



HU000032178T2

(19) **HU****MAGYARORSZÁG****Szellemi Tulajdon Nemzeti Hivatala**(11) Lajstromszám: **E 032 178**(13) **T2**

EURÓPAI SZABADALOM SZÖVEGÉNEK FORDÍTÁSA

(21) Magyar ügyszám: **E 14 153319**(22) A bejelentés napja: **2010. 02. 05.**(51) Int. Cl.: **C12N 15/82** (2006.01)**A01H 5/00** (2006.01)**C07K 14/325** (2006.01)

(96) Az európai bejelentés bejelentési száma:

EP 20100153319

(97) Az európai bejelentés közzétételi adatai:

EP 2728007 A2 **2014. 05. 07.**

(97) Az európai szabadalom megadásának meghirdetési adatai:

EP 2728007 B1 **2017. 01. 25.**

(30) Elsőbbségi adatok:

150309 P **2009. 02. 05.** **US****229567 P** **2009. 07. 29.** **US**

(73) Jogosult(ak):

**Athenix Corporation, Research Triangle Park,
NC 27709 (US)**

(72) Feltaláló(k):

Heinrichs, Volker, 30900 Wedemark (DE)

(74) Képviselő:

SBGK Szabadalmi Ügyvivői Iroda, Budapest

(54)

Variáns Axmi-R1 delta-endotoxin gének és eljárások azok alkalmazására

Az európai szabadalom ellen, megadásának az Európai Szabadalmi Közlönyben való meghirdetésétől számított kilenc hónapon belül, felszólalást lehet benyújtani az Európai Szabadalmi Hivatalnál. (Európai Szabadalmi Egyezmény 99. cikk(1))

A fordítást a szabadalmas az 1995. évi XXXIII. törvény 84/H. §-a szerint nyújtotta be. A fordítás tartalmi helyességét a Szellemi Tulajdon Nemzeti Hivatala nem vizsgálta.



(11)

EP 2 728 007 B1

(12)

EUROPEAN PATENT SPECIFICATION

(45) Date of publication and mention
of the grant of the patent:
25.01.2017 Bulletin 2017/04

(51) Int Cl.:
C12N 15/82 ^(2006.01) **C07K 14/325** ^(2006.01)
A01H 5/00 ^(2006.01)

(21) Application number: **14153319.0**

(22) Date of filing: **05.02.2010**

(54) **Variant Axmi-R1 delta-endotoxin genes and methods for their use**

Varianten der Axmi-R1-delta-Endotoxingene und Anwendungsverfahren dafür

Gène de delta-endotoxine Axmi-R1 variant et procédés pour l'utiliser

(84) Designated Contracting States:
**AT BE BG CH CY CZ DE DK EE ES FI FR GB GR
HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL
PT RO SE SI SK SM TR**
Designated Extension States:
AL BA RS

(30) Priority: **05.02.2009 US 150309 P**
29.07.2009 US 229567 P

(43) Date of publication of application:
07.05.2014 Bulletin 2014/19

(62) Document number(s) of the earlier application(s) in
accordance with Art. 76 EPC:
10703770.7 / 2 393 929

(73) Proprietor: **Athenix Corporation**
Research Triangle Park, NC 27709 (US)

(72) Inventor: **Heinrichs, Volker**
30900 Wedemark (DE)

(74) Representative: **Power, David**
J A Kemp
14 South Square
Gray's Inn
London WC1R 5JJ (GB)

(56) References cited:
WO-A2-03/018810 US-A- 5 659 123
US-A- 6 023 013

- **SHENG-JIUN WU ET AL: "Functional Significance of Loops in The Receptor Binding Domain of Bacillus thuringiensis CryIIIa [delta]-Endotoxin", JOURNAL OF MOLECULAR BIOLOGY, vol. 255, no. 4, 2 February 1996 (1996-02-02), pages 628-640, XP55105111, ISSN: 0022-2836, DOI: 10.1006/jmbi.1996.0052**
- **WU S-J ET AL: "Enhanced toxicity of Bacillus thuringiensis Cry3A delta-endotoxin in coleopterans by mutagenesis in a receptor binding loop", FEBS LETTERS, ELSEVIER, AMSTERDAM, NL, vol. 473, no. 2, 12 May 2000 (2000-05-12), pages 227-232, XP004337143, ISSN: 0014-5793, DOI: 10.1016/S0014-5793(00)01505-2**
- **SCHNEPF E ET AL: "BACILLUS THURINGIENSIS AND ITS PESTICIDAL CRYSTAL PROTEINS", MICROBIOLOGY AND MOLECULAR BIOLOGY REVIEWS, AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 62, no. 3, September 1998 (1998-09), pages 775-806, XP000986964, ISSN: 1092-2172**
- **PARK H-W ET AL: "Effect of specific mutations in helix [alpha]7 of domain I on the stability and crystallization of Cry3A in Bacillus thuringiensis", MOLECULAR BIOTECHNOLOGY, HUMANA PRESS, INC, US, vol. 27, no. 2, 1 June 2004 (2004-06-01), pages 89-100, XP002526267, ISSN: 1073-6085, DOI: 10.1385/MB:27:2:089**
- **WALTERS F S ET AL: "An engineered chymotrypsin/cathepsin G site in domain I renders Bacillus thuringiensis Cry3A active against western corn rootworm larvae", APPLIED AND ENVIRONMENTAL MICROBIOLOGY, AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 74, no. 2, 16 November 2007 (2007-11-16), pages 367-374, XP002526268, ISSN: 0099-2240, DOI: 10.1128/AEM.02165-07**

Note: Within nine months of the publication of the mention of the grant of the European patent in the European Patent Bulletin, any person may give notice to the European Patent Office of opposition to that patent, in accordance with the Implementing Regulations. Notice of opposition shall not be deemed to have been filed until the opposition fee has been paid. (Art. 99(1) European Patent Convention).

EP 2 728 007 B1

- C. PADILLA ET AL: "Role of Tryptophan Residues in Toxicity of Cry1Ab Toxin from *Bacillus thuringiensis*", *APPLIED AND ENVIRONMENTAL MICROBIOLOGY*, vol. 72, no. 1, January 2006 (2006-01), pages 901-907, XP55105142, ISSN: 0099-2240, DOI: 10.1128/AEM.72.1.901-907.2006

Description

FIELD OF THE INVENTION

[0001] This invention relates to the field of molecular biology. Provided are novel genes that encode pesticidal proteins. These proteins and the nucleic acid sequences that encode them are useful in preparing pesticidal formulations and in the production of transgenic pest-resistant plants.

BACKGROUND OF THE INVENTION

[0002] *Bacillus thuringiensis* (Bt) is a Gram-positive spore forming soil bacterium characterized by its ability to produce crystalline inclusions that are specifically toxic to certain orders and species of insects, but are harmless to plants and other non-targeted organisms. For this reason, compositions including *Bacillus thuringiensis* strains or their insecticidal proteins can be used as environmentally-acceptable insecticides to control agricultural insect pests or insect vectors for a variety of human or animal diseases.

[0003] Crystal (Cry) proteins (delta-endotoxins) from *Bacillus thuringiensis* have potent insecticidal activity against predominantly Lepidopteran, Dipteran, and Coleopteran larvae. These proteins also have shown activity against *Hymenoptera*, *Homoptera*, *Phthiraptera*, *Mallophaga*, and *Acari* pest orders, as well as other invertebrate orders such as Nematelminthes, Platyhelminthes, and Sarcostigophora (Feitelson (1993) The *Bacillus Thuringiensis* family tree. In Advanced Engineered Pesticides, Marcel Dekker, Inc., New York, N.Y.) These proteins were originally classified as CryI to CryV based primarily on their insecticidal activity. The major classes were *Lepidoptera*-specific (I), *Lepidoptera*- and *Diptera*-specific (II), *Coleoptera*-specific (III), *Diptera*-specific (IV), and nematode-specific (V) and (VI). The proteins were further classified into subfamilies; more highly related proteins within each family were assigned divisional letters such as *Cry1A*, *Cry1B*, *Cry1C*, etc. Even more closely related proteins within each division were given names such as *Cry1C1*, *Cry1C2*, etc.

[0004] A new nomenclature was recently described for the Cry genes based upon amino acid sequence homology rather than insect target specificity (Crickmore et al. (1998) Microbiol. Mol. Biol. Rev. 62:807-813). In the new classification, each toxin is assigned a unique name incorporating a primary rank (an Arabic number), a secondary rank (an uppercase letter), a tertiary rank (a lowercase letter), and a quaternary rank (another Arabic number). In the new classification, Roman numerals have been exchanged for Arabic numerals in the primary rank. Proteins with less than 45% sequence identity have different primary ranks, and the criteria for secondary and tertiary ranks are 78% and 95%, respectively.

[0005] The crystal protein does not exhibit insecticidal activity until it has been ingested and solubilized in the insect midgut. The ingested protoxin is hydrolyzed by proteases in the insect digestive tract to an active toxic molecule. (Höfte and Whiteley (1989) Microbiol. Rev. 53:242-255). This toxin binds to apical brush border receptors in the midgut of the target larvae and inserts into the apical membrane creating ion channels or pores, resulting in larval death.

[0006] Delta-endotoxins generally have five conserved sequence domains, and three conserved structural domains (see, for example, de Maagd et al. (2001) Trends Genetics 17:193-199). The first conserved structural domain consists of seven alpha helices and is involved in membrane insertion and pore formation. Domain II consists of three beta-sheets arranged in a Greek key configuration, and domain III consists of two antiparallel beta-sheets in "jelly-roll" formation (de Maagd et al., 2001, supra). Domains II and III are involved in receptor recognition and binding, and are therefore considered determinants of toxin specificity.

[0007] Cry3 type delta endotoxins were first identified in the early 1980's. Cry3Aa1 delta endotoxin (also previously known as cryC and cryIIIA) has been previously isolated from strains *Bacillus thuringiensis* var *san diego* (Herrnstadt et al. (1987) Gene. 57:37-46), *Bacillus thuringiensis tenebrionis* (Hofte et al. (1987) Nucleic acids Res. 15: 7183; McPherson et al. (1988) Bio/Technology 6:61-66; Sekar et al. (1987) Proc. Natl. Acad. Sci. USA 84: 7036-7040) and EG2158 (Donovan et al. (1988) Mol Gen Genet. 214(3):365-72).

[0008] Cry3Aa is often observed as a major component of a rhomboid crystal in certain native *Bacillus* strains, and is produced as a 72kDa protein that is subsequently processed to a 66kDa toxin by proteolytic processing by sporulation associated proteases. This 66kDa protein has been known to produce activity on the coleopteran Colorado Potato Beetle.

[0009] Because of the devastation that insects can confer, and the improvement in yield by controlling insect pests, there is a continual need to discover new forms of pesticidal toxins.

SUMMARY OF INVENTION

[0010] Compositions and methods for conferring pesticidal activity to bacteria, plants, plant cells, tissues and seeds are provided. Compositions include nucleic acid molecules encoding sequences for pesticidal and insecticidal polypeptides, vectors comprising those nucleic acid molecules, and host cells comprising the vectors. Compositions also include the pesticidal polypeptide sequences. The nucleotide sequences can be used in DNA constructs or expression cassettes

for transformation and expression in organisms, including microorganisms and plants. The nucleotide or amino acid sequences may be synthetic sequences that have been designed for expression in an organism including, but not limited to, a microorganism or a plant. Compositions also comprise transformed bacteria, plants, plant cells, tissues, and seeds.

[0011] In particular, isolated nucleic acid molecules are provided that encode a pesticidal protein. Additionally, amino acid sequences corresponding to the pesticidal protein are encompassed. Hence, the present invention provides a recombinant nucleic acid molecule comprising a nucleotide sequence encoding a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID NO: 2.

[0012] The present invention further provides:

- a vector comprising the nucleic acid molecule of the invention, preferably further comprising a nucleic acid molecule encoding a heterologous polypeptide;
- a host cell comprising the vector of the invention, preferably that is a bacterial host cell or a plant host cell;
- a transgenic plant comprising the plant host cell of the invention, preferably wherein said plant is selected from the group consisting of maize, sorghum, wheat, cabbage, sunflower, tomato, crucifers, peppers, potato, cotton, rice, soybean, sugarbeet, sugarcane, tobacco, barley, and oilseed rape; and
- a seed comprising the nucleic acid molecule of the invention.

[0013] The invention further provides a recombinant polypeptide comprising a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID No: 2, more preferably further comprising heterologous amino acid sequences.

[0014] The invention further provides a composition comprising a polypeptide of the invention, preferably wherein said composition comprising the polypeptide of the invention, preferably wherein said composition:

- (a) is selected from the group consisting of a powder, dust, pellet, granule, spray, emulsion, colloid, and solution;
- (b) is prepared by desiccation, lyophilization, homogenization, extraction, filtration, centrifugation, sedimentation, or concentration of a culture of *Bacillus thuringiensis* cells; and/or
- (c) comprises from about 1% to about 99% by weight of said polypeptide.

[0015] Methods are provided for producing the polypeptides of the invention, and for using those polypeptides for controlling or killing a coleopteran pest. Hence, the present invention provides a method for controlling or killing a coleopteran pest population comprising contacting said population with a pesticidally-effective amount of the polypeptide of the invention. The present invention also provides a method for producing a polypeptide with pesticidal activity toward a coleopteran pest, comprising culturing a host cell comprising the vector of the invention.

[0016] The compositions and methods of the invention are useful for the production of organisms with enhanced pest resistance or tolerance. These organisms and compositions comprising the organisms are desirable for agricultural purposes.

[0017] Hence, the present invention provides a method for protecting a plant from a pest, comprising expressing in a plant or cell thereof a nucleotide sequence encoding a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID No: 2.

[0018] The present invention also provides a plant having stably incorporated into its genome a DNA construct comprising nucleic acid molecule comprising a nucleotide sequence encoding a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID NO: 2.

BRIEF DESCRIPTION OF THE FIGURES

[0019]

Figure 1 shows the annotated AXMI-R1 sequence (SEQ ID NO:2). The underlined regions represent loop regions (L1, L2 and L3). The vertical bars represent the boundaries between domain I (DI), domain II (DII), and domain III (DIII). The arrows note some of the regions targeted for generation of variants.

Figure 2 shows an alignment of Axmi164 (SEQ ID NO:13), Axmi161 (SEQ ID NO:44), Axmi152 (SEQ ID NO:45), Axmi151 (SEQ ID NO:26), Axmi146 (SEQ ID NO:27), Axmi141 (SEQ ID NO:28), Axmi129 (SEQ ID NO:29), Axmi128 (SEQ ID NO:30), Axmi127 (SEQ ID NO:31), Axmi120 (SEQ ID NO:32), Axmi116 (SEQ ID NO:33), Axmi114 (SEQ ID NO:34), Axmi101 (SEQ ID NO:35), Axmi091 (SEQ ID NO:36), Axmi087 (SEQ ID NO:37), Axmi037 (SEQ ID NO:38), Axmi029 (SEQ ID NO:39), Axmi028 (SEQ ID NO:40), Cry8Bb1 (SEQ ID NO:41), Cry8Bc1 (SEQ ID NO:42), Cry7Aa (SEQ ID NO:43), AxmiR1 PermutP3c7 (evo21) (SEQ ID NO:13), and Axmi-R1 (SEQ ID NO:2).

[0020] DETAILED DESCRIPTION

The present invention is drawn to compositions and methods for regulating pest resistance or tolerance in organisms, particularly plants or plant cells. By "resistance" is intended that the pest (e.g., insect) is killed upon ingestion or other contact with the polypeptides of the invention. By "tolerance" is intended an impairment or reduction in the movement, feeding, reproduction, or other functions of the pest. The methods involve transforming organisms with a nucleotide sequence encoding a pesticidal protein of the invention. In particular, the nucleotide sequences of the invention are useful for preparing plants and microorganisms that possess pesticidal activity. Thus, transformed bacteria, plants, plant cells, plant tissues and seeds are provided.

[0021] Provided herein are compositions comprising nucleic acid sequences encoding variant Cry3 amino acid sequences wherein the variant has pesticidal activity, particularly pesticidal activity against coleopteran pests.

[0022] A recombinant nucleic acid molecule of the invention is one comprising a nucleotide sequence encoding a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID NO: 2.

[0023] A recombinant polypeptide of the invention is one comprising a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID No: 2, more preferably further comprising heterologous amino acid sequences.

[0024] For a list of Cry3 sequences, see Crickmore et al. (1998), Microbiol. Mol. Biol. Rev. 62:807-813, and for regular updates see Crickmore et al. (2003) "Bacillus thuringiensis toxin nomenclature," at www.biol.susx.ac.uk/Home/Neil_Crickmore/Bt/index.

[0025] The naturally-occurring, or "wild-type," Cry3 sequence is the Axmi-R1 nucleotide sequence set forth in SEQ ID NO:1, which encodes the amino acid sequence set forth in SEQ ID NO:2. The AXMI-R1 sequence corresponds to the cry3Aa sequence described in GENBANK® Accession No. P0A379. However, it will be understood that the substitutions described in Table 16 can be made at corresponding positions of any Cry3 protein, such as any Cry3A, Cry3B, or Cry3C protein. The "corresponding positions" can be determined by aligning the target sequence with SEQ ID NO:2. See, for example, the alignment shown in Figure 2. A Cry3 variant of the invention will have at least 95% amino acid sequence identity to SEQ ID NO: 2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID NO: 2.

[0026] The crystal structure of the cry3Aa protein has been determined previously (Li et al, 1991, Nature 353:815-821). This crystal structure delineates the various loop regions, and shows sites of proteolytic processing relative to the three dimensional structure of the protein. This structure suggests that the toxin is arranged into three domains consistent with the structures of other delta-endotoxin sequences (typically referred to as Domains I, II, and III). Each domain of the toxin has loop regions that are defined based on the crystal structure. Prior to and since the publication of this crystal structure, there have been multiple attempts to describe broad simple rules related to the structure and function of toxicity

of Bt endotoxins, and in particular the cry3-type endotoxins, and the role of proteolysis in this activity.

[0027] For example, Van Rie et al., 1997 (U.S. Patent 5,659,123) suggest the identification of amino acids leading to improved toxicity by performing modifications of Domain II in the areas regarded as "loops" by identifying positions negatively impacting toxicity, followed by random replacement of amino acids at certain positions within these loops. Similarly, random alanine insertion into Loop II residues by Wu and Dean (J.Mol. Biol., 1996, 255: 628-640) reduced protein function. Random mutagenesis of Loop I residues by Wu et al (Febs Letters, 2000, 473:227-232) in most cases resulted in unstable protein and reduced protein function, and in two cases was reported to yield proteins with increased toxicity and altered binding properties. For the cry3Bb toxin (English et al, U.S. patent 6,023,013 re-issued as RE39,580) it was reported that certain substitutions in that toxin led to improved corn rootworm activity, but in most cases these alterations occurred in different residues than those suggested by Van Rie, or studied by Wu and Dean.

[0028] In addition, modifications in the regions of the cry3A toxin that are normally cleaved by trypsin- or chymotrypsin-like proteases have been made in attempts to improve cry3A activity on coleopteran and notably western corn rootworm. Chen et al (U.S. patent 7,030,295) report that insertion of the synthetic tetrapeptide AAPF (SEQ ID NO:20), described as a "Cathepsin G cleavage site" (or a "chymotrypsin/Cathepsin G cleavage site"; Walters et al, 2008, Applied and Environ. Micro. 74: 367-374), at specific locations in the protein can lead to improved cry3A activity.

[0029] Trypsin cleavage of cry3A is well known in the art, and has been shown to naturally occur in the region of approximately R158-N159 in the native cry3A peptide (Carroll et al 1989 Biochem J. 261:99-105). Furthermore, chymotrypsin is also known to cleave in this region at the His161-Ser162 junction (Carroll et al 1997 J Invert. Biol. 70: 41-49). Walters et al (2008) showed cleavage of a modified Cry3A ("mCry3A," which contains a chymotrypsin/cathepsin G protease recognition site) by chymotrypsin at its native location in this region (the His161-Ser162 junction). There are no reports of mutagenesis of the naturally occurring amino acid sequence in this region of Cry 3A resulting in improved pesticidal activity on coleopteran pests.

[0030] Thus, the invention provides variant Cry3 sequences having improved pesticidal activity relative to the corresponding wild-type sequence. In various embodiments, the variant Cry3 pesticidal sequences have improved pesticidal activity compared to the pesticidal activity of AXMI-R1. Hence a variant of the invention has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID NO: 2.

[0031] By "improved activity" is intended an increase in the mortality, reduction in feeding, or reduction in growth of a target pest. The improvement in activity is at least about 5%, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 100%, at least about 1.5-fold, at least about 2-fold, at least about 3-fold, at least about 4-fold, or greater increase in activity relative to the activity of the wild-type sequence, e.g., AXMI-R1. In some embodiments, the target pest is a coleopteran pest.

[0032] In some embodiments, the pesticidal sequences encompassed herein comprise variants of the axmi-R1 sequence set forth in SEQ ID NO:1. By "variants of axmi-R1" is intended a nucleotide or amino acid sequence corresponding to AXMI-R1, where one or more mutations has been introduced within certain regions (i.e., "target mutation region(s)") of the AXMI-R1 sequence. In particular, an amino acid sequence of the invention comprises a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID No: 2, more preferably further comprising heterologous amino acid sequences. A polynucleotide sequence of the invention encodes such a variant Cry3 amino acid sequence. Unless otherwise specified, the amino acid regions outside of the target mutation region(s) are identical to the AXMI-R1 sequence. The identical regions are either identical amino acid sequences, or a nucleotide sequence that encodes an identical amino acid sequence. It will be understood that nucleotide sequences may differ from the wild-type nucleotide sequence, yet still encode the wild-type amino acid sequence, due to the degeneracy of the genetic code.

[0033] In other embodiments, the target mutation region of Cry3 corresponds to the proposed processing and pore forming region described in Li et al. (1991, Nature 353:815-821, herein incorporated by reference in its entirety, particularly with respect to the structural descriptions of the cry3Aa protein). In various embodiments, the target mutation region corresponds to amino acid positions 480 to 490, and positions 510 to 530 of SEQ ID NO:2. A Cry3 variant of the invention comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID NO: 2. In some embodiments, such a variant Cry3 sequence contains any combination of the mutations listed in Table 16, up to and including mutation at every position described in Table 16.

[0034] In some embodiments, the variant Cry3 sequences of the invention also have one or more substitutions selected from the amino acid positions corresponding to positions 158, and 519 of SEQ ID NO:2. In another embodiment, the variant Cry3 sequences do not have the following substitutions: P154H, V155H, R315W, R315D, R315M, R315L. In yet

another embodiment, the variant Cry3 sequence of the invention does not have any of the combination of mutations listed in Table 2 of U.S. Patent 6,023,013.

[0035] In another embodiment, the variant Cry3 sequence is selected from the group consisting of SEQ ID NO:15, 17 or 38. In yet another embodiment, the variant Cry3 sequences encompassed herein consist of one or more mutations in the processing and pore formation region and one or more mutations in the receptor binding region. The variants encompassed herein have improved pesticidal activity relative to the pesticidal activity of the wild-type Cry3 and so have pesticidal activity which is improved relative to the pesticidal activity of SEQ ID NO: 2. In some embodiments, the improved pesticidal activity is against a coleopteran pests, for example, a rootworm pest.

[0036] The variant Cry3 sequences of the invention can be further modified to introduce one or more of the Cry3 mutations described in the art. For example, the variant AXMI-R1 sequence encompassed herein can comprise one or more of the substitutions listed in Table 16 in addition to one or more of the mutations described in U.S. Patents 5,659,123 and 6,023,013; Wu and Dean (J.Mol. Biol., 1996, 255: 628-640); or Wu et al (Febs Letters, 2000, 473:227-232), or any combination thereof provided that the variant has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2 and comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID NO: 2. Additionally, the variant AXMI-R1 sequence may comprise an insertion of one or more Cathepsin G cleavage sites as discussed *supra* (e.g., at or near the native chymotrypsin or trypsin cleavage site).

[0037] In yet another embodiment of the invention, the mutations described in Table 16 can be introduced into the corresponding positions of any amino acid sequences having homology to AXMI-R1 to introduce or improve toxicity to a pest of interest, particularly a coleopteran pest such as a rootworm pest. See, for example, the amino acid sequences aligned with AXMI-R1 in Figure 2, or the homologous amino acid sequences set forth in, for example, GENBANK® Accession No. P0A379.1, AAA22336.1, AAA22542.1, AAS79487.1, AAU29411.1, AAW82872.1, AAA73184.1, CAA51996.1, 1DLC_A, Q45744.1, Q06117.1, AAA74198.1, P17969.1. The homologous amino acid sequence can be aligned using one of the alignment programs described herein to identify the corresponding positions for mutation. Alternatively, a crystal structure or other 3-dimensional representation thereof of the homologous amino acid sequence can be superimposed onto the crystal structure of Cry3A (described in Li et al. 1991, Nature 353:815-821) and the corresponding positions aligned. The crystal structure of the Cry3B protein is described in U.S. Patent 6,023,013. A variant of the invention has at least 95% amino acid sequence identity to SEQ ID NO: 2 over the full length of SEQ ID NO: 2.

[0038] The sequences find use in the construction of expression vectors for subsequent transformation into organisms of interest, as probes for the isolation of other homologous (or partially homologous) genes, and for the generation of altered pesticidal proteins by methods known in the art, such as domain swapping or DNA shuffling. The proteins find use in controlling or killing lepidopteran, coleopteran, dipteran, and nematode pest populations and for producing compositions with pesticidal activity.

[0039] By "pesticidal toxin" or "pesticidal protein" is intended a toxin that has toxic activity against one or more pests, including, but not limited to, members of the *Lepidoptera*, *Diptera*, and *Coleoptera* orders, or the *Nematoda* phylum, or a protein that has homology to such a protein. Pesticidal proteins have been isolated from organisms including, for example, *Bacillus sp.*, *Clostridium bifermentans* and *Paenibacillus popilliae*. Pesticidal proteins include amino acid sequences deduced from the full-length nucleotide sequences disclosed herein, and amino acid sequences that are shorter than the full-length sequences, either due to the use of an alternate downstream start site, or due to processing that produces a shorter protein having pesticidal activity. Processing may occur in the organism the protein is expressed in, or in the pest after ingestion of the protein.

Isolated Nucleic Acid Molecules, and Variants and Fragments Thereof

[0040] One aspect of the invention pertains to isolated or recombinant nucleic acid molecules comprising nucleotide sequences encoding pesticidal proteins and polypeptides. In particular, the present invention provides a recombinant nucleic acid molecule comprising a nucleotide sequence encoding a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID NO: 2. As used herein, the term "nucleic acid molecule" is intended to include DNA molecules (e.g., recombinant DNA, cDNA or genomic DNA) and RNA molecules (e.g., mRNA) and analogs of the DNA or RNA generated using nucleotide analogs. The nucleic acid molecule can be single-stranded or double-stranded, but preferably is double-stranded DNA.

[0041] An "isolated" or "recombinant" nucleic acid sequence (or DNA) is used herein to refer to a nucleic acid sequence

(or DNA) that is no longer in its natural environment, for example in an *in vitro* or in a recombinant bacterial or plant host cell. In some embodiments, an isolated or recombinant nucleic acid is free of sequences (preferably protein encoding sequences) that naturally flank the nucleic acid (i.e., sequences located at the 5' and 3' ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For purposes of the invention, "isolated" when used to refer to nucleic acid molecules excludes isolated chromosomes. For example, in various embodiments, the isolated delta-endotoxin encoding nucleic acid molecule can contain less than about 5 kb, 4 kb, 3 kb, 2 kb, 1 kb, 0.5 kb, or 0.1 kb of nucleotide sequences that naturally flank the nucleic acid molecule in genomic DNA of the cell from which the nucleic acid is derived. In various embodiments, a delta-endotoxin protein that is substantially free of cellular material includes preparations of protein having less than about 30%, 20%, 10%, or 5% (by dry weight) of non-delta-endotoxin protein (also referred to herein as a "contaminating protein").

[0042] Nucleotide sequences encoding the proteins of the present invention include nucleotide sequences encoding variants of Cry3, as well as fragments and complements thereof. By "complement" is intended a nucleotide sequence that is sufficiently complementary to a given nucleotide sequence such that it can hybridize to the given nucleotide sequence to thereby form a stable duplex. Such nucleotide sequences will encode a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID NO: 2.

[0043] Nucleic acid molecules that are fragments of these nucleotide sequences encoding pesticidal proteins are also encompassed by the present invention provided that they encode a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID NO: 2. By "fragment" is intended a portion of the nucleotide sequence encoding a pesticidal protein. A fragment of a nucleotide sequence may encode a biologically active portion of a pesticidal protein. Nucleic acid molecules that are fragments of a nucleotide sequence encoding a pesticidal protein comprise at least about 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 1100, 1200, 1300, 1350, 1400 contiguous nucleotides, or up to the number of nucleotides present in a full-length nucleotide sequence encoding a pesticidal protein disclosed herein, depending upon the intended use. By "contiguous" nucleotides is intended nucleotide residues that are immediately adjacent to one another. Fragments of the nucleotide sequences of the present invention will encode protein fragments that retain the biological activity of the pesticidal protein and, hence, retain pesticidal activity. By "retains activity" is intended that the fragment will have at least about 30%, at least about 50%, at least about 70%, 80%, 90%, 95% or higher of the pesticidal activity of the reference pesticidal protein (i.e., the pesticidal variant Cry3 sequences disclosed herein). In one embodiment, the pesticidal activity is coleopterocidal activity. Methods for measuring pesticidal activity are well known in the art. See, for example, Czaplak and Lang (1990) J. Econ. Entomol. 83:2480-2485; Andrews et al. (1988) Biochem. J. 252:199-206; Marrone et al. (1985) J. of Economic Entomology 78:290-293; and U.S. Patent No. 5,743,477.

[0044] A fragment of a nucleotide sequence encoding a pesticidal protein that encodes a biologically active portion of a protein of the invention will encode at least about 15, 25, 30, 50, 75, 100, 125, 150, 175, 200, 250, 300, 350, 400, 450 contiguous amino acids, or up to the total number of amino acids present in a full-length pesticidal protein of the invention.

[0045] Preferred pesticidal proteins of the present invention are encoded by a nucleotide sequence sufficiently identical to the variant Cry3 sequences encompassed herein. By "sufficiently identical" is intended an amino acid or nucleotide sequence that has at least 95%, 96%, 97%, 98%, 99% or greater sequence identity compared to the reference sequence of SEQ ID NO:2) using one of the alignment programs described herein using standard parameters. One of skill in the art will recognize that these values can be appropriately adjusted to determine corresponding identity of proteins encoded by two nucleotide sequences by taking into account codon degeneracy, amino acid similarity, reading frame positioning, and the like.

[0046] To determine the percent identity of two amino acid sequences or of two nucleic acids, the sequences are aligned for optimal comparison purposes. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences (i.e., percent identity = number of identical positions/total number of positions (e.g., overlapping positions) x 100). In one embodiment, the two sequences are the same length. In another embodiment, the percent identity is calculated across the entirety of the reference sequence (i.e., variant Cry3 sequences encompassed herein). The percent identity between two sequences can be determined using techniques similar to those described below, with or without allowing gaps. In calculating percent identity, typically exact matches are counted.

[0047] The determination of percent identity between two sequences can be accomplished using a mathematical algorithm. A nonlimiting example of a mathematical algorithm utilized for the comparison of two sequences is the algorithm

of Karlin and Altschul (1990) Proc. Natl. Acad. Sci. USA 87:2264, modified as in Karlin and Altschul (1993) Proc. Natl. Acad. Sci. USA 90:5873-5877. Such an algorithm is incorporated into the BLASTN and BLASTX programs of Altschul et al. (1990) J. Mol. Biol. 215:403. BLAST nucleotide searches can be performed with the BLASTN program, score = 100, wordlength = 12, to obtain nucleotide sequences homologous to pesticidal-like nucleic acid molecules of the invention. BLAST protein searches can be performed with the BLASTX program, score = 50, wordlength = 3, to obtain amino acid sequences homologous to pesticidal protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST (in BLAST 2.0) can be utilized as described in Altschul et al. (1997) Nucleic Acids Res. 25:3389. Alternatively, PSI-Blast can be used to perform an iterated search that detects distant relationships between molecules. See Altschul *et al.* (1997) *supra*. When utilizing BLAST, Gapped BLAST, and PSI-Blast programs, the default parameters of the respective programs (e.g., BLASTX and BLASTN) can be used. Alignment may also be performed manually by inspection.

