatttt cccaatggtt ttgagctcct tgattacact cactgtcttc attcgttgtt    480
gttggttcat gatttataaa gttgggatgg gtaatgctgg agctgcttta tcagtcagca    540
tctgtgattg ggttgaagtg actgttcttg gtctttacat caaatactca ccttcttggt    600
agaaaaacac tgctccattc acctgggatg ctttcagagg gattggcagc ttcatgcggt    660
tggctgtacc atcagctggt atgctttgtc ttgaatgggt gtcatacagc cttctgttct    720
tgctttctgg gatcttacca aatccagcac ttgaaacttc tgtgctttct atatgcata    780
ctacagtgtg gttggtatgc aatctcccat ttggcatcgg aacagctgca agcgtgcgtg    840
tttcaaatga gctaggtgca gggaaaccag aaggtgcccg tttagtggta gttgtgcct    900
tatccattgt tgtttgctca gctatcctgg tgagcatgac tcttctatcg ttgcgccgtt    960
ttattggaat tgctttcagc aacgaggagg aggttataaa ttatgtcacc agaattggtt    1020
cgctgctttc aatttcagtt cttgcagaca atcttcaagg tgttctcaca ggtatctcta    1080
ggggctgtgg atggcagcat ttaggcgcct atgttaacct tggcgcggtc tatcttatcg    1140
gtgttcctgt ggggtgttgt ctcggtttta gatttcactc agggaggagt gggttttgga    1200
tgggcatgat agctggtggt gccactcagg tgcctctcct atctatcac actgcaatga    1260
caaaactggag gaagatgtca gacaaggcta gagagagagt gtttgatgaa aggcctccaa    1320
ctcaggcagc atgattgaat caacttacag ttgcacttga ttctctcga aagttttgccc    1380
acactgtagg tgatttttgt gtacgaggtg ctcattttcc acatatctgt aatgaagact    1440
tatactctgc tcaaaagggc tgtccaatga agctagatta gtgtattgct ccacggtctt    1500
aggctctggt ttgatcaaaa gtatttctag agttttgaaa gaatactaca gtttagcaaa    1560
atcgggtttt gagaggtatg gaggtgtttg gatggaacaa gttttgcagt tttaaaaacc    1620
atggtattgc taa                                     1633

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<210> 69

<211> 443

<212> PRT

<213> *Eragrostis nindensis*

<400> 69

```

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

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      195              200              205
Asp Ala Phe Arg Gly Ile Gly Ser Phe Met Arg Leu Ala Val Pro Ser
 210      215      220
Ala Val Met Leu Cys Leu Glu Trp Trp Ser Tyr Glu Leu Leu Val Leu
 225      230      235      240
Leu Ser Gly Ile Leu Pro Asn Pro Ala Leu Glu Thr Ser Val Leu Ser
      245      250      255
Ile Cys Ile Ser Thr Val Val Leu Val Tyr Asn Leu Pro Phe Gly Ile
      260      265      270
Gly Thr Ala Ala Ser Val Arg Val Ser Asn Glu Leu Gly Ala Gly Asn
 275      280      285
Pro Glu Gly Ala Arg Leu Val Val Val Ala Leu Ser Ile Val Val
 290      295      300
Cys Ser Ala Ile Leu Val Ser Met Thr Leu Leu Ser Leu Arg Arg Phe
 305      310      315      320
Ile Gly Ile Ala Phe Ser Asn Glu Glu Glu Val Ile Asn Tyr Val Thr
      325      330      335
Arg Met Val Pro Leu Leu Ser Ile Ser Val Leu Ala Asp Asn Leu Gln
      340      345      350
Gly Val Leu Thr Gly Ile Ser Arg Gly Cys Gly Trp Gln His Leu Gly
 355      360      365
Ala Tyr Val Asn Leu Gly Ala Phe Tyr Leu Ile Gly Val Pro Val Gly
 370      375      380
Val Val Leu Gly Phe Arg Phe His Leu Gly Gly Ala Gly Phe Trp Met
 385      390      395      400
Gly Met Ile Ala Gly Gly Ala Thr Gln Val Ala Leu Leu Ser Ile Ile
      405      410      415
Thr Ala Met Thr Asn Trp Arg Lys Met Ser Asp Lys Ala Arg Glu Arg
      420      425      430
Val Phe Asp Glu Arg Leu Pro Thr Gln Ala Ala
      435      440

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<210> 70

<211> 1305

<212> DNA

<213> *Eragrostis nindensis*

<400> 70

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cctccctcgc caccgtctcc gggttcagcc tcctcgttgg aatggcaagt gcattggaga      60
ctctatgtgg ccaagcttac ggtgcaaagc agtaccataa gctaggagtg caaacttaca      120
gagcaatagt caccctccta gtggctctgca tccccatcac agttctcttg cgttcatgg      180
gcaaaatcct ggttctcata gggcaggacc ccttgatcgc ccaggggacc gggagataca      240
tagtctggct gatccgggg ctcttcgcaa acgctgtgtt gcagccaatc accaagtcc      300
tgcagaccga gagcctata tttgcccgc tcgtctcatc agttgcaacg ctggcgatcc      360
acgtccctct gtgctatatg atggtgttca gaactgggtt tgggtatacc ggagctgctc      420
tgtogataag catatcttat tggctgaatg tgattatgct tgttgtgtac attgcgatgt      480
caagttcttg caaggagaca cgcacacctc caacgatcga ggccttcaag gaaattgatg      540
cgttcctgog tctagccctg ccctctgcac tgatgatctg tcttgaatgg tggtcatttg      600
agatccttat ccttctctca gggtttctac ccaaccacga gcttcagacc tgggtgcttt      660
caatctgtct atcaagcatt acattactct acactctacc atatggattt ggagctgctg      720
gaagcacaag agtagcaaat gaactgggtg cggggaaccc tgaaggagct cgattctctg      780
tccgtgttgt gatgtccatg gggcgatgg aggcggttat catcagtgga actcttttag      840
ctttacgaog tcttgcggt caggcataca gcagtggga ggaggtggtg tcattcgtcg      900
caaccatggt tcctttggtt agcatcactg tgattacaga tggccttcaa ggagttctct      960
caggcattgc tcgaggatgc ggttggcaac acctgggcgc gtacgtgaac ctcggtcgt      1020
tctacctgct ggggatgccg atggcgatcc tcctcggctt cgtgctgaac atgggaggca      1080
gagggctctg gatgggcgtc ctctcgggtt ccgtatcaca gactacgctc ctgtccgccca      1140
tcacgatatt cactgactgg cccaagatgg cagagaaaagc caggcagagg gtgttcgatg      1200
agaagccggc ggatcccag tcgagacacc tgctggaata gcttgactcc agattcaaac      1260
gattcagtta tctgattctg caggggctgc agaattcgtt gatga      1305

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<210> 71

<211> 412

<212> PRT

<213> *Eragrostis nindensis*

<400> 71

```

Ser Leu Ala Thr Val Ser Gly Phe Ser Leu Leu Val Gly Met Ala Ser
1      5      10      15
Ala Leu Glu Thr Leu Cys Gly Gln Ala Tyr Gly Ala Lys Gln Tyr His
20      25      30
Lys Leu Gly Val Gln Thr Tyr Arg Ala Ile Val Thr Leu Leu Val Val
35      40      45
Cys Ile Pro Ile Thr Val Leu Trp Ala Phe Met Gly Lys Ile Leu Val
50      55      60
Leu Ile Gly Gln Asp Pro Leu Ile Ala Gln Gly Ala Gly Arg Tyr Ile
65      70      75      80
Val Trp Leu Ile Pro Gly Leu Phe Ala Asn Ala Val Leu Gln Pro Ile
85      90      95
Thr Lys Phe Leu Gln Thr Gln Ser Leu Ile Phe Ala Pro Leu Val Ser
100     105     110
Ser Val Ala Thr Leu Ala Ile His Val Pro Leu Cys Tyr Met Met Val
115     120     125
Phe Arg Thr Gly Phe Gly Tyr Thr Gly Ala Ala Leu Ser Ile Ser Ile
130     135     140
Ser Tyr Trp Leu Asn Val Ile Met Leu Val Val Tyr Ile Ala Met Ser
145     150     155     160
Ser Ser Cys Lys Glu Thr Arg Thr Pro Pro Thr Ile Glu Ala Phe Lys
165     170     175
Glu Ile Asp Ala Phe Leu Arg Leu Ala Leu Pro Ser Ala Leu Met Ile
180     185     190
Cys Leu Glu Trp Trp Ser Phe Glu Ile Leu Ile Leu Leu Ser Gly Phe
195     200     205
Leu Pro Asn Pro Glu Leu Gln Thr Ser Val Leu Ser Ile Cys Leu Ser
210     215     220
Ser Ile Thr Leu Leu Tyr Thr Leu Pro Tyr Gly Phe Gly Ala Ala Gly
225     230     235     240
Ser Thr Arg Val Ala Asn Glu Leu Gly Ala Gly Asn Pro Glu Gly Ala
245     250     255
Arg Phe Ser Val Arg Val Val Met Ser Met Ala Ala Met Glu Ala Val
260     265     270
Ile Ile Ser Gly Thr Leu Leu Ala Leu Arg Arg Leu Val Gly Gln Ala
275     280     285
Tyr Ser Ser Glu Glu Glu Val Val Ser Phe Val Ala Thr Met Val Pro
290     295     300
Leu Val Ser Ile Thr Val Ile Thr Asp Gly Leu Gln Gly Val Leu Ser
305     310     315     320
Gly Ile Ala Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr Val Asn
325     330     335
Leu Gly Ser Phe Tyr Leu Leu Gly Met Pro Met Ala Ile Leu Leu Gly
340     345     350
Phe Val Leu Asn Met Gly Gly Arg Gly Leu Trp Met Gly Val Leu Cys
355     360     365
Gly Ser Val Ser Gln Thr Thr Leu Leu Ser Ala Ile Thr Ile Phe Thr
370     375     380
Asp Trp Pro Lys Met Ala Glu Lys Ala Arg Gln Arg Val Phe Asp Glu
385     390     395     400
Lys Pro Ala Asp Pro Glu Ser Arg His Leu Leu Glu
405     410

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<210> 72

<211> 1520

<212> DNA

<213> *Eragrostis nindensis*

<400> 72

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gagcctgtcg cagtacgcgg tgcaggtggc gtccaacatg atggtcgggc acctccccgg      60
cgtcctcccg ctctccgcct ccgccatcgc cactccctcc gccaccgtct cggccttcag      120
cctcctcatt ggaatggcaa gtggattgga aactctatgc ggccaagcgt acggggctaa      180
acagtatgac aaattgggac tgcaaacata cagagctata gtcacactcc tagttgtgag      240

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cattccaatc tcaatattgt gggccttcat aggcacaactc ctgatoctca taggacaaga      300
tccattgata tcaaaggaag ctgggagata catagcctgg ttgattccag ggctctttgc      360
gtatgcagtc agccaacctc tcacaaaatt tctgcagtc cagagctcca taattcctat      420
gctttggtcc tccatagcga cactgctctt gcacatccct ctttgttggg tgttgggttt      480
caagacaagc ctgggggttta ttggagcttc tttagcgata agcttatcat attggctgaa      540
tgtgatcatg cttgctgctt acatccgata ctcaagtgtc tgtaaaagaga cccgctcgcc      600
tctactactg gaggccttca aaggagttgg ttgttccctg cgcttggctc tgccatctgc      660
actaatgttg tgtttcgaat ggtgttcctt tgaggttctt attcttctct ctggacttct      720
gcccaatcca gagctgcaaa cttcagtcct ctcgatttgc ctaacgacta tcacgttgat      780
gtatactata ccttatggac ttggagcggc agcaagcacg cgagtggcca atgaattagg      840
tgctagcaac cctgaaggag ctgcagtcgc tgttcgaatt gttatgacta tcgcagcgct      900
agaggcaggt ctcgttacaa ttctattgtt agcatcacaa cacatcgtgg gctatgcata      960
tagcagcgat aaggaggtgg tcgcttatgt caatgcaatg gttccctttg tgtgcgtctc      1020
agttgctgct gatagccttc aaggagtctc ctcaggtatt gcccgaggaa gcgggtggca      1080
gcacttgggt gcttatgtga acctcggttc gttctatctg attgggattc cagtggcact      1140
cttcctcggc ttgttcttga agatggaagg aaaagggttt tggatgggca tttcctgcgg      1200
ttcgtagtgt cagttcttat tactcgaggt gataacattc ttcagcaact ggcaaaaagt      1260
gtctgagaaa gcaagggaaa ggggtgtcag cgaagagctg tctaataagg aaccattgga      1320
atcggtatga ccatcttga tctaatttta acatgcgtcg actaatctcc tgacctgaat      1380
gtgaagaagc agttgttga cattagtaca gaataactct ttcgatataa aagaggatac      1440
gaactgtgga tgcatgtgat gtgtgcacgt tgtaactttc attttactaa aaaatagttg      1500
gaagagatcg gaagagcgtc

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<210> 73

<211> 447

<212> PRT

<213> *Eragrostis nindensis*

<400> 73

```

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

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

```

<210> 74

<211> 653

<212> DNA

<213> *Paspalum notatum*

<400> 74

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ccagccgcgc gacactccaa tcgcatacac gaacacgact cctcggaacg cggctcgatc    60
gacgcgacaa cggcagccgc catggaggag aggggtgccg ttctgcagca gcagtggacg    120
ctgcgagacg gcgcgacgg accggaggag aagcgcggcg gcctgaggtg gtggtggtgg    180
agggaccttg cgcgggagcg cgggaagtgc ggtacgtcg ccctgcgatg ggcggcgtg    240
agcgtgtcgc agtcggcggt gcaggtggcg tccaacatga tggtcggcca cctccccggc    300
gtcctccgcg ttctggcctc cgtatcgca acctccctcg ccaccgtctc cggtttcagc    360
ctcctcattg gaatggcaag tggcttgaa actctatgtg gtcaagccta cggggcgaaa    420
cagtacgata aattggggat gcacacctat agggccatag tcacgctcat agttgtgagc    480
attccaatct ccttctctg ggtattcata ggcaaatcc tgatcctcat aggccaaagac    540
cctttgatct caaaggaagc tgggagatat atagtctggt tgattccagg actctttgca    600
tatgcaatca gccagcctct cacgaaattt ctgcagtctc agagtctgat aat          653

```

<210> 75

<211> 501

<212> PRT

<213> *Paspalum notatum*

<220>

<221> misc_feature
 <222> (191)..(192)
 <223> Xaa can be any naturally occurring amino acid

<220>
 <221> misc_feature
 <222> (407)..(409)
 <223> Xaa can be any naturally occurring amino acid

<400> 75

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