[0048] Another non-limiting example of a mathematical algorithm utilized for the comparison of sequences is the ClustalW algorithm (Higgins et al. (1994) Nucleic Acids Res. 22:4673-4680). ClustalW compares sequences and aligns the entirety of the amino acid or DNA sequence, and thus can provide data about the sequence conservation of the entire amino acid sequence. The ClustalW algorithm is used in several commercially available DNA/amino acid analysis software packages, such as the ALIGNX module of the Vector NTI Program Suite (Invitrogen Corporation, Carlsbad, CA). After alignment of amino acid sequences with ClustalW, the percent amino acid identity can be assessed. A non-limiting example of a software program useful for analysis of ClustalW alignments is GENEDOC™. GENEDOC™ (Karl Nicholas) allows assessment of amino acid (or DNA) similarity and identity between multiple proteins. Another non-limiting example of a mathematical algorithm utilized for the comparison of sequences is the algorithm of Myers and Miller (1988) CABIOS 4:11-17. Such an algorithm is incorporated into the ALIGN program (version 2.0), which is part of the GCG Wisconsin Genetics Software Package, Version 10 (available from Accelrys, Inc., 9685 Scranton Rd., San Diego, CA, USA). When utilizing the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used.

[0049] Unless otherwise stated, GAP Version 10, which uses the algorithm of Needleman and Wunsch (1970) J. Mol. Biol. 48(3):443-453, will be used to determine sequence identity or similarity using the following parameters: % identity and % similarity for a nucleotide sequence using GAP Weight of 50 and Length Weight of 3, and the nws gapdna.cmp scoring matrix; % identity or % similarity for an amino acid sequence using GAP weight of 8 and length weight of 2, and the BLOSUM62 scoring program. Equivalent programs may also be used. By "equivalent program" is intended any sequence comparison program that, for any two sequences in question, generates an alignment having identical nucleotide residue matches and an identical percent sequence identity when compared to the corresponding alignment generated by GAP Version 10.

[0050] The invention also encompasses variant nucleic acid molecules. Such nucleic acid molecules will comprise a nucleotide sequence encoding a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID NO: 2. "Variants" of the pesticidal variant Cry3 protein-encoding nucleotide sequences include those sequences that encode the variant pesticidal proteins disclosed herein but that differ conservatively because of the degeneracy of the genetic code as well as those that are sufficiently identical as discussed above. Variant nucleotide sequences also include synthetically derived nucleotide sequences that have been generated, for example, by using site-directed mutagenesis but which still encode the pesticidal proteins disclosed in the present invention as discussed below. Variant proteins encompassed by the present invention are biologically active, that is they continue to possess the desired biological activity of the reference protein (i.e., variant Cry3 sequences encompassed herein), that is, pesticidal activity. By "retains activity" is intended that the variant will have at least about 30%, at least about 50%, at least about 70%, or at least about 80% of the pesticidal activity of the reference protein. In some embodiments, the variant pesticidal proteins described herein show improved activity relative to the AXMIR1 protein set forth in SEQ ID NO:2. Methods for measuring pesticidal activity are well known in the art. See, for example, Czaplak and Lang (1990) J. Econ. Entomol. 83: 2480-2485; Andrews et al. (1988) Biochem. J. 252:199-206; Marrone et al. (1985) J. of Economic Entomology 78:290-293; and U.S. Patent No. 5,743,477.

[0051] The skilled artisan will further appreciate that changes can be introduced by mutation of the nucleotide sequences of the invention thereby leading to changes in the amino acid sequence of the encoded pesticidal proteins, without altering the biological activity of the proteins. Thus, variant isolated nucleic acid molecules can be created by introducing one or more nucleotide substitutions, additions, or deletions into the corresponding nucleotide sequence disclosed herein, such that one or more amino acid substitutions, additions or deletions are introduced into the target mutation region(s) of the encoded protein. Mutations can be introduced by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Such variant nucleotide sequences are also encompassed by the present invention

provided that they encode a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID NO: 2.

[0052] For example, conservative amino acid substitutions may be made at one or more, predicted, nonessential amino acid residues. A "nonessential" amino acid residue is a residue that can be altered from the reference sequence of a pesticidal protein without substantially altering the biological activity, whereas an "essential" amino acid residue is required for biological activity. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine).

[0053] Delta-endotoxins generally have five conserved sequence domains, and three conserved structural domains (see, for example, de Maagd *et al.* (2001) *Trends Genetics* 17:193-199). The first conserved structural domain consists of seven alpha helices and is involved in membrane insertion and pore formation. Domain II consists of three beta-sheets arranged in a Greek key configuration, and domain III consists of two antiparallel beta-sheets in "jelly-roll" formation (de Maagd *et al.*, 2001, *supra*). Domains II and III are involved in receptor recognition and binding, and are therefore considered determinants of toxin specificity.

[0054] Amino acid substitutions may be made in nonconserved regions that retain function. In general, such substitutions would not be made for conserved amino acid residues, or for amino acid residues residing within a conserved motif, where such residues are essential for protein activity. Examples of residues that are conserved and that may be essential for protein activity include, for example, residues that are identical between all proteins contained in an alignment of similar or related toxins to the sequences of the invention (e.g., residues that are identical in an alignment of homologous proteins). Examples of residues that are conserved but that may allow conservative amino acid substitutions and still retain activity include, for example, residues that have only conservative substitutions between all proteins contained in an alignment of similar or related toxins to the sequences of the invention (e.g., residues that have only conservative substitutions between all proteins contained in the alignment homologous proteins). However, one of skill in the art would understand that functional variants may have minor conserved or nonconserved alterations in the conserved residues.

[0055] Alternatively, variant nucleotide sequences can be made by introducing mutations randomly along all or part of the target mutation region(s), such as by permutation or saturation mutagenesis, and the resultant mutants can be screened for ability to confer pesticidal activity to identify mutants that retain activity or show improved activity. Following mutagenesis, the encoded protein can be expressed recombinantly, and the activity of the protein can be determined using standard assay techniques.

[0056] Using methods such as PCR, hybridization, and the like corresponding pesticidal sequences can be identified, such sequences having substantial identity to the sequences of the invention. See, for example, Sambrook and Russell (2001) *Molecular Cloning: A Laboratory Manual*. (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY) and Innis, *et al.* (1990) *PCR Protocols: A Guide to Methods and Applications* (Academic Press, NY).

[0057] In a hybridization method, all or part of the pesticidal nucleotide sequence can be used to screen cDNA or genomic libraries. Methods for construction of such cDNA and genomic libraries are generally known in the art and are disclosed in Sambrook and Russell, 2001, *supra*. The so-called hybridization probes may be genomic DNA fragments, cDNA fragments, RNA fragments, or other oligonucleotides, and may be labeled with a detectable group such as ³²P, or any other detectable marker, such as other radioisotopes, a fluorescent compound, an enzyme, or an enzyme co-factor. Probes for hybridization can be made by labeling synthetic oligonucleotides based on the known pesticidal protein-encoding nucleotide sequence disclosed herein. Degenerate primers designed on the basis of conserved nucleotides or amino acid residues in the nucleotide sequence or encoded amino acid sequence can additionally be used. The probe typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, at least about 25, at least about 50, 75, 100, 125, 150, 175, or 200 consecutive nucleotides of nucleotide sequence encoding a pesticidal protein of the invention or a fragment or variant thereof. Methods for the preparation of probes for hybridization are generally known in the art and are disclosed in Sambrook and Russell, 2001, *supra*.

[0058] For example, an entire pesticidal protein sequence disclosed herein, or one or more portions thereof, may be used as a probe capable of specifically hybridizing to corresponding pesticidal protein-like sequences and messenger RNAs. To achieve specific hybridization under a variety of conditions, such probes include sequences that are unique and are preferably at least about 10 nucleotides in length, or at least about 20 nucleotides in length. Such probes may be used to amplify corresponding pesticidal sequences from a chosen organism by PCR. This technique may be used

to isolate additional coding sequences from a desired organism or as a diagnostic assay to determine the presence of coding sequences in an organism. Hybridization techniques include hybridization screening of plated DNA libraries (either plaques or colonies; see, for example, Sambrook et al. (1989) *Molecular Cloning: A Laboratory Manual* (2d ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York).

[0059] Hybridization of such sequences may be carried out under stringent conditions. By "stringent conditions" or "stringent hybridization conditions" is intended conditions under which a probe will hybridize to its target sequence to a detectably greater degree than to other sequences (e.g., at least 2-fold over background). Stringent conditions are sequence-dependent and will be different in different circumstances. By controlling the stringency of the hybridization and/or washing conditions, target sequences that are 100% complementary to the probe can be identified (homologous probing). Alternatively, stringency conditions can be adjusted to allow some mismatching in sequences so that lower degrees of similarity are detected (heterologous probing). Generally, a probe is less than about 1000 nucleotides in length, preferably less than 500 nucleotides in length.

[0060] Typically, stringent conditions will be those in which the salt concentration is less than about 1.5 M Na ion, typically about 0.01 to 1.0 M Na ion concentration (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30°C for short probes (e.g., 10 to 50 nucleotides) and at least about 60°C for long probes (e.g., greater than 50 nucleotides). Stringent conditions may also be achieved with the addition of destabilizing agents such as formamide. Exemplary low stringency conditions include hybridization with a buffer solution of 30 to 35% formamide, 1 M NaCl, 1% SDS (sodium dodecyl sulphate) at 37°C, and a wash in 1X to 2X SSC (20X SSC = 3.0 M NaCl/0.3 M trisodium citrate) at 50 to 55°C. Exemplary moderate stringency conditions include hybridization in 40 to 45% formamide, 1.0 M NaCl, 1% SDS at 37°C, and a wash in 0.5X to 1X SSC at 55 to 60°C. Exemplary high stringency conditions include hybridization in 50% formamide, 1 M NaCl, 1% SDS at 37°C, and a wash in 0.1X SSC at 60 to 65°C. Optionally, wash buffers may comprise about 0.1% to about 1% SDS. Duration of hybridization is generally less than about 24 hours, usually about 4 to about 12 hours.

[0061] Specificity is typically the function of post-hybridization washes, the critical factors being the ionic strength and temperature of the final wash solution. For DNA-DNA hybrids, the T_m can be approximated from the equation of Meinkoth and Wahl (1984) *Anal. Biochem.* 138:267-284: $T_m = 81.5^\circ\text{C} + 16.6 (\log M) + 0.41 (\%GC) - 0.61 (\% \text{ form}) - 500/L$; where M is the molarity of monovalent cations, %GC is the percentage of guanosine and cytosine nucleotides in the DNA, % form is the percentage of formamide in the hybridization solution, and L is the length of the hybrid in base pairs. The T_m is the temperature (under defined ionic strength and pH) at which 50% of a complementary target sequence hybridizes to a perfectly matched probe. T_m is reduced by about 1°C for each 1% of mismatching; thus, T_m , hybridization, and/or wash conditions can be adjusted to hybridize to sequences of the desired identity. For example, if sequences with $\geq 90\%$ identity are sought, the T_m can be decreased 10°C. Generally, stringent conditions are selected to be about 5°C lower than the thermal melting point (T_m) for the specific sequence and its complement at a defined ionic strength and pH. However, severely stringent conditions can utilize a hybridization and/or wash at 1, 2, 3, or 4°C lower than the thermal melting point (T_m); moderately stringent conditions can utilize a hybridization and/or wash at 6, 7, 8, 9, or 10°C lower than the thermal melting point (T_m); low stringency conditions can utilize a hybridization and/or wash at 11, 12, 13, 14, 15, or 20°C lower than the thermal melting point (T_m). Using the equation, hybridization and wash compositions, and desired T_m , those of ordinary skill will understand that variations in the stringency of hybridization and/or wash solutions are inherently described. If the desired degree of mismatching results in a T_m of less than 45°C (aqueous solution) or 32°C (formamide solution), it is preferred to increase the SSC concentration so that a higher temperature can be used. An extensive guide to the hybridization of nucleic acids is found in Tijssen (1993) *Laboratory Techniques in Biochemistry and Molecular Biology-Hybridization with Nucleic Acid Probes*, Part I, Chapter 2 (Elsevier, New York); and Ausubel et al., eds. (1995) *Current Protocols in Molecular Biology*, Chapter 2 (Greene Publishing and Wiley-Interscience, New York). See Sambrook et al. (1989) *Molecular Cloning: A Laboratory Manual* (2d ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York).

Isolated Proteins and Variants and Fragments Thereof

[0062] Pesticidal proteins are also encompassed within the present invention. By "pesticidal protein" is intended the pesticidal variant Cry3 sequences encompassed herein. Fragments, biologically active portions, and variants thereof are also provided, and may be used to practice the methods of the present invention. An "isolated protein" or a "recombinant protein" is used to refer to a protein that is no longer in its natural environment, for example in vitro or in a recombinant bacterial or plant host cell. A pesticidal protein of the invention is a recombinant polypeptide comprising a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID No: 2, more preferably further comprising heterologous amino acid sequences.

[0063] "Fragments" or "biologically active portions" are polypeptide fragments of the variant Cry3 sequences encompassed herein, and that exhibit pesticidal activity. They will comprise a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID No: 2, more preferably further comprising heterologous amino acid sequences. Such biologically active portions can be prepared by recombinant techniques and evaluated for pesticidal activity. Methods for measuring pesticidal activity are well known in the art. See, for example, Czapla and Lang (1990) J. Econ. Entomol. 83:2480-2485; Andrews et al. (1988) Biochem. J. 252:199-206; Marrone et al. (1985) J. of Economic Entomology 78:290-293; and U.S. Patent No. 5,743,477. As used here, a fragment comprises at least 20, 30, 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, or more amino acids.

[0064] By "variants" is intended proteins or polypeptides having an amino acid sequence that is at least about 95%, 96%, 97%, 98% or 99% identical to the amino acid sequence of SEQ ID NO:2. A variant will comprise a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID No: 2, more preferably further comprising heterologous amino acid sequences. Variants may include polypeptides encoded by a nucleic acid molecule that hybridizes to the nucleic acid molecule encoding the variant Cry3 sequences encompassed herein, or a complement thereof, under stringent conditions. Variants include polypeptides that differ in amino acid sequence due to mutagenesis. Variant proteins encompassed by the present invention are biologically active, that is they continue to possess the desired biological activity of the variant Cry3 protein, that is, retain pesticidal activity. The variants have improved activity relative to the reference protein (e.g., relative to SEQ ID NO:2, or relative to a specific variant Cry3 protein). Methods for measuring pesticidal activity are well known in the art. See, for example, Czapla and Lang (1990) J. Econ. Entomol. 83:2480-2485; Andrews et al. (1988) Biochem. J. 252:199-206; Marrone et al. (1985) J. of Economic Entomology 78:290-293; and U.S. Patent No. 5,743,477.

[0065] Bacterial genes, such as the *axmi* genes of this invention, quite often possess multiple methionine initiation codons in proximity to the start of the open reading frame. Often, translation initiation at one or more of these start codons will lead to generation of a functional protein. These start codons can include ATG codons. However, bacteria such as *Bacillus sp.* also recognize the codon GTG as a start codon, and proteins that initiate translation at GTG codons contain a methionine at the first amino acid. On rare occasions, translation in bacterial systems can initiate at a TTG codon, though in this event the TTG encodes a methionine. Furthermore, it is not often determined *a priori* which of these codons are used naturally in the bacterium. Thus, it is understood that use of one of the alternate methionine codons may also lead to generation of pesticidal proteins. These pesticidal proteins are encompassed in the present invention and may be used in the methods of the present invention. It will be understood that, when expressed in plants, it will be necessary to alter the alternate start codon to ATG for proper translation.

[0066] Antibodies to the polypeptides of the present invention, or to variants or fragments thereof, are also referred to. Methods for producing antibodies are well known in the art (see, for example, Harlow and Lane (1988) Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY; U.S. Patent No. 4,196,265).

Altered or Improved Variants

[0067] It is recognized that DNA sequences of a pesticidal protein may be further altered by various methods, and that these alterations may result in DNA sequences encoding proteins with amino acid sequences different than that encoded by a pesticidal protein of the present invention. This protein may be altered in various ways including amino acid substitutions, deletions, truncations, and insertions of one or more amino acids of the variant Cry3 sequences encompassed herein, including up to about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, about 10, about 15, about 20, about 25, about 30, about 35, amino acid substitutions, deletions or insertions in one or more of the target mutation region(s). A nucleic acid molecule of the invention will still comprise a nucleotide sequence encoding a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID NO: 2. Methods for such manipulations are generally known in the art. For example, amino acid sequence variants of a pesticidal protein can be prepared by mutations in the DNA. This may also be accomplished by one of several forms of mutagenesis and/or in

directed evolution. In some aspects, the changes encoded in the amino acid sequence will not substantially affect the function of the protein. Such variants will possess the desired (or improved) pesticidal activity. However, it is understood that the ability of a pesticidal protein to confer pesticidal activity may be improved by the use of such techniques upon the compositions of this invention. For example, one may express a pesticidal protein in host cells that exhibit high rates of base misincorporation during DNA replication, such as XL-1 Red (Stratagene, La Jolla, CA). After propagation in such strains, one can isolate the DNA (for example by preparing plasmid DNA, or by amplifying by PCR and cloning the resulting PCR fragment into a vector), culture the pesticidal protein mutations in a non-mutagenic strain, and identify mutated genes with pesticidal activity, for example by performing an assay to test for pesticidal activity. Generally, the protein is mixed and used in feeding assays. See, for example Marrone et al. (1985) J. of Economic Entomology 78:290-293. Such assays can include contacting plants with one or more pests and determining the plant's ability to survive and/or cause the death of the pests. Examples of mutations that result in increased toxicity are found in Schnepf et al. (1998) Microbiol. Mol. Biol. Rev. 62:775-806.

[0068] Alternatively, alterations may be made to the protein sequence of many proteins at the amino or carboxy terminus without substantially affecting activity. This can include insertions, deletions, or alterations introduced by modern molecular methods, such as PCR, including PCR amplifications that alter or extend the protein coding sequence by virtue of inclusion of amino acid encoding sequences in the oligonucleotides utilized in the PCR amplification. Alternatively, the protein sequences added can include entire protein-coding sequences, such as those used commonly in the art to generate protein fusions. Such fusion proteins are often used to (1) increase expression of a protein of interest (2) introduce a binding domain, enzymatic activity, or epitope to facilitate either protein purification, protein detection, or other experimental uses known in the art (3) target secretion or translation of a protein to a subcellular organelle, such as the periplasmic space of Gram-negative bacteria, or the endoplasmic reticulum of eukaryotic cells, the latter of which often results in glycosylation of the protein.

[0069] Variant nucleotide and amino acid sequences of the present invention also encompass sequences derived from mutagenic and recombinogenic procedures such as DNA shuffling. With such a procedure, one or more different pesticidal protein coding regions can be used to create a new pesticidal protein possessing the desired properties. In this manner, libraries of recombinant polynucleotides are generated from a population of related sequence polynucleotides comprising sequence regions that have substantial sequence identity and can be homologously recombined *in vitro* or *in vivo*. For example, using this approach, sequence motifs encoding a domain of interest may be shuffled between a pesticidal gene of the invention and other known pesticidal genes to obtain a new gene coding for a protein with an improved property of interest, such as an increased insecticidal activity. Strategies for such DNA shuffling are known in the art. See, for example, Stemmer (1994) Proc. Natl. Acad. Sci. USA 91:10747-10751; Stemmer (1994) Nature 370:389-391; Crameri et al. (1997) Nature Biotech. 15:436-438; Moore et al. (1997) J. Mol. Biol. 272:336-347; Zhang et al. (1997) Proc. Natl. Acad. Sci. USA 94:4504-4509; Crameri et al. (1998) Nature 391:288-291; and U.S. Patent Nos. 5,605,793 and 5,837,458.

[0070] Domain swapping or shuffling is another mechanism for generating altered pesticidal proteins. Domains may be swapped between pesticidal proteins, resulting in hybrid or chimeric toxins with improved pesticidal activity or target spectrum. Methods for generating recombinant proteins and testing them for pesticidal activity are well known in the art (see, for example, Naimov et al. (2001) Appl. Environ. Microbiol. 67:5328-5330; de Maagd et al. (1996) Appl. Environ. Microbiol. 62:1537-1543; Ge et al. (1991) J. Biol. Chem. 266:17954-17958; Schnepf et al. (1990) J. Biol. Chem. 265:20923-20930; Rang et al. (1999) Appl. Environ. Microbiol. 65:2918-2925).

Vectors

[0071] A pesticidal sequence of the invention may be provided in an expression cassette for expression in a plant of interest. By "plant expression cassette" is intended a DNA construct that is capable of resulting in the expression of a protein from an open reading frame in a plant cell. Typically these contain a promoter and a coding sequence. Often, such constructs will also contain a 3' untranslated region. Such constructs may contain a "signal sequence" or "leader sequence" to facilitate co-translational or post-translational transport of the peptide to certain intracellular structures such as the chloroplast (or other plastid), endoplasmic reticulum, or Golgi apparatus.

[0072] By "signal sequence" is intended a sequence that is known or suspected to result in cotranslational or post-translational peptide transport across the cell membrane. In eukaryotes, this typically involves secretion into the Golgi apparatus, with some resulting glycosylation. Insecticidal toxins of bacteria are often synthesized as protoxins, which are protolytically activated in the gut of the target pest (Chang (1987) Methods Enzymol. 153:507-516). In some embodiments of the present invention, the signal sequence is located in the native sequence, or may be derived from a sequence of the invention. By "leader sequence" is intended any sequence that when translated, results in an amino acid sequence sufficient to trigger co-translational transport of the peptide chain to a subcellular organelle. Thus, this includes leader sequences targeting transport and/or glycosylation by passage into the endoplasmic reticulum, passage to vacuoles, plastids including chloroplasts, mitochondria, and the like.

[0073] By "plant transformation vector" is intended a DNA molecule that is necessary for efficient transformation of a plant cell. Such a molecule may consist of one or more plant expression cassettes, and may be organized into more than one "vector" DNA molecule. For example, binary vectors are plant transformation vectors that utilize two non-contiguous DNA vectors to encode all requisite cis- and trans-acting functions for transformation of plant cells (Hellens and Mullineaux (2000) Trends in Plant Science 5:446-451). "Vector" refers to a nucleic acid construct designed for transfer between different host cells. "Expression vector" refers to a vector that has the ability to incorporate, integrate and express heterologous DNA sequences or fragments in a foreign cell. The cassette will include 5' and 3' regulatory sequences operably linked to a sequence of the invention. By "operably linked" is intended a functional linkage between a promoter and a second sequence, wherein the promoter sequence initiates and mediates transcription of the DNA sequence corresponding to the second sequence. Generally, operably linked means that the nucleic acid sequences being linked are contiguous and, where necessary to join two protein coding regions, contiguous and in the same reading frame. The cassette may additionally contain at least one additional gene to be cotransformed into the organism. Alternatively, the additional gene(s) can be provided on multiple expression cassettes.

[0074] "Promoter" refers to a nucleic acid sequence that functions to direct transcription of a downstream coding sequence. The promoter together with other transcriptional and translational regulatory nucleic acid sequences (also termed "control sequences") are necessary for the expression of a DNA sequence of interest.

[0075] Such an expression cassette is provided with a plurality of restriction sites for insertion of the pesticidal sequence to be under the transcriptional regulation of the regulatory regions.

[0076] The expression cassette will include in the 5'-3' direction of transcription, a transcriptional and translational initiation region (i.e., a promoter), a DNA sequence of the invention, and a translational and transcriptional termination region (i.e., termination region) functional in plants. The promoter may be native or analogous, or foreign or heterologous, to the plant host and/or to the DNA sequence of the invention. Additionally, the promoter may be the natural sequence or alternatively a synthetic sequence. Where the promoter is "native" or "homologous" to the plant host, it is intended that the promoter is found in the native plant into which the promoter is introduced. Where the promoter is "foreign" or "heterologous" to the DNA sequence of the invention, it is intended that the promoter is not the native or naturally occurring promoter for the operably linked DNA sequence of the invention.

[0077] The termination region may be native with the transcriptional initiation region, may be native with the operably linked DNA sequence of interest, may be native with the plant host, or may be derived from another source (i.e., foreign or heterologous to the promoter, the DNA sequence of interest, the plant host, or any combination thereof). Convenient termination regions are available from the Ti-plasmid of *A. tumefaciens*, such as the octopine synthase and nopaline synthase termination regions. See also Guerineau et al. (1991) Mol. Gen. Genet. 262:141-144; Proudfoot (1991) Cell 64:671-674; Sanfacon et al. (1991) Genes Dev. 5:141-149; Mogen et al. (1990) Plant Cell 2:1261-1272; Munroe et al. (1990) Gene 91:151-158; Ballas et al. (1989) Nucleic Acids Res. 17:7891-7903; and Joshi et al. (1987) Nucleic Acid Res. 15:9627-9639.

[0078] Where appropriate, the gene(s) may be optimized for increased expression in the transformed host cell. That is, the genes can be synthesized using host cell-preferred codons for improved expression, or may be synthesized using codons at a host-preferred codon usage frequency. Generally, the GC content of the gene will be increased. See, for example, Campbell and Gowri (1990) Plant Physiol. 92:1-11 for a discussion of host-preferred codon usage. Methods are available in the art for synthesizing plant-preferred genes. See, for example, U.S. Patent Nos. 5,380,831, and 5,436,391, and Murray et al. (1989) Nucleic Acids Res. 17:477-498.

[0079] In one embodiment, the pesticidal protein is targeted to the chloroplast for expression. In this manner, where the pesticidal protein is not directly inserted into the chloroplast, the expression cassette will additionally contain a nucleic acid encoding a transit peptide to direct the pesticidal protein to the chloroplasts. Such transit peptides are known in the art. See, for example, Von Heijne et al. (1991) Plant Mol. Biol. Rep. 9:104-126; Clark et al. (1989) J. Biol. Chem. 264:17544-17550; Della-Cioppa et al. (1987) Plant Physiol. 84:965-968; Romer et al. (1993) Biochem. Biophys. Res. Commun. 196:1414-1421; and Shah et al. (1986) Science 233:478-481.

[0080] The pesticidal gene to be targeted to the chloroplast may be optimized for expression in the chloroplast to account for differences in codon usage between the plant nucleus and this organelle. In this manner, the nucleic acids of interest may be synthesized using chloroplast-preferred codons. See, for example, U.S. Patent No. 5,380,831.

Plant Transformation

[0081] Methods of the invention involve introducing a nucleotide construct into a plant. By "introducing" is intended to present to the plant the nucleotide construct in such a manner that the construct gains access to the interior of a cell of the plant. The methods of the invention do not require that a particular method for introducing a nucleotide construct to a plant is used, only that the nucleotide construct gains access to the interior of at least one cell of the plant. Methods for introducing nucleotide constructs into plants are known in the art including, but not limited to, stable transformation methods, transient transformation methods, and virus-mediated methods.

[0082] By "plant" is intended whole plants, plant organs (e.g., leaves, stems, roots, etc.), seeds, plant cells, propagules, embryos and progeny of the same. Plant cells can be differentiated or undifferentiated (e.g. callus, suspension culture cells, protoplasts, leaf cells, root cells, phloem cells, pollen).

[0083] "Transgenic plants" or "transformed plants" or "stably transformed" plants or cells or tissues refers to plants that have incorporated or integrated exogenous nucleic acid sequences or DNA fragments into the plant cell. These nucleic acid sequences include those that are exogenous, or not present in the untransformed plant cell, as well as those that may be endogenous, or present in the untransformed plant cell. "Heterologous" generally refers to the nucleic acid sequences that are not endogenous to the cell or part of the native genome in which they are present, and have been added to the cell by infection, transfection, microinjection, electroporation, microprojection, or the like.

[0084] The transgenic plants of the invention express one or more of the variant Cry3 sequences disclosed herein. In various embodiments, the transgenic plant further comprises one or more additional genes for insect resistance, for example, one or more additional genes for controlling coleopteran pests (e.g., Cry1, such as members of the Cry1A, Cry1B, Cry1C, Cry1D, Cry1E, and Cry1F families; Cry2, such as members of the Cry2A family; Cry9, such as members of the Cry9A, Cry9B, Cry9C, Cry9D, Cry9E, and Cry9F families; Cry34/35; VIPs, such as VIP3; or any of the modified Cry3A or Cry3B sequences known in the art as having toxicity against coleopteran pests. It will be understood by one of skill in the art that the transgenic plant may comprise any gene imparting an agronomic trait of interest.

[0085] Transformation of plant cells can be accomplished by one of several techniques known in the art. The pesticidal gene of the invention may be modified to obtain or enhance expression in plant cells. Typically a construct that expresses such a protein would contain a promoter to drive transcription of the gene, as well as a 3' untranslated region to allow transcription termination and polyadenylation. The organization of such constructs is well known in the art. In some instances, it may be useful to engineer the gene such that the resulting peptide is secreted, or otherwise targeted within the plant cell. For example, the gene can be engineered to contain a signal peptide to facilitate transfer of the peptide to the endoplasmic reticulum. It may also be preferable to engineer the plant expression cassette to contain an intron, such that mRNA processing of the intron is required for expression.

[0086] Typically this "plant expression cassette" will be inserted into a "plant transformation vector". This plant transformation vector may be comprised of one or more DNA vectors needed for achieving plant transformation. For example, it is a common practice in the art to utilize plant transformation vectors that are comprised of more than one contiguous DNA segment. These vectors are often referred to in the art as "binary vectors". Binary vectors as well as vectors with helper plasmids are most often used for *Agrobacterium*-mediated transformation, where the size and complexity of DNA segments needed to achieve efficient transformation is quite large, and it is advantageous to separate functions onto separate DNA molecules. Binary vectors typically contain a plasmid vector that contains the cis-acting sequences required for T-DNA transfer (such as left border and right border), a selectable marker that is engineered to be capable of expression in a plant cell, and a "gene of interest" (a gene engineered to be capable of expression in a plant cell for which generation of transgenic plants is desired). Also present on this plasmid vector are sequences required for bacterial replication. The cis-acting sequences are arranged in a fashion to allow efficient transfer into plant cells and expression therein. For example, the selectable marker gene and the pesticidal gene are located between the left and right borders. Often a second plasmid vector contains the trans-acting factors that mediate T-DNA transfer from *Agrobacterium* to plant cells. This plasmid often contains the virulence functions (Vir genes) that allow infection of plant cells by *Agrobacterium*, and transfer of DNA by cleavage at border sequences and vir-mediated DNA transfer, as is understood in the art (Hellens and Mullineaux (2000) Trends in Plant Science 5:446-451). Several types of *Agrobacterium* strains (e.g. LBA4404, GV3101, EHA101, EHA105, etc.) can be used for plant transformation. The second plasmid vector is not necessary for transforming the plants by other methods such as microprojection, microinjection, electroporation, polyethylene glycol, etc.

[0087] In general, plant transformation methods involve transferring heterologous DNA into target plant cells (e.g. immature or mature embryos, suspension cultures, undifferentiated callus, protoplasts, etc.), followed by applying a maximum threshold level of appropriate selection (depending on the selectable marker gene) to recover the transformed plant cells from a group of untransformed cell mass. Explants are typically transferred to a fresh supply of the same medium and cultured routinely. Subsequently, the transformed cells are differentiated into shoots after placing on regeneration medium supplemented with a maximum threshold level of selecting agent. The shoots are then transferred to a selective rooting medium for recovering rooted shoot or plantlet. The transgenic plantlet then grows into a mature plant and produces fertile seeds (e.g. Hiei et al. (1994) The Plant Journal 6:271-282; Ishida et al. (1996) Nature Biotechnology 14:745-750). Explants are typically transferred to a fresh supply of the same medium and cultured routinely. A general description of the techniques and methods for generating transgenic plants are found in Ayres and Park (1994) Critical Reviews in Plant Science 13:219-239 and Bommineni and Jauhar (1997) Maydica 42:107-120. Since the transformed material contains many cells; both transformed and non-transformed cells are present in any piece of subjected target callus or tissue or group of cells. The ability to kill non-transformed cells and allow transformed cells to proliferate results in transformed plant cultures. Often, the ability to remove non-transformed cells is a limitation to rapid recovery of transformed plant cells and successful generation of transgenic plants.

[0088] Transformation protocols as well as protocols for introducing nucleotide sequences into plants may vary depending on the type of plant or plant cell, i.e., monocot or dicot, targeted for transformation. Generation of transgenic plants may be performed by one of several methods, including, but not limited to, microinjection, electroporation, direct gene transfer, introduction of heterologous DNA by *Agrobacterium* into plant cells (*Agrobacterium*-mediated transformation), bombardment of plant cells with heterologous foreign DNA adhered to particles, ballistic particle acceleration, aerosol beam transformation (U.S. Published Application No. 20010026941; U.S. Patent No. 4,945,050; International Publication No. WO 91/00915; U.S. Published Application No. 2002015066), Lec1 transformation, and various other non-particle direct-mediated methods to transfer DNA.