```
Gly Met Ala Ser Gly Leu Glu Thr Leu Cys Gly Gln Ala Tyr Gly Ala
100      105      110
Lys Gln Tyr Asp Lys Leu Gly Met His Thr Tyr Arg Ala Ile Val Thr
115      120      125
Leu Ile Val Val Ser Ile Pro Ile Ser Leu Leu Trp Val Phe Ile Gly
130      135      140
Lys Leu Leu Ile Leu Ile Gly Gln Asp Pro Leu Ile Ser Lys Glu Ala
145      150      155      160
Gly Arg Tyr Ile Val Trp Leu Ile Pro Gly Leu Phe Ala Tyr Ala Ile
165      170      175
Ser Gln Pro Leu Thr Lys Phe Leu Gln Ser Gln Ser Leu Ile Xaa Xaa
180      185      190
Pro Met Leu Trp Ser Ser Ile Ala Thr Leu Leu Leu His Ile Pro Leu
195      200      205
Cys Trp Leu Leu Val Phe Lys Thr Ser Leu Gly Tyr Ile Gly Ala Ser
210      215      220
Leu Ala Ile Ser Leu Ser Tyr Trp Leu Asn Val Ile Met Leu Ala Ala
225      230      235      240
Tyr Ile Ile Phe Ser Asn Ser Cys Lys Glu Thr Arg Ser Pro Pro Thr
245      250      255
Ile Glu Ala Phe Lys Gly Val Gly Ile Phe Leu Arg Leu Ala Leu Pro
260      265      270
Ser Ala Leu Met Leu Cys Phe Glu Trp Trp Ser Phe Glu Ile Leu Ile
275      280      285
Leu Leu Ser Gly Ile Leu Pro Asn Pro Glu Leu Gln Thr Ser Val Leu
290      295      300
Ser Ile Cys Leu Thr Thr Ile Thr Leu Thr Tyr Thr Ile Pro Tyr Gly
305      310      315      320
Leu Gly Ala Ala Ala Ser Thr Arg Val Ala Asn Glu Leu Gly Gly Gly
325      330      335
Asn Pro Glu Gly Ala Arg Ser Ala Val Arg Val Val Met Cys Ile Ala
340      345      350
Val Ile Gly Ala Thr Ile Val Thr Ile Ile Leu Leu Ser Ser Gln His
355      360      365
Ile Leu Gly Tyr Ala Phe Ser Ser Asp Lys Glu Val Val Ala Tyr Val
370      375      380
Asn Ala Met Val Pro Phe Val Cys Val Ser Val Ala Ala Asp Ser Leu
385      390      395      400
Gln Gly Val Leu Ser Gly Xaa Xaa Xaa Gly Cys Gly Trp Gln His Leu
405      410      415
Gly Ala Tyr Val Asn Leu Gly Ser Phe Tyr Leu Val Gly Ile Pro Thr
420      425      430
Ala Leu Leu Leu Gly Phe Val Leu Lys Met Glu Gly Lys Gly Leu Trp
435      440      445
Met Gly Ile Ser Cys Gly Ser Ile Val Gln Phe Leu Leu Ala Ile
450      455      460
Ile Thr Phe Phe Ser Asn Trp Gln Lys Met Ser Asp Lys Ala Arg Glu
465      470      475      480
Arg Val Phe Asn Asp Glu Gln Ser Asn Lys Glu Pro Leu Glu Ser Asp
485      490      495
Gly Ser Gly Ser Val
500
```

<210> 76
 <211> 1355
 <212> DNA
 <213> Paspalum notatum

<400> 76

```

ggggcgctoga ggggggggtgg gtgggggtatc tggcgctgcc catgggtggtg gtgaacctgt      60
cgcagtagcgc cgtgcagggtg tcttccaaca tgatggtcgg gcacctcccc ggctgtgctcc      120
cgctctcctc caccgccatc gccacatccc tcgccaaagt ctccggcttc agcctcctga      180
ttggaatggc aagtgcactg gagacgctat gtggccaagc ctacggcgca aaacagtacc      240
acaaactagg tgtagatact tatagagcag tagtcaccct ccttgtggtc tgcacccctc      300
tctcgcttct ctgggtgttc atggataaaa tcctggtcgt catagggcaa gacccctca      360

```

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tctccaagg agctggaagg tacatgacct ggctgatccc cgggctcttc gogaatgcgg      420
tgatccagcc ggtcaccaag ttctgcaga cgcagagcct catatacccc ttgctgctgt      480
cgtctgtggc gacgatggcg atccacatcc ctctatgcta cttgatggtg ttcaagactg      540
gctttgggta cacaggtgct gctttgacta taggcatatc atactggctg aatgtaggca      600
tgcttgttgg gtacatcatg ttctcaaatt cttgcaagga gacacgcaca cgcccaacga      660
ttgaagcctt caagggaatc gatgcgttcc tgcgtctagc cctgccctct gcactaatga      720
tgtgttttga atggtgttca tttgagctcc ttattctctt gtcagggttc ctaccaacc      780
cagagctgca gacctcagtg ctttcaattt gtctcacaag tataacgtta ctcttcaata      840
taccttttgg acctggggct gctggaagca cccgagtagc aaatgaactg ggtgctggga      900
acctgatggg agctcgatct gcagtcogog ttgtgctgtc catgacggcg atcgacgcag      960
ttatcgtggg cggaaactct ctacggcgac ggcgctcgtt gggcatggct tacagcagcg      1020
aggaggaggt catatcttct gttgccacca tggttcctct ggtctgcatc actgtggtaa      1080
ctgactgtgt acaggaggtt ctctcaggcg ttgcccaggg gtgctgggtg cagcacctgg      1140
gcgcttatgt caatctggcg tcattctacc tgctggggat cccgatggcg atccttctcg      1200
gcttcgtgct gcacctgggg tcgagagggg tctggatggg catcgtctgc ggtcctttgt      1260
ctcagacaat actcatgtcc gtcatcacat tcttcaccaa ctggcccaag atgctgaca      1320
aggccaggga gaggtgttc agcgagaagc caccg      1355

```

<210> 77

<211> 451

<212> PRT

<213> Paspalum notatum

<400> 77

```

Ala Leu Glu Ala Gly Trp Val Gly Tyr Leu Ala Leu Pro Met Val Val
1      5      10      15
Val Asn Leu Ser Gln Tyr Ala Val Gln Val Ser Ser Asn Met Met Val
20      25      30
Gly His Leu Pro Gly Val Leu Pro Leu Ser Ser Thr Ala Ile Ala Thr
35      40      45
Ser Leu Ala Asn Val Ser Gly Phe Ser Leu Leu Ile Gly Met Ala Ser
50      55      60
Ala Leu Glu Thr Leu Cys Gly Gln Ala Tyr Gly Ala Lys Gln Tyr His
65      70      75      80
Lys Leu Gly Val Asp Thr Tyr Arg Ala Val Val Thr Leu Leu Val Val
85      90      95
Cys Ile Pro Leu Ser Leu Leu Trp Val Phe Met Asp Lys Ile Leu Val
100      105      110
Val Ile Gly Gln Asp Pro Leu Ile Ser Gln Gly Ala Gly Arg Tyr Met
115      120      125
Thr Trp Leu Ile Pro Gly Leu Phe Ala Asn Ala Val Ile Gln Pro Val
130      135      140
Thr Lys Phe Leu Gln Thr Gln Ser Leu Ile Tyr Pro Leu Leu Leu Ser
145      150      155      160
Ser Val Ala Thr Met Ala Ile His Ile Pro Leu Cys Tyr Leu Met Val
165      170      175
Phe Lys Thr Gly Phe Gly Tyr Thr Gly Ala Ala Leu Thr Ile Gly Ile
180      185      190
Ser Tyr Trp Leu Asn Val Gly Met Leu Val Gly Tyr Ile Met Phe Ser
195      200      205
Asn Ser Cys Lys Glu Thr Arg Thr Arg Pro Thr Ile Glu Ala Phe Lys
210      215      220
Gly Val Asp Ala Phe Leu Arg Leu Ala Leu Pro Ser Ala Leu Met Met
225      230      235      240
Cys Phe Glu Trp Trp Ser Phe Glu Leu Leu Ile Leu Leu Ser Gly Phe
245      250      255
Leu Pro Asn Pro Glu Leu Gln Thr Ser Val Leu Ser Ile Cys Leu Thr
260      265      270
Ser Ile Thr Leu Leu Phe Asn Ile Pro Phe Gly Leu Gly Ala Ala Gly
275      280      285
Ser Thr Arg Val Ala Asn Glu Leu Gly Ala Gly Asn Pro Asp Gly Ala
290      295      300
Arg Ser Ala Val Arg Val Val Leu Ser Met Thr Ala Ile Asp Ala Val
305      310      315      320
Ile Val Gly Gly Thr Leu Leu Ala Ala Arg Leu Val Gly Met Ala

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325      330      335
Tyr Ser Ser Glu Glu Glu Val Ile Ser Ser Val Ala Thr Met Val Pro
340      345      350
Leu Val Cys Ile Thr Val Val Thr Asp Cys Val Gln Gly Val Leu Ser
355      360      365
Gly Val Ala Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr Val Asn
370      375      380
Leu Gly Ser Phe Tyr Leu Leu Gly Ile Pro Met Ala Ile Leu Leu Gly
385      390      395      400
Phe Val Leu His Leu Gly Ser Arg Gly Leu Trp Met Gly Ile Val Cys
405      410      415
Gly Ser Leu Ser Gln Thr Ile Leu Met Ser Val Ile Thr Phe Phe Thr
420      425      430
Asn Trp Pro Lys Met Ala Asp Lys Ala Arg Glu Arg Val Phe Ser Glu
435      440      445
Lys Pro Pro
450

```

<210> 78

<211> 1375

<212> DNA

<213> Paspalum notatum

<400> 78

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gctgctgcag ctacagatgc agctcatctc caccgtcatg gtggggcacc tcggcgagat    60
gccgctcgcc ggccgccgcca tcgccaaactc gctcaccacac gtctccggat tcagcgtgct    120
tatgggactg gcatgcggat tggaaactat ttgtggacag gcctacgggg cagaacagta    180
tcataagcta gctttattta cctacaggtc tataattgta ctocctatac tgtgtgtgcc    240
cattgccatt atatgggttt tcatcccaga catactccct ctcataggtc aggatccgca    300
agtagcaagt gaggtcgga agtatgcctt atggcttacc cctggtttat ttgccttcag    360
tgtggctcag tgcctttcaa agttcctcca gtctcagagc ttaattttcc ccttgggttt    420
gagctcctta acaacactca ctctctttat tcctttgtgc tggttcatgg tttacaaagt    480
tgggatgggt aatgctggag ctgcttttagc agtcagcatc tgtgattggg ttgaaatcat    540
ggtccttggt ctttatatta agctctcacc ttogtgtgag aaaactcgtg ctccattcac    600
gcgggaagct tttcgaggga ttgggagttt catgcggttg gcagtacctt cagcacttat    660
gatatgcatt gaatggtggt cgtacgagct gottgttctg ctttcaggga tcttaccaaa    720
tccagcactt gaaacttcgg tactatctat atgcatgtct accatatgtt tgggtgtacaa    780
tatcccatat ggcacccggag cagctgcaag tgtgcgtgtg tccaatgagc taggtgcagg    840
gaacccagat ggtgcccgct tagtagtagt tgtcgcccta tccaccataa tttgttcagc    900
agtctcgttg agcgttaactc ttctatcact gcgccatttc atcggaattg ctttcagcaa    960
tgaagaggag gttgttagact atgtcaccag aatggtaccg ttgctttcaa tttcagttct   1020
taatgacaac ctccaaggag tcctttcagg tattttctaga ggctgtggat ggcagaattt   1080
aggagcatat gttaacctgg gcgcgttcta tcttgttggc attcctgtgg cacttggttt   1140
cggttttgca ttgcatctag gaggagctgg gttctggatt ggcataatag ctggtggagt   1200
tacacaggtc actctcctat cagtcatcac tgcaatgaca aactggggga agatgggtga   1260
tatggctagg gatagggtat atgagggaag tcttccaaca caggtagatt gaatgcgccca   1320
actttaagtc atattggatt ggattctatt aatcttcacc tacgttaaata agccg      1375

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<210> 79

<211> 436

<212> PRT

<213> Paspalum notatum

<400> 79

```

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

```

	85		90		95
Gln Asp Pro	Gln Val Ala Ser Glu	Ala Gly Lys Tyr Ala Leu Trp Leu			
	100	105	110		
Ile Pro Gly	Leu Phe Ala Phe Ser Val	Ala Gln Cys Leu Ser Lys Phe			
	115	120	125		
Leu Gln Ser	Gln Ser Leu Ile Phe Pro	Leu Val Leu Ser Ser Leu Thr			
	130	135	140		
Thr Leu Thr	Leu Phe Ile Pro Leu Cys Trp Phe Met Val Tyr Lys Val				
	145	150	155		160
Gly Met Gly	Asn Ala Gly Ala Ala Leu Ala Val Ser Ile Cys Asp Trp				
	165	170	175		
Val Glu Ile	Met Val Leu Gly Leu Tyr Ile Lys Leu Ser Pro Ser Cys				
	180	185	190		
Glu Lys Thr	Arg Ala Pro Phe Thr Arg Glu Ala Phe Arg Gly Ile Gly				
	195	200	205		
Ser Phe Met	Arg Leu Ala Val Pro Ser Ala Leu Met Ile Cys Ile Glu				
	210	215	220		
Trp Trp Ser	Tyr Glu Leu Leu Val Leu Leu Ser Gly Ile Leu Pro Asn				
	225	230	235		240
Pro Ala Leu	Glu Thr Ser Val Leu Ser Ile Cys Met Ser Thr Ile Leu				
	245	250	255		
Leu Val Tyr	Asn Ile Pro Tyr Gly Ile Gly Ala Ala Ala Ser Val Arg				
	260	265	270		
Val Ser Asn	Glu Leu Gly Ala Gly Asn Pro Asp Gly Ala Arg Leu Val				
	275	280	285		
Val Val Val	Ala Leu Ser Thr Ile Ile Cys Ser Ala Val Leu Val Ser				
	290	295	300		
Val Thr Leu	Leu Ser Leu Arg His Phe Ile Gly Ile Ala Phe Ser Asn				
	305	310	315		320
Glu Glu Glu	Val Val Asp Tyr Val Thr Arg Met Val Pro Leu Leu Ser				
	325	330	335		
Ile Ser Val	Leu Asn Asp Asn Leu Gln Gly Val Leu Ser Gly Ile Ser				
	340	345	350		
Arg Gly Cys	Gly Trp Gln Asn Leu Gly Ala Tyr Val Asn Leu Gly Ala				
	355	360	365		
Phe Tyr Leu	Val Gly Ile Pro Val Ala Leu Val Phe Gly Phe Ala Leu				
	370	375	380		
His Leu Gly	Gly Ala Gly Phe Trp Ile Gly Ile Ile Ala Gly Gly Val				
	385	390	395		400
Thr Gln Val	Thr Leu Leu Ser Val Ile Thr Ala Met Thr Asn Trp Gly				
	405	410	415		
Lys Met Val	Asp Met Ala Arg Asp Arg Val Tyr Glu Gly Ser Leu Pro				
	420	425	430		
Thr Gln Val	Asp				
	435				

<210> 80

<211> 1960

<212> DNA

<213> Paspalum notatum

<400> 80

cgccccacgg	tgggggacgga	ggcgcgcgcg	cagggtggggc	tcgcggcgcc	gctgggtggcg	60
tgcagcctgc	tgcagtcacag	cttcgaggtg	gtctccgtca	tggtcgcggg	ccacctcggg	120
gagctctccc	tctccggcgc	ctccgtcgct	gcctccttcg	ccaacgtcac	cggcttcagc	180
gtcctcgtcg	gcattgggag	cgcatctgat	accttttgtg	gacaatcata	tggagcaagg	240
caatatgac	tgctcgggac	acacacacaa	agggcctatag	ttgttcttat	gcttacaggt	300
gttcctttgg	catttgtttt	ggccttctot	ggtcaaatcc	tggttgctct	tggtcaaaaat	360
cctgaaatat	catttcaagc	tggactgtac	gctcagtggt	tgatccctgg	tcttttcgca	420
tacgggtttg	tccagtgcc	taccagattt	ctgcagaccc	aaaatatgtg	cogaatattg	480
gtagtttctc	ctggacttac	tttgctactt	cacattatgc	tgtgctgggt	cctgggtcaa	540
agttttggcc	ttggccacaa	aggcgcagct	ctggcgaccc	caatatotta	ctgggttcaat	600
gtggcattgc	tagcaatata	tgtgaaagcc	tctgaaagtg	gcagaagaag	ctggcatgga	660
tggtcaaggg	aggcactaaa	gttaaaggat	gtaaaactat	atctatgggt	ggccattcca	720
tctacattta	tgacotgctt	ggagtattgg	gcatttgaga	tggtgggttct	cctagcagga	780

tttcttcag	atccaaaact	ggaaacttoa	attttatcca	tcagcctaaa	cacaatgtgg	840
atggtttata	caattccaag	tgccctcagt	agtgaataaa	gtattagagt	gtccaatgaa	900
ctaggtgctg	ggaaccacaca	ggcagcacgc	ctgtcagttt	atatttcagg	aatcatgtgc	960
ctaactgaag	gcctttttgt	agctatcatc	acagtattag	tgcgagatat	ctggggttat	1020
ttgtacagca	atgaagaaaa	ggtcgtgaag	catgtatcga	tgatgatgcc	aattcttgct	1080
acttctgact	tcatggatgg	aatacagtcg	acactatcag	gcgcggctcg	aggatgtggc	1140
tggcagaag	tatgctcact	tatcaacctg	tttgcttact	atgttattgg	tctcccttca	1200
gctgtcactt	tgtcatttgt	tttgaagatt	ggtggttaagg	gcctttggct	gggaattata	1260
tgtgctatgg	cagtgcaaat	atttgctttg	gtagtatga	tgcttcgaac	cagctggaa	1320
gaagaggctg	aaaaggcccc	ggctagagtt	cagtgttcag	atggcagcat	tacattggac	1380
tgaatcttat	cagttgtgaa	ttgtgattat	agatccctta	aggtgcagtg	tataggttta	1440
tatgagtcct	ttgggccaag	gcagcagctc	tggatctggc	gggactgagc	tatcagccta	1500
aaagcagggag	tacttggttt	gcaattgatg	gccttgaggt	acgtttcttt	ctggtttctg	1560
cggtcctaat	atagcatcgt	gaaaggcgag	gaagcaaccg	aaatttggtta	gctccggaag	1620
tggagggttg	cgtggagcgt	gagctgtttc	caaatcccaa	atactccacc	tgctcacogt	1680
gtgggttaat	cagctctcac	ctgaaagata	tttgctatta	ctacaattga	tgtttgctct	1740
gaaaggaaag	aaggagagag	ggtgtaaaact	tttcatgcta	ctacgcttca	ggagttcagg	1800
tgtcagtcctg	tcagggtggt	tccttggaat	gaaagcttca	gggtgcgctc	aggatgccat	1860
gtcagctagc	ggtctgttgc	gtgggcgttt	tatacagagc	tgatcgatgg	catctgcgat	1920
cgcgtctgta	tagataatgt	atggatggct	cagaccatcc			1960

<210> 81

<211> 460

<212> PRT

<213> Paspalum notatum

<400> 81

```

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

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

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<210> 82

<211> 1761

<212> DNA

<213> Paspalum notatum

<400> 82

```

cagtctogct cactctaaag tccaaaactac gaccagctcaa acaccgacgg agagagggcg 60
agagggcacac accgagagac acgaactaga agagctttgc gtaccatggc gaaggggaagc 120
gcggagggaag cgcttctcgc cgcgcccca cccgaggagg accagagcgt gcgggtcgag 180
gtgaagaagc agctatggct ggcaggggccc atgatctccg gcgcgctcct gcagaacgtc 240
atccagatga tctccgtcat gtatgtgggc caccctcggcg agctccccct cgcggcgccc 300
tccatggcca actccttcgc caccgtcacg ggcttcagcc tgctgcttgg aatggccagt 360
gctctggata ctctgtcggg gcaagcgttc ggagcccgcc agtactacct cctgggcatt 420
tacaagcaac gtgccatgtt tctactcacc ctcgtgagcg tccccctcgc cgtgatctgg 480
ttgtacacgg gcgagatcct cgcctcgtg ggcagggacc ccgacatcgc cgcggaggca 540
ggcaggtacg caccgtggat gatccacgg gtcttcgcct acgggcttct gcagtgcac 600
gtccgggttc tgacagacga gaatgtcgtg gtgcccgta tggcgagcgc tggcgcgggc 660
gcgggggtgcc acctggtggt atgctggcg ctctgtacg cgctcgggtt ggcagcaag 720
ggtgcggcgc ttagcaacgc catctcgtac tgggtcaacg tggcctgctt ggccgtgtac 780
gtcaggggtgt cgcagcacct caaggaagc tggactggct tctccacgga ggccttcgt 840
gatgctctcg gcttcttcgc gctcgtctc ccatccgcta tgatggctgt cttgggaatg 900
tggctcgttg agctcattgt gottctatcg ggccttctgc ctaaccccaa actggagaca 960
tccgtgctgt ccatcagcct taacactgct gccttcgtgt ggaatgatcc cttggggtt 1020
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cgccttcgcy tgcccgtagt cctgtttctg gccgtctcgg aagggtggt gatggggtt 1140
atcctcgtct cgcgtcgcta catctggggc caccggtaca gcaacgtcga ggaggtggt 1200
acatacgtgg ccaagatgat gctcgtcatt gccgtgtcga actttttcga tggaaatccag 1260
tgtgtttctt caggcgtggc aagaggtggt ggaatggcga agattggtg ttgcgttaac 1320
cttgggtgcct actatttggg cggcattcct tcagcatacc tcatagcttt tgttctcgt 1380
gttggcgga cgggcctgtg gttgggcac atctgtggcg tcttgggtga agtctcgtg 1440
ctaagatcg tcacgctgtg tacgaactgg gatagtgagg caaccaaggc gaaggacaga 1500
gtttacagtt cttctcgtcc tcgggatttt gaaacatgac cgaatgcagt gtagtgaaga 1560
agcgttttac cacacaacct agctgggtga atcccaaaga gaagagacac ttaacttaat 1620
tatacttatt acagagtttc catcagcatt atcaatatgc agttacagat tatctaaaat 1680
aagctttcca tgtattctca caggcaagct gtccagcata cttatgatgt gtactccatt 1740
ttttttgttt gatgccaatgc a 1761

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<210> 83

<211> 477

<212> PRT

<213> Paspalum notatum

<400> 83

Met Ala Lys Gly Ser Ala Glu Glu Ala Leu Leu Ala Ala Ala Gln Pro

```

1           5           10           15
Glu Glu Asp Gln Ser Val Arg Val Glu Val Lys Lys Gln Leu Trp Leu
20          25          30
Ala Gly Pro Met Ile Ser Gly Ala Leu Leu Gln Asn Val Ile Gln Met
35          40          45
Ile Ser Val Met Tyr Val Gly His Leu Gly Glu Leu Pro Leu Ala Gly
50          55          60
Ala Ser Met Ala Asn Ser Ser Phe Ala Thr Val Thr Gly Phe Ser Leu Leu
65          70          75          80
Leu Gly Met Ala Ser Ala Leu Asp Thr Leu Cys Gly Gln Ala Phe Gly
85          90          95
Ala Arg Gln Tyr Tyr Leu Leu Gly Ile Tyr Lys Gln Arg Ala Met Phe
100         105         110
Leu Leu Thr Leu Val Ser Val Pro Leu Ala Val Ile Trp Leu Tyr Thr
115         120         125
Gly Glu Ile Leu Ala Leu Leu Gly Gln Asp Pro Asp Ile Ala Ala Glu
130         135         140
Ala Gly Arg Tyr Ala Arg Trp Met Ile Pro Ala Val Phe Ala Tyr Gly
145         150         155         160
Leu Leu Gln Cys His Val Arg Phe Leu Gln Thr Gln Asn Val Val Val
165         170         175
Pro Val Met Ala Ser Ala Gly Ala Ala Ala Gly Cys His Leu Val Val
180         185         190
Cys Trp Ala Leu Val Tyr Ala Leu Gly Leu Gly Ser Lys Gly Ala Ala
195         200         205
Leu Ser Asn Ala Ile Ser Tyr Trp Val Asn Val Ala Val Leu Ala Val
210         215         220
Tyr Val Arg Val Ser Ser Thr Cys Lys Glu Thr Trp Thr Gly Phe Ser
225         230         235         240
Thr Glu Ala Phe Arg Asp Ala Leu Gly Phe Phe Arg Leu Ala Val Pro
245         250         255
Ser Ala Met Met Val Cys Leu Glu Met Trp Ser Phe Glu Leu Ile Val
260         265         270
Leu Leu Ser Gly Leu Leu Pro Asn Pro Lys Leu Glu Thr Ser Val Leu
275         280         285
Ser Ile Ser Leu Asn Thr Ala Ala Phe Val Trp Met Ile Pro Phe Gly
290         295         300
Leu Gly Ser Ala Ile Ser Thr Arg Val Ser Asn Glu Leu Gly Ala Gly
305         310         315         320
Arg Pro Arg Ala Ala Arg Leu Ala Val Arg Val Val Leu Phe Leu Ala
325         330         335
Val Ser Glu Gly Leu Val Met Gly Phe Ile Leu Val Cys Val Arg Tyr
340         345         350
Ile Trp Gly His Ala Tyr Ser Asn Val Glu Glu Val Val Thr Tyr Val
355         360         365
Ala Lys Met Met Leu Val Ile Ala Val Ser Asn Phe Phe Asp Gly Ile
370         375         380
Gln Cys Val Leu Ser Gly Val Ala Arg Gly Cys Gly Trp Gln Lys Ile
385         390         395         400
Gly Ala Cys Val Asn Leu Gly Ala Tyr Tyr Leu Val Gly Ile Pro Ser
405         410         415
Ala Tyr Leu Ile Ala Phe Val Leu Arg Val Gly Gly Thr Gly Leu Trp
420         425         430
Leu Gly Ile Ile Cys Gly Leu Leu Val Gln Val Leu Leu Met Ile
435         440         445
Val Thr Leu Cys Thr Asn Trp Asp Ser Glu Ala Thr Lys Ala Lys Asp
450         455         460
Arg Val Tyr Ser Ser Ser Arg Pro Ala Asp Phe Glu Thr
465         470         475

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<210> 84

<211> 1385

<212> DNA

<213> Paspalum notatum

<400> 84

```

aacgtcacog gcttcagcct tctctacggc atggcgagcg cgctggacac gctgtgcggg      60
caggccttcg gagccaggca gtacggccgc ctgggcctct acaagcagcg agcgatgctg      120
gtgctcgcgc tcacctgcgt tctgatcgcc gcgctctggg ccaacgccgg caagatcctc      180
gtcctcatcg gccaggaccc cgacatcgcc gccgaggccg gcgcctactc acggtggctc      240
ataccgtgcc tcgtccctct cgtccgcctc gtgtgccaca tccgtttcct acaggccacg      300
agcatcgctg tgcgggtaat ggtgagctct ggtgcgacgg cgctgagcca cgtcttggtg      360
tgctgggcgc tgggtgtcaa ggccggaatg gggagcaaa gcgctgcgct ggcagcgccc      420
atttcctaca ccatcaacct gacctgcta gctctctacg tcaggctctc aagcgctgct      480
aggaggacat ggactggatt ctccacggag gctttcagag agcttctccg attcaccgag      540
ctcgccatcc cgtctgcgat gatggtctgt ttggagtgtt ggtcctttga actgcttggt      600
cttctatccg gctactacc caatcctacg cttgaaactt cagtctgttc aatatgcctc      660
aacaccgggt cactcttgtt catggtacog tttggtctct gcacagccat aagcacagct      720
gtttcaaatg aacttggtgc tggtcagccc caagcagcaa agctagcaac tcgtgtgggt      780
atgtttatcg ctttatctgc gggcttgctg ctgggatctg ccattgattt gctacgcaat      840
ttctgggggtt atatgtacag caatgaacct gaagtgtgtg catacattgc tagaatgata      900
ccggttcttg caatatcggt cttcacagat gggcttcaca gttctctatc aggagtgttg      960
actggatgtg gtgagcagaa gattggtgca cgtgttaatc tcgctgcggt ctacttggtg      1020
ggcattccca tggcctgtgt gcttgcatct gtccctccatc taaatggaat gggctctgtg      1080
ctgggcatcg tttgtggcag cctttccaag cttgtgttgc tcactctggat cacaatgcgg      1140
ataaactggg agaaaaggcg aatcaaggca aaagaaaacg cttttaattc atctcttcca      1200
gttacatgac agagtatga gcaaccagac atcaagacca caacatggca cttgcaaaact      1260
gagagatatt aggttctctg gttattttaa tttaggatat gatgagataa gatatgcctc      1320
tattcatcat agcggctctca tgtttaaaca ttgtaacttc tctattaact tcatcagaat      1380
ttaac

```

<210> 85

<211> 402

<212> PRT

<213> Paspalum notatum

<400> 85