[0089] Methods for transformation of chloroplasts are known in the art. See, for example, Svab et al. (1990) Proc. Natl. Acad. Sci. USA 87:8526-8530; Svab and Maliga (1993) Proc. Natl. Acad. Sci. USA 90:913-917; Svab and Maliga (1993) EMBO J. 12:601-606. The method relies on particle gun delivery of DNA containing a selectable marker and targeting of the DNA to the plastid genome through homologous recombination. Additionally, plastid transformation can be accomplished by transactivation of a silent plastid-borne transgene by tissue-preferred expression of a nuclear-encoded and plastid-directed RNA polymerase. Such a system has been reported in McBride et al. (1994) Proc. Natl. Acad. Sci. USA 91:7301-7305.

[0090] Following integration of heterologous foreign DNA into plant cells, one then applies a maximum threshold level of appropriate selection in the medium to kill the untransformed cells and separate and proliferate the putatively transformed cells that survive from this selection treatment by transferring regularly to a fresh medium. By continuous passage and challenge with appropriate selection, one identifies and proliferates the cells that are transformed with the plasmid vector. Molecular and biochemical methods can then be used to confirm the presence of the integrated heterologous gene of interest into the genome of the transgenic plant.

[0091] The cells that have been transformed may be grown into plants in accordance with conventional ways. See, for example, McCormick et al. (1986) Plant Cell Reports 5:81-84. These plants may then be grown, and either pollinated with the same transformed strain or different strains, and the resulting hybrid having constitutive expression of the desired phenotypic characteristic identified. Two or more generations may be grown to ensure that expression of the desired phenotypic characteristic is stably maintained and inherited and then seeds harvested to ensure expression of the desired phenotypic characteristic has been achieved. In this manner, the present invention provides transformed seed (also referred to as "transgenic seed") having a nucleotide construct of the invention, for example, an expression cassette of the invention, stably incorporated into their genome.

Evaluation of Plant Transformation

[0092] Following introduction of heterologous foreign DNA into plant cells, the transformation or integration of heterologous gene in the plant genome is confirmed by various methods such as analysis of nucleic acids, proteins and metabolites associated with the integrated gene.

[0093] PCR analysis is a rapid method to screen transformed cells, tissue or shoots for the presence of incorporated gene at the earlier stage before transplanting into the soil (Sambrook and Russell (2001) Molecular Cloning: A Laboratory Manual. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY). PCR is carried out using oligonucleotide primers specific to the gene of interest or *Agrobacterium* vector background, etc.

[0094] Plant transformation may be confirmed by Southern blot analysis of genomic DNA (Sambrook and Russell, 2001, *supra*). In general, total DNA is extracted from the transformant, digested with appropriate restriction enzymes, fractionated in an agarose gel and transferred to a nitrocellulose or nylon membrane. The membrane or "blot" is then probed with, for example, radiolabeled ³²P target DNA fragment to confirm the integration of introduced gene into the plant genome according to standard techniques (Sambrook and Russell, 2001, *supra*).

[0095] In Northern blot analysis, RNA is isolated from specific tissues of transformant, fractionated in a formaldehyde agarose gel, and blotted onto a nylon filter according to standard procedures that are routinely used in the art (Sambrook and Russell, 2001, *supra*). Expression of RNA encoded by the pesticidal gene is then tested by hybridizing the filter to a radioactive probe derived from a pesticidal gene, by methods known in the art (Sambrook and Russell, 2001, *supra*).

[0096] Western blot, biochemical assays and the like may be carried out on the transgenic plants to confirm the presence of protein encoded by the pesticidal gene by standard procedures (Sambrook and Russell, 2001, *supra*) using antibodies that bind to one or more epitopes present on the pesticidal protein.

Pesticidal Activity in Plants

[0097] In another aspect of the invention, one may generate transgenic plants expressing a pesticidal protein that has pesticidal activity. Methods described above by way of example may be utilized to generate transgenic plants, but the manner in which the transgenic plant cells are generated is not critical to this invention. Methods known or described in the art such as *Agrobacterium*-mediated transformation, biolistic transformation, and non-particle-mediated methods

may be used at the discretion of the experimenter. Plants expressing a pesticidal protein may be isolated by common methods described in the art, for example by transformation of callus, selection of transformed callus, and regeneration of fertile plants from such transgenic callus. In such process, one may use any gene as a selectable marker so long as its expression in plant cells confers ability to identify or select for transformed cells.

[0098] A number of markers have been developed for use with plant cells, such as resistance to chloramphenicol, the aminoglycoside G418, hygromycin, or the like. Other genes that encode a product involved in chloroplast metabolism may also be used as selectable markers. For example, genes that provide resistance to plant herbicides such as glyphosate, bromoxynil, or imidazolinone may find particular use. Such genes have been reported (Stalker et al. (1985) J. Biol. Chem. 263:6310-6314 (bromoxynil resistance nitrilase gene); and Sathasivan et al. (1990) Nucl. Acids Res. 18:2188 (AHAS imidazolinone resistance gene). Additionally, the genes disclosed herein are useful as markers to assess transformation of bacterial or plant cells. Methods for detecting the presence of a transgene in a plant, plant organ (e.g., leaves, stems, roots, etc.), seed, plant cell, propagule, embryo or progeny of the same are well known in the art. In one embodiment, the presence of the transgene is detected by testing for pesticidal activity.

[0099] Fertile plants expressing a pesticidal protein may be tested for pesticidal activity, and the plants showing optimal activity selected for further breeding. Methods are available in the art to assay for pest activity. Generally, the protein is mixed and used in feeding assays. See, for example Marrone et al. (1985) J. of Economic Entomology 78:290-293.

[0100] The present invention may be used for transformation of any plant species, including, but not limited to, monocots and dicots. Examples of plants of interest include, but are not limited to, corn (maize), sorghum, wheat, sunflower, tomato, crucifers, peppers, potato, cotton, rice, soybean, sugarbeet, sugarcane, tobacco, barley, and oilseed rape, *Brassica* sp., alfalfa, rye, millet, safflower, peanuts, sweet potato, cassava, coffee, coconut, pineapple, citrus trees, cocoa, tea, banana, avocado, fig, guava, mango, olive, papaya, cashew, macadamia, almond, oats, vegetables, ornamentals, and conifers.

[0101] Vegetables include, but are not limited to, tomatoes, lettuce, green beans, lima beans, peas, and members of the genus *Curcumis* such as cucumber, cantaloupe, and musk melon. Ornamentals include, but are not limited to, azalea, hydrangea, hibiscus, roses, tulips, daffodils, petunias, carnation, poinsettia, and chrysanthemum. Preferably, plants of the present invention are crop plants (for example, maize, sorghum, wheat, sunflower, tomato, crucifers, peppers, potato, cotton, rice, soybean, sugarbeet, sugarcane, tobacco, barley, oilseed rape, etc.).

Use in Pesticidal Control

[0102] General methods for employing strains comprising a nucleotide sequence of the present invention, or a variant thereof, in pesticide control or in engineering other organisms as pesticidal agents are known in the art. See, for example U.S. Patent No. 5,039,523 and EP 0480762A2.

[0103] The *Bacillus* strains containing a nucleotide sequence of the present invention, or a variant thereof, or the microorganisms that have been genetically altered to contain a pesticidal gene and protein may be used for protecting agricultural crops and products from pests. In one aspect of the invention, whole, i.e., unlysed, cells of a toxin (pesticide)-producing organism are treated with reagents that prolong the activity of the toxin produced in the cell when the cell is applied to the environment of target pest(s).

[0104] Alternatively, the pesticide is produced by introducing a pesticidal gene into a cellular host. Expression of the pesticidal gene results, directly or indirectly, in the intracellular production and maintenance of the pesticide. In one aspect of this invention, these cells are then treated under conditions that prolong the activity of the toxin produced in the cell when the cell is applied to the environment of target pest(s). The resulting product retains the toxicity of the toxin. These naturally encapsulated pesticides may then be formulated in accordance with conventional techniques for application to the environment hosting a target pest, e.g., soil, water, and foliage of plants. See, for example EPA 0192319, and the references cited therein. Alternatively, one may formulate the cells expressing a gene of this invention such as to allow application of the resulting material as a pesticide.

[0105] The active ingredients of the present invention are normally applied in the form of compositions and can be applied to the crop area or plant to be treated, simultaneously or in succession, with other compounds. These compounds can be fertilizers, weed killers, cryoprotectants, surfactants, detergents, pesticidal soaps, dormant oils, polymers, and/or time-release or biodegradable carrier formulations that permit long-term dosing of a target area following a single application of the formulation. They can also be selective herbicides, chemical insecticides, virucides, microbicides, amoebicides, pesticides, fungicides, bacteriocides, nematocides, molluscicides or mixtures of several of these preparations, if desired, together with further agriculturally acceptable carriers, surfactants or application-promoting adjuvants customarily employed in the art of formulation. Suitable carriers and adjuvants can be solid or liquid and correspond to the substances ordinarily employed in formulation technology, e.g. natural or regenerated mineral substances, solvents, dispersants, wetting agents, tackifiers, binders or fertilizers. Likewise the formulations may be prepared into edible "baits" or fashioned into pest "traps" to permit feeding or ingestion by a target pest of the pesticidal formulation.

[0106] Methods of applying an active ingredient of the present invention or an agrochemical composition of the present invention that contains at least one of the pesticidal proteins produced by the bacterial strains of the present invention

include leaf application, seed coating and soil application. The number of applications and the rate of application depend on the intensity of infestation by the corresponding pest.

[0107] The composition may be formulated as a powder, dust, pellet, granule, spray, emulsion, colloid, solution, or such like, and may be prepared by such conventional means as desiccation, lyophilization, homogenation, extraction, filtration, centrifugation, sedimentation, or concentration of a culture of cells comprising the polypeptide. In all such compositions that contain at least one such pesticidal polypeptide, the polypeptide may be present in a concentration of from about 1% to about 99% by weight.

[0108] Lepidopteran, dipteran, or coleopteran pests may be killed or reduced in numbers in a given area by the methods of the invention, or may be prophylactically applied to an environmental area to prevent infestation by a susceptible pest. Preferably the pest ingests, or is contacted with, a pesticidally-effective amount of the polypeptide. By "pesticidally-effective amount" is intended an amount of the pesticide that is able to bring about death to at least one pest, or to noticeably reduce pest growth, feeding, or normal physiological development. This amount will vary depending on such factors as, for example, the specific target pests to be controlled, the specific environment, location, plant, crop, or agricultural site to be treated, the environmental conditions, and the method, rate, concentration, stability, and quantity of application of the pesticidally-effective polypeptide composition. The formulations may also vary with respect to climatic conditions, environmental considerations, and/or frequency of application and/or severity of pest infestation.

[0109] The pesticide compositions described may be made by formulating either the bacterial cell, crystal and/or spore suspension, or isolated protein component with the desired agriculturally-acceptable carrier. The compositions may be formulated prior to administration in an appropriate means such as lyophilized, freeze-dried, desiccated, or in an aqueous carrier, medium or suitable diluent, such as saline or other buffer. The formulated compositions may be in the form of a dust or granular material, or a suspension in oil (vegetable or mineral), or water or oil/water emulsions, or as a wettable powder, or in combination with any other carrier material suitable for agricultural application. Suitable agricultural carriers can be solid or liquid and are well known in the art. The term "agriculturally-acceptable carrier" covers all adjuvants, inert components, dispersants, surfactants, tackifiers, binders, etc. that are ordinarily used in pesticide formulation technology; these are well known to those skilled in pesticide formulation. The formulations may be mixed with one or more solid or liquid adjuvants and prepared by various means, e.g., by homogeneously mixing, blending and/or grinding the pesticidal composition with suitable adjuvants using conventional formulation techniques. Suitable formulations and application methods are described in U.S. Patent No. 6,468,523.

[0110] "Pest" includes but is not limited to, insects, fungi, bacteria, nematodes, mites, ticks, and the like. Insect pests include insects selected from the orders *Coleoptera*, *Diptera*, *Hymenoptera*, *Lepidoptera*, *Mallophaga*, *Homoptera*, *Hemiptera*, *Orthoptera*, *Thysanoptera*, *Dermaptera*, *Isoptera*, *Anoplura*, *Siphonaptera*, *Trichoptera*, etc., particularly *Coleoptera*, *Lepidoptera*, and *Diptera*.

[0111] The order *Coleoptera* includes the suborders *Adephaga* and *Polyphaga*. Suborder *Adephaga* includes the superfamilies *Caraboidea* and *Gyrinoidea*, while suborder *Polyphaga* includes the superfamilies *Hydrophiloidea*, *Staphylinidea*, *Cantharoidea*, *Cleroidea*, *Elateroidea*, *Dascilloidea*, *Dryopoidea*, *Byrrhoidea*, *Cucujoidea*, *Meloidea*, *Mordelloidea*, *Tenebrionoidea*, *Bostrichoidea*, *Scarabaeoidea*, *Cerambycoidea*, *Chrysomeloidea*, and *Curculionoidea*. Superfamily *Caraboidea* includes the families *Cicindelidae*, *Carabidae*, and *Dytiscidae*. Superfamily *Gyrinoidea* includes the family *Gyrinidae*. Superfamily *Hydrophiloidea* includes the family *Hydrophilidae*. Superfamily *Staphylinidea* includes the families *Silphidae* and *Staphylinidae*. Superfamily *Cantharoidea* includes the families *Cantharidae* and *Lampyridae*. Superfamily *Cleroidea* includes the families *Cleridae* and *Dermentidae*. Superfamily *Elateroidea* includes the families *Elateridae* and *Buprestidae*. Superfamily *Cucujoidea* includes the family *Coccinellidae*. Superfamily *Meloidea* includes the family *Meloidae*. Superfamily *Tenebrionoidea* includes the family *Tenebrionidae*. Superfamily *Scarabaeoidea* includes the families *Passalidae* and *Scarabaeidae*. Superfamily *Cerambycoidea* includes the family *Cerambycidae*. Superfamily *Chrysomeloidea* includes the family *Chrysomelidae*. Superfamily *Curculionoidea* includes the families *Curculionidae* and *Scolytidae*.

[0112] The order *Diptera* includes the Suborders *Nematocera*, *Brachycera*, and *Cyclorrhapha*. Suborder *Nematocera* includes the families *Tipulidae*, *Psychodidae*, *Culicidae*, *Ceratopogonidae*, *Chironomidae*, *Simuliidae*, *Bibionidae*, and *Cecidomyiidae*. Suborder *Brachycera* includes the families *Stratiomyidae*, *Tabanidae*, *Therevidae*, *Asilidae*, *Mydidae*, *Bombyliidae*, and *Dolichopodidae*. Suborder *Cyclorrhapha* includes the Divisions *Aschiza* and *Aschiza*. Division *Aschiza* includes the families *Phoridae*, *Syrphidae*, and *Conopidae*. Division *Aschiza* includes the Sections *Acalyptratae* and *Calypttratae*. Section *Acalyptratae* includes the families *Otitidae*, *Tephritidae*, *Agromyzidae*, and *Drosophilidae*. Section *Calypttratae* includes the families *Hippoboscidae*, *Oestridae*, *Tachinidae*, *Anthomyiidae*, *Muscidae*, *Calliphoridae*, and *Sarcophagidae*.

[0113] The order *Lepidoptera* includes the families *Papilionidae*, *Pieridae*, *Lycaenidae*, *Nymphalidae*, *Danaidae*, *Satyridae*, *Hesperiidae*, *Sphingidae*, *Saturniidae*, *Geometridae*, *Arctiidae*, *Noctuidae*, *Lymantriidae*, *Sesiidae*, and *Tineidae*.

[0114] Insect pests of the invention for the major crops include: Maize: *Ostrinia nubilalis*, European corn borer; *Agrotis ipsilon*, black cutworm; *Helicoverpa zea*, corn earworm; *Spodoptera frugiperda*, fall armyworm; *Diatraea grandiosella*, southwestern corn borer; *Elasmopalpus lignosellus*, lesser cornstalk borer; *Diatraea saccharalis*, sugarcane borer;

Diabrotica virgifera, western corn rootworm; *Diabrotica longicornis barberi*, northern corn rootworm; *Diabrotica undecimpunctata howardi*, southern corn rootworm; *Melanotus* spp., wireworms; *Cyclocephala borealis*, northern masked chafer (white grub); *Cyclocephala immaculata*, southern masked chafer (white grub); *Popillia japonica*, Japanese beetle; *Chaetocnema pulicaria*, corn flea beetle; *Sphenophorus maidis*, maize billbug; *Rhopalosiphum maidis*, corn leaf aphid; *Anuraphis maidiradicis*, corn root aphid; *Blissus leucopterus leucopterus*, chinch bug; *Melanoplus femurrubrum*, redlegged grasshopper; *Melanoplus sanguinipes*, migratory grasshopper; *Hylemya platura*, seedcorn maggot; *Agromyza parvicornis*, corn blot leafminer; *Anaphothrips obscurus*, grass thrips; *Solenopsis milesta*, thief ant; *Tetranychus urticae*, twospotted spider mite; *Sorghum*: *Chilo partellus*, sorghum borer; *Spodoptera frugiperda*, fall armyworm; *Helicoverpa zea*, corn earworm; *Elasmopalpus lignosellus*, lesser cornstalk borer; *Feltia subterranea*, granulate cutworm; *Phyllophaga crinita*, white grub; *Eleodes*, *Conoderus*, and *Aeolus* spp., wireworms; *Oulema melanopus*, cereal leaf beetle; *Chaetocnema pulicaria*, corn flea beetle; *Sphenophorus maidis*, maize billbug; *Rhopalosiphum maidis*, corn leaf aphid; *Sipha flava*, yellow sugarcane aphid; *Blissus leucopterus leucopterus*, chinch bug; *Contarinia sorghicola*, sorghum midge; *Tetranychus cinnabarinus*, carmine spider mite; *Tetranychus urticae*, twospotted spider mite; Wheat: *Pseudaletia unipunctata*, army worm; *Spodoptera frugiperda*, fall armyworm; *Elasmopalpus lignosellus*, lesser cornstalk borer; *Agrotis orthogonia*, western cutworm; *Elasmopalpus lignosellus*, lesser cornstalk borer; *Oulema melanopus*, cereal leaf beetle; *Hypera punctata*, clover leaf weevil; *Diabrotica undecimpunctata howardi*, southern corn rootworm; Russian wheat aphid; *Schizaphis graminum*, greenbug; *Macrosiphum avenae*, English grain aphid; *Melanoplus femurrubrum*, redlegged grasshopper; *Melanoplus differentialis*, differential grasshopper; *Melanoplus sanguinipes*, migratory grasshopper; *Mayetiola destructor*, Hessian fly; *Sitodiplosis mosellana*, wheat midge; *Meromyza americana*, wheat stem maggot; *Hylemya coarctata*, wheat bulb fly; *Frankliniella fusca*, tobacco thrips; *Cephus cinctus*, wheat stem sawfly; *Aceria tulipae*, wheat curl mite; Sunflower: *Suleima helianthana*, sunflower bud moth; *Homoeosoma electellum*, sunflower moth; *zygogramma exclamationis*, sunflower beetle; *Bothyrus gibbosus*, carrot beetle; *Neolasioptera murtfeldtiana*, sunflower seed midge; Cotton: *Heliothis virescens*, cotton budworm; *Helicoverpa zea*, cotton bollworm; *Spodoptera exigua*, beet armyworm; *Pectinophora gossypiella*, pink bollworm; *Anthonomus grandis*, boll weevil; *Aphis gossypii*, cotton aphid; *Pseudatomoscelis seriatus*, cotton fleahopper; *Trialeurodes abutilonea*, bandedwinged whitefly; *Lygus lineolaris*, tarnished plant bug; *Melanoplus femurrubrum*, redlegged grasshopper; *Melanoplus differentialis*, differential grasshopper; *Thrips tabaci*, onion thrips; *Frankliniella fusca*, tobacco thrips; *Tetranychus cinnabarinus*, carmine spider mite; *Tetranychus urticae*, twospotted spider mite; Rice: *Diatraea saccharalis*, sugarcane borer; *Spodoptera frugiperda*, fall armyworm; *Helicoverpa zea*, corn earworm; *Colaspis brunnea*, grape colaspis; *Lissorhoptrus oryzophilus*, rice water weevil; *Sitophilus oryzae*, rice weevil; *Nephotettix nigropictus*, rice leafhopper; *Blissus leucopterus leucopterus*, chinch bug; *Acrosternum hilare*, green stink bug; Soybean: *Pseudoplusia includens*, soybean looper; *Anticarsia gemmatilis*, velvetbean caterpillar; *Platyphena scabra*, green cloverworm; *Ostrinia nubilalis*, European corn borer; *Agrotis ipsilon*, black cutworm; *Spodoptera exigua*, beet armyworm; *Heliothis virescens*, cotton budworm; *Helicoverpa zea*, cotton bollworm; *Epilachna varivestis*, Mexican bean beetle; *Myzus persicae*, green peach aphid; *Empoasca fabae*, potato leafhopper; *Acrosternum hilare*, green stink bug; *Melanoplus femurrubrum*, redlegged grasshopper; *Melanoplus differentialis*, differential grasshopper; *Hylemya platura*, seedcorn maggot; *Sericothrips variabilis*, soybean thrips; *Thrips tabaci*, onion thrips; *Tetranychus turkestanii*, strawberry spider mite; *Tetranychus urticae*, twospotted spider mite; Barley: *Ostrinia nubilalis*, European corn borer; *Agrotis ipsilon*, black cutworm; *Schizaphis graminum*, greenbug; *Blissus leucopterus leucopterus*, chinch bug; *Acrosternum hilare*, green stink bug; *Euschistus servus*, brown stink bug; *Delia platura*, seedcorn maggot; *Mayetiola destructor*, Hessian fly; *Petrobia latens*, brown wheat mite; Oil Seed Rape: *Brevicoryne brassicae*, cabbage aphid; *Phyllotreta cruciferae*, Flea beetle; *Mamestra configurata*, Bertha armyworm; *Plutella xylostella*, Diamond-back moth; *Delia* spp., Root maggots.

[0115] Nematodes include parasitic nematodes such as root-knot, cyst, and lesion nematodes, including *Heterodera* spp., *Meloidogyne* spp., and *Globodera* spp.; particularly members of the cyst nematodes, including, but not limited to, *Heterodera glycines* (soybean cyst nematode); *Heterodera schachtii* (beet cyst nematode); *Heterodera avenae* (cereal cyst nematode); and *Globodera rostochiensis* and *Globodera pallida* (potato cyst nematodes). Lesion nematodes include *Pratylenchus* spp.

[0116] The plants can also be treated with one or more chemical compositions, including one or more herbicide, insecticides, or fungicides. Exemplary chemical compositions include: Fruits/Vegetables Herbicides: Atrazine, Bromacil, Diuron, Glyphosate, Linuron, Metribuzin, Simazine, Trifluralin, Fluazifop, Glufosinate, Halosulfuron Gowan, Paraquat, Propyzamide, Sethoxydim, Butafenacil, Halosulfuron, Indaziflam; Fruits/Vegetables Insecticides: Aldicarb, Bacillus thuringiensis, Carbaryl, Carbofuran, Chlorpyrifos, Cypermethrin, Deltamethrin, Diazinon, Malathion, Abamectin, Cyfluthrin/beta-cyfluthrin, Esfenvalerate, Lambda-cyhalothrin, Acequinocyl, Bifenazate, Methoxyfenozide, Novaluron, Chromafenozide, Thiacloprid, Dinotefuran, Fluacrypyrim, Tolfenpyrad, Clothianidin, Spirodiclofen, Gamma-cyhalothrin, Spiromesifen, Spinosad, Rynaxypyr, Cyazypyr, Spinoteram, Triflumuron, Spirotetramat, Imidacloprid, Flubendiamide, Thiodicarb, Metaflumizone, Sulfoxaflor, Cyflumetofen, Cyanopyrafen, Imidacloprid, Clothianidin, Thiamethoxam, Spinetoram, Thiodicarb, Flonicamid, Methiocarb, Emamectin-benzoate, Indoxacarb, Fozthiazate, Fenamiphos, Cadusaphos, Pyriproxifen, Fenbutatin-oxid, Hexthiazox, Methomyl, 4-[[[6-Chlorpyridin-3-yl)methyl](2,2-difluorethyl)amino]furan-

2(5H)-on; Fruits/Vegetables Fungicides: Carbendazim, Chlorothalonil, EBDCs, Sulphur, Thiophanate-methyl, Azoxystrobin, Cymoxanil, Fluazinam, Fosetyl, Iprodione, Kresoxim-methyl, Metalaxyl/mefenoxam, Trifloxystrobin, Ethaboxam, Iprovalicarb, Trifloxystrobin, Fenhexamid, Oxpoconazole fumarate, Cyazofamid, Fenamidone, Zoxamide, Picoxystrobin, Pyraclostrobin, Cyflufenamid, Boscalid; Cereals Herbicides: Isoproturon, Bromoxynil, Ioxynil, Phenoxies, Chlorsulfuron, Clodinafop, Diclofop, Diflufenican, Fenoxaprop, Florasulam, Fluroxypyr, Metsulfuron, Triasulfuron, Flucarbazone, Iodosulfuron, Propoxycarbazone, Picolinafen, Mesosulfuron, Bflubutamid, Pinoxaden, Amidosulfuron, Thifensulfuron, Tribenuron, Flupyrasulfuron, Sulfosulfuron, Pyrasulfotole, Pyroxulam, Flufenacet, Tralkoxydim, Pyroxasulfon; Cereals Fungicides: Carbendazim, Chlorothalonil, Azoxystrobin, Cyproconazole, Cyprodinil, Fenpropimorph, Epoxiconazole, Kresoxim-methyl, Quinoxifen, Tebuconazole, Trifloxystrobin, Simeconazole, Picoxystrobin, Pyraclostrobin, Dimoxystrobin, Prothioconazole, Fluoxastrobin; Cereals Insecticides: Dimethoate, Lambda-cyhalothrin, Deltamethrin, alpha-Cypermethrin, B-cyfluthrin, Bifenthrin, Imidacloprid, Clothianidin, Thiamethoxam, Thiacloprid, Acetamiprid, Dinotofuran, Chlorpyrifos, Metamidophos, Oxidemethon-methyl, Pirimicarb, Methiocarb; Maize Herbicides: Atrazine, Alachlor, Bromoxynil, Acetochlor, Dicamba, Clopyralid, (S)-Dimethenamid, Glufosinate, Glyphosate, Isoxaflutole, (S)-Metolachlor, Mesotrione, Nicosulfuron, Primisulfuron, Rimsulfuron, Sulcotrione, Foramsulfuron, Topramezone, Tembotrione, Saflufenacil, Thiencarbazone, Flufenacet, Pyroxasulfon; Maize Insecticides: Carbofuran, Chlorpyrifos, Bifenthrin, Fipronil, Imidacloprid, Lambda-Cyhalothrin, Tefluthrin, Terbufos, Thiamethoxam, Clothianidin, Spiromesifen, Flubendiamide, Triflumuron, Rynaxypyr, Deltamethrin, Thiodicarb, β -Cyfluthrin, Cypermethrin, Bifenthrin, Lufenuron, Triflumuron, Tefluthrin, Tebupirimphos, Ethiprole, Cyazypyr, Thiacloprid, Acetamiprid, Dinotofuran, Avermectin, Methiocarb, Spirodiclofen, Spirotetramat; Maize Fungicides: Fenitropan, Thiram, Prothioconazole, Tebuconazole, Trifloxystrobin; Rice Herbicides: Butachlor, Propanil, Azimsulfuron, Bensulfuron, Cyhalofop, Daimuron, Fentrazamide, Imazosulfuron, Mefenacet, Oxaziclomefone, Pyrazosulfuron, Pyributicarb, Quinclorac, Thiobencarb, Indanofan, Flufenacet, Fentrazamide, Halosulfuron, Oxaziclomefone, Benzobicyclon, Pyriftalid, Penoxsulam, Bispyribac, Oxadiargyl, Ethoxysulfuron, Pretilachlor, Mesotrione, Tefuryltrione, Oxadiazon, Fenoxaprop, Pyrimisulfan; Rice Insecticides: Diazinon, Fenitrothion, Fenobucarb, Monocrotophos, Benfuracarb, Buprofezin, Dinotofuran, Fipronil, Imidacloprid, Isoprocarb, Thiacloprid, Chromafenozide, Thiacloprid, Dinotofuran, Clothianidin, Ethiprole, Flubendiamide, Rynaxypyr, Deltamethrin, Acetamiprid, Thiamethoxam, Cyazypyr, Spinosad, Spinotoram, Emamectin-Benzoate, Cypermethrin, Chlorpyrifos, Cartap, Methamidophos, Etofenprox, Triazophos, 4-[[[6-Chlorpyridin-3-yl)methyl](2,2-difluorethyl)amino]furan-2(5H)-on, Carbofuran, Benfuracarb; Rice Fungicides: Thiophanate-methyl, Azoxystrobin, Carpropamid, Edifenphos, Ferimzone, Iprobenfos, Isoprothiolane, Pencycuron, Probenazole, Pyroquilon, Tricyclazole, Trifloxystrobin, Diclocymet, Fenoxanil, Simeconazole, Tiadinil; Cotton Herbicides: Diuron, Fluometuron, MSMA, Oxyfluorfen, Prometryn, Trifluralin, Carfentrazon, Clethodim, Fluazifop-butyl, Glyphosate, Norflurazon, Pendimethalin, Pyriothobac-sodium, Trifloxysulfuron, Tepraloxymid, Glufosinate, Flumioxazin, Thidiazuron; Cotton Insecticides: Acephate, Aldicarb, Chlorpyrifos, Cypermethrin, Deltamethrin, Malathion, Monocrotophos, Abamectin, Acetamiprid, Emamectin Benzoate, Imidacloprid, Indoxacarb, Lambda-Cyhalothrin, Spinosad, Thiodicarb, Gamma-Cyhalothrin, Spiromesifen, Pyridalyl, Flonicamid, Flubendiamide, Triflumuron, Rynaxypyr, Beta-Cyfluthrin, Spirotetramat, Clothianidin, Thiamethoxam, Thiacloprid, Dinotofuran, Flubendiamide, Cyazypyr, Spinosad, Spinotoram, gamma Cyhalothrin, 4-[[[6-Chlorpyridin-3-yl)methyl](2,2-difluorethyl)amino]furan-2(5H)-on, Thiodicarb, Avermectin, Flonicamid, Pyridalyl, Spiromesifen, Sulfoxaflor, Profenophos, Thiazophos, Endosulfan; Cotton Fungicides: Etridiazole, Metalaxyl, Quintozene; Soybean Herbicides: Alachlor, Bentazone, Trifluralin, Chlorimuron-Ethyl, Cloransulam-Methyl, Fenoxaprop, Fomesafen, Fluazifop, Glyphosate, Imazamox, Imazaquin, Imazethapyr, (S)-Metolachlor, Metribuzin, Pendimethalin, Tepraloxymid, Glufosinate; Soybean Insecticides: Lambda-cyhalothrin, Methomyl, Parathion, Thiocarb, Imidacloprid, Clothianidin, Thiamethoxam, Thiacloprid, Acetamiprid, Dinotofuran, Flubendiamide, Rynaxypyr, Cyazypyr, Spinosad, Spinotoram, Emamectin-Benzoate, Fipronil, Ethiprole, Deltamethrin, β -Cyfluthrin, gamma and lambda Cyhalothrin, 4-[[[6-Chlorpyridin-3-yl)methyl](2,2-difluorethyl)amino]furan-2(5H)-on, Spirotetramat, Spinodiclofen, Triflumuron, Flonicamid, Thiodicarb, beta-Cyfluthrin; Soybean Fungicides: Azoxystrobin, Cyproconazole, Epoxiconazole, Flutriafol, Pyraclostrobin, Tebuconazole, Trifloxystrobin, Prothioconazole, Tetraconazole; Sugarbeet Herbicides: Chloridazon, Desmedipham, Ethofumesate, Phenmedipham, Triallate, Clopyralid, Fluazifop, Lenacil, Metamitron, Quinmerac, Cycloxydim, Triflurosulfuron, Tepraloxymid, Quizalofop; Sugarbeet Insecticides: Imidacloprid, Clothianidin, Thiamethoxam, Thiacloprid, Acetamiprid, Dinotofuran, Deltamethrin, β -Cyfluthrin, gamma/lambda Cyhalothrin, 4-[[[6-Chlorpyridin-3-yl)methyl](2,2-difluorethyl)amino]furan-2(5H)-on, Tefluthrin, Rynaxypyr, Cyazypyr, Fipronil, Carbofuran; Canola Herbicides: Clopyralid, Diclofop, Fluazifop, Glufosinate, Glyphosate, Metazachlor, Trifluralin Ethametsulfuron, Quinmerac, Quizalofop, Clethodim, Tepraloxymid; Canola Fungicides: Azoxystrobin, Carbendazim, Fludioxonil, Iprodione, Prochloraz, Vinclozolin; Canola Insecticides: Carbofuran, Organophosphates, Pyrethroids, Thiacloprid, Deltamethrin, Imidacloprid, Clothianidin, Thiamethoxam, Acetamiprid, Dinotofuran, β -Cyfluthrin, gamma and lambda Cyhalothrin, tau-Fluvalerate, Ethiprole, Spinosad, Spinotoram, Flubendiamide, Rynaxypyr, Cyazypyr, 4-[[[6-Chlorpyridin-3-yl)methyl](2,2-difluorethyl)amino]furan-2(5H)-on.