```

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

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Ser Ala Met Ile Leu Leu Arg Asn Phe Trp Gly Tyr Met Tyr Ser Asn
260    265    270
Glu Pro Glu Val Val Ala Tyr Ile Ala Arg Met Ile Pro Val Leu Ala
275    280    285
Ile Ser Phe Phe Thr Asp Gly Leu His Ser Ser Leu Ser Gly Val Leu
290    295    300
Thr Gly Cys Gly Glu Gln Lys Ile Gly Ala Arg Val Asn Leu Ala Ala
305    310    315    320
Phe Tyr Leu Ala Gly Ile Pro Met Ala Val Leu Leu Ala Phe Val Leu
325    330    335
His Leu Asn Gly Met Gly Leu Trp Leu Gly Ile Val Cys Gly Ser Leu
340    345    350
Ser Lys Leu Val Leu Leu Ile Trp Ile Thr Met Arg Ile Asn Trp Glu
355    360    365
Lys Glu Ala Ile Lys Ala Lys Glu Thr Ala Phe Asn Ser Ser Leu Pro
370    375    380
Val Thr
385    390    395    400

```

<210> 86

<211> 2023

<212> DNA

<213> Artificial Sequence

<220>

<223> Pn_NODE_22180 N-terminus complete

<400> 86

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atggcggaaga agccagtgga ggaagcgctc ctgcgagcgg cagacgagca ggagagcctg    60
agccgcgccca cgggtgggggc ggaggcgcgg cggcaggtgg ggctcgcggc gccgctggtg    120
gcgtgcagcc tgctgcagta cagcttgtag gtggtctccg tcatgttcgc cggccacctc    180
ggggagctct cctctccggg cgcctccgtc gctgcctcct tcgccaacgt caccggcttc    240
agcgtcctgc tgggcacggg gagcgcaatt gatacctttt gtggacaatc atatggagca    300
aggcaatatg atctgctcgg gacacacaca caaagggtta tagttgttct tatgcttaca    360
ggtgttcctt tggcatttgt tttggccttc tctggtcaaa tctggttgc tcttgggtcaa    420
aatcctgaaa tatcatttca agctggactg tacgctcagt ggttgatccc tggctctttc    480
gcatacgggt tgcctcagtg ccttaccaga tttctgcaga cccaaaatat tgtccgaata    540
ttggtagttt cctctggact tactttgcta cttcacatta tgcgtgctg gtctcctggtt    600
caaagttttg gccctggcca caaaggcgca gctctggcga cctcaatate ttactggttc    660
aatgtggcat tgctagcaat atatgtgaaa gcctctgaag ctggcagaag aagctggcat    720
ggatggtcaa gggaggcact aaagttaaag gatgtaaaac tatatctatg gttggccatt    780
ccatctacat ttatgacctg cttggagtat tgggcatttg agatggtggt tctcctagca    840
ggatctcttc cagatccaaa actggaaact tcaattttat ccatcagcct aaacacaatg    900
tggatggttt atacaattcc aagtggcctc agtagtgcaa taagtattag agtgtccaat    960
gaactaggtg ctgggaaccc acaggcagca cgcctgtcag tttatatttc aggaatcatg    1020
tgctaaactg aaggcctttt ttagctatc atcacagtat tagtgcgaga tatctggggt    1080
tatttgcaca gcaatgaaga aaaggtcgtg aagcatgtat cgatgatgat gccaatctct    1140
gctacttctg acttcacgga tggatacag tgcaactat caggcgcggc tcgaggatgt    1200
ggctggcaga aagtatgctc acttatcaac ctgtttgctt actatgttat tggctcctcc    1260
tcagctgtca cttttgcatt tgttttgaag attggtggta agggcctttg gctgggaatt    1320
atatgtgcta tggcagtgca aatatattgt ttggtagtga tgatgcttcg aaccagctgg    1380
aatgaagagg ctgaaaaggg cgggctaga gttcagtggt cagatggcag cattacattg    1440
gactgaatct tatcagttgt gaattgtgat tatagatccc ttaaggtgca gtgtataggt    1500
ttatatgagt cctttgggcc aaggcagcag ctctggatct ggcgggactg agctatcagc    1560
ctaaaagcag gagtacttgg cttgcaattg atggccttgg agtacgtttc tttctggttt    1620
ctgcggctca atgatagcac cgtgaaaggg gaggaagcaa ccgaaatttg gtagctccgg    1680
aagtggaggt tgtcgtggac gctgagctgt ttccaaatcc caaatactcc acctgctcac    1740
cgtgtgggtt aatcgactct cacctgaaag atatttgcta ttactacaat tgatgtttgc    1800
tctgaaagga aggaaggaga gaggtgttaa acttttcatg ctactacgct tcaggagttc    1860
aggtgtcagt ctgtcagggg gtttccctgg aatgaaagct tcagggtgcg ctccaggatgc    1920
catgtcagct agcgggtctg tgcgtggcg ttttatacag agctgatcga tggcatctgc    1980
gatcgctct gtatagataa tgtatggatg gctcagacca tcc    2023

```

<210> 87

<211> 481

<212> PRT

<213> Artificial Sequence

<220>

<223> Pn_NODE21180 N-terminus complete

<400> 87

```

Met Ala Lys Lys Pro Val Glu Glu Ala Leu Leu Ala Ala Ala Asp Glu
1      5      10      15
Gln Glu Ser Leu Ser Arg Pro Thr Val Gly Ala Glu Ala Arg Arg Gln
20      25      30
Val Gly Leu Ala Ala Pro Leu Val Ala Cys Ser Leu Leu Gln Tyr Ser
35      40      45
Leu Gln Val Val Ser Val Met Phe Ala Gly His Leu Gly Glu Leu Ser
50      55      60
Leu Ser Gly Ala Ser Val Ala Ala Ser Phe Ala Asn Val Thr Gly Phe
65      70      75      80
Ser Val Leu Leu Gly Met Gly Ser Ala Leu Asp Thr Phe Cys Gly Gln
85      90      95
Ser Tyr Gly Ala Arg Gln Tyr Asp Leu Leu Gly Thr His Thr Gln Arg
100      105      110
Ala Ile Val Val Leu Met Leu Thr Gly Val Pro Leu Ala Phe Val Leu
115      120      125
Ala Phe Ser Gly Gln Ile Leu Val Ala Leu Gly Gln Asn Pro Glu Ile
130      135      140
Ser Phe Gln Ala Gly Leu Tyr Ala Gln Trp Leu Ile Pro Gly Leu Phe
145      150      155      160
Ala Tyr Gly Leu Leu Gln Cys Leu Thr Arg Phe Leu Gln Thr Gln Asn
165      170      175
Ile Val Arg Ile Leu Val Val Ser Ser Gly Leu Thr Leu Leu Leu His
180      185      190
Ile Met Leu Cys Trp Phe Leu Val Gln Ser Phe Gly Leu Gly His Lys
195      200      205
Gly Ala Ala Leu Ala Thr Ser Ile Ser Tyr Trp Phe Asn Val Ala Leu
210      215      220
Leu Ala Ile Tyr Val Lys Ala Ser Glu Ala Gly Arg Arg Ser Trp His
225      230      235      240
Gly Trp Ser Arg Glu Ala Leu Lys Leu Lys Asp Val Lys Leu Tyr Leu
245      250      255
Trp Leu Ala Ile Pro Ser Thr Phe Met Thr Cys Leu Glu Tyr Trp Ala
260      265      270
Phe Glu Met Val Val Leu Leu Ala Gly Phe Leu Pro Asp Pro Lys Leu
275      280      285
Glu Thr Ser Ile Leu Ser Ile Ser Leu Asn Thr Met Trp Met Val Tyr
290      295      300
Thr Ile Pro Ser Gly Leu Ser Ser Ala Ile Ser Ile Arg Val Ser Asn
305      310      315      320
Glu Leu Gly Ala Gly Asn Pro Gln Ala Ala Arg Leu Ser Val Tyr Ile
325      330      335
Ser Gly Ile Met Cys Leu Thr Glu Gly Leu Phe Val Ala Ile Ile Thr
340      345      350
Val Leu Val Arg Asp Ile Trp Gly Tyr Leu Tyr Ser Asn Glu Glu Lys
355      360      365
Val Val Lys His Val Ser Met Met Met Pro Ile Leu Ala Thr Ser Asp
370      375      380
Phe Met Asp Gly Ile Gln Cys Thr Leu Ser Gly Ala Ala Arg Gly Cys
385      390      395      400
Gly Trp Gln Lys Val Cys Ser Leu Ile Asn Leu Phe Ala Tyr Tyr Val
405      410      415
Ile Gly Leu Pro Ser Ala Val Thr Phe Ala Phe Val Leu Lys Ile Gly
420      425      430
Gly Lys Gly Leu Trp Leu Gly Ile Ile Cys Ala Met Ala Val Gln Ile
435      440      445
Phe Ala Leu Val Val Met Met Leu Arg Thr Ser Trp Asn Glu Glu Ala
450      455      460
Glu Lys Ala Arg Ala Arg Val Gln Cys Ser Asp Gly Ser Ile Thr Leu

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465      470      475      480
Asp

```

<210> 88

<211> 488

<212> PRT

<213> *Panicum virgatum*

<400> 88

```

Met Gly Ser Ser Pro Glu Ala Pro Leu Leu Pro Pro Gln Arg Gly Gly
1      5      10
Glu Glu Ala Gly Arg Cys Arg Trp Trp Arg Gly Gly Ala Ser Trp Ala
20      25      30
Ala Ala Thr Ala Glu Ala Gly Arg Leu Ala Ala Leu Gly Ala Pro Met
35      40      45
Ile Ala Val Ala Leu Leu Gln Leu Met Met Gln Leu Ile Ser Thr Val
50      55      60
Met Val Gly His Leu Gly Glu Val Pro Leu Ala Gly Ala Ala Ile Ala
65      70      75      80
Asn Ser Leu Thr Asn Val Ser Gly Phe Ser Val Leu Met Gly Leu Ala
85      90      95
Cys Gly Leu Glu Thr Ile Cys Gly Gln Ala Tyr Gly Ala Glu Gln Tyr
100     105     110
His Lys Leu Ala Leu Phe Thr Tyr Arg Ser Ile Val Val Leu Leu Val
115     120     125
Ala Ser Val Pro Ile Ala Ile Ile Trp Leu Phe Ile Pro Asp Val Leu
130     135     140
Pro Leu Ile Gly Gln Asp Ala Gln Ile Ala Ser Glu Ala Gly Arg Tyr
145     150     155     160
Ala Leu Trp Leu Ile Pro Gly Leu Phe Ala Tyr Ser Val Ala Gln Cys
165     170     175
Leu Ser Lys Phe Leu Gln Ser Gln Ser Leu Ile Phe Pro Met Val Leu
180     185     190
Ser Ser Leu Thr Thr Leu Thr Leu Phe Ile Pro Leu Cys Trp Phe Met
195     200     205
Val Tyr Lys Val Gly Met Gly Asn Ala Gly Ala Ala Phe Ala Val Ser
210     215     220
Ile Cys Asp Trp Val Glu Val Thr Val Leu Gly Leu Tyr Ile Lys Phe
225     230     235     240
Ser Pro Ser Cys Asp Lys Thr Arg Ala Ala Pro Thr Trp Glu Thr Phe
245     250     255
Arg Gly Ile Gly Ser Phe Met Arg Leu Ala Val Pro Ser Thr Leu Met
260     265     270
Ile Cys Leu Glu Trp Trp Ser Tyr Glu Leu Leu Val Leu Val Ser Gly
275     280     285
Asn Leu Pro Asn Pro Ala Leu Glu Thr Ser Val Leu Ser Ile Cys Ile
290     295     300
Ser Thr Val Val Leu Val Tyr Asn Leu Pro Tyr Gly Ile Gly Asn Ala
305     310     315     320
Ala Ser Val Arg Val Ser Asn Glu Leu Gly Ala Gly Asn Pro Asp Gly
325     330     335
Ala Arg Leu Val Val Val Val Ser Leu Ser Ile Ile Ile Cys Thr Ala
340     345     350
Val Leu Val Ser Val Thr Leu Leu Ser Leu Arg His Phe Ile Gly Ile
355     360     365
Ala Phe Ser Asn Glu Glu Glu Val Val Asn Tyr Val Thr Arg Met Val
370     375     380
Pro Leu Leu Ser Ile Ser Val Leu Ile Asp Asn Leu Gln Gly Val Leu
385     390     395     400
Ser Gly Ile Ser Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr Val
405     410     415
Asn Leu Gly Ala Phe Tyr Leu Ile Gly Ile Pro Val Ala Leu Val Leu
420     425     430
Gly Phe Ala Phe His Leu Gly Gly Ala Gly Phe Trp Ile Gly Met Ile

435     440     445
Ala Gly Gly Ala Thr Gln Val Thr Leu Leu Ser Val Ile Thr Ala Met
450     455     460
Thr Asn Trp Gly Lys Met Ala Glu Lys Ala Arg Asp Arg Val Phe Glu
465     470     475     480
Glu Ser Leu Pro Thr Gln Ala Asp
485

```

<210> 89

<211> 491

<212> PRT

<213> Oryza sativa

<400> 89

```

Met Ala Ala Ala Ala Arg Glu Glu Gln Pro Leu Leu Leu Arg Arg Glu
1      5      10      15
Glu Gly Glu Glu Glu Gly Glu Glu Val Gly Trp Arg Arg Arg Trp Gly
20      25      30
Ser Glu Ala Gly Lys Leu Ala Tyr Leu Ala Leu Pro Met Val Ala Val
35      40      45
Ser Leu Thr Asn Tyr Ala Val Gln Val Phe Ser Asn Met Met Val Gly
50      55      60
His Leu Pro Gly Val Leu Pro Leu Ser Ser Ala Ala Ile Ala Thr Ser
65      70      75      80
Leu Ala Ser Val Thr Gly Phe Ser Leu Leu Ile Gly Met Ala Ser Ala
85      90      95
Leu Glu Thr Leu Cys Gly Gln Ala Tyr Gly Ala Lys Gln Tyr His Thr
100     105     110
Leu Gly Val His Thr Tyr Arg Ala Ile Leu Thr Leu Leu Val Val Cys
115     120     125
Ile Pro Leu Ser Leu Leu Trp Val Phe Met Gly Lys Ile Leu Val Leu
130     135     140
Ile Gly Gln Asp Pro Leu Ile Ser His Gly Ala Gly Arg Tyr Ile Val
145     150     155     160
Trp Leu Ile Pro Gly Leu Phe Ala Asn Ala Leu Ile Gln Pro Ile Thr
165     170     175
Lys Phe Leu Gln Ser Gln Ser Leu Ile Met Pro Met Leu Val Ala Ser
180     185     190
Val Ala Thr Leu Val Phe His Ile Pro Leu Cys Trp Leu Met Val Phe
195     200     205
Lys Thr Gly Leu Gly Tyr Thr Gly Ala Ala Leu Ser Ile Ser Ile Ser
210     215     220
Tyr Trp Leu Asn Val Ala Met Leu Val Ala Tyr Ile Leu Leu Ser Ser
225     230     235     240
Ser Cys Lys Glu Thr Arg Thr Pro Pro Thr Ile Glu Ala Phe Lys Gly
245     250     255
Leu Asp Gly Phe Leu Arg Leu Ala Leu Pro Ser Ala Leu Met Ile Cys
260     265     270
Leu Glu Trp Trp Ser Phe Glu Leu Leu Ile Leu Met Ser Gly Leu Leu
275     280     285
Pro Asn Pro Glu Leu Gln Thr Ser Val Leu Ser Ile Cys Leu Thr Ser
290     295     300
Ile Thr Leu Leu Phe Thr Ile Pro Tyr Gly Leu Gly Ala Gly Gly Ser
305     310     315     320
Thr Arg Val Ala Asn Glu Leu Gly Ala Gly Asn Pro Glu Gly Ala Arg
325     330     335
Ser Ala Val Tyr Val Val Leu Ser Val Ala Val Thr Glu Ala Leu Ile
340     345     350
Val Cys Gly Thr Leu Leu Ala Ser Arg Arg Leu Leu Gly Arg Ala Tyr
355     360     365
Ser Ser Glu Glu Glu Val Ile Ser Phe Val Ala Met Met Val Pro Leu
370     375     380
Val Cys Ile Thr Val Val Thr Asp Gly Leu Gln Gly Val Met Ser Gly
385     390     395     400
Ile Ala Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr Val Asn Leu
405     410     415
Gly Ser Phe Tyr Leu Leu Gly Ile Pro Met Ala Ile Leu Leu Gly Phe
420     425     430
Val Leu His Met Gly Ala Lys Gly Leu Trp Met Gly Ile Val Cys Gly
435     440     445
Ser Ile Ser Gln Ile Thr Leu Leu Ser Ala Ile Thr Phe Phe Thr Asn
450     455     460
Trp Gln Lys Met Ala Glu Asn Ala Arg Glu Arg Val Phe Ser Glu Lys
465     470     475     480
Pro Thr Glu Pro Ser Arg Tyr His Leu Val Glu
485     490