Methods for Increasing Plant Yield

[0117] Methods for increasing plant yield are provided. The methods comprise introducing into a plant or plant cell a polynucleotide comprising a pesticidal sequence disclosed herein. As defined herein, the "yield" of the plant refers to the quality and/or quantity of biomass produced by the plant. By "biomass" is intended any measured plant product. An increase in biomass production is any improvement in the yield of the measured plant product. Increasing plant yield has several commercial applications. For example, increasing plant leaf biomass may increase the yield of leafy vegetables for human or animal consumption. Additionally, increasing leaf biomass can be used to increase production of plant-derived pharmaceutical or industrial products. An increase in yield can comprise any statistically significant increase including, but not limited to, at least a 1% increase, at least a 3% increase, at least a 5% increase, at least a 10% increase, at least a 20% increase, at least a 30%, at least a 50%, at least a 70%, at least a 100% or a greater increase in yield compared to a plant not expressing the pesticidal sequence.

[0118] The following examples are offered by way of illustration and not by way of limitation.

EXPERIMENTAL

Example 1. Expression Construct.

[0119] pAX 5510 is an expression vector, based on the pRSF1b1 vector system (Invitrogen) that contains the open reading frame SEQ ID NO:1 (Designated herein as axmi-R1, which encodes the sequence described in GENBANK® Accession No. POA379) downstream of the T7 promoter, such that induction of transcription of the T7 promoter (for example, in BL21: DE3 strains) results in accumulation of the cry-R1 protein (SEQ ID NO:2, which corresponds to the sequence described in GENBANK® Accession No. POA379), with an N-terminal His tag, in *E. coli* cells.

Example 2. Western corn rootworm (WCRW) and Southern corn rootworm (SCRW) Bioassays

[0120] Western and Southern corn rootworm eggs (*Diabrotica virgifera* and *Diabrotica undecimpunctata*, respectively) (Crop Characteristics, MN) were washed and incubated at 25 °C until near-hatch. Molten artificial diet was prepared as previously described (US Patent No. 7,351,881), placed in 1 ml aliquots and allowed to cool in 24-well tissue culture plates (Corning 3527) for 1 hour. Once solidified, 40 µl of sample was placed in each well and allowed to diffuse into the diet. After the sample was absorbed, 7.5 µl of egg:0.15% agar slurry (approximately 25 rootworm eggs per well) were delivered onto the side of each well and allowed to dry. Once dry, the plates were sealed with a BREATHE-EASY® gas permeable membrane (Research Products International) and placed in a dark growth chamber (25 °C, 90% relative humidity (RH)).

[0121] After 24 hours, each plate had its membrane and then unhatched eggs removed, resealed with gas permeable membranes and returned to the dark growth chamber (25 °C, 90% RH) for an additional four days. After a total of five days, insects in sample wells were compared to in-plate controls and assessed for stunting and mortality (See Table 1 for the scoring system).

Table 1. Scoring System used in WCRW and SCRW Bioassays

Score	Definition
0	No Activity
1	Slight, non-uniform stunt
2	Non-uniform stunt
3	Uniform stunt
4	Uniform stunt with mortality (expressed as a percentage)
5	Uniform stunt with 100% mortality

Example 3. Mutagenesis Strategy, and creation of first mutagenized library.

[0122] The first generation point mutation library (PM Library 1, PM1) targeted 4 regions of SEQ ID NO:2, comprising twenty eight (28) positions. Using pAX5510 as a template, several individual positions were randomized using the QUIKCHANGE® Site-directed mutagenesis kit, and the DNA sequences of a large number of variants were determined. By analysis of the DNA sequences, desirable variants were pooled, while undesired clones (such as wild-type clones,

duplicate mutants and frame shift mutants) were eliminated. Two hundred and ninety-four (294) unique variants were identified from PM Library1 for further testing.

[0123] Primary screening. The pooled library variants, as well as pAX5510, were transformed into BL21*DE3 cells and plated on LB+ Kanamycin (100 µg/ml). Fresh colonies were picked into 8.5 ml LB + Kanamycin (100ug/ml) liquid medium and were grown in 24 deep well blocks at 37°C and 250 rpm until an OD600 nm of 0.3-0.4 was reached. IPTG was added to a final concentration of 0.5 mM and the cultures were incubated for an additional 18 hours at 20°C. The OD600 nm was determined and the cells were collected by centrifugation (10 minutes at 4500 rpm, 4 degrees C). The cell pellets were resuspended in 50 mM Sodium carbonate pH 10.5, 1 mM DTT at a density of 10 OD600/ml. The cells were disrupted by bead beating and soluble extracts were obtained after centrifugation at 4000 rpm for 15 minutes at 4°C.

[0124] The extracts were assayed for activity against WCRW and SCRW at 4 replicates per variant each. After 5 days, rootworm toxicity scores were determined by averaging the scores from 4 replicates. Variants (436 total) were screened in this primary screen, providing a 1.5x coverage of the library.

[0125] Re-assays and scale-up. Forty-three variants scoring ≥ 3 in the primary screen were re-assayed using the same experimental conditions as in the primary screen. The scores obtained from primary screen and re-assay, including scores from repeat isolates due to oversampling, were averaged, and 20 variants were prioritized for more extensive scale-ups.

[0126] For scale-ups, 5 freshly transformed colonies were picked into 135 ml LB+Kanamycin (100 µg/ml) and grown in 1 liter shaker flasks at 37°C and 250 rpm until an OD600 nm of 0.3-0.4 was reached. IPTG was added to a final concentration of 0.5 mM and the cultures were incubated for an additional 18 hours at 20°C. The OD600 nm was determined and the cells were collected by centrifugation (10 minutes at 5000 rpm, 4 degrees C). The cell pellets were resuspended in 50 mM Sodium carbonate pH10.5, 1 mM DTT at a density of 10 OD600/ml. The cells were disrupted by bead beating and soluble extracts were obtained after centrifugation at 4000 rpm for 15 minutes at 4° C. AXMI-R1 variants in those extracts were quantitated on SDS-PAGE stained with Coomassie by comparing serial dilutions of extract to a BSA standard of known concentration. The concentrations of the AXMI-R1 variants studied were close, ranging from 0.13-0.22 µg/ul.

[0127] For assaying, serial dilutions of extracts containing AXMI-R1 variant were prepared in a control extract from BL21*DE3 transformed with pRSF1b. The dilutions range from 40 to 1.25 µl of extract containing AXMI-R1 variants. Thus, the concentration of AXMI-R1 variants was titrated, while the amount of BL21#DE3 proteins was held constant. Forty replicates per variant and dilution were assayed on WCRW. The average score for each dilution was determined, as well as the EC50.

[0128] The AXMI-R1 variants were ranked according to the average bioassay score (n=40) at 40 µl of extract (Table 2). For comparison, 6 biological replicates of AXMI-R1 wild-type (wt) were prepared, and the data and standard deviations are provided.

[0129] Variants D4F11, H9, G5, H4, D5D8, and D4A2 showed a significantly improved activity against WCRW. The nucleotide sequence encoding D5D8 is set forth in SEQ ID NO:5, and the amino acid sequence is set forth in SEQ ID NO:6.

Table 2. Variants with Improved Activity on WCRW.

Amino acid Position relative to SEQ ID NO:2	Variant Protein ID	Amino Acid Change
154	D4F11	P154A
160	H9	P160I
160	G5	P160A
160	H4	P160F
316	D5D8	G316T
316	D4A2	G316Q

[0130] Thus, while not bound by any particular theory or mechanism, improved WCRW activity may be linked to mutations in three positions of AXMI-R1 (Table 2). Positions 154 and 160 of AXMI-R1 are in the proposed processing and pore formation region, while position 316 is in the proposed receptor binding region (Li et al, 1991, Nature 353:815-821).

Example 4. Combination variants:

[0131] Variants were generated that combine favorable mutations at position 316 with favorable mutations at positions 154 and 160 to identify combinations of mutations providing cumulative improvements of processing and receptor rec-

EP 2 728 007 B1

ognition. Table 3 lists the results of such testing; the bioassay data indicate that the combination mutants P160I; G316T (H9 + D5D8) and P160F; G316T (H4 + D5D8) provide cumulative improvements in activity. The nucleotide sequence encoding H9 + D5D8 is set forth in SEQ ID NO:7, and the amino acid sequence is set forth in SEQ ID NO:8. The amino acid sequence for H4+D5D8 is set forth in SEQ ID NO:26.

Table 3a. Activity of Combined Variants on SCRW

	Score							
	0	1	2	3	4	5	AVG	Std Dev
AXMI-R1	2	12	6	0	0	0	1.2	0.62
H4	0	0	12	8	0	0	2.4	0.5
H9	0	0	16	4	0	0	2.2	0.41
G5	0	0	13	7	0	0	2.35	0.49
D4F11	0	0	18	2	0	0	2.1	0.31
D5D8	0	0	13	7	0	0	2.35	0.49
D4A2	0	0	16	4	0	0	2.2	0.41
H9+D5D8	0	0	2	15	3	0	3.05	0.51
H4+D5D8	0	0	3	17	0	0	2.85	0.37
G5+D5D8	0	0	14	6	0	0	2.3	0.47
D4F1 + D5D8	0	0	18	2	0	0	2.1	0.31
H9+ D4A2	0	1	10	9	0	0	2.4	0.6
H4+ D4A2	0	0	17	3	0	0	2.15	0.37
G5+ D4A2	0	0	8	12	0	0	2.6	0.5
D4F11 + D4A2	0	0	18	2	0	0	2.1	0.31
Vector	20	0	0	0	0	0	0	0

Table 3b. Activity of Combined Variants on WCRW

	Score							
	0	1	2	3	4	5	AVG	Std Dev
AXMI-R1	0	3	37	0	0	0	1.93	0.27
H4	0	0	33	7	0	0	2.18	0.38
H9	0	0	40	0	0	0	2.00	0.00
G5	0	0	35	5	0	0	2.13	0.33
D4F11	0	0	40	0	0	0	2.00	0.00
D5D8	0	0	40	0	0	0	2.00	0.00
D4A2	0	0	40	0	0	0	2.00	0.00
H9+D5D8	0	0	40	0	0	0	2.00	0.00
H4+D5D8	0	0	39	1	0	0	2.03	0.16
G5+D5D8	0	0	40	0	0	0	2.00	0.00
D4F1 + D5D8	0	0	34	0	0	0	1.85	0.36
H9+ D4A2	0	0	40	0	0	0	2.00	0.00
H4+ D4A2	0	32	7	0	0	0	1.18	0.39

EP 2 728 007 B1

(continued)

	Score							
	0	1	2	3	4	5	AVG	Std Dev
G5+ D4A2	0	16	24	0	0	0	1.60	0.50
D4F11 + D4A2	0	18	21	0	0	0	1.54	0.51
Vector	20	0	0	0	0	0	0.0	0.00

Example 5. Point mutant library 2: residues flanking position 316

[0132] Given the improved pesticidal activity generated in PM Library 1 (PM1) from mutations in residue 316, a second point mutation library (PM library 2, PM2) was generated for positions 313, 314, 315, 317, and 318 relative to SEQ ID NO:2. This library has a calculated diversity of 61 variants. Ninety two (92) variants were assayed, and five variants (R315F, R315M, R315W, Y317E, Y317N) flanking position 316 showed some improvement in the primary screen. Variants R315M and R315W were scaled up and assayed at protein concentrations in the range of 125-250 µg/ml. The data indicates that alterations of position 315 can generate improved activity against CRW.

Table 4a. Activity of Variants on WCRW

Frequency of Score (0-5)				
WCRW				
Score	pAX5510 (AXMI-R1)	L3F1 (R315M)	L3G2 (R315W)	pRSF1b (control)
0	0	0	0	20
1	0	0	0	0
2	32	30	31	0
3	8	9	9	0
4	0	0	0	0
5	0	0	0	0
AVG	2.20	2.23	2.23	0
Std Dev	0.41	0.43	0.42	0

Table 4b. Activity of Variants on SCRW

Frequency of Score (0-5)				
WCRW				
Score	pAX5510 (AXMI-R1)	L3F1 (R315M)	L3G2 (R315W)	pRSF1b (control)
0	0	0	0	17
1	0	0	0	0
2	14	2	0	3
3	6	15	16	0
4	0	3	4	0
5	0	0	0	0
AVG	2.30	3.05	3.20	0.30

Example 6. Permutational Library 1.

[0133] A permutational mutagenesis library was generated targeting positions 154, 155, 158 and 160. This library (Library P1; P1) was generated using oligo-directed mutagenesis methods as known in the art, resulting in a library with a theoretical complexity of 768 variants. The diversity incorporated in the library is as follows:

Table 5. Positions altered in Library 2.

Position relative to SEQ ID NO:2	Amino Acids Observed in Variants	Amino Acid Changes in Library (PI)
154	P,A,E	P,A,E,D,H,Q
155	V,E,K	V,E,K,M
158	R,V	R,V,G,L
160	P,A,F,I	P,A,F,I,L,S,T,V

[0134] Five hundred seventy three (573) clones were analyzed in a 24 well format (4 reps each), and 155 clones were identified for further testing. Seventy-three clones were retested, and ultimately eight clones were tested after scale up (as described herein).

Example 7. Mortality of variants on WCRW and SCRW

[0135] Several variants from P1 showing desired activity were selected for scale up experiments as described herein. The resulting protein was tested at protein concentrations in the range of 125-250 µg/ml. Several variants showed the ability to kill WCRW and SCRW in these assays, whereas control protein AXMI-R1 wt showed no mortality on either WCRW or SCRW in these assays.

[0136] In a first set of experiments, CRW eggs were deposited into wells, samples were added, and, after 5 days, damage to CRW and % CRW mortality (if applicable) were scored (Table 6). The average scores and average mortality were based on 40 replicates for WCRW and 20 replicates for SCRW. The data showed that variants PermutP3c6 and PermutP3c7 give 8-9% mortality against WCRW and 60-80% mortality against SCRW, while the AXMI-R1wt showed no mortality (Table 7). The nucleotide sequence encoding the 3c7 variant is set forth in SEQ ID NO:12, and the amino acid sequence is set forth in SEQ ID NO:13.

[0137] Analysis of the proteins by SDS-PAGE shows that the expression levels of AXMI-R1wt, 3c6, and 3c7 are indistinguishable and likely identical.

Table 6. Activity of Variants on Corn Rootworm

	Score: Western Corn Rootworm		Score: Southern Corn Rootworm	
	Avg score (n=40)	SD	Avg score (n=20)	SD
Vector Control	0.00	0.00	0.25	0.44
AXMI-R1	2.50	0.51	2.65	0.49
3c6	3.03	0.62	4.70	0.57
3c7	3.03	0.62	4.10	0.85

Table 7. Mortality of Variants on Corn Rootworm

	Mortality: Western Corn Rootworm		Mortality: Southern Corn Rootworm	
	Percent Mortality (n=40)	SD	Percent Mortality (n=20)	SD
Vector Control	0.00	0.00	0.00	0.00
AXMI-R1	0.00	0.00	0.00	0.00
3c6	8.75	18.72	86.50	29.07
3c7	7.75	17.02	59.00	38.78

[0138] In a subsequent experiment, CRW eggs were deposited into wells, sample was added, and after 1 day unhatched eggs were removed. This method gives a more synchronized population of early hatching CRW larvae that encounter the sample within 1-2 days of sample application. Under these conditions, variant 3c7 achieved 44% mortality against WCRW and 86% mortality against SCRW (Table 8).

Table 8. Mortality of Variant PermutP3c7 in modified Corn Rootworm assay

	Mortality: Western Corn Rootworm		Mortality: Southern Corn Rootworm	
	Percent Mortality (n=40)	SD	Percent Mortality (n=20)	SD
Vector Control	0.00	0.00	0.00	0.00
3c7	44.00	26.44	86.50	13.09

[0139] A third variant, 3a11 (V155K; R158G; P160T), also induced mortality against WCRW compared to the AXMI-R1 controls. In this experiment, CRW eggs were deposited into wells, sample was added, and after 1 day unhatched eggs were removed. Mortality of 36% was observed in rootworms exposed to 3a11 in this assay (Table 9).

Table 9. Activity of Variants 3a11 on Corn Rootworm

	Western Corn Rootworm	
	Avg score (n=40)	SD
Vector Control	0.05	0.22
AXMI-R1	2.45	0.71
3a11	3.8	0.69

Table 10. Summary of Amino Acid changes of certain variants

Protein ID	Amino Acid Changes relative to SEQ ID NO:2
3c7	P154A; V155K; P160V
3c6	P154Q; V155E; P160L
3a11	V155K; R158G; P160T

Example 8. Combinatorial Variants.

[0140] A variant that combined 3c7 (P154A, V155K, P160V) and the variant D5D8 (G316T) from Library PM1 was generated and tested for CRW activity, and showed mortality against WCRW and SCRW at protein concentrations in the range of 125-250 μ g/ml. The nucleotide sequence encoding the 3c7 + D5D8 variant is set forth in SEQ ID NO:9, and the amino acid sequence is set forth in SEQ ID NO:10.

Example 9. Library PM2

[0141] A second generation point mutation library (PM2) was generated to combine alterations in positions 482 and 483 with alterations in positions 315 and 316. This library contains 756 variants. More than 1,100 clones were picked and tested for activity. Variants '1g8' (G316E, Q482L, G483K) and '2b11' (G316A, Q482L, G483K) were found to show improved activity on a rootworm pest compared to AXMI-R1. Variant 1g8 showed in most cases superior activity compared to 3c7. The nucleotide sequence encoding the 1g8 variant is set forth in SEQ ID NO:14, and the amino acid sequence is set forth in SEQ ID NO:15.

Table 11. Percentage of wells with 50% or greater mortality

	WCRW	SCRW
AXMI-R1 (pAX5510)	0	0
3c7	56	13

EP 2 728 007 B1

(continued)

	WCRW	SCRW
1g8	100	50
Vector Control	6	0

Example 10. Library P3

[0142] A library (Library P3) of variants in the positions corresponding to positions 481 through 486 of AXMI-R1 (designated herein as 'Loop 3') was generated. Individual clones were tested to assess the contribution of each residue to pesticidal activity. Residues 482 and 483 were found to contribute to activity, since variants in these residues demonstrated improved activity on corn rootworm (Table 12).

Table 12. Improved Variants from Residues 482 and 483

AA change relative to SEQ ID NO:2		WCRW (score)	SCRW (score)
None	Test 1	1	0
	Test 2	2	0
	Test 3	2	2
Q482I	Test 1	4	2
	Test 2	3	2
G483K	Test 1	4	3
	Test 2	4	4
G483S	Test 1	3	1
	Test 2	4	3
G438Q	Test 1	2	3
	Test 2	4	3

Example 11 Combination variants

[0143] Clones were generated that combined the alterations observed in variants 1g8 and 2b11 with that in 3c7. The resulting clones AXMI-R1 (3c7+1g8) and AXMI-R1 (3c7+2b11) were tested and found to retain activity on corn rootworm. Notably, AXMI-R1 (3c7+1g8) appeared to exhibit higher mortality on corn rootworm than 3c7 alone. AXMI-R1 (3c7+2b11) also appeared in some tests to exhibit activity greater than 3c7 alone.

Example 12. Generation of AXMI-R1(EVO23)

[0144] A second generation permutational library for the processing region was cloned into AXMI-R1(1g8) (SEQ ID NO:15), thus allowing a diversity screen in the processing region in the context of variant AXMI-R1(1g8), which contains mutations in the receptor binding region. The diversity of that library is 573. Variants (n=813) were screened, 163 clones were re-assayed, and 40 variants were scaled up. AXMI-R1(EVO23) (SEQ ID NO:17) had the highest activity from that library. The nucleotide sequence encoding AXMI-R1(EVO23) is set forth in SEQ ID NO:16. The activity of EVO23 on WCRW is shown in Table 13.

Table 13. Activity of EVO23 on Western Corn Rootworm

	WCRW avg mortality (%)	std dev
AXMI-R1	1.67	3.79
Evo23	23.44	6.15
pRSF1b	0.20	0.78

Example 13. Generation of domain II/III interface variants

[0145] Modeling of axmi-R1 has identified 3 regions contributing to the interface between domain 2 and domain 3. These regions correspond to positions 331-335, positions 368-373, and positions 518-524 of SEQ ID NO:2. Variant libraries targeting these regions were generated. The diversity of the library corresponding to positions 518-524 was eight (Table 14). Twelve variants were screened, and L61E11 was re-assayed and scaled up.

Table 14. Domain II/III interface variant library

position	518	519	520	521	522	523	524
wt	Y	K	L	Q	S	G	A
diversity		S		K			
codons	tat	aag	tta	caa	tct	ggg	gct
		agt		aaa			
permut dna	tat	ark	tta	maa	tct	ggg	gct
permut prot	Y	KSRN	L	QK	S	G	A

[0146] The activity of the L61E11 variant against WCRW is show in Table 15.

Table 15. Activity of L61E11 on Western Corn Rootworm

	WCRW avg mortality (%)	Stdv
AXMI-R1	13	14.2
L61e11	18	14.5
pRSF1b	0	0

[0147] The present invention demonstrates that alteration of the residues described herein result in variants with improved activity on pests. A summary of the residues that were altered in the present invention is provided in Table 16.

Table 16. Summary of Positions Altered in Improved Variants

SEQ ID NO:	Identifier	Summary of mutations	154	155	158	160	315	316	482	483	519
2	wt	wt	P	V	R	P	R	G	Q	G	K
21	D4F11	P154A	A								
22	H9	P160I				I					
23	G5	P160A				A					
24	H4	P160F				F					
6	D5D8	G316T						T			
25	D4A2	G316Q						Q			
8	H9+D5D8	P160I; G316T				I		T			
26	H4+D5D8	P160F; G316T				F		T			
27	H9+D4A2	P160I; G316Q				I		Q			

(continued)

SEQ ID NO:	Identifier	Summary of mutations	154	155	158	160	315	316	482	483	519
28	G5+D4A2	P160A; G316Q				A		Q			
29	R315M	R315M					M				
30	R315W	R315W					W				
31	3c6	P154Q; V155E; P160L	Q	E		L					
13	3c7	P154A; V155K; P160V	A	K		V					
32	3a11	V155K; R158G; P160T		K	G		T				
15	1g8	G316E; Q482L; G483K						E	L	K	
33	2b11	G316A; Q482L; G483K						A	L	K	
34	Q482I	Q482I							I		
35	G483K	G483K								K	
36	G483S	G483S								S	
37	G483Q	G483Q								Q	
38	3c7+1g8	P154A; V155K; P160V; G316E; Q482L; G483K	A	K	V			E	L	K	
39	3c7+2b11	P154A; V155K; P160V; G316A; Q482L; G483K	A	K	V			A	L	K	
17	Evo23	P154H; P160L; G316E; Q482L; G483K	H			L		E	L	K	
19	L61E11	K519N									N
10	3c7+D5D8 (Evo20)	P154A; V155K; P160V; G316T	A	K		V		T			
40	G5+D5D8	P160A; G316T				A		T			
41	D4F11+D5D8	P154A; G316T	A					T			
42	H4+D4A2	P160F; G316Q				F		Q			
43	D4F11+D4A2	P154A; G316Q	A					Q			

Example 14. Use of evolved AXMI-R1 sequences in other Cry proteins:

[0148] AXMI-R1 sequence segments containing favorable mutations could be inserted into other, homologous Cry proteins to improve processing, receptor binding and activity. For example, a sequence segment from an evolved AXMI-R1 variant covering the processing region could be used to replace the homologous region in axmi008, axmi028, and other Cry proteins. Since the 3D folding of Cry proteins is conserved, improved processing and potency of the hybrid protein may be achieved. Further mutagenesis of these AXMI-R1 variant sequences may help to adapt and improve the AXMI-R1 variant sequences in the context of the host proteins.

Example 15. Additional assays for Pesticidal Activity

[0149] The nucleotide sequences of the invention can be tested for their ability to produce pesticidal proteins. The ability of a pesticidal protein to act as a pesticide upon a pest is often assessed in a number of ways. One way well known in the art is to perform a feeding assay. In such a feeding assay, one exposes the pest to a sample containing either compounds to be tested or control samples. Often this is performed by placing the material to be tested, or a suitable dilution of such material, onto a material that the pest will ingest, such as an artificial diet. The material to be tested may be composed of a liquid, solid, or slurry. The material to be tested may be placed upon the surface and then allowed to dry. Alternatively, the material to be tested may be mixed with a molten artificial diet, then dispensed into the assay chamber. The assay chamber may be, for example, a cup, a dish, or a well of a microtiter plate.

[0150] Assays for sucking pests (for example aphids) may involve separating the test material from the insect by a partition, ideally a portion that can be pierced by the sucking mouth parts of the sucking insect, to allow ingestion of the test material. Often the test material is mixed with a feeding stimulant, such as sucrose, to promote ingestion of the test compound.

[0151] Other types of assays can include microinjection of the test material into the mouth, or gut of the pest, as well as development of transgenic plants, followed by test of the ability of the pest to feed upon the transgenic plant. Plant testing may involve isolation of the plant parts normally consumed, for example, small cages attached to a leaf, or isolation of entire plants in cages containing insects.

[0152] Other methods and approaches to assay pests are known in the art, and can be found, for example in Robertson and Preisler, eds. (1992) *Pesticide bioassays with arthropods*, CRC, Boca Raton, FL. Alternatively, assays are commonly described in the journals *Arthropod Management Tests* and *Journal of Economic Entomology* or by discussion with members of the Entomological Society of America (ESA).

Example 16. Vectoring of Genes for Plant Expression

[0153] The coding regions of the invention are connected with appropriate promoter and terminator sequences for expression in plants. Such sequences are well known in the art and may include the rice actin promoter or maize ubiquitin promoter for expression in monocots, the *Arabidopsis* UBQ3 promoter or CaMV 35S promoter for expression in dicots, and the nos or PinII terminators. Techniques for producing and confirming promoter - gene - terminator constructs also are well known in the art.

[0154] In one aspect of the invention, synthetic DNA sequences are designed and generated. These synthetic sequences have altered nucleotide sequence relative to the parent sequence, but encode proteins that are essentially identical to the parent sequence.

[0155] In another aspect of the invention, modified versions of the synthetic genes are designed such that the resulting peptide is targeted to a plant organelle, such as the endoplasmic reticulum or the apoplast. Peptide sequences known to result in targeting of fusion proteins to plant organelles are known in the art. For example, the N-terminal region of the acid phosphatase gene from the White Lupin *Lupinus albus* (GENBANK® ID GI:14276838, Miller et al. (2001) *Plant Physiology* 127: 594-606) is known in the art to result in endoplasmic reticulum targeting of heterologous proteins. If the resulting fusion protein also contains an endoplasmic reticulum retention sequence comprising the peptide N-terminus-lysine-aspartic acid-glutamic acid-leucine (i.e., the "KDEL" motif, SEQ ID NO:11) at the C-terminus, the fusion protein will be targeted to the endoplasmic reticulum. If the fusion protein lacks an endoplasmic reticulum targeting sequence at the C-terminus, the protein will be targeted to the endoplasmic reticulum, but will ultimately be sequestered in the apoplast.

[0156] Thus, this gene encodes a fusion protein that contains the N-terminal thirty-one amino acids of the acid phosphatase gene from the White Lupin *Lupinus albus* (GENBANK® ID GI:14276838, Miller et al., 2001, *supra*) fused to the N-terminus of the amino acid sequence of the invention, as well as the KDEL sequence at the C-terminus. Thus, the resulting protein is predicted to be targeted the plant endoplasmic reticulum upon expression in a plant cell.

[0157] The plant expression cassettes described above are combined with an appropriate plant selectable marker to aid in the selection of transformed cells and tissues, and ligated into plant transformation vectors. These may include binary vectors from *Agrobacterium*-mediated transformation or simple plasmid vectors for aerosol or biolistic transformation.

Example 17. Transformation of Maize Cells with the pesticidal protein genes described herein

[0158] Maize ears are best collected 8-12 days after pollination. Embryos are isolated from the ears, and those embryos 0.8-1.5 mm in size are preferred for use in transformation. Embryos are plated scutellum side-up on a suitable incubation media, such as DN62ASS media (3.98 g/L N6 Salts; 1 mL/L (of 1000x Stock) N6 Vitamins; 800 mg/L L-Asparagine; 100 mg/L Myo-inositol; 1.4 g/L L-Proline; 100 mg/L Casamino acids; 50 g/L sucrose; 1 mL/L (of 1 mg/mL Stock) 2,4-D).

However, media and salts other than DN62A5S are suitable and are known in the art. Embryos are incubated overnight at 25°C in the dark. However, it is not necessary *per se* to incubate the embryos overnight.

[0159] The resulting explants are transferred to mesh squares (30-40 per plate), transferred onto osmotic media for about 30-45 minutes, then transferred to a beaming plate (see, for example, PCT Publication No. WO/0138514 and U.S. Patent No. 5,240,842).

[0160] DNA constructs designed to the genes of the invention in plant cells are accelerated into plant tissue using an aerosol beam accelerator, using conditions essentially as described in PCT Publication No. WO/0138514. After beaming, embryos are incubated for about 30 min on osmotic media, and placed onto incubation media overnight at 25°C in the dark. To avoid unduly damaging beamed explants, they are incubated for at least 24 hours prior to transfer to recovery media. Embryos are then spread onto recovery period media, for about 5 days, 25°C in the dark, then transferred to a selection media. Explants are incubated in selection media for up to eight weeks, depending on the nature and characteristics of the particular selection utilized. After the selection period, the resulting callus is transferred to embryo maturation media, until the formation of mature somatic embryos is observed. The resulting mature somatic embryos are then placed under low light, and the process of regeneration is initiated by methods known in the art. The resulting shoots are allowed to root on rooting media, and the resulting plants are transferred to nursery pots and propagated as transgenic plants.

Materials

DN62A5S Media

[0161]

Components	Per Liter	Source
Chu's N6 Basal Salt Mixture (Prod. No. C 416)	3.98 g/L	Phytotechnology Labs
Chu's N6 Vitamin Solution (Prod. No. C 149)	1 mL/L (of 1000x Stock)	Phytotechnology Labs
L-Asparagine	800 mg/L	Phytotechnology Labs
Myo-inositol	100 mg/L	Sigma
L-Proline	1.4 g/L	Phytotechnology Labs
Casamino acids	100 mg/L	Fisher Scientific
Sucrose	50 g/L	Phytotechnology Labs
2,4-D (Prod. No. D-7299)	1 mL/L (of 1 mg/mL Stock)	Sigma

[0162] The pH of the solution is adjusted to pH 5.8 with 1N KOH/1N KCl, Gelrite (Sigma) is added at a concentration up to 3g/L, and the media is autoclaved. After cooling to 50°C, 2 mL/L of a 5 mg/ml stock solution of silver nitrate (Phytotechnology Labs) is added.

Example 18. Transformation of genes of the invention in Plant Cells by *Agrobacterium*-Mediated Transformation

[0163] Ears are best collected 8-12 days after pollination. Embryos are isolated from the ears, and those embryos 0.8-1.5 mm in size are preferred for use in transformation. Embryos are plated scutellum side-up on a suitable incubation media, and incubated overnight at 25°C in the dark. However, it is not necessary *per se* to incubate the embryos overnight. Embryos are contacted with an *Agrobacterium* strain containing the appropriate vectors for Ti plasmid mediated transfer for about 5-10 min, and then plated onto co-cultivation media for about 3 days (25°C in the dark). After co-cultivation, explants are transferred to recovery period media for about five days (at 25°C in the dark). Explants are incubated in selection media for up to eight weeks, depending on the nature and characteristics of the particular selection utilized. After the selection period, the resulting callus is transferred to embryo maturation media, until the formation of mature somatic embryos is observed. The resulting mature somatic embryos are then placed under low light, and the process of regeneration is initiated as known in the art.

[0164] All publications and patent applications mentioned in the specification are indicative of the level of skill of those skilled in the art to which this invention pertains.

[0165] Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, it will be obvious that certain changes and modifications may be practiced within

the scope of the appended claims.

SEQUENCE LISTING

5 **[0166]**

 <110> Volker Heinrichs

10 <120> Variant Axmi-R1 Delta-Endotoxin Genes
 and Methods for Their Use

 <130> 45600/384850

15 <150> 61/229,567
 <151> 2009-07-29

 <150> 61/150,309
 <151> 2009-02-05

20 <160> 64

 <170> FastSEQ for Windows Version 4.0

25 <210> 1
 <211> 1935
 <212> DNA
 <213> Bacillus thuringiensis

30 <400> 1

35

40

45

50

55

atgaatccga acaatcgaag tgaacatgat acaataaaaa ctactgaaaa taatgaggtg 60
 ccaactaacc atgttcaata tccttttagcg gaaactccaa atccaacact agaagattta 120
 aattataaag agtttttaag aatgactgca gataataata cggaagcact agatagctct 180
 acaacaaaag atgtcattca aaaaggcatt tccgtagtag gtgatctcct aggcgtagta 240
 ggtttcccggt ttggtggagc gcttgtttcg ttttatacaa acttttttaa tactatttgg 300
 ccaagtgaag acccggtgga ggcttttatg gaacaagtag aagcattgat ggatcagaaa 360
 atagctgatt atgcaaaaaa taaagctctt gcagagttac agggccttca aaataatgtc 420
 gaagattatg tgagtgcatt gagttcatgg caaaaaaatc ctgtgagttc acgaaatcca 480
 catagccagg ggcgataag agagctgttt tctcaagcag aaagtcattt tcgtaattca 540
 atgccttcgt ttgcaatttc tggatacgag gttctatttc taacaacata tgcacaagct 600
 gccaacacac atttattttt actaaaagac gctcaaattt atggagaaga atggggatac 660
 gaaaaagaag atattgctga attttataaa agacaactaa aacttacgca agaataact 720
 gccattgtg tcaaatggta taatgttgga ttagataaat taagaggttc atcttatgaa 780
 tcttgggtaa actttaaccg ttatcgcgaga gagatgacat taacagtatt agatttaatt 840
 gcactatttc cattgtatga tgttcggcta taccctaaaag aagttaaaac cgaattaaca 900
 agagacgttt taacagatcc aattgtcggg gtcaacaacc ttaggggcta tggaacaacc 960
 ttctctaata tagaaaatta tattcgaaaa ccacatctat ttgactatct gcatagaatt 1020
 caatttcaca cgcggttcca accaggatat tatggaaatg actctttcaa ttattgggtcc 1080
 ggtaattatg tttcaactag accaagcata ggatcaaatg atataatcac atctccattc 1140
 tatggaaata aatccagtga acctgtacaa aatttagaat ttaatggaga aaaagtctat 1200
 agagccgtag caaatacaaa tcttgccgtc tggccgtccg ctgtatattc aggtgttaca 1260
 aaagtggaat ttagccaata taatgatcaa acagatgaag caagtacaca aacgtacgac 1320
 tcaaaaagaa atgttggcgc ggtcagctgg gattctatcg atcaattgcc tccagaaaca 1380
 acagatgaac ctctagaaaa gggatatagc catcaactca attatgtaat gtgcttttta 1440
 atgcagggtg gtagaggaac aatcccagtg ttaacttggg cacataaaaag tgtagacttt 1500
 tttaacatga ttgattcgaa aaaaattaca caacttccgt tagtaaaggc atataagtta 1560
 caatctggtg cttccgttgt cgcaggtcct aggtttacag gaggagatat cattcaatgc 1620
 acagaaaatg gaagtgcggc aactatttac gttacaccgg atgtgtcgta ctctcaaaa 1680
 tatcgagcta gaattcatta tgcttctaca tctcagataa catttacact cagtttagac 1740
 ggggcaccat ttaatcaata ctatttcgat aaaacgataa ataaaggaga cacattaacg 1800
 tataattcat ttaatttagc aagtttcagc acaccattcg aattatcagg gaataactta 1860
 caaataggcg tcacaggatt aagtgtcgga gataaagttt atatagacaa aattgaattt 1920
 attccagtga attag 1935

<210> 2

<211> 644

<212> PRT

<213> *Bacillus thuringiensis*

<400> 2

EP 2 728 007 B1

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

EP 2 728 007 B1

				500					505				510			
	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515					520					525			
5	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
		530					535					540				
	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
	545					550					555					560
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
				565						570					575	
10	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
			580						585					590		
	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
		595					600						605			
	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
	610					615						620				
15	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625					630					635					640
	Ile	Pro	Val	Asn												

20 <210> 3
 <211> 1965
 <212> DNA
 <213> Artificial Sequence

 25 <220>
 <223> axmi-R1 with histidine tag

 <400> 3

30

35

40

45

50

55

atggcacatc accaccacca tcacggatcc atgaatccga acaatcgaag tgaacatgat 60
 acaataaaaa ctactgaaaa taatgagggtg ccaactaacc atgttcaata tccttttagcg 120
 gaaactccaa atccaacact agaagattta aattataaag agtttttaag aatgactgca 180
 gataataata cggaagcact agatagctct acaacaaaag atgtcattca aaaaggcatt 240
 tccgtagtag gtgatctcct aggcgtagta ggtttcccg tttgggtggagc gcttgtttcg 300
 ttttatacaa acttttttaa tactatttgg ccaagtgaag acccggtgaa ggcttttatg 360
 gaacaagtag aagcattgat ggatcagaaa atagctgatt atgcaaaaaa taaagctctt 420
 gcagagttac agggccttca aaataaatgtc gaagattatg tgagtgcatt gagttcatgg 480
 caaaaaaatc ctgtgagttc acgaaatcca catagccagg ggcggataag agagctgttt 540
 tctcaagcag aaagtcattt tcgtaattca atgccttcgt ttgcaatttc tggatacgag 600
 gttctatttt taacaacata tgcacaagct gccaacacac atttattttt actaaaagac 660
 gctcaaattt atggagaaga atggggatac gaaaaagaag atattgctga attttataaa 720
 agacaactaa aacttacgca agaataatct gaccattgtg tcaaattgga taatgttggg 780
 ttagataaat taagagggtt atcttatgaa tcttgggtaa actttaaccg ttatcgcgaga 840
 gagatgacat taacagtatt agattttaatt gcactatttc cattgtatga tgttcggcta 900
 tacccaaaaag aagttaaaac cgaattaaca agagacgttt taacagatcc aattgtcggg 960
 gtcaacaacc ttaggggcta tggaacaacc ttctctaata tagaaaatta tattcgaaaa 1020
 ccacatctat ttgactatct gcatagaatt caatttcaca cgcggttcca accaggatat 1080
 tatggaaatg actctttcaa ttattggtcc ggtaattatg tttcaactag accaagcata 1140
 ggatcaaatg atataatcac atctccattc tatggaaata aatccagtga acctgtacaa 1200
 aatttagaat ttaatggaga aaaagtctat agagccgtag caaatacaaa tcttgcggtc 1260
 tggccgtccg ctgtatatct aggtgttaca aaagtggaat ttagccaata taatgatcaa 1320
 acagatgaag caagtacaca aacgtacgac tcaaaaagaa atgttggcgc ggtcagctgg 1380
 gattctatcg atcaattgcc tccagaaaca acagatgaac ctctagaaaa gggatatagc 1440
 catcaactca attatgtaat gtgcttttta atgcagggtg gtagaggaaac aatccagtg 1500
 ttaacttgga cacataaaaag tgtagacttt tttaacatga ttgattcgaa aaaaattaca 1560
 caacttccgt tagtaaaggc atataagtta caatctggtg cttccgttgt cgcaggtcct 1620
 aggtttacag gaggagatat cattcaatgc acagaaaatg gaagtgcggc aactatttac 1680
 gttacaccgg atgtgtcgta ctctcaaaaa tatcgagcta gaattcatta tgcttctaca 1740
 tctcagataa catttacact cagtttagac ggggcacat ttaatcaata ctatttcgat 1800
 aaaacgataa ataaaggaga cacattaacg tataattcat ttaatttagc aagtttcagc 1860
 acaccattcg aattatcagg gaataactta caaataggcg tcacaggatt aagtgtcgga 1920
 gataaagttt atatagacaa aattgaattt attccagtga attag 1965

<210> 4

<211> 654

<212> PRT

<213> Artificial Sequence

<220>

<223> Axmi-R1 with histidine tag

<400> 4

EP 2 728 007 B1

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

EP 2 728 007 B1

		450				455				460						
	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro	Leu	Glu	Lys	Gly	Tyr	Ser
	465					470					475					480
5	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu	Met	Gln	Gly	Ser	Arg	Gly
				485						490					495	
	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys	Ser	Val	Asp	Phe	Phe	Asn
				500					505					510		
	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu	Pro	Leu	Val	Lys	Ala	Tyr
			515					520					525			
10	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala	Gly	Pro	Arg	Phe	Thr	Gly
		530					535					540				
	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly	Ser	Ala	Ala	Thr	Ile	Tyr
	545				550					555						560
	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys	Tyr	Arg	Ala	Arg	Ile	His
15				565					570						575	
	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr	Leu	Ser	Leu	Asp	Gly	Ala
				580					585					590		
	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr	Ile	Asn	Lys	Gly	Asp	Thr
			595				600					605				
20	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser	Phe	Ser	Thr	Pro	Phe	Glu
		610					615					620				
	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val	Thr	Gly	Leu	Ser	Ala	Gly
	625				630					635						640
	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe	Ile	Pro	Val	Asn		
				645					650							

<210> 5

<211> 1935

<212> DNA

<213> Artificial Sequence

<220>

<223> synthetic nucleotide sequence encoding AXMI-R1(evo18)

<400> 5

	atgaacccca	acaacaggag	cgagcatgac	accatcaaga	caacagagaa	caatgaagtt	60
	ccaacaaacc	atgttcaata	tcctcttgct	gaaacaccaa	atccaacctt	ggaggacctc	120
	aactacaagg	agttcttgag	gatgacagct	gacaacaaca	cagaagctct	ggattcaagc	180
5	accaccaagg	atgtcatcca	gaagggcatc	tctgttggtg	gagatctgct	gggctgggtg	240
	ggcttcccct	tcggcggcgc	gctggtgagc	ttctacacca	acttcctcaa	caccatctgg	300
	ccatcagaag	atccatggaa	ggccttcatg	gagcaagtgg	aggcgctgat	ggaccagaag	360
	attgctgatt	atgccaagaa	caaggcgctg	gcggagctgc	aaggcctcca	gaacaatgtg	420
	gaggattatg	tttctgctct	gagcagctgg	cagaagaacc	ctgtttcttc	aagaaatcct	480
	cacagccaag	gaaggatcag	ggagctcttc	tcccaagcag	aaagccactt	cagaaacagc	540
10	atgccctcct	tcgccatctc	aggatatgag	gtgctcttcc	tcaccacata	tgctcaagct	600
	gccaacaccc	acctcttcct	gctgaaggat	gctcaaattt	atggagaaga	atggggatat	660
	gagaaggagg	acattgctga	gttctacaag	aggcagctaa	agctcaccca	ggagtacaca	720
	gatcactgcg	tcaaattgta	caatgttggg	ctggacaagc	tccgcggcag	cagctatgaa	780
	agctgggtga	acttcaacag	atacaggagg	gagatgacct	tcaccgtgct	ggacctcatt	840
15	gctctcttcc	ctctctatga	tgtccgcctc	tacccaagg	aggtgaaaac	agagctaaca	900
	agagatgtgc	tgacagatcc	catcgtcggc	gtcaacaact	tgaggacata	tggcaccacc	960
	ttcagcaaca	tcgagaacta	catcaggaag	cctcatctct	tcgactacct	ccacaggatt	1020
	cagttccaca	caaggttcca	gcctggatat	tatggaaatg	acagcttcaa	ctactggagc	1080
	ggcaactatg	tttcaacaag	gccaagcatt	ggaagcaatg	acatcataac	ttctcccttc	1140
20	tatggcaaca	agagcagcga	gcctgttcag	aacctggagt	tcaatggaga	gaaggtgtac	1200
	cgcgcgctcg	ccaacaccaa	cctcgccgtc	tggccatcag	ctgtctacag	cggcgtgacc	1260
	aaggtggagt	tcagccagta	caatgatcaa	acagatgaag	caagcaccca	aacatatgac	1320
	agcaagagaa	atgttggagc	tgtttcatgg	gacagcatcg	accagctgcc	gccggagaca	1380
	acagatgagc	cgctggagaa	gggctacagc	caccagctca	actatgtgat	gtgcttcttg	1440
	atgcaaggaa	gcagaggcac	catccccgtg	ctgacatgga	cccacaaatc	agtggacttc	1500
25	ttcaacatga	ttgacagcaa	gaagatcacc	cagctgccgc	tggtgaaggc	ctacaagctg	1560
	caaagcggcg	cctccgtggt	ggctgggccc	cgcttcaactg	gaggagacat	catccaatgc	1620
	acagaaaatg	gcagcgccgc	caccatctat	gtcaccctcg	atgtcagcta	cagccagaag	1680
30	tacagagcaa	ggattcatta	tgcttcaaca	agccagatca	ccttcacctt	gagcttggat	1740
	ggagctccct	tcaaccagta	ctacttcgac	aagaccatca	acaaaggaga	caccctcacc	1800
	tacaacagct	tcaacctcgc	ctccttctcc	acgccatttg	agctctcagg	aaacaacctc	1860
	cagatcggcg	tcaccggcct	ctccgccggc	gacaagggtg	acatcgacaa	gatcgagttc	1920
	atccccgtca	actaa					1935
35	<210> 6						
	<211> 644						
	<212> PRT						
	<213> Artificial Sequence						
40	<220>						
	<223> Axmi-R1 variant sequence (AXMI-R1(evo18))						
	<400> 6						

EP 2 728 007 B1

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

EP 2 728 007 B1

	Arg	Ala	Val	Ala	Asn	Thr	Asn	Leu	Ala	Val	Trp	Pro	Ser	Ala	Val	Tyr
				405						410					415	
	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp
				420					425					430		
5	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
			435					440					445			
	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
		450					455					460				
	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
10		465				470					475					480
	Met	Gln	Gly	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
				485						490					495	
	Ser	Val	Asp	Phe	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu
			500						505					510		
15	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515					520					525			
	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
		530					535					540				
	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
		545				550					555					560
20	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
				565						570					575	
	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
			580					585					590			
	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
25			595					600					605			
	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
		610					615					620				
	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
		625				630					635					640
30	Ile	Pro	Val	Asn												

<210> 7

<211> 1935

<212> DNA

<213> Artificial Sequence

<220>

<223> synthetic nucleotide sequence encoding AXMI-R1 variant sequence (AXMI-R1(evo19))

<400> 7

	atgaacccca	acaacaggag	cgagcatgac	accatcaaga	caacagagaa	caatgaagtt	60
	ccaacaaatc	atgtgcagta	cccgtctggcg	gagacaccaa	atccaacatt	ggaggacctc	120
	aactacaagg	agttcttgag	gatgacggcg	gacaacaaca	cagaagctct	ggacagcagc	180
5	accaccaagg	atgtcatcca	gaagggcatc	tcagtgggtg	gagatcttct	tggagtgggtg	240
	ggcttccctt	tcggcggcgc	gctggttagc	ttctacacca	acttcctcaa	caccatctgg	300
	ccatcagaag	atccatggaa	ggccttcatg	gagcaagtgg	aggcgctgat	ggaccagaag	360
	atcgccgact	acgccaagaa	caaggcgctg	gcggagctgc	aaggcctcca	gaacaatgtt	420
	gaagattatg	tctcggcgc	gagcagctgg	cagaagaacc	cggtgagctc	aagaaatatc	480
	cattctcaag	gaaggatcag	ggagctcttc	agccaagcag	aaagccactt	cagaaacagc	540
10	atgccgagct	tcgccatctc	aggatatgag	gtgctcttcc	tcaccaccta	tgctcaagct	600
	gccaacaccc	acctcttcct	gctgaaggat	gctcaaattt	atggagaaga	atggggctat	660
	gagaaggagg	acattgctga	gttctacaag	aggcagctaa	agctgacaca	agagtacacc	720
	gaccactgcg	tcaagtggta	caatgttggg	ctggacaagc	tccgcggcag	cagctatgaa	780
	agctgggtga	acttcaacag	atacaggagg	gagatgacgc	tcaccgtgct	ggacctcatt	840
15	gctctcttcc	cgctctatga	tgtgaggctc	taccccaagg	aggtcaagac	agagctgaca	900
	agagatgtgc	taacagatcc	catcgtcggc	gtcaacaacc	tccgcacctt	tggcaccacc	960
	ttcagcaaca	tcgagaacta	catcaggaag	ccgcacctct	tcgactacct	ccaccgcctc	1020
	cagttccaca	caaggttcca	acctggatat	tatggaaatg	acagcttcaa	ctactggagc	1080
	ggcaactatg	tttcaacaag	gccaaagcata	ggaagcaacg	acatcatcac	ctcgcccttc	1140
	tacggcaaca	agagctccga	gccggtgcaa	aatttgaggt	tcaatggaga	gaaggtgtac	1200
20	cgcgccgctc	ccaacaccaa	cctcgccgtc	tggccatcag	ctgtctacag	cggcgtgacc	1260

	aaggtggagt	tcagccagta	caatgatcaa	acagatgaag	caagcaccca	gacctacgac	1320
	agcaagagga	acgtcggcgc	cgtgtcatgg	gacagcatcg	accagctgcc	gccggagaca	1380
25	acagatgagc	cgctggagaa	gggtacagc	caccagctca	actatgtgat	gtgcttcttg	1440
	atgcaaggaa	gccgcggcac	catcccgggtg	ctgacatgga	cccacaagag	cgtggacttc	1500
	ttcaacatga	ttgattcaaa	gaagatcacc	cagctgccgc	tggtgaaggc	ctacaagctg	1560
	caaagcggcg	cctccgtggt	ggctgggcca	aggttcaccg	gcggcgacat	catccaatgc	1620
	acagaaaatg	gaagcgccgc	caccatctat	gtgacacctg	atgtgagcta	cagccagaag	1680
	tacagagcaa	ggattcatta	tgcttcaaca	agccagatca	ccttcacctt	gagcttggat	1740
30	ggagctccct	tcaaccagta	ctacttcgac	aagaccatca	acaaaggaga	caccttgacc	1800
	tacaacagct	tcaacctcgc	cagcttctca	acaccatttg	agctgagcgg	caacaacctc	1860
	cagatcggcg	tcaccggcct	ctccgccggc	gacaaggtct	acatcgacaa	gattgagttc	1920
	atcccgggtga	actaa					1935

35 <210> 8
 <211> 644
 <212> PRT
 <213> Artificial Sequence

40 <220>
 <223> AXMI-R1 variant sequence (AXMI-R1(evo19))

<400> 8

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

				340				345				350				
	Asn	Asp	Ser	Phe	Asn	Tyr	Trp	Ser	Gly	Asn	Tyr	Val	Ser	Thr	Arg	Pro
			355					360					365			
5	Ser	Ile	Gly	Ser	Asn	Asp	Ile	Ile	Thr	Ser	Pro	Phe	Tyr	Gly	Asn	Lys
			370				375						380			
	Ser	Ser	Glu	Pro	Val	Gln	Asn	Leu	Glu	Phe	Asn	Gly	Glu	Lys	Val	Tyr
	385					390					395					400
	Arg	Ala	Val	Ala	Asn	Thr	Asn	Leu	Ala	Val	Trp	Pro	Ser	Ala	Val	Tyr
					405					410						415
10	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp
				420					425					430		
	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
			435					440					445			
	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
15			450				455					460				
	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
	465					470					475					480
	Met	Gln	Gly	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
					485					490					495	
20	Ser	Val	Asp	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu	
				500				505					510			
	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515					520					525			
	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
		530					535					540				
25	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
	545					550					555					560
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
					565					570					575	
	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
				580				585					590			
30	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
			595					600					605			
	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
		610					615					620				
35	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625					630					635					640
	Ile	Pro	Val	Asn												

<210> 9

<211> 1935

40 <212> DNA

<213> Artificial Sequence

<220>

<223> synthetic nucleotide sequence encoding AXMI-R1 variant sequence (AXMI-R1(evo20))

45

<400> 9

50

55

EP 2 728 007 B1

atgaacccca acaacaggag cgagcatgac accatcaaga caacagagaa caatgaagtt 60
 ccaacaaatc atgtgcagta cccgctggcg gagacaccaa atccaacatt ggaggacctc 120
 aactacaagg agttcttgag gatgacggcg gacaacaaca cagaagctct ggacagcagc 180
 accaccaagg atgtcatcca gaagggcatc tcagtgggtg gagatcttct tggagtgggtg 240
 ggcttcccct tcggcggcgc gctggttagc ttctacacca acttcctcaa caccatctgg 300
 ccatcagaag atccatggaa ggccttcatg gagcaagtgg aggcgctgat ggaccagaag 360
 atcgccgact acgccaagaa caaggcgtg gcggagctgc aaggcctcca gaacaatgtt 420
 gaagattatg tctcggcgtc gagcagctgg cagaagaacg cgaagagctc aagaaatgtg 480
 cattctcaag gaaggatcag ggagctcttc agccaagcag aaagccactt cagaaacagc 540
 atgccgagct tcgccatctc aggatatgag gtgctcttcc tcaccaccta tgctcaagct 600
 gccaacaccc acctcttctc gctgaaggat gctcaaattt atggagaaga atggggctat 660
 gagaaggagg acattgctga gttctacaag aggcagctaa agctgacaca agagtacacc 720
 gaccactgag tcaagtggta caatgttggg ctggacaagc tccgcggcag cagctatgaa 780
 agctgggtga acttcaacag atacaggagg gagatgacgc tcaccgtgct ggacctcatt 840

gctctcttcc cgctctatga tgtgaggctc taccccaagg aggtcaagac agagctgaca 900
 agagatgtgc taacagatcc catcgctggc gtcaacaacc tccgcacctc tggcaccacc 960
 ttcagcaaca tcgagaacta catcaggaag ccgcacctct tcgactacct ccaccgcatc 1020
 cagttccaca caaggttcca acctggatat tatggaaatg acagcttcaa ctactggagc 1080
 ggcaactatg tttcaacaag gccaagcata ggaagcaacg acatcatcac ctcgcccttc 1140
 tacggcaaca agagctccga gccggtgcaa aatttggagt tcaatggaga gaaggtgtac 1200
 cgcgccgtcg ccaacaccaa cctcgccgtc tggccatcag ctgtctacag cggcgtgacc 1260
 aaggtggagt tcagccagta caatgatcaa acagatgaag caagcaccca gacctacgac 1320
 agcaagagga acgtcggcgc cgtgtcatgg gacagcatcg accagctgcc gccggagaca 1380
 acagatgagc cgctggagaa gggctacagc caccagctca actatgtgat gtgcttcttg 1440
 atgcaaggaa gccgcggcac catcccgtg ctgacatgga ccacaagag cgtggacttc 1500
 ttcaacatga ttgattcaaa gaagatcacc cagctgccgc tgggtgaaggc ctacaagctg 1560
 caaagcggcg cctccgtggt ggctgggcca aggttcaccg gcggcgacat catccaatgc 1620
 acagaaaatg gaagcgccgc caccatctat gtgacacctg atgtgagcta cagccagaag 1680
 tacagagcaa ggattcatta tgcttcaaca agccagatca cttcacctt gagcttggat 1740
 ggagctccct tcaaccagta ctacttcgac aagaccatca acaaaggaga caccttgacc 1800
 tacaacagct tcaacctcgc cagcttctca acaccatttg agctgagcgg caacaacctc 1860
 cagatcggcg tcaccggcct ctccgccggc gacaaggctc acatcgacaa gattgagttc 1920
 atcccgtgga actaa 1935

<210> 10
 <211> 644
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> AXMI-R1 variant sequence (AXMI-R1(evo20))

<400> 10

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

	Arg	Leu	Tyr	Pro	Lys	Glu	Val	Lys	Thr	Glu	Leu	Thr	Arg	Asp	Val	Leu
	290						295					300				
	Thr	Asp	Pro	Ile	Val	Gly	Val	Asn	Asn	Leu	Arg	Thr	Tyr	Gly	Thr	Thr
5	305					310					315					320
	Phe	Ser	Asn	Ile	Glu	Asn	Tyr	Ile	Arg	Lys	Pro	His	Leu	Phe	Asp	Tyr
					325					330					335	
	Leu	His	Arg	Ile	Gln	Phe	His	Thr	Arg	Phe	Gln	Pro	Gly	Tyr	Tyr	Gly
				340					345					350		
10	Asn	Asp	Ser	Phe	Asn	Tyr	Trp	Ser	Gly	Asn	Tyr	Val	Ser	Thr	Arg	Pro
		355						360					365			
	Ser	Ile	Gly	Ser	Asn	Asp	Ile	Ile	Thr	Ser	Pro	Phe	Tyr	Gly	Asn	Lys
	370						375					380				
	Ser	Ser	Glu	Pro	Val	Gln	Asn	Leu	Glu	Phe	Asn	Gly	Glu	Lys	Val	Tyr
	385					390					395					400
15	Arg	Ala	Val	Ala	Asn	Thr	Asn	Leu	Ala	Val	Trp	Pro	Ser	Ala	Val	Tyr
				405					410						415	
	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp
				420					425					430		
	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
		435						440					445			
20	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
	450						455					460				
	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
	465					470					475					480
25	Met	Gln	Gly	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
				485						490					495	
	Ser	Val	Asp	Phe	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu
			500						505					510		
	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515						520				525			
30	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
	530						535					540				
	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
	545					550				555						560
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
				565						570					575	
35	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
				580					585					590		
	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
			595					600					605			
40	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
		610					615					620				
	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625					630					635					640
	Ile	Pro	Val	Asn												

45 <210> 11
 <211> 4
 <212> PRT
 <213> Artificial Sequence

50 <220>
 <223> endoplasmic reticulum signal sequence

<400> 11

55 Lys Asp Glu Leu
 1

<210> 12

EP 2 728 007 B1

<211> 1932
 <212> DNA
 <213> Artificial Sequence

5 <220>
 <223> nucleotide sequence encoding variant of Axmi-R1 (Axmi-R1(3c7))

<400> 12

```

10      atgaatccga acaatcgaag tgaacatgat acaataaaaa ctactgaaaa taatgaggtg 60
      ccaactaacc atgttcaata tccttttagcg gaaactccaa atccaacact agaagattta 120
      aattataaag agttttttaag aatgactgca gataataata cggaagcact agatagctct 180
      acaacaaaag atgtcattca aaaaggcatt tccgtagtag gtgatctcct aggcgtagta 240
15      ggtttcccg tgggtggagc gcttgtttcg ttttatacaa acttttttaa tactatttgg 300
      ccaagtgaag acccggtgga ggcttttatg gaacaagtag aagcattgat ggatcagaaa 360
      atagctgatt atgcaaaaaa taaagctctt gcagagttac agggccttca aaataatgtc 420
      gaagattatg tgagtgcatt gagttcatgg caaaaaaatg caaagagttc acgaaatgta 480
      catagccagg ggcggataag agagctgttt tctcaagcag aaagtcattt tcgtaattca 540
      tgcccttcgt ttgcaatttc tggatacagag gttctatttc taacaacata tgcacaagct 600
20      gccacacac atttattttt actaaaagac gctcaaattt atggagaaga atggggatag 660
      gaaaaagaag atattgctga attttataaa agacaactaa aacttacgca agaataact 720
      gaccattgtg tcaaattggt taatgttggg ttagataaat taagaggttc atcttatgaa 780
      tcttgggtaa actttaaccg ttatcgcaga gagatgacat taacagtatt agatttaatt 840
      gcactatttc cattgtatga tgttcggcta taccctaaag aagttaaaac cgaattaaca 900
25      agagacgttt taacagatcc aattgtcggg gtcaacaacc ttaggggcta tggacaacc 960
      ttctctaata tagaaaatta tattcgaaaa ccacatctat ttgactatct gcatagaatt 1020
      caatttcaca cgcggttcca accaggatat tatggaaatg actctttcaa ttattggtcc 1080
      ggtaattatg tttcaactag accaagcata ggatcaaag atataatcac atctccattc 1140
      tatggaaata aatccagtga acctgtacaa aatttagaat ttaatggaga aaaagtctat 1200
30      agagccgtag caaatacaaa tcttgcggtc tggccgtccg ctgtatattc aggtgttaca 1260
      aaagtggat ttagccaata taatgatcaa acagatgaag caagtacaca aacgtacgac 1320
      tcaaaaagaa atgttggcgc ggtcagctgg gattctatcg atcaattgcc tccagaaaca 1380
      acagatgaac ctctagaaaa gggatatagc catcaactca attatgtaat gtgcttttta 1440
      atgcagggtg gtagaggaac aatcccagtg ttaacttggg cacataaaag tgtagacttt 1500
      tttaacatga ttgattcgaa aaaaattaca caacttccgt tagtaaaggc atataagtta 1560
35      caatctggtg cttccggtgt cgcaggtcct aggtttacag gaggagatat cattcaatgc 1620
      acagaaaatg gaagtgcggc aactatttac gttacaccgg atgtgtcgta ctctcaaaaa 1680
      tatcgagcta gaattcatta tgcttctaca tctcagataa catttacact cagtttagac 1740
      ggggcaccat ttaatcaata ctatttcgat aaaacgataa ataaaggaga cacattaacg 1800
      tataattcat ttaatttagc aagtttcagc acaccattcg aattatcagg gaataactta 1860
40      caaataggcg tcacaggatt aagtgtcgga gataaagttt atatagacaa aattgaattt 1920
      attccagtga at 1932
  
```

<210> 13
 <211> 644
 45 <212> PRT
 <213> Artificial Sequence

<220>
 <223> variant of Axmi-R1 (Axmi-R1(3c7))

<400> 13

EP 2 728 007 B1

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

20

25

30

35

40

45

50

55

EP 2 728 007 B1

	Ala	Leu	Ala	Glu	Leu	Gln	Gly	Leu	Gln	Asn	Asn	Val	Glu	Asp	Tyr	Val
	130						135					140				
	Ser	Ala	Leu	Ser	Ser	Trp	Gln	Lys	Asn	Ala	Lys	Ser	Ser	Arg	Asn	Val
	145					150					155					160
5	His	Ser	Gln	Gly	Arg	Ile	Arg	Glu	Leu	Phe	Ser	Gln	Ala	Glu	Ser	His
					165					170					175	
	Phe	Arg	Asn	Ser	Met	Pro	Ser	Phe	Ala	Ile	Ser	Gly	Tyr	Glu	Val	Leu
					180				185					190		
	Phe	Leu	Thr	Thr	Tyr	Ala	Gln	Ala	Ala	Asn	Thr	His	Leu	Phe	Leu	Leu
					195				200				205			
10	Lys	Asp	Ala	Gln	Ile	Tyr	Gly	Glu	Glu	Trp	Gly	Tyr	Glu	Lys	Glu	Asp
	210						215					220				
	Ile	Ala	Glu	Phe	Tyr	Lys	Arg	Gln	Leu	Lys	Leu	Thr	Gln	Glu	Tyr	Thr
	225					230						235				240
	Asp	His	Cys	Val	Lys	Trp	Tyr	Asn	Val	Gly	Leu	Asp	Lys	Leu	Arg	Gly
					245					250					255	
15	Ser	Ser	Tyr	Glu	Ser	Trp	Val	Asn	Phe	Asn	Arg	Tyr	Arg	Arg	Glu	Met
				260					265					270		
	Thr	Leu	Thr	Val	Leu	Asp	Leu	Ile	Ala	Leu	Phe	Pro	Leu	Tyr	Asp	Val
				275				280					285			
	Arg	Leu	Tyr	Pro	Lys	Glu	Val	Lys	Thr	Glu	Leu	Thr	Arg	Asp	Val	Leu
	290					295						300				
20	Thr	Asp	Pro	Ile	Val	Gly	Val	Asn	Asn	Leu	Arg	Gly	Tyr	Gly	Thr	Thr
	305					310						315				320
	Phe	Ser	Asn	Ile	Glu	Asn	Tyr	Ile	Arg	Lys	Pro	His	Leu	Phe	Asp	Tyr
					325					330					335	
	Leu	His	Arg	Ile	Gln	Phe	His	Thr	Arg	Phe	Gln	Pro	Gly	Tyr	Tyr	Gly
				340					345					350		
25	Asn	Asp	Ser	Phe	Asn	Tyr	Trp	Ser	Gly	Asn	Tyr	Val	Ser	Thr	Arg	Pro
				355				360					365			
	Ser	Ile	Gly	Ser	Asn	Asp	Ile	Ile	Thr	Ser	Pro	Phe	Tyr	Gly	Asn	Lys
	370					375						380				
	Ser	Ser	Glu	Pro	Val	Gln	Asn	Leu	Glu	Phe	Asn	Gly	Glu	Lys	Val	Tyr
	385					390					395					400
30	Arg	Ala	Val	Ala	Asn	Thr	Asn	Leu	Ala	Val	Trp	Pro	Ser	Ala	Val	Tyr
					405					410					415	
	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp
				420				425						430		
	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
				435				440					445			
35	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
	450					455						460				
	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
	465					470					475					480
	Met	Gln	Gly	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
					485					490					495	
40	Ser	Val	Asp	Phe	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu
				500					505					510		
	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
				515				520						525		
	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
	530					535						540				
45	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
	545					550					555					560
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
					565					570					575	
50	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
				580					585					590		
	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
				595				600					605			
	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
	610					615						620				
55	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625					630					635					640
	Ile	Pro	Val	Asn												