```

<210> 90

<211> 491

<212> PRT

<213> Oryza sativa

<400> 90

```

Met Ala Ala Ala Ala Arg Glu Glu Gln Pro Leu Leu Leu Arg Arg Glu
1      5      10      15
Glu Gly Glu Glu Glu Gly Glu Glu Val Gly Trp Arg Arg Arg Trp Gly
20      25      30
Ser Glu Ala Gly Lys Leu Ala Tyr Leu Ala Leu Pro Met Val Ala Val
35      40      45
Ser Leu Thr Asn Tyr Ala Val Gln Val Phe Ser Asn Met Met Val Gly
50      55      60
His Leu Pro Gly Val Leu Pro Leu Ser Ser Ala Ala Ile Ala Thr Ser
65      70      75      80
Leu Ala Ser Val Thr Gly Phe Ser Leu Leu Ile Gly Met Ala Ser Ala
85      90      95
Leu Glu Thr Leu Cys Gly Gln Ala Tyr Gly Ala Lys Gln Tyr His Thr
100     105     110
Leu Gly Val His Thr Tyr Arg Ala Ile Leu Thr Leu Leu Val Val Cys
115     120     125
Ile Pro Leu Ser Leu Leu Trp Val Phe Met Gly Lys Ile Leu Val Leu
130     135     140
Ile Gly Gln Asp Pro Leu Ile Ser His Gly Ala Gly Arg Tyr Ile Val
145     150     155     160
Trp Leu Ile Pro Gly Leu Phe Ala Asn Ala Leu Ile Gln Pro Ile Thr
165     170     175
Lys Phe Leu Gln Ser Gln Ser Leu Ile Met Pro Met Leu Val Ala Ser
180     185     190
Val Ala Thr Leu Val Phe His Ile Pro Leu Cys Trp Leu Met Val Phe
195     200     205
Lys Thr Gly Leu Gly Tyr Thr Gly Ala Ala Leu Ser Ile Ser Ile Ser
210     215     220
Tyr Trp Leu Asn Val Ala Met Leu Val Ala Tyr Ile Leu Leu Ser Ser
225     230     235     240
Ser Cys Lys Glu Thr Arg Thr Pro Pro Thr Ile Glu Ala Phe Lys Gly
245     250     255
Leu Asp Gly Phe Leu Arg Leu Ala Leu Pro Ser Ala Leu Met Ile Cys
260     265     270
Leu Glu Trp Trp Ser Phe Glu Leu Leu Ile Leu Met Ser Gly Leu Leu
275     280     285
Pro Asn Pro Glu Leu Gln Thr Ser Val Leu Ser Ile Cys Leu Thr Ser
290     295     300
Ile Thr Leu Leu Phe Thr Ile Pro Tyr Gly Leu Gly Ala Gly Gly Ser
305     310     315     320
Thr Arg Val Ala Asn Glu Leu Gly Ala Gly Asn Pro Glu Gly Ala Arg
325     330     335
Ser Ala Val Tyr Val Val Leu Ser Val Ala Val Thr Glu Ala Leu Ile
340     345     350
Val Cys Gly Thr Leu Leu Ala Ser Arg Arg Leu Leu Gly Arg Ala Tyr
355     360     365
Ser Ser Glu Glu Glu Val Ile Ser Phe Val Ala Met Met Val Pro Leu
370     375     380
Val Cys Ile Thr Val Val Thr Asp Gly Leu Gln Gly Val Met Ser Gly
385     390     395     400
Ile Ala Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr Val Asn Leu
405     410     415
Gly Ser Phe Tyr Leu Leu Gly Ile Pro Met Ala Ile Leu Leu Gly Phe
420     425     430
Val Leu His Met Gly Ala Lys Gly Leu Trp Met Gly Ile Val Cys Gly
435     440     445
Ser Ile Ser Gln Ile Thr Leu Leu Ser Ala Ile Thr Phe Phe Thr Asn
450     455     460
Trp Gln Lys Met Ala Glu Asn Ala Arg Glu Arg Val Phe Ser Glu Lys
465     470     475     480
Pro Thr Glu Pro Ser Arg Tyr His Leu Val Glu
485     490

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<210> 91

<211> 408

<212> PRT

<213> Oryza sativa

<400> 91

```

Met Glu Glu Arg Ile Pro Leu Leu Ser Lys Arg Phe Pro Ala Asp Gly
1      5      10      15
Thr Ala Gly Val Gly Gly Gly Arg Glu Glu Gly Gly Asp Arg Trp
20      25      30
Trp Ser Gly Leu Ala Arg Glu Ala Gly Lys Val Gly Ser Met Ala Leu
35      40      45
Pro Met Ala Ala Met Ser Val Ala Gln Asn Ala Val Gln Val Ala Ser
50      55      60
Asn Met Met Val Gly His Leu Pro Gly Val Leu Pro Leu Ser Ala Ser
65      70      75      80
Ala Ile Ala Thr Ser Leu Ala Ser Val Ser Gly Phe Ser Leu Leu Val
85      90      95
Gly Met Ala Ser Gly Leu Glu Thr Leu Cys Gly Gln Ala Tyr Gly Ala
100     105     110
Lys Gln Tyr Asp Lys Leu Gly Val Gln Thr Tyr Arg Ala Ile Val Thr
115     120     125
Leu Thr Val Val Thr Ile Pro Ile Ser Leu Leu Trp Val Phe Ile Gly
130     135     140
Lys Leu Leu Thr Leu Ile Gly Gln Asp Pro Val Ile Ser His Glu Ala
145     150     155     160
Gly Arg Tyr Ile Val Trp Leu Ile Pro Gly Leu Phe Ala Tyr Ala Val
165     170     175
Cys Gln Pro Leu Thr Lys Phe Leu Gln Ser Gln Ser Leu Ile Phe Pro
180     185     190
Met Leu Trp Ser Ser Ile Ala Thr Leu Leu Leu His Ile Pro Leu Ser
195     200     205
Trp Leu Leu Val Phe Lys Thr Ser Met Gly Phe Thr Gly Ala Ala Leu
210     215     220
Ala Ile Ser Ile Ser Tyr Trp Leu Asn Thr Phe Met Leu Ala Ala Tyr
225     230     235     240
Ile Arg Phe Ser Cys Ser Cys Lys Val Thr Arg Ser Pro Pro Thr Ile
245     250     255
Glu Ala Phe Arg Gly Val Gly Leu Phe Leu Arg Ile Ala Leu Pro Ser
260     265     270
Ala Leu Met Leu Cys Phe Glu Trp Trp Ser Phe Glu Ile Leu Val Leu
275     280     285
Leu Ser Gly Leu Leu Pro Asn Pro Glu Leu Glu Ser Ser Val Leu Ser
290     295     300
Ile Cys Leu Thr Thr Ser Leu Met Tyr Thr Ile Pro Tyr Gly Leu
305     310     315     320
Gly Gly Ala Ala Ser Thr Arg Val Ala Asn Glu Leu Gly Ala Gly Asn
325     330     335
Pro Glu Gly Ala Arg Ser Ala Val His Leu Val Met Ser Ile Ala Gly

340      345      350
Thr Glu Ala Val Leu Val Thr Gly Met Leu Phe Ala Ala Gln Arg Ile
355     360     365
Leu Gly Tyr Ala Tyr Ser Ser Asp Glu Glu Val Val Thr Tyr Phe Thr
370     375     380
Ser Met Val Pro Phe Val Cys Ile Ser Val Ala Ala Asp Ser Leu Gln
385     390     395     400
Gly Val Leu Ser Gly Tyr Ile Ser
405

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<210> 92

<211> 408

<212> PRT

<213> Oryza sativa

<400> 92

```

Met Glu Glu Arg Ile Pro Leu Leu Ser Lys Arg Phe Pro Ala Asp Gly
1      5      10      15
Thr Ala Gly Val Gly Gly Gly Arg Glu Glu Gly Gly Asp Arg Trp
20      25      30
Trp Ser Gly Leu Ala Arg Glu Ala Gly Lys Val Gly Ser Met Ala Leu
35      40      45
Pro Met Ala Ala Met Ser Val Ala Gln Asn Ala Val Gln Val Ala Ser
50      55      60
Asn Met Met Val Gly His Leu Pro Gly Val Leu Pro Leu Ser Ala Ser
65      70      75      80
Ala Ile Ala Thr Ser Leu Ala Ser Val Ser Gly Phe Ser Leu Leu Val
85      90      95
Gly Met Ala Ser Gly Leu Glu Thr Leu Cys Gly Gln Ala Tyr Gly Ala
100     105     110
Lys Gln Tyr Asp Lys Leu Gly Val Gln Thr Tyr Arg Ala Ile Val Thr
115     120     125
Leu Thr Val Val Thr Ile Pro Ile Ser Leu Leu Trp Val Phe Ile Gly
130     135     140
Lys Leu Leu Thr Leu Ile Gly Gln Asp Pro Val Ile Ser His Glu Ala
145     150     155     160
Gly Arg Tyr Ile Val Trp Leu Ile Pro Gly Leu Phe Ala Tyr Ala Val
165     170     175
Cys Gln Pro Leu Thr Lys Phe Leu Gln Ser Gln Ser Leu Ile Phe Pro
180     185     190
Met Leu Trp Ser Ser Ile Ala Thr Leu Leu Leu His Ile Pro Leu Ser
195     200     205
Trp Leu Leu Val Phe Lys Thr Ser Met Gly Phe Thr Gly Ala Ala Leu
210     215     220
Ala Ile Ser Ile Ser Tyr Trp Leu Asn Thr Phe Met Leu Ala Ala Tyr
225     230     235     240
Ile Arg Phe Ser Cys Ser Cys Lys Val Thr Arg Ser Pro Pro Thr Ile
245     250     255
Glu Ala Phe Arg Gly Val Gly Leu Phe Leu Arg Ile Ala Leu Pro Ser
260     265     270
Ala Leu Met Leu Cys Phe Glu Trp Trp Ser Phe Glu Ile Leu Val Leu
275     280     285
Leu Ser Gly Leu Leu Pro Asn Pro Glu Leu Glu Ser Ser Val Leu Ser
290     295     300
Ile Cys Leu Thr Thr Thr Ser Leu Met Tyr Thr Ile Pro Tyr Gly Leu
305     310     315     320
Gly Gly Ala Ala Ser Thr Arg Val Ala Asn Glu Leu Gly Ala Gly Asn
325     330     335
Pro Glu Gly Ala Arg Ser Ala Val His Leu Val Met Ser Ile Ala Gly
340     345     350
Thr Glu Ala Val Leu Val Thr Gly Met Leu Phe Ala Ala Gln Arg Ile
355     360     365
Leu Gly Tyr Ala Tyr Ser Ser Asp Glu Glu Val Val Thr Tyr Phe Thr
370     375     380
Ser Met Val Pro Phe Val Cys Ile Ser Val Ala Ala Asp Ser Leu Gln
385     390     395     400
Gly Val Leu Ser Gly Tyr Ile Ser
405

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<210> 93

<211> 408

<212> PRT

<213> Panicum virgatum

<400> 93

```

Met Glu Glu Arg Ile Pro Leu Leu Ser Lys Arg Phe Pro Ala Asp Gly
1      5      10      15
Thr Ala Gly Val Gly Gly Gly Arg Glu Glu Gly Gly Asp Arg Trp
20      25      30
Trp Ser Gly Leu Ala Arg Glu Ala Gly Lys Val Gly Ser Met Ala Leu
35      40      45
Pro Met Ala Ala Met Ser Val Ala Gln Asn Ala Val Gln Val Ala Ser
50      55      60
Asn Met Met Val Gly His Leu Pro Gly Val Leu Pro Leu Ser Ala Ser
65      70      75      80
Ala Ile Ala Thr Ser Leu Ala Ser Val Ser Gly Phe Ser Leu Leu Val
85      90      95
Gly Met Ala Ser Gly Leu Glu Thr Leu Cys Gly Gln Ala Tyr Gly Ala
100     105     110
Lys Gln Tyr Asp Lys Leu Gly Val Gln Thr Tyr Arg Ala Ile Val Thr
115     120     125
Leu Thr Val Val Thr Ile Pro Ile Ser Leu Leu Trp Val Phe Ile Gly
130     135     140
Lys Leu Leu Thr Leu Ile Gly Gln Asp Pro Val Ile Ser His Glu Ala
145     150     155     160
Gly Arg Tyr Ile Val Trp Leu Ile Pro Gly Leu Phe Ala Tyr Ala Val
165     170     175
Cys Gln Pro Leu Thr Lys Phe Leu Gln Ser Gln Ser Leu Ile Phe Pro
180     185     190
Met Leu Trp Ser Ser Ile Ala Thr Leu Leu Leu His Ile Pro Leu Ser
195     200     205
Trp Leu Leu Val Phe Lys Thr Ser Met Gly Phe Thr Gly Ala Ala Leu
210     215     220
Ala Ile Ser Ile Ser Tyr Trp Leu Asn Thr Phe Met Leu Ala Ala Tyr
225     230     235     240
Ile Arg Phe Ser Cys Ser Cys Lys Val Thr Arg Ser Pro Pro Thr Ile
245     250     255
Glu Ala Phe Arg Gly Val Gly Leu Phe Leu Arg Ile Ala Leu Pro Ser
260     265     270
Ala Leu Met Leu Cys Phe Glu Trp Trp Ser Phe Glu Ile Leu Val Leu
275     280     285
Leu Ser Gly Leu Leu Pro Asn Pro Glu Leu Glu Ser Ser Val Leu Ser
290     295     300
Ile Cys Leu Thr Thr Thr Ser Leu Met Tyr Thr Ile Pro Tyr Gly Leu
305     310     315     320
Gly Gly Ala Ala Ser Thr Arg Val Ala Asn Glu Leu Gly Ala Gly Asn
325     330     335
Pro Glu Gly Ala Arg Ser Ala Val His Leu Val Met Ser Ile Ala Gly
340     345     350
Thr Glu Ala Val Leu Val Thr Gly Met Leu Phe Ala Ala Gln Arg Ile
355     360     365
Leu Gly Tyr Ala Tyr Ser Ser Asp Glu Glu Val Val Thr Tyr Phe Thr
370     375     380
Ser Met Val Pro Phe Val Cys Ile Ser Val Ala Ala Asp Ser Leu Gln
385     390     395     400
Gly Val Leu Ser Gly Tyr Ile Ser
405