<210> 14
 <211> 1932
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> nucleotide sequence encoding variant of Axmi-R1 (Axmi-R1(1g8))

<400> 14

```

atgaatccga acaatcgaag tgaacatgat acaataaaaa ctactgaaaa taatgaggtg 60
ccaactaacc atgttcaata tccttttagcg gaaactccaa atccaacact agaagattta 120
aattataaag agttttttaag aatgactgca gataataata cggaagcact agatagctct 180
acaacaaaag atgtcattca aaaaggcatt tccgtagtag gtgatctcct aggcgtagta 240
ggtttcccggt ttggtggagc gcttgtttcg ttttatacaa acttttttaa tactatttgg 300
ccaagtgaag acccggtgga ggcttttatg gaacaagtag aagcattgat ggatcagaaa 360
atagctgatt atgcaaaaaa taaagctctt gcagagttac agggccttca aaataatgtc 420
gaagattatg tgagtgcatt gagttcatgg caaaaaaatc ctgtgagttc acgaaatcca 480
catagccagg ggcggataag agagctgttt tctcaagcag aaagtcattt tcgtaattca 540
atgccttcgt ttgcaatttc tggatacgag gttctatttc taacaacata tgcacaagct 600
gccaacacac atttattttt actaaaagac gctcaaattt atggagaaga atggggatag 660
gaaaaagaag atattgctga attttataaa agacaactaa aacttacgca agaataact 720
gaccattgtg tcaaatggta taatgttggg ttagataaat taagaggttc atcttatgaa 780
tcttgggtaa actttaaccg ttatcgcgag gagatgacat taacagtatt agatttaatt 840
gcactatttc cattgtatga tggtcggcta taccctaaaag aagttaaaac cgaattaaca 900
agagacgttt taacagatcc aattgtcggg gtcaacaacc ttagggaata tggaacaacc 960
ttctctaata tagaaaatta tattcgaaaa ccacatctat ttgactatct gcatagaatt 1020
caatttcaca cgcggttcca accaggatat tatggaaatg actctttcaa ttattggtcc 1080
ggtaattatg tttcaactag accaagcata ggatcaaag atataatcac atctccattc 1140
tatggaaata aatccagtga acctgtacaa aatttagaat ttaatggaga aaaagtctat 1200
agagccgtag caaatacaaa tcttgcggtc tggccgtccg ctgtatattc aggtgttaca 1260
aaagtggaa tttagccaata taatgatcaa acagatgaag caagtacaca aacgtacgac 1320
tcaaaaagaa atgttggcgc ggtcagctgg gattctatcg atcaattgcc tccagaaaca 1380
acagatgaac ctctagaaaa gggatatagc catcaactca attatgtaat gtgcttttta 1440
atgctgaaaa gtagaggaac aatcccagtg ttaacttggg cacataaaaag tgtagacttt 1500
tttaacatga ttgattcgaa aaaaattaca caacttccgt tagtaaaggc atataagtta 1560
caatctggtg cttccgttgt cgcaggtcct aggtttacag gaggagatat cattcaatgc 1620
acagaaaatg gaagtgcggc aactatttac gttacaccgg atgtgtcgta ctctcaaaaa 1680
tatcgagcta gaattcatta tgcttctaca tctcagataa catttacact cagtttagac 1740
ggggcaccat ttaatcaata ctatttcgat aaaacgataa ataaaggaga cacattaacg 1800
tataattcat ttaatttagc aagtttcagc acaccattcg aattatcagg gaataactta 1860
caaataggcg tcacaggatt aagtgtgga gataaagttt atatagacaa aattgaattt 1920
attccagtga at 1932

```

<210> 15
 <211> 644
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> variant of Axmi-R1 (Axmi-R1(Ig8))

<400> 15

EP 2 728 007 B1

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

15

20

25

30

35

40

45

50

55

EP 2 728 007 B1

	65				70				75				80			
	Gly	Phe	Pro	Phe	Gly	Gly	Ala	Leu	Val	Ser	Phe	Tyr	Thr	Asn	Phe	Leu
				85						90					95	
	Asn	Thr	Ile	Trp	Pro	Ser	Glu	Asp	Pro	Trp	Lys	Ala	Phe	Met	Glu	Gln
5				100					105					110		
	Val	Glu	Ala	Leu	Met	Asp	Gln	Lys	Ile	Ala	Asp	Tyr	Ala	Lys	Asn	Lys
			115					120					125			
	Ala	Leu	Ala	Glu	Leu	Gln	Gly	Leu	Gln	Asn	Asn	Val	Glu	Asp	Tyr	Val
		130					135					140				
	Ser	Ala	Leu	Ser	Ser	Trp	Gln	Lys	Asn	Pro	Val	Ser	Ser	Arg	Asn	Pro
10	145					150					155				160	
	His	Ser	Gln	Gly	Arg	Ile	Arg	Glu	Leu	Phe	Ser	Gln	Ala	Glu	Ser	His
				165						170					175	
	Phe	Arg	Asn	Ser	Met	Pro	Ser	Phe	Ala	Ile	Ser	Gly	Tyr	Glu	Val	Leu
				180					185					190		
15	Phe	Leu	Thr	Thr	Tyr	Ala	Gln	Ala	Ala	Asn	Thr	His	Leu	Phe	Leu	Leu
			195					200					205			
	Lys	Asp	Ala	Gln	Ile	Tyr	Gly	Glu	Glu	Trp	Gly	Tyr	Glu	Lys	Glu	Asp
		210					215					220				
	Ile	Ala	Glu	Phe	Tyr	Lys	Arg	Gln	Leu	Lys	Leu	Thr	Gln	Glu	Tyr	Thr
	225					230					235				240	
20	Asp	His	Cys	Val	Lys	Trp	Tyr	Asn	Val	Gly	Leu	Asp	Lys	Leu	Arg	Gly
				245						250					255	
	Ser	Ser	Tyr	Glu	Ser	Trp	Val	Asn	Phe	Asn	Arg	Tyr	Arg	Arg	Glu	Met
				260					265					270		
	Thr	Leu	Thr	Val	Leu	Asp	Leu	Ile	Ala	Leu	Phe	Pro	Leu	Tyr	Asp	Val
			275					280					285			
25	Arg	Leu	Tyr	Pro	Lys	Glu	Val	Lys	Thr	Glu	Leu	Thr	Arg	Asp	Val	Leu
		290					295					300				
	Thr	Asp	Pro	Ile	Val	Gly	Val	Asn	Asn	Leu	Arg	Glu	Tyr	Gly	Thr	Thr
	305					310					315				320	
	Phe	Ser	Asn	Ile	Glu	Asn	Tyr	Ile	Arg	Lys	Pro	His	Leu	Phe	Asp	Tyr
				325						330					335	
30	Leu	His	Arg	Ile	Gln	Phe	His	Thr	Arg	Phe	Gln	Pro	Gly	Tyr	Tyr	Gly
				340					345					350		
	Asn	Asp	Ser	Phe	Asn	Tyr	Trp	Ser	Gly	Asn	Tyr	Val	Ser	Thr	Arg	Pro
			355						360				365			
	Ser	Ile	Gly	Ser	Asn	Asp	Ile	Ile	Thr	Ser	Pro	Phe	Tyr	Gly	Asn	Lys
		370					375					380				
35	Ser	Ser	Glu	Pro	Val	Gln	Asn	Leu	Glu	Phe	Asn	Gly	Glu	Lys	Val	Tyr
	385					390					395				400	
	Arg	Ala	Val	Ala	Asn	Thr	Asn	Leu	Ala	Val	Trp	Pro	Ser	Ala	Val	Tyr
				405						410					415	
	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp
				420					425					430		
40	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
			435					440					445			
	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
		450					455					460				
	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
	465					470					475				480	
45	Met	Leu	Lys	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
				485						490					495	
	Ser	Val	Asp	Phe	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu
				500					505					510		
	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515						520					525		
50	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
		530					535					540				
	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
	545					550					555				560	
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
				565						570					575	
55	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
				580					585					590		

EP 2 728 007 B1

	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
			595					600					605			
	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
		610					615				620					
5	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625					630					635					640
	Ile	Pro	Val	Asn												

<210> 16

10 <211> 1932

<212> DNA

<213> Artificial Sequence

<220>

15 <223> nucleotide sequence encoding variant of Axmi-R1 (Axmi-R1(Evo23))

<400> 16

20	atgaatccga	acaatcgaag	tgaacatgat	acaataaaaa	ctactgaaaa	taatgaggtg	60
	ccaactaacc	atgttcaata	tccttttagcg	gaaactccaa	atccaacact	agaagattta	120
	aattataaag	agtttttaag	aatgactgca	gataataata	cggaagcact	agatagctct	180
	acaacaaaag	atgtcattca	aaaaggcatt	tccgtagtag	gtgatctcct	aggcgtagta	240
	ggtttcccg	ttggtggagc	gcttgtttcg	ttttatacaa	acttttttaa	tactatttgg	300
	ccaagtgaag	acccgtggaa	ggcttttatg	gaacaagtag	aagcattgat	ggatcagaaa	360
25	atagctgatt	atgcaaaaaa	taaagctctt	gcagagttac	agggccttca	aaataatgtc	420
	gaagattatg	tgagtgcatt	gagttcatgg	caaaaaaatc	atgtgagttc	acgaaatctt	480
	catagccagg	ggcggataag	agagctgttt	tctcaagcag	aaagtcattt	tcgtaattca	540
	atgccttcgt	ttgcaatttc	tggatcacgag	gttctatttc	taacaacata	tgcaacaagc	600
	gccaacacac	atttattttt	actaaaagac	gctcaaattt	atggagaaga	atggggatac	660
30	gaaaaagaag	atattgctga	atttttataaa	agacaactaa	aacttacgca	agaatatact	720
	gaccattgtg	tcaaattggt	taattgttga	ttagataaat	taagaggttc	atcttatgaa	780
	tcttggtgta	actttaaccg	ttatcgcaga	gagatgacat	taacagattt	agattttaatt	840
	gcactatttc	cattgtatga	tgttcggcta	tacccaaaag	aagttaaaac	cgaattaaca	900
	agagacgttt	taacagatcc	aattgtcggg	gtcaacaacc	ttagggaata	tggacaacc	960
35	ttctctaata	tagaaaatta	tattcgaaaa	ccacatctat	ttgactatct	gcatagaatt	1020
	caatttcaca	cgcggttcca	accaggatat	tatggaaatg	actctttcaa	ttattgggtc	1080
	ggtaattatg	tttcaactag	accaagcata	ggatcaaag	atataatcac	atctccattc	1140
	tatggaaata	aatccagtg	acctgtacaa	aatttagaat	ttaatggaga	aaaagtctat	1200
	agagccgtag	caaatacaaa	tcttgcggtc	tggccgtccg	ctgtatattc	aggtgttaca	1260
	aaagtgggaat	ttagccaata	taatgatcaa	acagatgaag	caagtacaca	aacgtacgac	1320
40	tcaaaaagaa	atgttggcgc	ggtcagctgg	gattctatcg	atcaattgcc	tccagaaaca	1380
	acagatgaac	ctctagaaaa	gggatatagc	catcaactca	attatgtaat	gtgcttttta	1440
	atgctgaaaa	gtagaggaac	aatcccagtg	ttaacttgga	cacataaaaag	tgtagacttt	1500
	tttaacatga	ttgattcgaa	aaaaattaca	caacttccgt	tagtaaaggc	atataagtta	1560
	caatctggtg	cttccgttgt	cgcaggtcct	aggtttacag	gaggagatat	cattcaatgc	1620
45	acagaaaatg	gaagtgcggc	aactatttac	gttacaccgg	atgtgtcgta	ctctcaaaaa	1680
	tatcgagcta	gaattcatta	tgcttctaca	tctcagataa	catttacact	cagtttagac	1740
	ggggcaccat	ttaatcaata	ctatttcgat	aaaacgataa	ataaaggaga	cacattaacg	1800
	tataattcat	ttaatttagc	aagtttcagc	acaccattcg	aattatcagg	gaataactta	1860
	caaataggcg	tcacaggatt	aagtgcgtga	gataaagttt	atatagacaa	aattgaattt	1920
50	attccagtg	at					1932

<210> 17

<211> 644

<212> PRT

55 <213> Artificial Sequence

<220>

<223> variant of Axmi-R1 (Axmi-R1(Evo23))

EP 2 728 007 B1

<400> 17

	Met	Asn	Pro	Asn	Asn	Arg	Ser	Glu	His	Asp	Thr	Ile	Lys	Thr	Thr	Glu
5	1				5					10					15	
10																
15																
20																
25																
30																
35																
40																
45																
50																
55																

EP 2 728 007 B1

	Asn	Asn	Glu	Val	Pro	Thr	Asn	His	Val	Gln	Tyr	Pro	Leu	Ala	Glu	Thr
				20					25					30		
	Pro	Asn	Pro	Thr	Leu	Glu	Asp	Leu	Asn	Tyr	Lys	Glu	Phe	Leu	Arg	Met
			35					40					45			
5	Thr	Ala	Asp	Asn	Asn	Thr	Glu	Ala	Leu	Asp	Ser	Ser	Thr	Thr	Lys	Asp
		50					55					60				
	Val	Ile	Gln	Lys	Gly	Ile	Ser	Val	Val	Gly	Asp	Leu	Leu	Gly	Val	Val
	65					70					75				80	
	Gly	Phe	Pro	Phe	Gly	Gly	Ala	Leu	Val	Ser	Phe	Tyr	Thr	Asn	Phe	Leu
					85					90				95		
10	Asn	Thr	Ile	Trp	Pro	Ser	Glu	Asp	Pro	Trp	Lys	Ala	Phe	Met	Glu	Gln
				100					105					110		
	Val	Glu	Ala	Leu	Met	Asp	Gln	Lys	Ile	Ala	Asp	Tyr	Ala	Lys	Asn	Lys
			115					120					125			
	Ala	Leu	Ala	Glu	Leu	Gln	Gly	Leu	Gln	Asn	Asn	Val	Glu	Asp	Tyr	Val
			130				135					140				
15	Ser	Ala	Leu	Ser	Ser	Trp	Gln	Lys	Asn	His	Val	Ser	Ser	Arg	Asn	Leu
	145					150					155				160	
	His	Ser	Gln	Gly	Arg	Ile	Arg	Glu	Leu	Phe	Ser	Gln	Ala	Glu	Ser	His
					165					170				175		
	Phe	Arg	Asn	Ser	Met	Pro	Ser	Phe	Ala	Ile	Ser	Gly	Tyr	Glu	Val	Leu
				180					185					190		
20	Phe	Leu	Thr	Thr	Tyr	Ala	Gln	Ala	Ala	Asn	Thr	His	Leu	Phe	Leu	Leu
			195					200					205			
	Lys	Asp	Ala	Gln	Ile	Tyr	Gly	Glu	Glu	Trp	Gly	Tyr	Glu	Lys	Glu	Asp
		210					215					220				
	Ile	Ala	Glu	Phe	Tyr	Lys	Arg	Gln	Leu	Lys	Leu	Thr	Gln	Glu	Tyr	Thr
	225					230					235				240	
25	Asp	His	Cys	Val	Lys	Trp	Tyr	Asn	Val	Gly	Leu	Asp	Lys	Leu	Arg	Gly
				245					250					255		
	Ser	Ser	Tyr	Glu	Ser	Trp	Val	Asn	Phe	Asn	Arg	Tyr	Arg	Arg	Glu	Met
				260					265					270		
	Thr	Leu	Thr	Val	Leu	Asp	Leu	Ile	Ala	Leu	Phe	Pro	Leu	Tyr	Asp	Val
			275					280					285			
30	Arg	Leu	Tyr	Pro	Lys	Glu	Val	Lys	Thr	Glu	Leu	Thr	Arg	Asp	Val	Leu
		290					295						300			
	Thr	Asp	Pro	Ile	Val	Gly	Val	Asn	Asn	Leu	Arg	Glu	Tyr	Gly	Thr	Thr
		305				310					315				320	
	Phe	Ser	Asn	Ile	Glu	Asn	Tyr	Ile	Arg	Lys	Pro	His	Leu	Phe	Asp	Tyr
				325						330				335		
35	Leu	His	Arg	Ile	Gln	Phe	His	Thr	Arg	Phe	Gln	Pro	Gly	Tyr	Tyr	Gly
				340					345					350		
	Asn	Asp	Ser	Phe	Asn	Tyr	Trp	Ser	Gly	Asn	Tyr	Val	Ser	Thr	Arg	Pro
			355					360					365			
	Ser	Ile	Gly	Ser	Asn	Asp	Ile	Ile	Thr	Ser	Pro	Phe	Tyr	Gly	Asn	Lys
		370					375					380				
40	Ser	Ser	Glu	Pro	Val	Gln	Asn	Leu	Glu	Phe	Asn	Gly	Glu	Lys	Val	Tyr
						390					395				400	
	Arg	Ala	Val	Ala	Asn	Thr	Asn	Leu	Ala	Val	Trp	Pro	Ser	Ala	Val	Tyr
				405						410				415		
	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp
				420					425					430		
45	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
			435					440					445			
	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
		450					455					460				
	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
						470					475				480	
50	Met	Leu	Lys	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
				485						490				495		
	Ser	Val	Asp	Phe	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu
				500					505					510		
	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515					520					525			
55	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly

EP 2 728 007 B1

	530		535		540	
	Ser Ala Ala Thr Ile Tyr Val Thr Pro Asp Val Ser Tyr Ser Gln Lys					
	545		550		555	560
5	Tyr Arg Ala Arg Ile His Tyr Ala Ser Thr Ser Gln Ile Thr Phe Thr					
		565		570		575
	Leu Ser Leu Asp Gly Ala Pro Phe Asn Gln Tyr Tyr Phe Asp Lys Thr					
		580		585		590
	Ile Asn Lys Gly Asp Thr Leu Thr Tyr Asn Ser Phe Asn Leu Ala Ser					
		595		600		605
10	Phe Ser Thr Pro Phe Glu Leu Ser Gly Asn Asn Leu Gln Ile Gly Val					
		610		615		620
	Thr Gly Leu Ser Ala Gly Asp Lys Val Tyr Ile Asp Lys Ile Glu Phe					
		625		630		635
	Ile Pro Val Asn					640

<210> 18

<211> 1932

<212> DNA

<213> Artificial Sequence

<220>

<223> nucleotide sequence encoding variant of Axmi-R1 (Axmi-R1(L61E11)) (Axmi-R1(L61E11)) (Axmi-R1(Evo23))

<400> 18

	atgaatccga	acaatcgaag	tgaacatgat	acaataaaaa	ctactgaaaa	taatgaggtg	60
	ccaactaacc	atgttcaata	tccttttagcg	gaaactccaa	atccaacact	agaagattta	120
	aattataaaag	agttttttaag	aatgactgca	gataataata	cggaagcact	agatagctct	180
30	acaacaaaag	atgtcattca	aaaaggcatt	tccgtagtag	gtgatctcct	aggcgtagta	240
	ggtttcccgt	ttggtggagc	gcttgtttcg	ttttatacaa	actttttaaa	tactatttgg	300
	ccaagtgaag	acccgtggaa	ggcttttatg	gaacaagtag	aagcattgat	ggatcagaaa	360
	atagctgatt	atgcaaaaaa	taaagctcct	gcagagttac	agggccttca	aaataatgtc	420
	gaagattatg	tgagtgcatt	gagttcatgg	caaaaaaatc	ctgtgagttc	acgaaatcca	480
	catagccagg	ggcggataag	agagctgttt	tctcaagcag	aaagtcattt	tcgtaattca	540
35	atgccttcgt	ttgcaatttc	tggatacgag	gttctatttc	taacaacata	tgcacaagct	600
	gccaacacac	atttattttt	actaaaagac	gctcaaattt	atggagaaga	atgggggatac	660
	gaaaaagaag	atattgctga	attttataaa	agacaactaa	aacttacgca	agaatatact	720
	gaccattgtg	tcaaattgta	taatgttgga	ttagataaat	taagagggtc	atcttatgaa	780
	tcttgggtaa	actttaaccg	ttatcgcaga	gagatgacat	taacagtatt	agattttaatt	840
40	gcactatttc	cattgtatga	tggtcggcta	tacccaaaag	aagttaaaac	cgaattaaca	900
	agagacgttt	taacagatcc	aattgtcggg	gtcaacaacc	ttaggggcta	tggacaacac	960
	ttctctaata	tagaaaatta	tattcgaaaa	ccacatctat	ttgactatct	gcatagaatt	1020
	caatttcaca	cgcggttcca	accaggatat	tatggaaatg	actctttcaa	ttattggtcc	1080
	ggtaattatg	tttcaactag	accaagcata	ggatcaaatg	atataatcac	atctccattc	1140
45	tatggaaata	aatccagtga	acctgtacaa	aatttagaat	ttaatggaga	aaaagtctat	1200
	agagccgtag	caaatacaaa	tcttgcggtc	tggccgtccg	ctgtatattc	aggtgttaca	1260
	aaagtggaa	ttagccaata	taatgatcaa	acagatgaag	caagtacaca	aacgtacgac	1320
	tcaaaaagaa	atgttggcgc	ggtcagctgg	gattctatcg	atcaattgcc	tccagaaaca	1380
	acagatgaac	ctctagaaaa	gggatatagc	catcaactca	attatgtaat	gtgcttttta	1440
	atgcagggta	gtagaggaa	aatcccagtg	ttaacttgga	cacataaaaag	tgtagacttt	1500
50	tttaacatga	ttgattcgaa	aaaaattaca	caacttccgt	tagtaaaggc	atataattta	1560
	caatctgggtg	cttccgttgt	cgcaggtcct	aggtttacag	gaggagatat	cattcaatgc	1620
	acagaaaatg	gaagtgcggc	aactattttac	gttacaccgg	atgtgtcgtg	ctctcaaaaa	1680
	tatcgagcta	gaattcatta	tgcttctaca	tctcagataa	catttacact	cagtttagac	1740
	ggggcaccat	ttaatcaata	ctatttcgat	aaaaccgataa	ataaaggaga	cacattaacg	1800
55	tataattcat	ttaatttagc	aagtttcagc	acaccattcg	aattatcagg	gaataactta	1860
	caaataggcg	tcacaggatt	aagtgcgtgga	gataaagttt	atatagacaa	aattgaattt	1920
	attccagtga	at					1932

<210> 19
<211> 644
<212> PRT
<213> Artificial Sequence

5

<220>
<223> variant of Axmi-R1 (Axmi-R1(L61E11))

10

<400> 19

15

20

25

30

35

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

	465		470		475		480									
	Met	Gln	Gly	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
					485				490						495	
5	Ser	Val	Asp	Phe	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu
			500						505					510		
	Pro	Leu	Val	Lys	Ala	Tyr	Asn	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515						520					525		
	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
		530					535					540				
10	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
	545					550					555					560
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
				565						570					575	
	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
			580						585					590		
15	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
		595						600					605			
	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
		610					615					620				
	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
20	625					630					635					640
	Ile	Pro	Val	Asn												

<210> 20

<211> 4

25 <212> PRT

<213> Artificial Sequence

<220>

30 <223> synthetic tetrapeptide

<400> 20

Ala Ala Pro Phe

1

35

<210> 21

<211> 644

<212> PRT

<213> Artificial Sequence

40

<220>

<223> variant Axmi-R1 (D4F11)

<400> 21

45

50

55

EP 2 728 007 B1

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

20

25

30

35

40

45

50

55

EP 2 728 007 B1

	Ser	Ala	Leu	Ser	Ser	Trp	Gln	Lys	Asn	Ala	Val	Ser	Ser	Arg	Asn	Pro
	145					150					155					160
	His	Ser	Gln	Gly	Arg	Ile	Arg	Glu	Leu	Phe	Ser	Gln	Ala	Glu	Ser	His
				165						170					175	
5	Phe	Arg	Asn	Ser	Met	Pro	Ser	Phe	Ala	Ile	Ser	Gly	Tyr	Glu	Val	Leu
				180					185					190		
	Phe	Leu	Thr	Thr	Tyr	Ala	Gln	Ala	Ala	Asn	Thr	His	Leu	Phe	Leu	Leu
			195					200					205			
	Lys	Asp	Ala	Gln	Ile	Tyr	Gly	Glu	Glu	Trp	Gly	Tyr	Glu	Lys	Glu	Asp
	210						215					220				
10	Ile	Ala	Glu	Phe	Tyr	Lys	Arg	Gln	Leu	Lys	Leu	Thr	Gln	Glu	Tyr	Thr
	225					230					235					240
	Asp	His	Cys	Val	Lys	Trp	Tyr	Asn	Val	Gly	Leu	Asp	Lys	Leu	Arg	Gly
				245						250					255	
	Ser	Ser	Tyr	Glu	Ser	Trp	Val	Asn	Phe	Asn	Arg	Tyr	Arg	Arg	Glu	Met
				260					265					270		
15	Thr	Leu	Thr	Val	Leu	Asp	Leu	Ile	Ala	Leu	Phe	Pro	Leu	Tyr	Asp	Val
			275					280					285			
	Arg	Leu	Tyr	Pro	Lys	Glu	Val	Lys	Thr	Glu	Leu	Thr	Arg	Asp	Val	Leu
	290					295						300				
	Thr	Asp	Pro	Ile	Val	Gly	Val	Asn	Asn	Leu	Arg	Gly	Tyr	Gly	Thr	Thr
20	305					310					315					320
	Phe	Ser	Asn	Ile	Glu	Asn	Tyr	Ile	Arg	Lys	Pro	His	Leu	Phe	Asp	Tyr
				325						330					335	
	Leu	His	Arg	Ile	Gln	Phe	His	Thr	Arg	Phe	Gln	Pro	Gly	Tyr	Tyr	Gly
				340					345					350		
25	Asn	Asp	Ser	Phe	Asn	Tyr	Trp	Ser	Gly	Asn	Tyr	Val	Ser	Thr	Arg	Pro
			355					360					365			
	Ser	Ile	Gly	Ser	Asn	Asp	Ile	Ile	Thr	Ser	Pro	Phe	Tyr	Gly	Asn	Lys
	370					375						380				
	Ser	Ser	Glu	Pro	Val	Gln	Asn	Leu	Glu	Phe	Asn	Gly	Glu	Lys	Val	Tyr
	385					390					395					400
30	Arg	Ala	Val	Ala	Asn	Thr	Asn	Leu	Ala	Val	Trp	Pro	Ser	Ala	Val	Tyr
				405						410					415	
	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp
				420					425					430		
	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
			435				440						445			
35	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
	450					455						460				
	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
	465					470					475					480
	Met	Gln	Gly	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
				485						490					495	
40	Ser	Val	Asp	Phe	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu
				500					505					510		
	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
				515				520					525			
	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
45	530					535						540				
	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
	545					550					555					560
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
				565						570					575	
50	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
				580					585					590		
	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
			595					600					605			
	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
	610						615					620				
55	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625					630					635					640
	Ile	Pro	Val	Asn												

<210> 22
<211> 644
<212> PRT
<213> Artificial Sequence

5

<220>
<223> variant Axmi-R1 (H9)

10

15

20

25

30

35

40

45

50

55

EP 2 728 007 B1

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

55

EP 2 728 007 B1

			435				440					445				
	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
		450					455					460				
5	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
	465					470					475					480
	Met	Gln	Gly	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
					485					490					495	
	Ser	Val	Asp	Phe	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu
			500						505				510			
10	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515					520					525			
	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
		530				535					540					
	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
15	545					550					555					560
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
					565					570					575	
	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
			580					585					590			
20	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
			595					600				605				
	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
		610				615					620					
	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625				630						635					640
25	Ile	Pro	Val	Asn												

<210> 23

<211> 644

<212> PRT

30 <213> Artificial Sequence

<220>

<223> variant Axmi-R1 (G5)

35 <400> 23

40

45

50

55

EP 2 728 007 B1

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

30

35

40

45

50

55

EP 2 728 007 B1

	210		215		220	
	Ile Ala Glu Phe Tyr Lys Arg Gln Leu Lys Leu Thr Gln Glu Tyr Thr					
	225		230		235	240
5	Asp His Cys Val Lys Trp Tyr Asn Val Gly Leu Asp Lys Leu Arg Gly					
		245		250		255
	Ser Ser Tyr Glu Ser Trp Val Asn Phe Asn Arg Tyr Arg Arg Glu Met					
		260		265		270
	Thr Leu Thr Val Leu Asp Leu Ile Ala Leu Phe Pro Leu Tyr Asp Val					
		275		280		285
10	Arg Leu Tyr Pro Lys Glu Val Lys Thr Glu Leu Thr Arg Asp Val Leu					
		290		295		300
	Thr Asp Pro Ile Val Gly Val Asn Asn Leu Arg Gly Tyr Gly Thr Thr					
		305		310		315
	Phe Ser Asn Ile Glu Asn Tyr Ile Arg Lys Pro His Leu Phe Asp Tyr					
		325		330		335
15	Leu His Arg Ile Gln Phe His Thr Arg Phe Gln Pro Gly Tyr Tyr Gly					
		340		345		350
	Asn Asp Ser Phe Asn Tyr Trp Ser Gly Asn Tyr Val Ser Thr Arg Pro					
		355		360		365
	Ser Ile Gly Ser Asn Asp Ile Ile Thr Ser Pro Phe Tyr Gly Asn Lys					
20		370		375		380
	Ser Ser Glu Pro Val Gln Asn Leu Glu Phe Asn Gly Glu Lys Val Tyr					
		385		390		395
	Arg Ala Val Ala Asn Thr Asn Leu Ala Val Trp Pro Ser Ala Val Tyr					
		405		410		415
25	Ser Gly Val Thr Lys Val Glu Phe Ser Gln Tyr Asn Asp Gln Thr Asp					
		420		425		430
	Glu Ala Ser Thr Gln Thr Tyr Asp Ser Lys Arg Asn Val Gly Ala Val					
		435		440		445
	Ser Trp Asp Ser Ile Asp Gln Leu Pro Pro Glu Thr Thr Asp Glu Pro					
		450		455		460
30	Leu Glu Lys Gly Tyr Ser His Gln Leu Asn Tyr Val Met Cys Phe Leu					
		465		470		475
	Met Gln Gly Ser Arg Gly Thr Ile Pro Val Leu Thr Trp Thr His Lys					
		485		490		495
	Ser Val Asp Phe Phe Asn Met Ile Asp Ser Lys Lys Ile Thr Gln Leu					
35		500		505		510
	Pro Leu Val Lys Ala Tyr Lys Leu Gln Ser Gly Ala Ser Val Val Ala					
		515		520		525
	Gly Pro Arg Phe Thr Gly Gly Asp Ile Ile Gln Cys Thr Glu Asn Gly					
		530		535		540
40	Ser Ala Ala Thr Ile Tyr Val Thr Pro Asp Val Ser Tyr Ser Gln Lys					
		545		550		555
	Tyr Arg Ala Arg Ile His Tyr Ala Ser Thr Ser Gln Ile Thr Phe Thr					
		565		570		575
	Leu Ser Leu Asp Gly Ala Pro Phe Asn Gln Tyr Tyr Phe Asp Lys Thr					
45		580		585		590
	Ile Asn Lys Gly Asp Thr Leu Thr Tyr Asn Ser Phe Asn Leu Ala Ser					
		595		600		605
	Phe Ser Thr Pro Phe Glu Leu Ser Gly Asn Asn Leu Gln Ile Gly Val					
		610		615		620
50	Thr Gly Leu Ser Ala Gly Asp Lys Val Tyr Ile Asp Lys Ile Glu Phe					
		625		630		635
	Ile Pro Val Asn					640

<210> 24

<211> 644

<212> PRT

<213> Artificial Sequence

<220>

<223> variant Axmi-R1 (H4)

<400> 24

5

10

15

20

25

30

35

40

45

50

55

EP 2 728 007 B1

	Met	Asn	Pro	Asn	Asn	Arg	Ser	Glu	His	Asp	Thr	Ile	Lys	Thr	Thr	Glu
	1				5					10					15	
	Asn	Asn	Glu	Val	Pro	Thr	Asn	His	Val	Gln	Tyr	Pro	Leu	Ala	Glu	Thr
				20					25					30		
5	Pro	Asn	Pro	Thr	Leu	Glu	Asp	Leu	Asn	Tyr	Lys	Glu	Phe	Leu	Arg	Met
			35					40					45			
	Thr	Ala	Asp	Asn	Asn	Thr	Glu	Ala	Leu	Asp	Ser	Ser	Thr	Thr	Lys	Asp
		50					55					60				
	Val	Ile	Gln	Lys	Gly	Ile	Ser	Val	Val	Gly	Asp	Leu	Leu	Gly	Val	Val
	65					70					75					80
10	Gly	Phe	Pro	Phe	Gly	Gly	Ala	Leu	Val	Ser	Phe	Tyr	Thr	Asn	Phe	Leu
				85						90				95		
	Asn	Thr	Ile	Trp	Pro	Ser	Glu	Asp	Pro	Trp	Lys	Ala	Phe	Met	Glu	Gln
				100					105					110		
	Val	Glu	Ala	Leu	Met	Asp	Gln	Lys	Ile	Ala	Asp	Tyr	Ala	Lys	Asn	Lys
			115					120					125			
15	Ala	Leu	Ala	Glu	Leu	Gln	Gly	Leu	Gln	Asn	Asn	Val	Glu	Asp	Tyr	Val
		130					135					140				
	Ser	Ala	Leu	Ser	Ser	Trp	Gln	Lys	Asn	Pro	Val	Ser	Ser	Arg	Asn	Phe
	145					150					155					160
	His	Ser	Gln	Gly	Arg	Ile	Arg	Glu	Leu	Phe	Ser	Gln	Ala	Glu	Ser	His
				165						170					175	
20	Phe	Arg	Asn	Ser	Met	Pro	Ser	Phe	Ala	Ile	Ser	Gly	Tyr	Glu	Val	Leu
				180					185					190		
	Phe	Leu	Thr	Thr	Tyr	Ala	Gln	Ala	Ala	Asn	Thr	His	Leu	Phe	Leu	Leu
			195					200					205			
	Lys	Asp	Ala	Gln	Ile	Tyr	Gly	Glu	Glu	Trp	Gly	Tyr	Glu	Lys	Glu	Asp
25		210					215					220				
	Ile	Ala	Glu	Phe	Tyr	Lys	Arg	Gln	Leu	Lys	Leu	Thr	Gln	Glu	Tyr	Thr
	225					230					235					240
	Asp	His	Cys	Val	Lys	Trp	Tyr	Asn	Val	Gly	Leu	Asp	Lys	Leu	Arg	Gly
				245						250					255	
	Ser	Ser	Tyr	Glu	Ser	Trp	Val	Asn	Phe	Asn	Arg	Tyr	Arg	Arg	Glu	Met
30				260					265					270		
	Thr	Leu	Thr	Val	Leu	Asp	Leu	Ile	Ala	Leu	Phe	Pro	Leu	Tyr	Asp	Val
			275					280					285			
	Arg	Leu	Tyr	Pro	Lys	Glu	Val	Lys	Thr	Glu	Leu	Thr	Arg	Asp	Val	Leu
		290					295					300				
35	Thr	Asp	Pro	Ile	Val	Gly	Val	Asn	Asn	Leu	Arg	Gly	Tyr	Gly	Thr	Thr
	305					310					315					320
	Phe	Ser	Asn	Ile	Glu	Asn	Tyr	Ile	Arg	Lys	Pro	His	Leu	Phe	Asp	Tyr
				325						330					335	
	Leu	His	Arg	Ile	Gln	Phe	His	Thr	Arg	Phe	Gln	Pro	Gly	Tyr	Tyr	Gly
				340					345					350		
40	Asn	Asp	Ser	Phe	Asn	Tyr	Trp	Ser	Gly	Asn	Tyr	Val	Ser	Thr	Arg	Pro
			355					360					365			
	Ser	Ile	Gly	Ser	Asn	Asp	Ile	Ile	Thr	Ser	Pro	Phe	Tyr	Gly	Asn	Lys
		370					375					380				
	Ser	Ser	Glu	Pro	Val	Gln	Asn	Leu	Glu	Phe	Asn	Gly	Glu	Lys	Val	Tyr
	385					390					395					400
45	Arg	Ala	Val	Ala	Asn	Thr	Asn	Leu	Ala	Val	Trp	Pro	Ser	Ala	Val	Tyr
				405						410					415	
	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp
				420					425					430		
	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
			435					440					445			
50	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
		450					455					460				
	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
	465					470					475					480
	Met	Gln	Gly	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
				485						490					495	
55	Ser	Val	Asp	Phe	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu
				500					505					510		

EP 2 728 007 B1

	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515					520					525			
	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
		530					535					540				
5	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
	545					550					555					560
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
					565					570					575	
	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
10				580					585					590		
	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
			595					600					605			
	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
		610					615					620				
15	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625					630					635					640
	Ile	Pro	Val	Asn												

<210> 25

<211> 644

20 <212> PRT

<213> Artificial Sequence

<220>

25 <223> variant Axmi-R1 (D4A2)

<400> 25

30

35

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

	Arg	Leu	Tyr	Pro	Lys	Glu	Val	Lys	Thr	Glu	Leu	Thr	Arg	Asp	Val	Leu
	290						295					300				
	Thr	Asp	Pro	Ile	Val	Gly	Val	Asn	Asn	Leu	Arg	Gln	Tyr	Gly	Thr	Thr
5	305					310					315					320
	Phe	Ser	Asn	Ile	Glu	Asn	Tyr	Ile	Arg	Lys	Pro	His	Leu	Phe	Asp	Tyr
					325					330					335	
	Leu	His	Arg	Ile	Gln	Phe	His	Thr	Arg	Phe	Gln	Pro	Gly	Tyr	Tyr	Gly
				340					345					350		
10	Asn	Asp	Ser	Phe	Asn	Tyr	Trp	Ser	Gly	Asn	Tyr	Val	Ser	Thr	Arg	Pro
		355						360					365			
	Ser	Ile	Gly	Ser	Asn	Asp	Ile	Ile	Thr	Ser	Pro	Phe	Tyr	Gly	Asn	Lys
		370					375					380				
	Ser	Ser	Glu	Pro	Val	Gln	Asn	Leu	Glu	Phe	Asn	Gly	Glu	Lys	Val	Tyr
	385					390					395					400
15	Arg	Ala	Val	Ala	Asn	Thr	Asn	Leu	Ala	Val	Trp	Pro	Ser	Ala	Val	Tyr
				405					410						415	
	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp
				420					425					430		
	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
		435						440					445			
20	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
		450					455					460				
	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
	465					470					475					480
25	Met	Gln	Gly	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
				485						490					495	
	Ser	Val	Asp	Phe	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu
			500						505					510		
	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515						520				525			
30	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
		530					535					540				
	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
	545					550				555						560
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
				565						570					575	
35	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
				580					585					590		
	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
			595					600					605			
40	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
		610					615					620				
	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625					630					635					640
	Ile	Pro	Val	Asn												

45 <210> 26
 <211> 644
 <212> PRT
 <213> Artificial Sequence

50 <220>
 <223> variant Axmi-R1 (H4+D5D8)

<400> 26

55

EP 2 728 007 B1

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

EP 2 728 007 B1

	Val	Ile	Gln	Lys	Gly	Ile	Ser	Val	Val	Gly	Asp	Leu	Leu	Gly	Val	Val
	65					70					75					80
	Gly	Phe	Pro	Phe	Gly	Gly	Ala	Leu	Val	Ser	Phe	Tyr	Thr	Asn	Phe	Leu
					85						90				95	
5	Asn	Thr	Ile	Trp	Pro	Ser	Glu	Asp	Pro	Trp	Lys	Ala	Phe	Met	Glu	Gln
				100					105					110		
	Val	Glu	Ala	Leu	Met	Asp	Gln	Lys	Ile	Ala	Asp	Tyr	Ala	Lys	Asn	Lys
			115					120					125			
	Ala	Leu	Ala	Glu	Leu	Gln	Gly	Leu	Gln	Asn	Asn	Val	Glu	Asp	Tyr	Val
			130				135					140				
10	Ser	Ala	Leu	Ser	Ser	Trp	Gln	Lys	Asn	Pro	Val	Ser	Ser	Arg	Asn	Phe
	145					150					155					160
	His	Ser	Gln	Gly	Arg	Ile	Arg	Glu	Leu	Phe	Ser	Gln	Ala	Glu	Ser	His
					165					170					175	
	Phe	Arg	Asn	Ser	Met	Pro	Ser	Phe	Ala	Ile	Ser	Gly	Tyr	Glu	Val	Leu
				180				185						190		
15	Phe	Leu	Thr	Thr	Tyr	Ala	Gln	Ala	Ala	Asn	Thr	His	Leu	Phe	Leu	Leu
			195					200					205			
	Lys	Asp	Ala	Gln	Ile	Tyr	Gly	Glu	Glu	Trp	Gly	Tyr	Glu	Lys	Glu	Asp
			210				215					220				
	Ile	Ala	Glu	Phe	Tyr	Lys	Arg	Gln	Leu	Lys	Leu	Thr	Gln	Glu	Tyr	Thr
	225					230					235					240
20	Asp	His	Cys	Val	Lys	Trp	Tyr	Asn	Val	Gly	Leu	Asp	Lys	Leu	Arg	Gly
					245					250					255	
	Ser	Ser	Tyr	Glu	Ser	Trp	Val	Asn	Phe	Asn	Arg	Tyr	Arg	Arg	Glu	Met
				260				265						270		
	Thr	Leu	Thr	Val	Leu	Asp	Leu	Ile	Ala	Leu	Phe	Pro	Leu	Tyr	Asp	Val
			275					280					285			
25	Arg	Leu	Tyr	Pro	Lys	Glu	Val	Lys	Thr	Glu	Leu	Thr	Arg	Asp	Val	Leu
			290				295					300				
	Thr	Asp	Pro	Ile	Val	Gly	Val	Asn	Asn	Leu	Arg	Thr	Tyr	Gly	Thr	Thr
	305					310					315					320
	Phe	Ser	Asn	Ile	Glu	Asn	Tyr	Ile	Arg	Lys	Pro	His	Leu	Phe	Asp	Tyr
					325					330					335	
30	Leu	His	Arg	Ile	Gln	Phe	His	Thr	Arg	Phe	Gln	Pro	Gly	Tyr	Tyr	Gly
				340				345						350		
	Asn	Asp	Ser	Phe	Asn	Tyr	Trp	Ser	Gly	Asn	Tyr	Val	Ser	Thr	Arg	Pro
			355					360					365			
	Ser	Ile	Gly	Ser	Asn	Asp	Ile	Ile	Thr	Ser	Pro	Phe	Tyr	Gly	Asn	Lys
			370				375					380				
35	Ser	Ser	Glu	Pro	Val	Gln	Asn	Leu	Glu	Phe	Asn	Gly	Glu	Lys	Val	Tyr
	385					390					395					400
	Arg	Ala	Val	Ala	Asn	Thr	Asn	Leu	Ala	Val	Trp	Pro	Ser	Ala	Val	Tyr
					405					410					415	
	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp
				420					425					430		
40	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
			435					440					445			
	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
		450				455						460				
45	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
	465					470					475					480
	Met	Gln	Gly	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
					485					490					495	
	Ser	Val	Asp	Phe	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu
				500					505					510		
50	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515					520					525			
	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
			530				535					540				
	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
					550						555					560
55	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
					565					570					575	
	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr

EP 2 728 007 B1

[illegible]

10 <210> 27
 <211> 644
 <212> PRT
 <213> Artificial Sequence

15 <220>
<223> variant Axmi-R1 (H9+D4A2)

<400> 27

20

25

30

35

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

			355				360				365					
	Ser	Ile	Gly	Ser	Asn	Asp	Ile	Ile	Thr	Ser	Pro	Phe	Tyr	Gly	Asn	Lys
		370					375					380				
5	Ser	Ser	Glu	Pro	Val	Gln	Asn	Leu	Glu	Phe	Asn	Gly	Glu	Lys	Val	Tyr
	385					390					395					400
	Arg	Ala	Val	Ala	Asn	Thr	Asn	Leu	Ala	Val	Trp	Pro	Ser	Ala	Val	Tyr
					405					410					415	
	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp
				420					425					430		
10	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
			435					440					445			
	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
	450					455					460					
	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
15	465				470					475						480
	Met	Gln	Gly	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
				485					490						495	
	Ser	Val	Asp	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu	
			500					505					510			
20	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515					520					525			
	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
		530				535					540					
	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
	545				550				555							560
25	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
				565					570						575	
	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
			580					585					590			
	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
		595					600					605				
30	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
		610				615					620					
	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625				630				635							640
	Ile	Pro	Val	Asn												

<210> 28

<211> 644

<212> PRT

<213> Artificial Sequence

<220>

<223> variant Axmi-R1 (G5+D4A2)

<400> 28

EP 2 728 007 B1

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

20

25

30

35

40

45

50

55

EP 2 728 007 B1

[illegible]

<210> 29
<211> 644
<212> PRT
<213> Artificial Sequence

5

<220>
<223> variant Axmi-R1 (R315M)

10

<400> 29

15

20

25

30

35

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
			435					440					445			
	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
5		450				455						460				
	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
	465				470					475						480
	Met	Gln	Gly	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
				485					490					495		
10	Ser	Val	Asp	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu	
			500					505					510			
	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515					520					525			
	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
	530					535					540					
15	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
	545				550					555						560
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
				565					570						575	
	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
			580					585					590			
20	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
		595					600					605				
	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
	610					615					620					
25	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625					630					635					640
	Ile	Pro	Val	Asn												

<210> 30

<211> 644

30 <212> PRT

<213> Artificial Sequence

<220>

<223> variant Axmi-R1 (R315W)

35

<400> 30

40

45

50

55

EP 2 728 007 B1

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

30

35

40

45

50

55

EP 2 728 007 B1

	Lys	Asp	Ala	Gln	Ile	Tyr	Gly	Glu	Glu	Trp	Gly	Tyr	Glu	Lys	Glu	Asp
		210					215					220				
	Ile	Ala	Glu	Phe	Tyr	Lys	Arg	Gln	Leu	Lys	Leu	Thr	Gln	Glu	Tyr	Thr
	225					230					235					240
5	Asp	His	Cys	Val	Lys	Trp	Tyr	Asn	Val	Gly	Leu	Asp	Lys	Leu	Arg	Gly
					245					250					255	
	Ser	Ser	Tyr	Glu	Ser	Trp	Val	Asn	Phe	Asn	Arg	Tyr	Arg	Arg	Glu	Met
				260					265					270		
10	Thr	Leu	Thr	Val	Leu	Asp	Leu	Ile	Ala	Leu	Phe	Pro	Leu	Tyr	Asp	Val
			275					280					285			
	Arg	Leu	Tyr	Pro	Lys	Glu	Val	Lys	Thr	Glu	Leu	Thr	Arg	Asp	Val	Leu
		290					295					300				
	Thr	Asp	Pro	Ile	Val	Gly	Val	Asn	Asn	Leu	Trp	Gly	Tyr	Gly	Thr	Thr
	305					310					315					320
15	Phe	Ser	Asn	Ile	Glu	Asn	Tyr	Ile	Arg	Lys	Pro	His	Leu	Phe	Asp	Tyr
				325						330					335	
	Leu	His	Arg	Ile	Gln	Phe	His	Thr	Arg	Phe	Gln	Pro	Gly	Tyr	Tyr	Gly
				340					345					350		
	Asn	Asp	Ser	Phe	Asn	Tyr	Trp	Ser	Gly	Asn	Tyr	Val	Ser	Thr	Arg	Pro
			355					360					365			
20	Ser	Ile	Gly	Ser	Asn	Asp	Ile	Thr	Ser	Pro	Phe	Tyr	Gly	Asn	Lys	
		370					375				380					
	Ser	Ser	Glu	Pro	Val	Gln	Asn	Leu	Glu	Phe	Asn	Gly	Glu	Lys	Val	Tyr
						390					395					400
25	Arg	Ala	Val	Ala	Asn	Thr	Asn	Leu	Ala	Val	Trp	Pro	Ser	Ala	Val	Tyr
				405						410					415	
	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp
				420					425					430		
	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
			435					440					445			
30	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
		450					455					460				
	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
						470					475					480
	Met	Gln	Gly	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
					485					490					495	
35	Ser	Val	Asp	Phe	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu
				500					505					510		
	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
				515					520				525			
	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
		530					535					540				
40	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
		545				550					555					560
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
					565					570					575	
45	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
				580					585					590		
	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
			595					600					605			
	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
		610					615					620				
50	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
		625				630					635					640
	Ile	Pro	Val	Asn												

<210> 31

<211> 644

<212> PRT

<213> Artificial Sequence

<220>

<223> variant Axmi-R1 (3c6)

<400> 31

5

10

15

20

25

30

35

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

				500					505					510			
	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala	
			515					520					525				
5	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly	
		530					535					540					
	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys	
	545					550					555					560	
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr	
				565						570					575		
10	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr	
			580						585					590			
	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser	
		595					600						605				
	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val	
	610					615					620						
15	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe	
	625					630					635					640	
	Ile	Pro	Val	Asn													

<210> 32

20 <211> 644

<212> PRT

<213> Artificial Sequence

<220>

25 <223> variant Axmi-R1 (3all)

<400> 32

30

35

40

45

50

55

EP 2 728 007 B1

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

35

40

45

50

55

EP 2 728 007 B1

[illegible]

45

<210> 33
<211> 644
<212> PRT
<213> Artificial Sequence

50 <220>
<223> variant Axmi-R1 (2b11)

<400> 33

EP 2 728 007 B1

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

10

15

20

25

30

35

40

45

50

55

EP 2 728 007 B1

					50																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																							
--	--	--	--	--	----	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

EP 2 728 007 B1

	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
				580					585					590		
	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
			595					600					605			
5	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
	610					615					620					
	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625					630					635					640
	Ile	Pro	Val	Asn												

10

<210> 34
 <211> 644
 <212> PRT
 <213> Artificial Sequence

15

<220>
 <223> variant Axmi-R1 (Q482I)

<400> 34

20

25

30

35

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

	Asn	Asp	Ser	Phe	Asn	Tyr	Trp	Ser	Gly	Asn	Tyr	Val	Ser	Thr	Arg	Pro
			355					360					365			
	Ser	Ile	Gly	Ser	Asn	Asp	Ile	Ile	Thr	Ser	Pro	Phe	Tyr	Gly	Asn	Lys
		370					375					380				
5	Ser	Ser	Glu	Pro	Val	Gln	Asn	Leu	Glu	Phe	Asn	Gly	Glu	Lys	Val	Tyr
	385					390					395					400
	Arg	Ala	Val	Ala	Asn	Thr	Asn	Leu	Ala	Val	Trp	Pro	Ser	Ala	Val	Tyr
				405						410					415	
	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp
10				420					425					430		
	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
			435					440					445			
	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
	450					455						460				
15	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
	465				470						475					480
	Met	Ile	Gly	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
				485						490					495	
	Ser	Val	Asp	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu	
			500					505					510			
20	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515					520					525			
	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
		530					535					540				
	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
25	545					550					555					560
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
				565						570					575	
	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
			580					585					590			
30	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
		595						600					605			
	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
		610					615					620				
	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625					630					635					640
35	Ile	Pro	Val	Asn												

<210> 35

<211> 644

<212> PRT

40 <213> Artificial Sequence

<220>

<223> variant Axmi-R1 (G483K)

45 <400> 35

50

55

EP 2 728 007 B1

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

20

25

30

35

40

45

50

55

EP 2 728 007 B1

	Ala	Leu	Ala	Glu	Leu	Gln	Gly	Leu	Gln	Asn	Asn	Val	Glu	Asp	Tyr	Val
	130						135					140				
	Ser	Ala	Leu	Ser	Ser	Trp	Gln	Lys	Asn	Pro	Val	Ser	Ser	Arg	Asn	Pro
	145					150					155					160
5	His	Ser	Gln	Gly	Arg	Ile	Arg	Glu	Leu	Phe	Ser	Gln	Ala	Glu	Ser	His
					165					170					175	
	Phe	Arg	Asn	Ser	Met	Pro	Ser	Phe	Ala	Ile	Ser	Gly	Tyr	Glu	Val	Leu
					180				185					190		
	Phe	Leu	Thr	Thr	Tyr	Ala	Gln	Ala	Ala	Asn	Thr	His	Leu	Phe	Leu	Leu
					195				200				205			
10	Lys	Asp	Ala	Gln	Ile	Tyr	Gly	Glu	Glu	Trp	Gly	Tyr	Glu	Lys	Glu	Asp
	210						215					220				
	Ile	Ala	Glu	Phe	Tyr	Lys	Arg	Gln	Leu	Lys	Leu	Thr	Gln	Glu	Tyr	Thr
	225					230						235				240
	Asp	His	Cys	Val	Lys	Trp	Tyr	Asn	Val	Gly	Leu	Asp	Lys	Leu	Arg	Gly
					245					250					255	
15	Ser	Ser	Tyr	Glu	Ser	Trp	Val	Asn	Phe	Asn	Arg	Tyr	Arg	Arg	Glu	Met
				260					265					270		
	Thr	Leu	Thr	Val	Leu	Asp	Leu	Ile	Ala	Leu	Phe	Pro	Leu	Tyr	Asp	Val
				275				280					285			
	Arg	Leu	Tyr	Pro	Lys	Glu	Val	Lys	Thr	Glu	Leu	Thr	Arg	Asp	Val	Leu
	290					295						300				
20	Thr	Asp	Pro	Ile	Val	Gly	Val	Asn	Asn	Leu	Arg	Gly	Tyr	Gly	Thr	Thr
	305					310						315				320
	Phe	Ser	Asn	Ile	Glu	Asn	Tyr	Ile	Arg	Lys	Pro	His	Leu	Phe	Asp	Tyr
					325					330					335	
	Leu	His	Arg	Ile	Gln	Phe	His	Thr	Arg	Phe	Gln	Pro	Gly	Tyr	Tyr	Gly
				340					345					350		
25	Asn	Asp	Ser	Phe	Asn	Tyr	Trp	Ser	Gly	Asn	Tyr	Val	Ser	Thr	Arg	Pro
				355				360					365			
	Ser	Ile	Gly	Ser	Asn	Asp	Ile	Ile	Thr	Ser	Pro	Phe	Tyr	Gly	Asn	Lys
	370					375						380				
	Ser	Ser	Glu	Pro	Val	Gln	Asn	Leu	Glu	Phe	Asn	Gly	Glu	Lys	Val	Tyr
	385					390					395					400
30	Arg	Ala	Val	Ala	Asn	Thr	Asn	Leu	Ala	Val	Trp	Pro	Ser	Ala	Val	Tyr
					405					410					415	
	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp
				420				425						430		
	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
				435				440					445			
35	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
	450					455						460				
	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
	465					470					475					480
	Met	Gln	Lys	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
					485					490					495	
40	Ser	Val	Asp	Phe	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu
				500					505					510		
	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
				515				520						525		
	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
	530					535						540				
45	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
	545					550					555					560
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
					565					570					575	
	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
				580					585					590		
	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
				595				600					605			
	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
	610					615						620				
55	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625					630					635					640
	Ile	Pro	Val	Asn												

<210> 36
<211> 644
<212> PRT
<213> Artificial Sequence

5

<220>
<223> variant Axmi-R1 (G483S)

10

<400> 36

15

20

25

30

35

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

				420				425				430				
	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
			435					440				445				
5	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
		450				455						460				
	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
	465				470						475					480
	Met	Gln	Ser	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
				485						490					495	
10	Ser	Val	Asp	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu	
			500					505					510			
	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515					520					525			
	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
15		530				535						540				
	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
	545				550					555						560
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
				565						570						575
20	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
			580					585					590			
	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
			595					600					605			
	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
	610				615						620					
25	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625				630						635					640
	Ile	Pro	Val	Asn												

<210> 37

30 <211> 644

<212> PRT

<213> Artificial Sequence

<220>

35 <223> variant Axmi-R1 (G483Q)

<400> 37

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

				195						200				205			
	Lys	Asp	Ala	Gln	Ile	Tyr	Gly	Glu	Glu	Trp	Gly	Tyr	Glu	Lys	Glu	Asp	
		210					215					220					
5	Ile	Ala	Glu	Phe	Tyr	Lys	Arg	Gln	Leu	Lys	Leu	Thr	Gln	Glu	Tyr	Thr	
	225					230					235					240	
	Asp	His	Cys	Val	Lys	Trp	Tyr	Asn	Val	Gly	Leu	Asp	Lys	Leu	Arg	Gly	
					245					250					255		
	Ser	Ser	Tyr	Glu	Ser	Trp	Val	Asn	Phe	Asn	Arg	Tyr	Arg	Arg	Glu	Met	
				260					265					270			
10	Thr	Leu	Thr	Val	Leu	Asp	Leu	Ile	Ala	Leu	Phe	Pro	Leu	Tyr	Asp	Val	
				275				280					285				
	Arg	Leu	Tyr	Pro	Lys	Glu	Val	Lys	Thr	Glu	Leu	Thr	Arg	Asp	Val	Leu	
		290					295					300					
	Thr	Asp	Pro	Ile	Val	Gly	Val	Asn	Asn	Leu	Arg	Gly	Tyr	Gly	Thr	Thr	
15	305					310					315					320	
	Phe	Ser	Asn	Ile	Glu	Asn	Tyr	Ile	Arg	Lys	Pro	His	Leu	Phe	Asp	Tyr	
					325					330					335		
	Leu	His	Arg	Ile	Gln	Phe	His	Thr	Arg	Phe	Gln	Pro	Gly	Tyr	Tyr	Gly	
				340					345					350			
	Asn	Asp	Ser	Phe	Asn	Tyr	Trp	Ser	Gly	Asn	Tyr	Val	Ser	Thr	Arg	Pro	
20			355					360					365				
	Ser	Ile	Gly	Ser	Asn	Asp	Ile	Thr	Ser	Pro	Phe	Tyr	Gly	Asn	Lys		
		370					375				380						
	Ser	Ser	Glu	Pro	Val	Gln	Asn	Leu	Glu	Phe	Asn	Gly	Glu	Lys	Val	Tyr	
	385					390					395					400	
25	Arg	Ala	Val	Ala	Asn	Thr	Asn	Leu	Ala	Val	Trp	Pro	Ser	Ala	Val	Tyr	
					405					410					415		
	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp	
				420					425					430			
	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val	
			435					440					445				
30	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro	
		450					455					460					
	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu	
	465					470					475					480	
	Met	Gln	Gln	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys	
35					485					490					495		
	Ser	Val	Asp	Phe	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu	
				500					505					510			
	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala	
			515					520					525				
40	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly	
		530					535					540					
	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys	
	545					550					555					560	
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr	
					565					570					575		
45	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr	
				580					585					590			
	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser	
			595					600					605				
	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val	
50		610					615					620					
	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe	
	625					630					635					640	
	Ile	Pro	Val	Asn													

55 <210> 38
 <211> 644
 <212> PRT
 <213> Artificial Sequence

<220>

<223> variant Axmi-R1 (3c7+1g8)

<400> 38

5

10

15

20

25

30

35

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

	Ser	Val	Asp	Phe	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu
				500					505					510		
	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515					520					525			
5	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
		530				535						540				
	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
	545					550					555					560
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
10					565					570					575	
	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
				580					585					590		
	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
			595					600					605			
15	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
		610				615						620				
	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625					630					635					640
	Ile	Pro	Val	Asn												

20 <210> 39
 <211> 644
 <212> PRT
 <213> Artificial Sequence

25 <220>
 <223> variant Axmi-R1 (3c7+2b11)

<400> 39

30

35

40

45

50

55

EP 2 728 007 B1

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

35

40

45

50

55

EP 2 728 007 B1

	Thr	Leu	Thr	Val	Leu	Asp	Leu	Ile	Ala	Leu	Phe	Pro	Leu	Tyr	Asp	Val
			275					280					285			
	Arg	Leu	Tyr	Pro	Lys	Glu	Val	Lys	Thr	Glu	Leu	Thr	Arg	Asp	Val	Leu
		290					295					300				
5	Thr	Asp	Pro	Ile	Val	Gly	Val	Asn	Asn	Leu	Arg	Ala	Tyr	Gly	Thr	Thr
	305					310					315					320
	Phe	Ser	Asn	Ile	Glu	Asn	Tyr	Ile	Arg	Lys	Pro	His	Leu	Phe	Asp	Tyr
					325					330					335	
	Leu	His	Arg	Ile	Gln	Phe	His	Thr	Arg	Phe	Gln	Pro	Gly	Tyr	Tyr	Gly
10				340					345					350		
	Asn	Asp	Ser	Phe	Asn	Tyr	Trp	Ser	Gly	Asn	Tyr	Val	Ser	Thr	Arg	Pro
			355					360					365			
	Ser	Ile	Gly	Ser	Asn	Asp	Ile	Ile	Thr	Ser	Pro	Phe	Tyr	Gly	Asn	Lys
		370					375					380				
15	Ser	Ser	Glu	Pro	Val	Gln	Asn	Leu	Glu	Phe	Asn	Gly	Glu	Lys	Val	Tyr
	385					390					395					400
	Arg	Ala	Val	Ala	Asn	Thr	Asn	Leu	Ala	Val	Trp	Pro	Ser	Ala	Val	Tyr
					405					410					415	
	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp
				420					425					430		
20	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
			435					440					445			
	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
		450				455						460				
	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
25	465					470					475					480
	Met	Leu	Lys	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
					485					490					495	
	Ser	Val	Asp	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu	
				500				505					510			
30	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515					520					525			
	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
		530					535					540				
	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
	545					550					555					560
35	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
					565					570					575	
	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
				580					585					590		
	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
			595					600					605			
40	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
		610					615					620				
	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625					630					635					640
	Ile	Pro	Val	Asn												

<210> 40

<211> 644

<212> PRT

<213> Artificial Sequence

<220>

<223> variant Axmi-R1 (G5+D5D8)

<400> 40

EP 2 728 007 B1

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

10

15

20

25

30

35

40

45

50

55

EP 2 728 007 B1

	Thr	Ala	Asp	Asn	Asn	Thr	Glu	Ala	Leu	Asp	Ser	Ser	Thr	Thr	Lys	Asp
	50						55					60				
	Val	Ile	Gln	Lys	Gly	Ile	Ser	Val	Val	Gly	Asp	Leu	Leu	Gly	Val	Val
	65					70					75					80
5	Gly	Phe	Pro	Phe	Gly	Gly	Ala	Leu	Val	Ser	Phe	Tyr	Thr	Asn	Phe	Leu
					85					90					95	
	Asn	Thr	Ile	Trp	Pro	Ser	Glu	Asp	Pro	Trp	Lys	Ala	Phe	Met	Glu	Gln
				100					105					110		
	Val	Glu	Ala	Leu	Met	Asp	Gln	Lys	Ile	Ala	Asp	Tyr	Ala	Lys	Asn	Lys
			115						120					125		
10	Ala	Leu	Ala	Glu	Leu	Gln	Gly	Leu	Gln	Asn	Asn	Val	Glu	Asp	Tyr	Val
		130					135						140			
	Ser	Ala	Leu	Ser	Ser	Trp	Gln	Lys	Asn	Pro	Val	Ser	Ser	Arg	Asn	Ala
	145					150					155				160	
	His	Ser	Gln	Gly	Arg	Ile	Arg	Glu	Leu	Phe	Ser	Gln	Ala	Glu	Ser	His
					165					170					175	
15	Phe	Arg	Asn	Ser	Met	Pro	Ser	Phe	Ala	Ile	Ser	Gly	Tyr	Glu	Val	Leu
				180					185					190		
	Phe	Leu	Thr	Thr	Tyr	Ala	Gln	Ala	Ala	Asn	Thr	His	Leu	Phe	Leu	Leu
			195					200					205			
	Lys	Asp	Ala	Gln	Ile	Tyr	Gly	Glu	Glu	Trp	Gly	Tyr	Glu	Lys	Glu	Asp
		210					215					220				
20	Ile	Ala	Glu	Phe	Tyr	Lys	Arg	Gln	Leu	Lys	Leu	Thr	Gln	Glu	Tyr	Thr
	225					230					235				240	
	Asp	His	Cys	Val	Lys	Trp	Tyr	Asn	Val	Gly	Leu	Asp	Lys	Leu	Arg	Gly
					245					250					255	
	Ser	Ser	Tyr	Glu	Ser	Trp	Val	Asn	Phe	Asn	Arg	Tyr	Arg	Arg	Glu	Met
				260					265					270		
25	Thr	Leu	Thr	Val	Leu	Asp	Leu	Ile	Ala	Leu	Phe	Pro	Leu	Tyr	Asp	Val
			275					280					285			
	Arg	Leu	Tyr	Pro	Lys	Glu	Val	Lys	Thr	Glu	Leu	Thr	Arg	Asp	Val	Leu
		290					295					300				
	Thr	Asp	Pro	Ile	Val	Gly	Val	Asn	Asn	Leu	Arg	Thr	Tyr	Gly	Thr	Thr
	305					310					315				320	
30	Phe	Ser	Asn	Ile	Glu	Asn	Tyr	Ile	Arg	Lys	Pro	His	Leu	Phe	Asp	Tyr
					325					330					335	
	Leu	His	Arg	Ile	Gln	Phe	His	Thr	Arg	Phe	Gln	Pro	Gly	Tyr	Tyr	Gly
				340					345					350		
	Asn	Asp	Ser	Phe	Asn	Tyr	Trp	Ser	Gly	Asn	Tyr	Val	Ser	Thr	Arg	Pro
			355						360				365			
35	Ser	Ile	Gly	Ser	Asn	Asp	Ile	Ile	Thr	Ser	Pro	Phe	Tyr	Gly	Asn	Lys
		370					375					380				
	Ser	Ser	Glu	Pro	Val	Gln	Asn	Leu	Glu	Phe	Asn	Gly	Glu	Lys	Val	Tyr
						390					395				400	
	Arg	Ala	Val	Ala	Asn	Thr	Asn	Leu	Ala	Val	Trp	Pro	Ser	Ala	Val	Tyr
					405					410					415	
40	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp
				420					425					430		
	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
			435					440					445			
	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
		450					455					460				
45	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
						470					475				480	
	Met	Gln	Gly	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
					485					490					495	
	Ser	Val	Asp	Phe	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu
				500					505					510		
50	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515						520					525		
	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
			530				535					540				
55	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
						550					555				560	
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr