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<210> 94
<211> 306

<212> PRT

<213> Oryza sativa

<400> 94

```

Met Glu Glu Arg Ile Pro Leu Leu Ser Lys Arg Phe Pro Ala Asp Gly
1      5      10      15
Thr Ala Gly Val Gly Gly Gly Arg Glu Glu Gly Gly Asp Arg Trp
20      25      30
Trp Ser Gly Leu Ala Arg Glu Ala Gly Lys Val Gly Ser Met Ala Leu
35      40      45
Pro Met Ala Ala Met Ser Val Ala Gln Asn Ala Val Gln Val Ala Ser
50      55      60
Asn Met Met Val Gly His Leu Pro Gly Val Leu Pro Leu Ser Ala Ser
65      70      75      80
Ala Ile Ala Thr Ser Leu Ala Ser Val Ser Gly Phe Ser Leu Leu Val
85      90      95
Gly Met Ala Ser Gly Leu Glu Thr Leu Cys Gly Gln Ala Tyr Gly Ala
100     105     110
Lys Gln Tyr Asp Lys Leu Gly Val Gln Thr Tyr Arg Ala Ile Val Thr
115     120     125
Leu Thr Val Val Thr Ile Pro Ile Ser Leu Leu Trp Val Phe Ile Gly
130     135     140
Lys Leu Leu Thr Leu Ile Gly Gln Asp Pro Val Ile Ser His Glu Ala
145     150     155     160
Gly Arg Tyr Ile Val Trp Leu Ile Pro Gly Leu Phe Ala Tyr Ala Val
165     170     175
Cys Gln Pro Leu Thr Lys Phe Leu Gln Ser Gln Ser Leu Ile Phe Pro
180     185     190
Met Leu Trp Ser Ser Ile Ala Thr Leu Leu Leu His Ile Pro Leu Ser
195     200     205
Trp Leu Leu Val Phe Lys Thr Ser Met Gly Phe Thr Gly Ala Ala Leu
210     215     220
Ala Ile Ser Ile Ser Tyr Trp Leu Asn Thr Phe Met Leu Ala Ala Tyr
225     230     235     240
Ile Arg Phe Ser Cys Ser Cys Lys Val Thr Arg Ser Pro Pro Thr Ile
245     250     255
Glu Ala Phe Arg Gly Val Gly Leu Phe Leu Arg Ile Ala Leu Pro Ser
260     265     270
Ala Leu Met Leu Cys Phe Glu Trp Trp Ser Phe Glu Ile Leu Val Leu
275     280     285
Leu Ser Gly Leu Leu Pro Asn Pro Glu Leu Glu Ser Ser Val Leu Ser
290     295     300
Ile Trp
305

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<210> 95

<211> 487

<212> PRT

<213> Zea may

<400> 95

```

Met Ala Ala Ala Arg Glu Glu Asp Glu Ala Ala Arg Pro Leu Leu Leu
1      5      10      15
Leu Pro Arg Thr Ala Gln Glu Asp Gln Lys Trp Trp Arg Arg Trp Ala
20      25      30
Arg Glu Ala Gly Trp Val Gly Tyr Leu Ala Leu Pro Met Val Val Val
35      40      45
Asn Leu Ser Gln Tyr Ala Val Gln Val Ser Ser Asn Met Met Val Gly
50      55      60
His Leu Pro Gly Val Leu Pro Leu Ser Ser Ala Ala Ile Ala Thr Ser
65      70      75      80
Leu Ala Asn Val Ser Gly Phe Ser Leu Leu Ile Gly Met Ala Ser Ala
85      90      95
Leu Glu Thr Leu Cys Gly Gln Ala Tyr Gly Ala Lys Gln Tyr His Lys
100     105     110

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```

Leu Gly Leu Asp Thr Tyr Arg Ala Val Val Thr Leu Leu Val Val Cys
115 120 125
Val Pro Leu Ser Leu Leu Trp Val Phe Met Asp Lys Ile Leu Val Leu
130 135 140
Ile Gly Gln Asp Pro Leu Ile Ser Gln Gly Ala Gly Arg Tyr Met Val
145 150 155 160
Trp Leu Ile Pro Gly Leu Phe Ala Asn Ala Val Ile Gln Pro Leu Thr
165 170 175
Lys Phe Leu Gln Thr Gln Ser Leu Ile Tyr Pro Leu Leu Leu Ser Ser
180 185 190
Ala Ala Thr Ala Ala Val His Val Pro Leu Cys Tyr Val Met Val Phe
195 200 205
Lys Thr Gly Leu Gly Tyr Thr Gly Ala Ala Leu Thr Ile Ser Ile Ser
210 215 220
Tyr Trp Leu Asn Val Ala Met Leu Val Gly Tyr Ile Ala Phe Ser Ser
225 230 235 240
Ser Cys Lys Glu Thr Arg Ala Arg Pro Thr Val Glu Val Phe Arg Gly
245 250 255
Val Asp Ala Phe Leu Arg Leu Ala Leu Pro Ser Ala Leu Met Met Cys
260 265 270
Leu Glu Trp Trp Ser Phe Glu Leu Leu Thr Leu Met Ser Gly Leu Leu
275 280 285
Pro Asn Pro Glu Leu Gln Thr Ser Val Leu Ser Ile Cys Leu Thr Ser
290 295 300
Val Thr Leu Leu Phe Thr Ile Pro Phe Gly Leu Gly Ala Ala Gly Ser
305 310 315 320
Thr Arg Val Ala Asn Glu Leu Gly Ala Gly Asn Pro Asp Gly Ala Arg
325 330 335
Ser Ala Val Arg Val Val Leu Ser Met Ala Gly Ile Asp Ala Val Val
340 345 350
Val Ser Gly Ser Leu Leu Ala Ala Arg Arg Leu Val Gly Ile Ala Tyr
355 360 365
Ser Ser Glu Glu Glu Val Ile Ser Ala Val Ala Ala Met Val Pro Leu
370 375 380
Val Cys Ile Thr Ala Ile Thr Asp Cys Leu Gln Gly Ile Leu Ser Gly
385 390 395 400
Val Ala Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr Val Asn Leu
405 410 415
Gly Ser Phe Tyr Leu Leu Gly Ile Pro Met Ala Ile Leu Leu Gly Phe
420 425 430
Val Leu Arg Met Gly Ser Arg Gly Leu Trp Met Gly Ile Val Cys Gly
435 440 445
Ser Leu Ser Gln Thr Thr Leu Met Ser Ala Ile Thr Phe Phe Thr Asp
450 455 460
Trp Asn Lys Met Ala Glu Lys Ala Arg Glu Arg Val Phe Ser Asp Lys
465 470 475 480
Gln Pro Gln Glu Pro Gly Pro
485

```

<210> 96

<211> 441

<212> PRT

<213> zea mays

<400> 96

```

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

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```

Ile Ala Ser Val Pro Met Ala Ile Leu Trp Val Phe Leu Pro Asp Val
      85      90      95
Leu Pro Leu Ile Gly Gln Asp Pro Gln Ile Ala Ile Glu Ala Gly Arg
      100     105     110
Tyr Ala Leu Trp Leu Ile Pro Gly Leu Phe Ala Phe Ser Val Ala Gln
      115     120     125
Cys Leu Ser Lys Phe Leu Gln Ser Gln Ser Leu Ile Phe Pro Leu Val
      130     135     140
Leu Ser Ser Leu Thr Thr Leu Ala Val Phe Ile Pro Leu Cys Trp Phe
      145     150     155     160
Met Val Tyr Lys Val Gly Met Gly Asn Ala Gly Ala Ala Phe Ala Val
      165     170     175
Ser Ile Cys Asp Trp Val Glu Val Thr Val Leu Gly Leu Tyr Ile Lys
      180     185     190
Phe Ser Pro Ser Cys Glu Lys Thr Arg Ala Pro Phe Thr Trp Glu Ala
      195     200     205
Phe Gln Gly Ile Gly Ser Phe Met Arg Leu Ala Val Pro Ser Ala Leu
      210     215     220
Met Val Cys Leu Glu Trp Trp Ser Tyr Glu Leu Leu Val Leu Leu Ser
      225     230     235     240
Gly Met Leu Pro Asn Ala Ala Leu Glu Thr Ser Val Leu Ser Ile Cys
      245     250     255
Ile Ser Thr Val Ile Leu Val Tyr Asn Leu Pro Tyr Gly Ile Gly Thr
      260     265     270
Ala Ala Ser Val Arg Val Ser Asn Glu Leu Gly Ala Gly Asn Pro Asp
      275     280     285
Ser Ala Arg Leu Val Val Val Ala Leu Ser Ile Ile Ile Phe Thr
      290     295     300
Ala Val Leu Val Ser Val Thr Leu Leu Ser Leu Arg His Phe Ile Gly
      305     310     315     320
Ile Ala Phe Ser Asn Glu Glu Glu Val Val Asn Tyr Val Thr Arg Met
      325     330     335
Val Pro Leu Leu Ser Ile Ser Val Ile Thr Asp Asn Leu Gln Gly Val
      340     345     350
Leu Ser Gly Ile Ser Arg Gly Cys Gly Trp Gln His Leu Gly Ala Tyr
      355     360     365
Val Asn Leu Gly Ala Phe Tyr Leu Val Gly Ile Pro Val Ala Leu Val
      370     375     380
Ala Gly Phe Ala Leu His Leu Gly Gly Ala Gly Phe Trp Ile Gly Met
      385     390     395     400
Ile Ala Gly Gly Ala Thr Gln Val Thr Leu Leu Thr Ile Ile Thr Ala
      405     410     415
Met Thr Asn Trp Arg Lys Met Ala Asp Lys Ala Arg Asp Arg Val Tyr
      420     425     430
Glu Gly Ser Leu Pro Ile Gln Ala Asn
      435     440

```

<210> 97

<211> 483

<212> PRT

<213> Oryza sativa

<400> 97

```

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

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Gly Gln Ser Tyr Gly Ala Lys Gln Tyr Asp Met Leu Gly Thr His Ala
 100 105 110
 Gln Arg Ala Ile Phe Val Leu Met Leu Met Gly Val Pro Leu Ala Phe
 115 120 125
 Val Leu Ala Phe Ala Gly Gln Ile Leu Ile Ala Leu Gly Gln Asn Pro
 130 135 140
 Glu Ile Ser Ser Glu Ala Gly Leu Tyr Ala Val Trp Leu Ile Pro Gly
 145 150 155 160
 Leu Phe Ala Tyr Gly Leu Leu Gln Cys Leu Thr Lys Phe Leu Gln Thr
 165 170 175
 Gln Asn Ile Val His Pro Leu Val Val Cys Ser Gly Ala Thr Leu Val
 180 185 190
 Ile His Ile Leu Leu Cys Trp Val Met Val His Cys Phe Asp Leu Gly
 195 200 205
 Asn Arg Gly Ala Ala Leu Ser Ile Ser Leu Ser Tyr Trp Phe Asn Val
 210 215 220
 Ile Leu Leu Ala Ile Tyr Val Lys Val Ser Glu Val Gly Arg Arg Ser
 225 230 235 240
 Trp Pro Gly Trp Ser Arg Glu Ala Leu Lys Leu Lys Asp Val Asn Met
 245 250 255
 Tyr Leu Arg Leu Ala Ile Pro Ser Thr Phe Met Thr Cys Leu Glu Tyr
 260 265 270
 Trp Ala Phe Glu Met Val Val Leu Leu Ala Gly Phe Leu Pro Asn Pro
 275 280 285
 Lys Leu Glu Thr Ser Ile Leu Ser Ile Ser Leu Asn Thr Met Trp Met
 290 295 300
 Val Tyr Thr Ile Pro Ser Gly Leu Ser Ser Ala Ile Ser Ile Arg Val
 305 310 315 320
 Ser Asn Glu Leu Gly Ala Arg Asn Pro Gln Ala Ala Arg Leu Ser Val
 325 330 335
 Phe Val Ser Gly Ile Met Cys Leu Thr Glu Gly Ile Leu Val Ala Ile
 340 345 350
 Ile Thr Val Leu Val Arg Asp Ile Trp Gly Tyr Leu Tyr Ser Asn Glu
 355 360 365
 Glu Glu Val Val Lys Tyr Val Ala Ala Met Met Pro Ile Leu Ala Leu
 370 375 380
 Ser Asp Phe Met Asp Gly Ile Gln Cys Thr Leu Ser Gly Ala Ala Arg
 385 390 395 400
 Gly Cys Gly Trp Gln Lys Val Cys Ser Val Ile Asn Leu Cys Ala Tyr
 405 410 415
 Tyr Thr Ile Gly Ile Pro Ser Ala Val Thr Phe Ala Phe Val Leu Lys
 420 425 430
 Ile Asp Gly Lys Gly Leu Trp Leu Gly Ile Ile Cys Ala Met Thr Val
 435 440 445
 Gln Ile Leu Ala Leu Val Val Met Leu Leu Arg Thr Ser Trp Asn Glu
 450 455 460
 Glu Ala Glu Lys Ala Arg Ala Arg Val Gln Gly Ser Asp Gly Arg Ile
 465 470 475 480
 Thr Leu Ala

<210> 98

<211> 479

<212> PRT

<213> zea mays

<400> 98

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

```

Ser Ser Ala Ser Ile Ala Thr Ser Phe Ala Gly Val Thr Gly Phe Ser
65      70      75      80
Leu Leu Ser Gly Met Ala Ser Ser Leu Asp Thr Leu Cys Gly Gln Ser
85      90      95
Phe Gly Ala Lys Gln Tyr Tyr Leu Leu Gly Ile Tyr Lys Gln Arg Ala
100      105      110
Ile Leu Val Leu Thr Leu Val Ser Leu Val Val Ala Ile Ile Trp Ser
115      120      125
Tyr Thr Gly Gln Ile Leu Leu Leu Phe Gly Gln Asp Pro Glu Ile Ala
130      135      140
Ala Gly Ala Gly Ser Tyr Ile Arg Trp Met Ile Pro Ala Leu Phe Val
145      150      155      160
Tyr Gly Pro Leu Gln Cys His Val Arg Phe Leu Gln Thr Gln Asn Ile
165      170      175
Val Leu Pro Val Met Leu Ser Ser Gly Ala Thr Ala Leu Asn His Leu
180      185      190
Leu Val Cys Trp Leu Leu Val Tyr Lys Ile Gly Met Gly Asn Lys Gly
195      200      205
Ala Ala Leu Ala Asn Ala Ile Ser Tyr Phe Thr Asn Val Ser Ile Leu
210      215      220
Ala Ile Tyr Val Arg Leu Ala Pro Ala Cys Arg Asn Thr Trp Arg Gly
225      230      235      240
Phe Ser Lys Glu Ala Phe His Asp Ile Thr Ser Phe Leu Arg Leu Gly
245      250      255
Ile Pro Ser Ala Leu Met Val Cys Leu Glu Trp Trp Ser Phe Glu Leu
260      265      270
Leu Val Leu Leu Ser Gly Leu Leu Pro Asn Pro Lys Leu Glu Thr Ser
275      280      285
Val Leu Ser Ile Ser Leu Asn Thr Gly Ser Leu Ala Phe Met Ile Pro
290      295      300
Phe Gly Leu Ser Ala Ala Ile Ser Thr Arg Val Ser Asn Glu Leu Gly
305      310      315      320
Ala Gly Arg Pro His Ala Ala His Leu Ala Thr Arg Val Val Met Val
325      330      335
Leu Ala Ile Val Val Gly Val Leu Ile Gly Leu Ala Met Ile Leu Val
340      345      350
Arg Asn Ile Trp Gly Tyr Ala Tyr Ser Asn Glu Lys Glu Val Val Lys
355      360      365
Tyr Ile Ser Lys Met Met Pro Ile Leu Ala Val Ser Phe Leu Phe Asp
370      375      380
Cys Val Gln Cys Val Leu Ser Gly Val Ala Arg Gly Cys Gly Trp Gln
385      390      395      400
Lys Ile Gly Ala Cys Val Asn Leu Gly Ala Tyr Tyr Leu Ile Gly Ile
405      410      415
Pro Ala Ala Phe Cys Phe Ala Phe Met Tyr His Leu Gly Gly Met Gly
420      425      430
Leu Trp Leu Gly Ile Ile Cys Ala Leu Val Ile Gln Met Leu Leu Leu
435      440      445
Leu Thr Ile Thr Leu Cys Ser Asn Trp Glu Lys Glu Ala Leu Lys Ala
450      455      460
Lys Asp Arg Val Phe Ser Thr Ser Val Pro Ala Asp Met Met Thr
465      470      475

```

<210> 99

<211> 410

<212> PRT

<213> Zea may

<400> 99

```

Met Ala Asn Ser Phe Ala Thr Val Thr Gly Leu Ser Leu Leu Gly
1      5      10      15
Met Ala Ser Ala Leu Asp Thr Leu Cys Gly Gln Ala Phe Gly Ala Arg
20      25      30
Gln Tyr Tyr Leu Leu Gly Ile Tyr Lys Gln Arg Ala Met Phe Leu Leu
35      40      45

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```

Thr Leu Val Ser Val Pro Leu Ser Val Val Trp Phe Tyr Thr Gly Glu
50      55      60
Ile Leu Leu Leu Phe Gly Gln Asp Pro Asp Ile Ala Ala Glu Ala Gly
65      70      75      80
Thr Tyr Ala Arg Trp Met Ile Pro Leu Leu Phe Ala Tyr Gly Leu Leu
85      90      95
Gln Cys His Val Arg Phe Leu Gln Thr Gln Asn Ile Val Val Pro Val
100     105     110
Met Ala Ser Ala Gly Ala Ala Ala Cys His Val Val Val Cys Trp
115     120     125
Ala Leu Val Tyr Ala Leu Gly Met Gly Ser Lys Gly Ala Ala Leu Ser
130     135     140
Asn Ala Ile Ser Tyr Trp Val Asn Val Ala Val Leu Ser Val Tyr Val
145     150     155     160
Arg Val Ser Ser Ala Cys Lys Glu Thr Trp Thr Gly Phe Ser Thr Glu
165     170     175
Ala Phe Arg Asp Ala Leu Gly Phe Phe Arg Leu Ala Val Pro Ser Ala
180     185     190
Leu Met Val Cys Leu Glu Met Trp Ser Phe Glu Leu Ile Val Leu Leu
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Ser Gly Leu Leu Pro Asn Pro Lys Leu Glu Thr Ser Val Leu Ser Ile
210     215     220
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225     230     235     240
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Val Leu Ser Gly Val Ala Arg Gly Cys Gly Trp Gln Lys Ile Gly Ala
325     330     335
Cys Ile Asn Leu Gly Ala Tyr Tyr Ile Val Gly Ile Pro Ser Ala Tyr
340     345     350
Leu Ile Ala Phe Val Leu Arg Val Gly Gly Thr Gly Leu Trp Leu Gly
355     360     365
Ile Ile Cys Gly Leu Ile Val Gln Leu Leu Leu Ala Ile Ile Thr
370     375     380
Leu Cys Thr Asn Trp Asp Ser Glu Ala Thr Lys Ala Lys Asn Arg Val
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Phe Asn Ser Ser Ser Pro Ala Ser Gly Thr
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<212> PRT

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<400> 100

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Gly Pro Leu Val Ala Ser Cys Ile Leu Gln Asn Val Val Gln Leu Val
35     40     45
Ser Val Met Phe Val Gly His Leu Gly Glu Leu Pro Leu Ala Gly Ala
50     55     60
Ser Leu Ala Ser Ser Leu Ala Asn Val Thr Gly Phe Ser Leu Leu Val
65     70     75     80
Gly Met Ala Ser Ala Leu Asp Thr Leu Cys Gly Gln Ala Phe Gly Ala
85     90     95

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130 135 140
Gly Ala Tyr Ser Arg Trp Leu Ile Leu Ser Leu Val Pro Tyr Val Pro
145 150 155 160
Leu Ala Cys His Val Arg Phe Leu Gln Thr Gln Ser Ile Val Val Pro
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Val Met Ala Ser Ser Gly Ala Thr Ala Leu Gly His Val Leu Val Cys
180 185 190
Trp Ala Leu Val Phe Lys Ala Gly Met Gly Ser Lys Gly Ala Ala Leu
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Ser Gly Ala Ile Ser Tyr Ser Val Asn Leu Ala Met Leu Ala Leu Tyr
210 215 220
Val Arg Leu Ser Ser Ala Cys Lys Arg Thr Trp Thr Gly Phe Ser Thr
225 230 235 240
Glu Ala Phe Arg Asp Leu Leu Arg Phe Thr Glu Leu Ala Val Pro Ser
245 250 255
Ala Met Met Val Cys Leu Glu Trp Trp Ser Phe Glu Leu Leu Val Leu
260 265 270
Leu Ser Gly Leu Leu Pro Asn Pro Lys Leu Glu Thr Ser Val Leu Ser
275 280 285
Ile Cys Leu Asn Thr Gly Ala Leu Leu Phe Met Val Pro Tyr Gly Leu
290 295 300
Cys Thr Ala Ile Ser Thr Arg Val Ser Asn Glu Leu Gly Ala Gly Glu
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420 425 430
Gly Ile Val Cys Gly Ser Leu Thr Lys Leu Val Leu Leu Met Trp Ile
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Ser Leu Ala Ser Ser Leu Ala Asn Val Thr Gly Phe Ser Leu Leu Val
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 Gly Ala Tyr Ser Arg Trp Leu Ile Leu Ser Leu Val Pro Tyr Val Pro
 145 150 155 160
 Leu Ala Cys His Val Arg Phe Leu Gln Thr Gln Ser Ile Val Val Pro
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 Cys Thr Ala Ile Ser Thr Arg Val Ser Asn Glu Leu Gly Ala Gly Glu
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 Val Leu Leu Ala Phe Val Leu His Leu Asn Gly Met Gly Leu Trp Leu
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 Gly Ile Val Cys Gly Ser Leu Thr Lys Leu Val Leu Leu Met Trp Ile
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<212> PRT

<213> Zea may

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 Ala Cys Gly Leu Glu Thr Ile Cys Gly Gln Ala Phe Gly Ala Glu Gln
 50 55 60

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Tyr Ala Leu Trp Leu Ile Pro Gly Leu Phe Ala Phe Ser Val Ala Gln
115     120     125
Cys Leu Ser Lys Phe Leu Gln Ser Gln Ser Leu Ile Phe Pro Leu Val
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Leu Ser Ser Leu Thr Thr Leu Ala Val Phe Ile Pro Leu Cys Trp Phe
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Met Val Tyr Lys Val Gly Met Gly Asn Ala Gly Ala Ala Phe Ala Val
165     170     175
Ser Ile Cys Asp Trp Val Glu Val Thr Val Leu Gly Leu Tyr Ile Lys
180     185     190
Phe Ser Pro Ser Cys Glu Lys Thr Arg Ala Pro Phe Thr Trp Glu Ala
195     200     205
Phe Gln Gly Ile Gly Ser Phe Met Arg Leu Ala Val Pro Ser Ala Leu
210     215     220
Met Val Cys Leu Glu Trp Trp Ser Tyr Glu Leu Leu Val Leu Leu Ser
225     230     235     240
Gly Met Leu Pro Asn Ala Ala Gln Ala Ala His Met Thr Thr Ile Asp
245     250     255
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260     265     270
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REFERENCES CITED IN THE DESCRIPTION

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Patentkrav

1. Monoklonalt antistof eller et funktionelt fragment deraf, som hver binder til det ekstracellulære domæne af en PGE₂-receptor undertype EP4 og hæmmer funktionen af PGE₂-receptoren EP4 for at øge det intracellulære cAMP-niveau.

2. Monoklonalt antistof eller et funktionelt fragment deraf ifølge krav 1, hvori antistoffet er fremstillet af hybridomer med de internationale deponeringstilgangsnumre FERM BP-11402 (NBG016-mAb14) og FERM BP-11403 (NBG016-mAb21).

10

3. Monoklonalt antistof eller et funktionelt fragment deraf ifølge krav 1 eller 2, hvori antistoffet specifikt binder til det ekstracellulære domæne af EP4 og omfatter ethvert af følgende (A), (B) og (C) med hensyn til aminosyresekvenserne af dets komplementaritetsbestemmende regioner 1-3 (CDR1-3):

15

(A) antistoffet har

tung kæde af CDR1 omfattende aminosyresekvensen vist i SEQ ID NO: 5,

tung kæde af CDR2 omfattende aminosyresekvensen vist i SEQ ID NO: 6,

tung kæde af CDR3 omfattende aminosyresekvensen vist i SEQ ID NO: 7,

let kæde af CDR1 omfattende aminosyresekvensen vist i SEQ ID NO: 8,

20

let kæde af CDR2 omfattende aminosyresekvensen vist i SEQ ID NO: 9, og

let kæde af CDR3 omfattende aminosyresekvensen vist i SEQ ID NO: 10;

(B) antistoffet har

tung kæde af CDR1 omfattende aminosyresekvensen vist i SEQ ID NO: 15,

tung kæde af CDR2 omfattende aminosyresekvensen vist i SEQ ID NO: 16,

25

tung kæde af CDR3 omfattende aminosyresekvensen vist i SEQ ID NO: 17,

let kæde af CDR1 omfattende aminosyresekvensen vist i SEQ ID NO: 18,

let kæde af CDR2 omfattende aminosyresekvensen vist i SEQ ID NO: 19, og

let kæde af CDR3 omfattende aminosyresekvensen vist i SEQ ID NO: 20; eller

(C) antistoffet har

30

tung kæde af CDR1 omfattende aminosyresekvensen vist i SEQ ID NO: 45,

tung kæde af CDR2 omfattende aminosyresekvensen vist i SEQ ID NO: 46,

tung kæde af CDR3 omfattende aminosyresekvensen vist i SEQ ID NO: 47,

let kæde af CDR1 omfattende aminosyresekvensen vist i SEQ ID NO: 48,

let kæde af CDR2 omfattende aminosyresekvensen vist i SEQ ID NO: 49, og

35

let kæde af CDR3 omfattende aminosyresekvensen vist i SEQ ID NO: 50.

4. Antistoffet eller et funktionelt fragment deraf ifølge ethvert af krav 1 til 3, hvori antistoffet specifikt binder til det ekstracellulære domæne af EP4 og omfatter et-

hvert af følgende (a), b) og (c) med hensyn til aminosyresekvenserne af dets variable region af den tunge kæde og dets variable region af den lette kæde:

- 5 (a) antistoffet har en variabel region af den tunge kæde omfattende aminosyresekvensen vist i SEQ ID No. 2 og en variabel region af den lette kæde omfattende aminosyresekvensen vist i SEQ ID No. 4;
- (b) antistoffet har en variabel region af den tunge kæde omfattende aminosyresekvensen vist i SEQ ID No. 12 og en variabel region af den lette kæde omfattende aminosyresekvensen vist i SEQ ID No. 14; eller
- 10 (c) antistoffet har en variabel region af den tunge kæde omfattende aminosyresekvensen vist i SEQ ID No. 43 og en variabel region af den lette kæde omfattende aminosyresekvensen vist i SEQ ID No. 44.

15 5. Antistoffet eller et funktionelt fragment deraf ifølge ethvert af krav 1 til 4, hvori antistoffet er et humaniseret antistof eller et kimærisk antistof.

6. Antistoffet eller et funktionelt fragment deraf ifølge ethvert af krav 3 og 4, hvori den variable region af den tunge kæde eller den variable region af den lette kæde af antistoffet eller fragment deraf er kodet af en nukleinsyre som vist i SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 41 eller

20 SEQ ID NO: 42.

7. Farmaceutisk sammensætning omfattende antistoffet eller et funktionelt fragment deraf ifølge ethvert af krav 1 til 5.

25 8. Farmaceutisk sammensætning ifølge krav 7 til anvendelse i en fremgangsmåde til behandling af en immunsygdom.

9. Farmaceutisk sammensætning ifølge krav 7 til anvendelse i en fremgangsmåde til behandling af en tumor.

30

10. Farmaceutisk sammensætning ifølge krav 7 til anvendelse i en fremgangsmåde til behandling af smerte.

35 11. Antistof immobiliseret på en bærer, hvori anti-EP4 antistoffet eller et funktionelt fragment deraf ifølge ethvert af krav 1 til 5 er immobiliseret på en bærer.

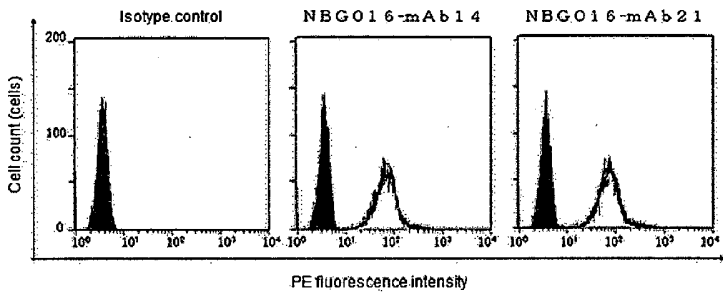
12. Fremgangsmåde til fjernelse af PGE₂-receptor EP4-eksprimerende celler fra blod, hvori et bærer-immobiliseret antistof ifølge krav 11 bringes i kontakt *ex vivo*

med blod indeholdende EP4-eksprimerende celler og efterfølgende fjernelse af de EP4-eksprimerende celler fra blodet.

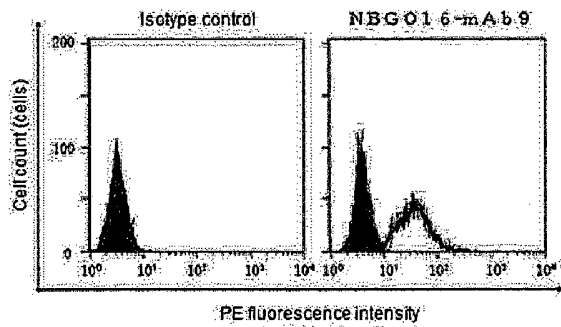
13. Kit til måling af ekspressionsniveauet for PGE₂-receptor EP4 på en celleover-
5 flade, som omfatter anti-EP4 antistoffet ifølge ethvert af krav 1 til 5.

DRAWINGS

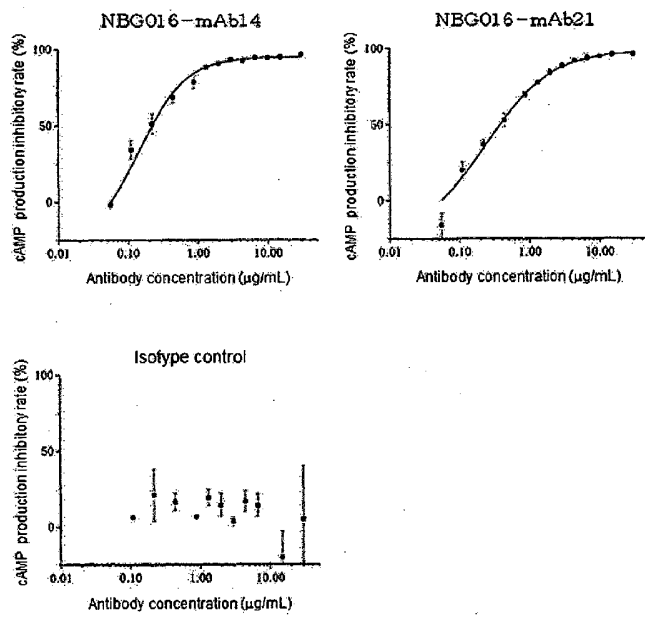
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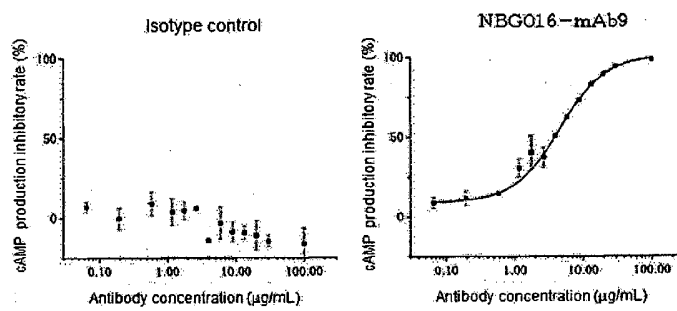
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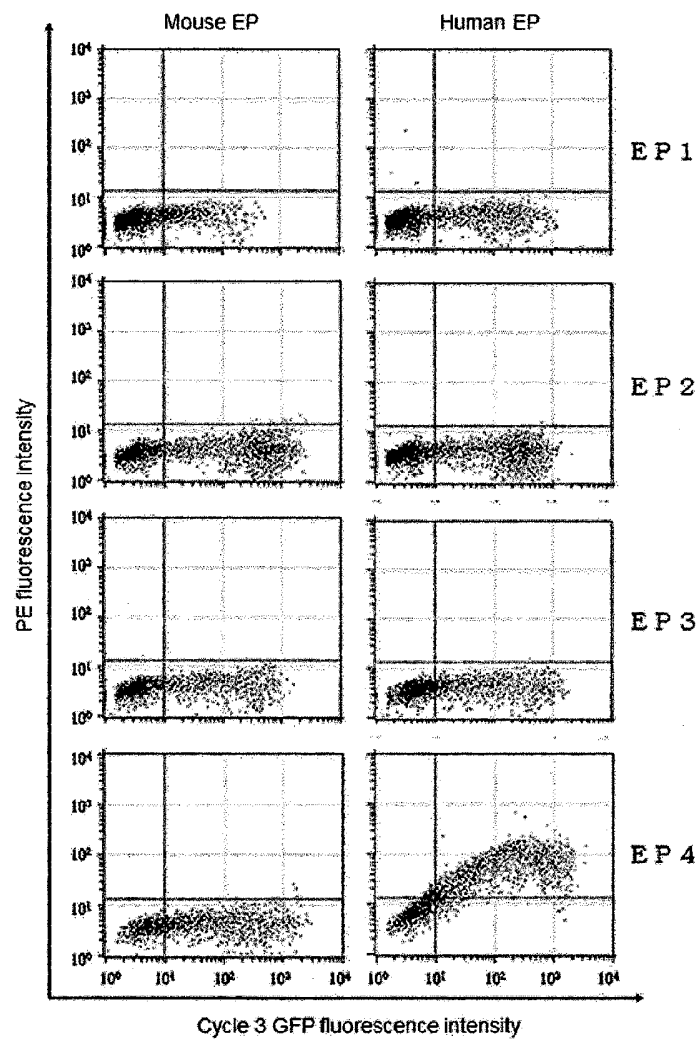
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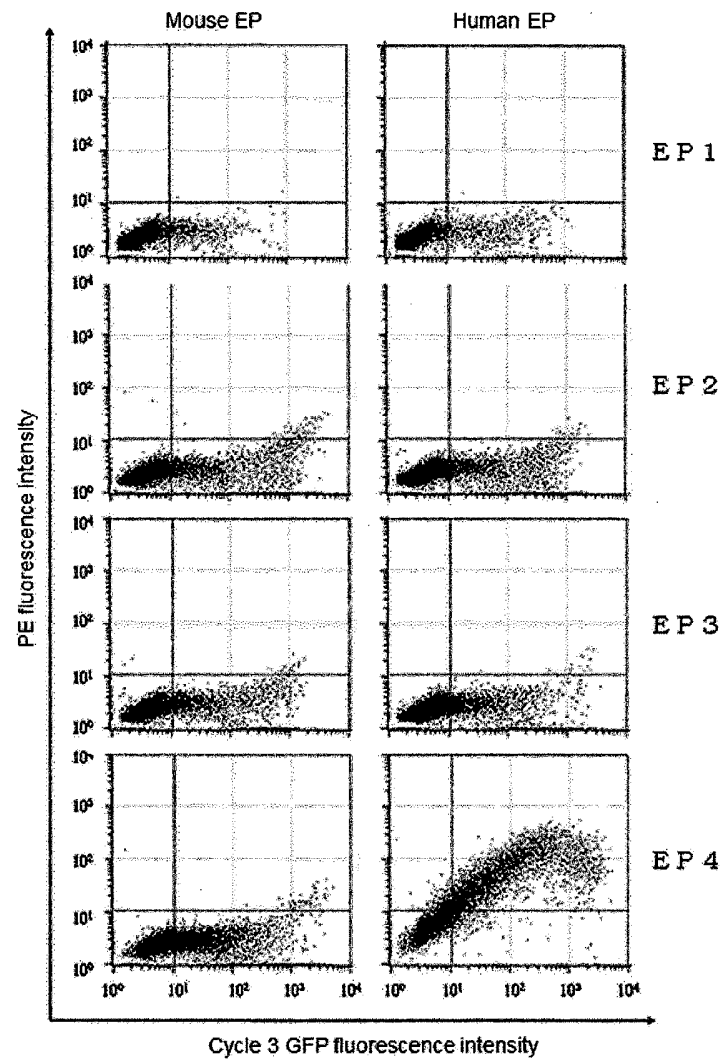
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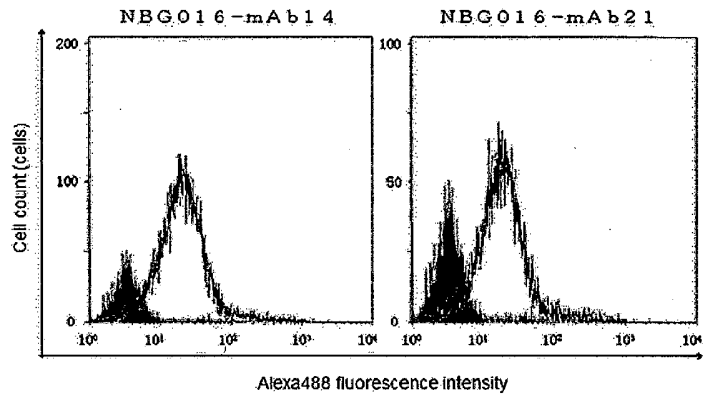
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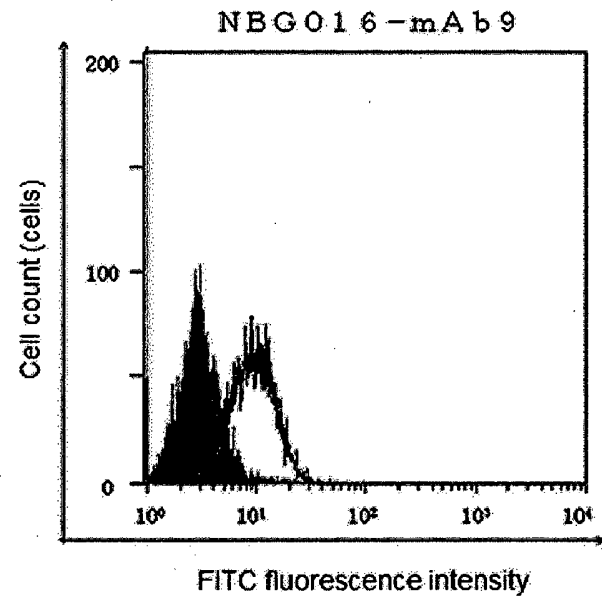
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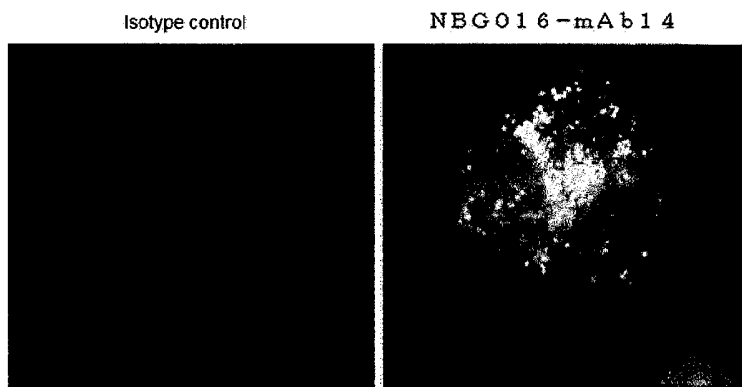
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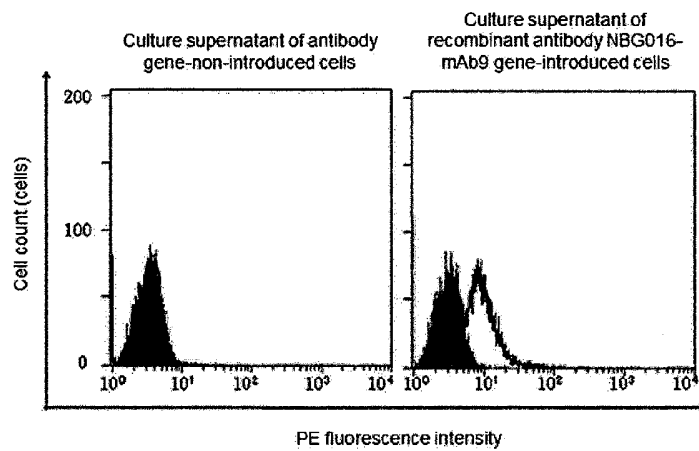
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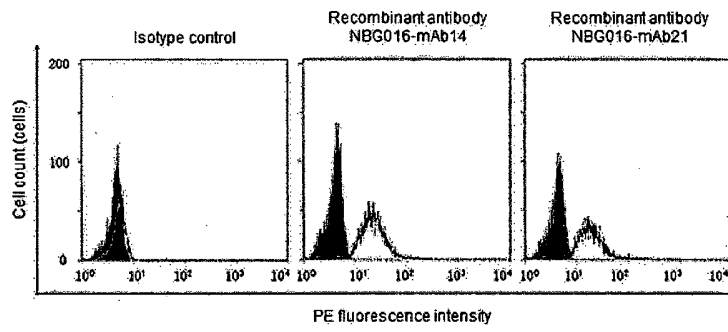
[Figure 9]



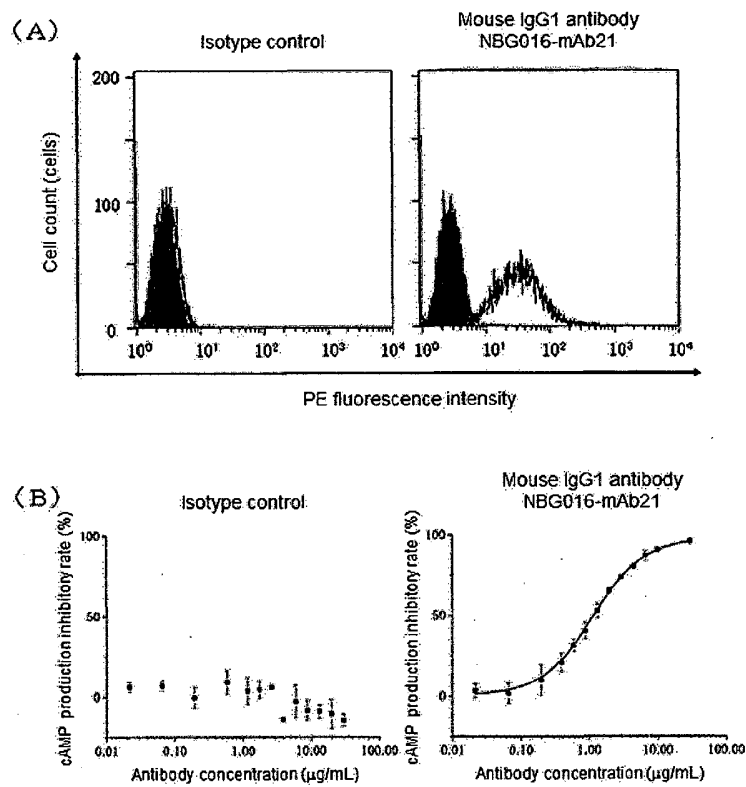
[Figure 10]



[Figure 11]



[Figure 12]



[Figure 13]