EP 2 728 007 B1

					565					570				575		
	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
				580					585					590		
5	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
			595					600					605			
	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
		610					615					620				
	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625					630					635					640
10	Ile	Pro	Val	Asn												

<210> 41

<211> 644

<212> PRT

15 <213> Artificial Sequence

<220>

<223> variant Axmi-R1 (D4F11+D5D8)

20 <400> 41

25

30

35

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

				340					345				350			
	Asn	Asp	Ser	Phe	Asn	Tyr	Trp	Ser	Gly	Asn	Tyr	Val	Ser	Thr	Arg	Pro
				355					360					365		
5	Ser	Ile	Gly	Ser	Asn	Asp	Ile	Ile	Thr	Ser	Pro	Phe	Tyr	Gly	Asn	Lys
				370					375					380		
	Ser	Ser	Glu	Pro	Val	Gln	Asn	Leu	Glu	Phe	Asn	Gly	Glu	Lys	Val	Tyr
	385					390					395					400
	Arg	Ala	Val	Ala	Asn	Thr	Asn	Leu	Ala	Val	Trp	Pro	Ser	Ala	Val	Tyr
					405						410					415
10	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp
				420						425				430		
	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
				435				440					445			
	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
	450						455					460				
15	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
	465					470					475					480
	Met	Gln	Gly	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
					485						490					495
	Ser	Val	Asp	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu	
20				500				505					510			
	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
				515				520					525			
	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
	530						535					540				
25	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
	545					550					555					560
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
					565						570					575
	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
				580					585					590		
30	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
				595				600					605			
	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
	610						615					620				
35	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625					630					635					640
	Ile	Pro	Val	Asn												

<210> 42

<211> 644

40 <212> PRT

<213> Artificial Sequence

<220>

<223> variant Axmi-R1 (H4+D4A2)

45

<400> 42

50

55

EP 2 728 007 B1

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

20

25

30

35

40

45

50

55

EP 2 728 007 B1

55

EP 2 728 007 B1

Ile Pro Val Asn

5 <210> 43
 <211> 644
 <212> PRT
 <213> Artificial Sequence

10 <220>
 <223> variant Axmi-R1 (D4F11+D4A2)

 <400> 43

15

20

25

30

35

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

	Ser	Gly	Val	Thr	Lys	Val	Glu	Phe	Ser	Gln	Tyr	Asn	Asp	Gln	Thr	Asp
				420					425					430		
	Glu	Ala	Ser	Thr	Gln	Thr	Tyr	Asp	Ser	Lys	Arg	Asn	Val	Gly	Ala	Val
			435					440					445			
5	Ser	Trp	Asp	Ser	Ile	Asp	Gln	Leu	Pro	Pro	Glu	Thr	Thr	Asp	Glu	Pro
		450				455						460				
	Leu	Glu	Lys	Gly	Tyr	Ser	His	Gln	Leu	Asn	Tyr	Val	Met	Cys	Phe	Leu
	465					470					475					480
10	Met	Gln	Gly	Ser	Arg	Gly	Thr	Ile	Pro	Val	Leu	Thr	Trp	Thr	His	Lys
					485					490					495	
	Ser	Val	Asp	Phe	Asn	Met	Ile	Asp	Ser	Lys	Lys	Ile	Thr	Gln	Leu	
			500					505					510			
	Pro	Leu	Val	Lys	Ala	Tyr	Lys	Leu	Gln	Ser	Gly	Ala	Ser	Val	Val	Ala
			515					520					525			
15	Gly	Pro	Arg	Phe	Thr	Gly	Gly	Asp	Ile	Ile	Gln	Cys	Thr	Glu	Asn	Gly
		530					535					540				
	Ser	Ala	Ala	Thr	Ile	Tyr	Val	Thr	Pro	Asp	Val	Ser	Tyr	Ser	Gln	Lys
	545					550					555					560
	Tyr	Arg	Ala	Arg	Ile	His	Tyr	Ala	Ser	Thr	Ser	Gln	Ile	Thr	Phe	Thr
					565					570					575	
20	Leu	Ser	Leu	Asp	Gly	Ala	Pro	Phe	Asn	Gln	Tyr	Tyr	Phe	Asp	Lys	Thr
			580						585					590		
	Ile	Asn	Lys	Gly	Asp	Thr	Leu	Thr	Tyr	Asn	Ser	Phe	Asn	Leu	Ala	Ser
			595					600					605			
25	Phe	Ser	Thr	Pro	Phe	Glu	Leu	Ser	Gly	Asn	Asn	Leu	Gln	Ile	Gly	Val
		610					615					620				
	Thr	Gly	Leu	Ser	Ala	Gly	Asp	Lys	Val	Tyr	Ile	Asp	Lys	Ile	Glu	Phe
	625					630					635					640
	Ile	Pro	Val	Asn												

30 <210> 44
 <211> 1166
 <212> PRT
 <213> Bacillus thuringiensis

35 <400> 44

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

		210				215				220							
		Ser	Glu	Ile	Ser	Thr	Tyr	Tyr	Asn	Arg	Gln	Val	Arg	Leu	Thr	Ser	Gln
		225					230					235					240
		Tyr	Ser	Asp	Tyr	Cys	Val	Lys	Trp	Tyr	Asn	Thr	Gly	Leu	Asp	Lys	Leu
5						245					250					255	
		Lys	Gly	Thr	Asn	Ser	Ala	Ser	Trp	Leu	Lys	Tyr	His	Gln	Phe	Arg	Arg
					260					265					270		
		Glu	Met	Thr	Leu	Met	Val	Leu	Asp	Val	Val	Ala	Leu	Phe	Pro	Asn	Tyr
				275					280					285			
10		Asn	Thr	Gln	Thr	Tyr	Pro	Ile	Glu	Thr	Arg	Ala	Gln	Leu	Thr	Arg	Asp
		290						295					300				
		Val	Tyr	Thr	Asp	Pro	Ala	Ala	Phe	Asn	Asn	Val	Ser	Asp	Tyr	Gly	Phe
		305				310						315				320	
		Cys	Asn	Pro	Trp	Ser	Thr	His	Ser	Gly	Ile	Leu	Phe	Ser	Glu	Val	Glu
					325						330					335	
15		Asn	Ala	Val	Ile	Arg	Ser	Pro	His	Leu	Phe	Asp	Ile	Leu	Ser	Ser	Ile
				340						345				350			
		Glu	Ile	Asn	Thr	Ala	Arg	Gly	Gly	Ile	Ala	Leu	Asn	Asn	Thr	Ala	Tyr
				355				360					365				
		Ile	Asn	Tyr	Trp	Ser	Gly	His	Ser	Leu	Lys	Tyr	His	Glu	Thr	Asn	Asn
		370					375					380					
20		Pro	Thr	Ile	Arg	Ala	Val	Asn	Tyr	Gly	Arg	Ile	Thr	Ser	Glu	Lys	Asn
		385				390						395				400	
		Ser	Leu	Val	Leu	Glu	Asp	Arg	Glu	Ile	Phe	Glu	Thr	Ile	Ser	Val	Val
					405						410				415		
		Ala	Asn	Leu	Ala	Asn	Val	Tyr	Gln	Lys	Ala	Tyr	Gly	Val	Pro	Glu	Ser
				420						425				430			
25		Tyr	Phe	Asn	Met	Thr	Arg	Arg	Gly	Thr	Ser	Ser	Thr	Ser	Tyr	Tyr	Phe
			435						440					445			
		Tyr	Ser	Lys	Thr	His	Thr	Thr	Pro	Tyr	Gly	Cys	Ser	Asp	Val	Tyr	Pro
		450					455					460					
		Ser	Tyr	Ser	Asp	Ile	Pro	Ile	Asp	Arg	Asn	Val	Pro	Val	Ala	Glu	Ser
		465				470						475				480	
30		Tyr	Ser	His	Arg	Leu	Ser	His	Ile	Thr	Phe	His	Ser	Phe	Ser	Lys	Asn
					485						490					495	
		Ser	Asn	Ala	Ile	Tyr	Gly	Ser	Phe	Pro	Val	Phe	Val	Trp	Thr	His	Val
				500					505					510			
		Ser	Ala	Asp	Leu	Thr	Asn	Thr	Ile	Tyr	Pro	Asp	Ala	Ile	Thr	Gln	Leu
			515					520					525				
35		Pro	Met	Val	Lys	Ala	Asn	Ala	Leu	Leu	Ser	Gly	Thr	Ser	Val	Ile	Lys
		530					535					540					
		Gly	Pro	Gly	Ser	Thr	Gly	Gly	Asp	Ile	Leu	Arg	Arg	Thr	Ser	Val	Gly
		545				550						555				560	
		Arg	Val	Gly	Asn	Phe	Lys	Val	Asn	Val	Asn	Gly	Pro	Leu	Thr	Gln	Arg
					565						570					575	
40		Tyr	Leu	Val	Arg	Ile	Arg	Tyr	Ala	Ser	Thr	Thr	Asp	Leu	Asp	Phe	Tyr
					580					585				590			
		Val	Tyr	Arg	Gly	Gly	Thr	Thr	Val	Ser	Asn	Tyr	Arg	Phe	Asn	Lys	Thr
			595					600					605				
		Met	Asn	Lys	Gly	Ala	Ser	Leu	Thr	Tyr	Asp	Ile	Phe	Lys	Phe	Ala	Ser
		610					615					620					
45		Phe	Ser	Thr	Pro	Phe	Thr	Phe	Thr	Lys	Thr	Gln	Asp	Glu	Leu	Gly	Ile
		625				630						635				640	
		Ser	Ile	Gln	Asn	Phe	Ser	Ser	Gly	Glu	Glu	Val	Tyr	Ile	Asp	Arg	Ile
					645						650				655		
		Glu	Val	Ile	Pro	Val	Gly	Thr	Thr	Tyr	Glu	Ala	Glu	Thr	Asp	Leu	Glu
				660					665					670			
50		Ile	Ala	Lys	Arg	Ala	Val	Asn	Thr	Leu	Phe	Thr	Asn	Thr	Lys	Asp	Gly
				675				680					685				
		Leu	Arg	Pro	Gly	Val	Thr	Asp	Tyr	Glu	Val	Asn	Gln	Ala	Ala	Asn	Leu
		690					695					700					
		Val	Glu	Cys	Leu	Ser	Asp	Asp	Leu	Tyr	Pro	Asn	Glu	Lys	Arg	Leu	Leu
55		705				710						715				720	
		Phe	Asp	Ala	Val	Lys	Glu	Ala	Lys	Arg	Leu	Ser	Gly	Val	Arg	Asn	Leu
					725						730					735	

EP 2 728 007 B1

	Leu	Gln	Asp	Ser	Asp	Phe	Gln	Glu	Ile	Asn	Gly	Glu	Asn	Gly	Trp	Thr
				740					745					750		
	Gly	Ser	Thr	Gly	Ser	Thr	Gly	Ile	Glu	Ile	Val	Glu	Gly	Asp	Ala	Leu
			755					760					765			
5	Phe	Lys	Gly	Arg	Tyr	Leu	Arg	Leu	Pro	Gly	Ala	Pro	Glu	Ile	Asp	Thr
		770					775					780				
	Glu	Thr	Tyr	Pro	Thr	Tyr	Leu	Tyr	Gln	Lys	Ile	Asp	Glu	Gly	Leu	Leu
		785				790					795					800
	Lys	Pro	Tyr	Thr	Arg	Tyr	Arg	Leu	Arg	Gly	Phe	Val	Gly	Ser	Ser	Gln
10					805					810					815	
	Gly	Leu	Glu	Ile	Tyr	Thr	Ile	Arg	His	Gln	Thr	Asn	Arg	Ile	Val	Lys
				820					825					830		
	Asn	Val	Pro	Asp	Asp	Leu	Leu	Pro	Asp	Val	Ser	Leu	Val	Ser	Ala	Gly
			835					840					845			
15	Asp	Gly	Ile	Asn	Arg	Cys	Ser	Glu	Gln	Lys	Tyr	Val	Asn	Ser	Arg	Leu
		850					855					860				
	Glu	Gly	Glu	Arg	Gly	Leu	Pro	Asn	Gly	Asn	Arg	Ser	Ala	Asp	Ala	His
		865				870					875					880
	Glu	Phe	Ser	Ile	Gln	Ile	Asp	Thr	Gly	Glu	Ile	Asp	Leu	Asn	Gly	Asn
				885						890					895	
20	Glu	Gly	Ile	Trp	Val	Gly	Phe	Lys	Val	Ala	Thr	Pro	Asp	Gly	Tyr	Ala
				900					905					910		
	Thr	Leu	Gly	Asn	Leu	Glu	Leu	Val	Glu	Glu	Gly	Pro	Leu	Ser	Gly	Asp
			915					920					925			
	Ala	Leu	Glu	Arg	Val	Gln	Arg	Glu	Glu	Gln	Gln	Trp	Lys	Ile	Arg	Met
25		930					935					940				
	Thr	Lys	Arg	Arg	Glu	Glu	Thr	Asp	Arg	Lys	Tyr	Thr	Ala	Ala	Lys	Gln
		945				950					955					960
	Ala	Val	Asp	Arg	Leu	Tyr	Ala	Asp	Tyr	Gln	Asp	Gln	Gln	Leu	Asn	Pro
				965					970						975	
30	Asn	Val	Glu	Ile	Thr	Asp	Ile	Thr	Ala	Ala	Gln	Asn	Leu	Ile	Gln	Ser
			980						985					990		
	Ile	Pro	Tyr	Val	Tyr	Asn	Asp	Val	Phe	Pro	Gly	Leu	Pro	Gly	Met	Asn
			995					1000					1005			
	Tyr	Ala	Lys	Tyr	Thr	Glu	Leu	Thr	Asn	Arg	Leu	Gln	Gln	Ala	Trp	Ser
		1010					1015					1020				
35	Leu	Tyr	Glu	Gln	Arg	Asn	Val	Ile	Pro	Asn	Gly	Asp	Phe	Arg	Asn	Glu
		1025				1030					1035					1040
	Leu	Asn	Asn	Trp	Asn	Thr	Thr	Ser	Gly	Val	Asn	Val	Gln	Gln	Ile	Asn
				1045						1050					1055	
	Asp	Arg	Ser	Val	Leu	Val	Ile	Pro	Asn	Trp	Asp	Glu	Gln	Val	Ser	Gln
				1060					1065					1070		
40	Gln	Phe	Thr	Val	Gln	Pro	Asn	Gln	Arg	Tyr	Val	Leu	Arg	Val	Thr	Ala
			1075					1080					1085			
	Arg	Lys	Glu	Gly	Val	Gly	Asn	Gly	Tyr	Val	Ser	Ile	Arg	Asp	Gly	Gly
		1090					1095					1100				
45	Asn	Gln	Thr	Glu	Thr	Leu	Thr	Phe	Ser	Ala	Asn	Glu	Tyr	Asp	Thr	Asn
		1105				1110					1115					1120
	Gly	Val	Tyr	Asn	Asp	Gln	Ile	Gly	Tyr	Ile	Thr	Lys	Thr	Val	Ala	Phe
				1125						1130					1135	
	Ile	Pro	Tyr	Thr	Asp	Gln	Val	Trp	Met	Asp	Ile	Ser	Glu	Thr	Glu	Gly
				1140					1145				1150			
50	Val	Leu	Tyr	Ile	Glu	Gly	Val	Lys	Leu	Val	Val	Asp	Val	Glu		
			1155					1160					1165			

<210> 45

<211> 1168

55 <212> PRT

<213> Bacillus thuringiensis

<400> 45

EP 2 728 007 B1

Met Lys Val Arg Leu Leu Met Asn Lys Asn Tyr Leu Ser Lys Ser Gln
1 5 10 15
Asp Leu Thr Gln Ile Ser Glu Ile Phe Gly Tyr Asp Pro Ile His Pro

5

10

15

20

25

30

35

40

45

50

55

EP 2 728 007 B1

				20				25				30				
	Leu	Val	Asn	Pro	Lys	Asn	His	Ile	Glu	Ser	Leu	Arg	Val	Asn	Arg	Asn
			35					40					45			
	Glu	Leu	Arg	Thr	Leu	Pro	Glu	Gly	Phe	Ala	Ser	Ser	Thr	Glu	Ser	Ala
5		50					55					60				
	Ile	Thr	Asn	Thr	Leu	Asn	Ile	Ile	Ser	Ile	Leu	Leu	Asp	Ala	Ser	Gly
	65					70					75					80
	His	Pro	Ala	Ala	Ala	Arg	Val	Leu	Gly	Val	Ile	Thr	Gly	Ile	Ile	Gly
					85					90					95	
	Ile	Leu	Trp	Pro	Gly	Gly	Ser	Gln	Lys	Thr	Trp	Glu	Glu	Phe	Met	Ala
10				100					105					110		
	Ala	Val	Glu	Ala	Leu	Ile	Asp	Glu	Lys	Ile	Thr	Glu	Ser	Phe	Lys	Asn
			115					120						125		
	Glu	Ala	Ile	Ser	Lys	Leu	Asn	Gly	Leu	Ala	Asp	Leu	Tyr	Thr	Val	Tyr
	130						135					140				
15	Leu	Ser	Glu	Leu	Glu	Leu	Trp	Leu	Glu	His	Pro	His	Asp	Pro	Ser	Ile
	145					150					155					160
	Ile	Gln	Ser	Val	Arg	Thr	Arg	Phe	Leu	Asp	Leu	Asp	Ser	Glu	Phe	Ile
				165					170						175	
	Ser	Ser	Met	Pro	Gln	Phe	Ala	Ile	Ser	Gly	Phe	Glu	Val	Ser	Phe	Leu
				180					185					190		
20	Pro	Val	Tyr	Ala	Gln	Ala	Ala	Asn	Leu	His	Leu	Leu	Leu	Leu	Arg	Asp
			195					200						205		
	Leu	Ser	Tyr	Tyr	Gly	Asn	Asp	Trp	Gly	Leu	Gln	Gln	Pro	Glu	Ile	Glu
	210					215						220				
	Asn	Tyr	Tyr	Asn	Arg	Gln	Ile	Asn	Asn	Ile	Gln	Lys	Tyr	Thr	Asp	His
	225					230					235					240
25	Cys	Val	Lys	Trp	Tyr	Gln	Leu	Gly	Leu	Gln	Asp	Val	Tyr	Asn	Lys	Tyr
				245					250						255	
	Asn	Ser	Thr	Ile	Asn	Glu	Asp	Gly	Gly	Leu	Pro	Trp	Thr	His	Tyr	
			260					265					270			
	Asn	Arg	Tyr	Arg	Arg	Glu	Met	Thr	Ile	Leu	Val	Leu	Asp	Leu	Val	Ala
			275					280					285			
30	Thr	Phe	Ser	Thr	Asn	Asp	Trp	Lys	Lys	Tyr	Tyr	Leu	Glu	Thr	Asn	Val
	290					295						300				
	Glu	Leu	Ser	Arg	Glu	Ile	Tyr	Thr	Asp	Pro	Leu	Gly	Tyr	Glu	Asp	Ser
	305					310					315					320
	Asp	Glu	Gly	Asn	Ile	Thr	Asp	Val	Asp	Trp	Tyr	Ser	Glu	Gly	Val	Ser
				325					330						335	
35	Phe	Ser	Thr	Ile	Glu	Asn	Leu	His	Ser	Pro	Lys	Leu	Val	Glu	Trp	Leu
				340					345					350		
	Lys	Arg	Ile	Thr	Ile	Gln	Thr	Asp	Tyr	Phe	Ser	Ala	Gly	Ser	Asp	Glu
			355					360					365			
	Ser	Tyr	Cys	Trp	Ala	Gly	His	Tyr	Ile	Tyr	Thr	Thr	Phe	Thr	Asp	Ser
	370					375						380				
40	Asp	Lys	Glu	Tyr	Ser	Arg	Tyr	Tyr	Gly	Asn	Pro	Glu	Asn	Val	Glu	Ser
	385					390					395					400
	Thr	Thr	Ser	Tyr	Thr	Phe	Ala	Pro	Ala	Glu	Val	Tyr	Lys	Val	Glu	Ser
				405						410					415	
	Val	Val	Gly	Ser	Glu	Arg	Asn	Ala	Thr	Tyr	Asp	Asn	Tyr	Val	Asn	Ser
				420					425					430		
45	Ala	Asn	Thr	Phe	Tyr	Gln	Val	Thr	Pro	Thr	Asn	Glu	Leu	Lys	Lys	Phe
			435					440					445			
	Ile	Tyr	Ser	Tyr	Arg	Asn	Asp	Tyr	Asp	Lys	Lys	Thr	Leu	Tyr	Ser	Asp
	450					455						460				
	Asp	Gln	Leu	Pro	Leu	Glu	Thr	Asp	Pro	Pro	Lys	Tyr	Gly	Glu	Tyr	Ser
	465					470					475					480
50	His	Arg	Leu	Ser	Asn	Ile	Thr	Cys	Ala	Pro	Leu	Asn	Ser	Asp	Asp	Phe
				485					490						495	
	Gly	Leu	Val	Pro	Ile	Leu	Gly	Trp	Thr	His	Thr	Ser	Leu	Lys	Arg	Glu
				500					505					510		
	Asn	Ile	Ile	Tyr	Pro	Asp	Lys	Ile	Thr	Gln	Ile	Pro	Ala	Val	Lys	Ser
			515					520					525			
55	Phe	Ser	Thr	Glu	Gly	Thr	Trp	Glu	Arg	Val	Ala	Ala	Gly	Pro	Gly	Phe
	530						535					540				

EP 2 728 007 B1

	Thr	Gly	Gly	Asn	Val	Thr	Gln	Ala	Thr	Asn	Thr	Val	Thr	Ser	Gly	Ile
	545					550					555					560
	Lys	Thr	Thr	Asp	Leu	Val	Lys	Ile	Arg	Val	Arg	Ile	Asp	Ser	Thr	Ala
					565					570						575
5	Ser	Ser	Lys	Gln	Tyr	Arg	Val	Arg	Leu	Arg	Tyr	Ala	Ser	Asn	Gln	Asp
				580					585					590		
	Phe	Ser	His	Ala	His	Phe	Tyr	Thr	Gly	Thr	Gly	Ser	Asn	Glu	Thr	Thr
			595					600					605			
	Phe	Ser	Leu	Lys	Lys	Thr	Thr	Asp	Phe	Pro	Phe	Ala	Asn	Tyr	Asn	Ser
		610					615					620				
10	Phe	Gly	Tyr	Val	Glu	Ile	Pro	Arg	Val	Leu	Lys	Phe	Ser	Ser	Gly	Ser
						630						635				640
	Glu	Ile	Ile	Asn	Val	Tyr	Val	Tyr	Pro	Glu	Asn	Gly	Leu	Lys	Val	Gln
					645					650					655	
	Val	Asp	Lys	Ile	Glu	Phe	Ile	Pro	Val	Asp	Asp	Asn	Tyr	Glu	Asp	Arg
				660					665					670		
15	Val	Thr	Leu	Glu	Lys	Ala	Gln	Lys	Ala	Val	Asn	Thr	Leu	Phe	Thr	Val
			675					680					685			
	Gly	Arg	Asn	Ala	Leu	Gln	Thr	Asp	Val	Thr	Asp	Tyr	Lys	Val	Asp	Gln
		690					695					700				
	Val	Ser	Ile	Leu	Val	Asp	Cys	Val	Ser	Glu	Glu	Leu	Tyr	Pro	Asn	Glu
		705				710					715					720
20	Lys	Lys	Glu	Leu	Gln	Asn	Leu	Val	Lys	Tyr	Ala	Lys	Arg	Leu	Ser	Ile
					725					730					735	
	Ser	Arg	Asn	Leu	Leu	Leu	Asp	Pro	Asn	Phe	Thr	Ser	Ile	Asn	Ala	Pro
				740					745					750		
	Lys	Ile	Arg	Gly	Trp	His	Gly	Ser	Gln	Gly	Ile	Phe	Val	Gly	Asn	Gly
		755					760						765			
25	Asn	Tyr	Ile	Phe	Lys	Gly	Pro	Tyr	Val	His	Leu	Gln	Gly	Thr	Asn	Asp
		770					775					780				
	Ala	Gln	Tyr	Pro	Thr	Tyr	Leu	Tyr	Gln	Lys	Ile	Asp	Glu	Ser	Lys	Leu
		785				790					795					800
	Lys	Glu	Tyr	Ile	Arg	Tyr	Lys	Leu	Arg	Gly	Phe	Ile	Glu	Ser	Ser	Gln
				805						810					815	
30	Asp	Leu	Glu	Val	Tyr	Val	Ile	Arg	Tyr	Asp	Val	Lys	Arg	Glu	Thr	Leu
				820					825					830		
	Asp	Val	Ser	Asn	Asn	Leu	Ser	Ser	Asp	Asp	Thr	Pro	Ala	Asn	Ala	Cys
			835					840					845			
	Gly	Gly	Pro	Asn	Arg	Cys	Ile	Glu	Gln	Gln	Tyr	Leu	Asp	Asp	Asn	Pro
		850					855					860				
35	Thr	Leu	Glu	Cys	Ser	Ser	Ile	Gln	Asp	Gly	Ile	Leu	Phe	Asp	Ser	His
		865				870					875					880
	Ser	Phe	Ser	Leu	Asn	Ile	Asp	Thr	Gly	Ser	Ile	Asp	Tyr	Asn	Glu	Asn
				885						890					895	
	Val	Gly	Ile	Trp	Val	Val	Phe	Lys	Ile	Ser	Thr	Leu	Glu	Gly	Tyr	Ala
				900					905					910		
40	Lys	Leu	Gly	Asn	Val	Glu	Val	Ile	Glu	Asp	Gly	Pro	Leu	Val	Gly	Glu
		915						920					925			
	Ala	Leu	Ala	Arg	Val	Lys	Arg	Gln	Glu	Thr	Lys	Trp	Arg	Asn	Lys	Leu
		930					935						940			
	Ala	Gln	Leu	Arg	Thr	Glu	Thr	Gln	Ala	Ile	Tyr	Thr	Arg	Ala	Lys	Gln
		945				950					955					960
45	Ser	Leu	Asp	Asn	Leu	Phe	Ile	Asp	Ala	Gln	Asp	Ala	His	Leu	Lys	Ile
				965						970					975	
	Gly	Thr	Pro	Phe	Ala	Ala	Ile	Val	Ala	Ala	Arg	Glu	Ala	Val	Gln	Ser
			980						985					990		
	Ile	Arg	Glu	Val	Tyr	Met	Pro	Trp	Leu	Ser	Val	Val	Ala	Gly	Val	Asn
		995						1000						1005		
50	Tyr	Pro	Ile	Phe	Thr	Glu	Leu	Asn	Leu	Arg	Val	Arg	Arg	Ala	Leu	Gln
		1010					1015					1020				
	Leu	Tyr	Asp	Leu	Arg	Asn	Val	Val	Arg	Asn	Gly	Arg	Phe	Arg	Asn	Gly
		1025				1030					1035					1040
55	Leu	Ser	Asn	Trp	Asn	Val	Thr	Ser	Asp	Val	Glu	Val	Gln	Glu	Glu	Asn
				1045						1050					1055	
	Gly	Asn	Asn	Val	Leu	Val	Leu	Ser	Asn	Trp	Asp	Ala	Gln	Val	Leu	Gln

EP 2 728 007 B1

					1060					1065					1070		
	Cys	Ile	Lys	Leu	Tyr	Gln	Asp	Arg	Gly	Tyr	Ile	Leu	Arg	Val	Thr	Ala	
5	Arg	Lys	Glu	Gly	Leu	Gly	Glu	Gly	Tyr	Ile	Thr	Ile	Thr	Asp	Glu	Glu	
	Gly	Asn	Thr	Asp	Gln	Leu	Thr	Phe	Gly	Ser	Cys	Glu	Glu	Ile	Asp	Ala	
	Ser	Asn	Ser	Phe	Val	Ser	Thr	Gly	Tyr	Met	Thr	Lys	Glu	Leu	Glu	Phe	
10	Phe	Pro	Asp	Thr	Glu	Lys	Val	Arg	Ile	Glu	Ile	Gly	Glu	Thr	Glu	Gly	
	Thr	Phe	Lys	Val	Glu	Ser	Val	Glu	Leu	Phe	Leu	Met	Glu	Asp	Leu	Cys	

15 <210> 46
 <211> 1134
 <212> PRT
 <213> Bacillus thuringiensis

20 <400> 46

25

30

35

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

	Tyr	Phe	Trp	Thr	Ala	His	Lys	Gly	Lys	Tyr	Lys	Leu	Ser	Ala	Ser	Thr
			355					360					365			
	Asp	Val	His	Asp	Thr	Ala	Leu	Tyr	Gly	Ser	Thr	Ser	Gly	Ser	Ile	Ser
		370					375					380				
5	Glu	Lys	Asn	Tyr	Ser	Phe	Asn	Gly	Asn	Asn	Ile	Tyr	Gln	Thr	Leu	Ala
		385				390					395					400
	Ala	Pro	Ser	Ala	Val	Phe	Thr	Thr	Ser	Lys	Gln	Tyr	Tyr	Gly	Ile	Glu
					405					410					415	
	Gln	Val	Glu	Phe	Tyr	Gly	Asp	Lys	Gly	Lys	Ile	His	Tyr	Tyr	Gly	Asp
				420					425					430		
10	Arg	Lys	Tyr	Pro	Leu	Ser	Val	Asp	Ser	Ala	Asn	Gln	Leu	Pro	Pro	Asp
			435					440					445			
	Glu	Glu	Pro	Ile	Ser	Glu	Asn	Tyr	Asp	His	Ile	Leu	Thr	His	Ala	Ser
		450					455					460				
	Ala	Val	Asn	Val	Leu	Asp	Gly	Gly	Thr	Val	Pro	Ile	Phe	Ala	Trp	Thr
		465				470					475					480
15	His	Arg	Ser	Ala	Asp	Tyr	Tyr	Asn	Thr	Ile	Tyr	Ser	Asp	Lys	Ile	Thr
					485					490					495	
	Gln	Ile	Pro	Ala	Val	Lys	Ile	Asn	Lys	Leu	Glu	Asn	Pro	Ser	Thr	Val
				500					505					510		
	Val	Lys	Gly	Pro	Gly	Phe	Thr	Gly	Gly	Asp	Leu	Val	Lys	Arg	Gly	Ser
			515					520					525			
20	Thr	Gly	Ile	Leu	Gly	Tyr	Leu	Asn	Val	Thr	Val	Asn	Ser	Pro	Leu	Ser
		530					535						540			
	Gln	Arg	Tyr	Ala	Val	Lys	Ile	Arg	Tyr	Ala	Ser	Thr	Ile	Ser	Gly	Asp
		545				550					555					560
	Phe	His	Val	Gln	Ile	Asp	Gly	Val	Ala	Thr	Leu	Glu	Gly	His	Cys	Glu
					565					570					575	
25	Ser	Thr	Ile	Asn	Ser	Gly	Asp	Glu	Leu	Ser	Phe	Glu	Ser	Phe	Ser	Tyr
				580					585					590		
	Lys	Glu	Phe	Ser	Thr	Thr	Val	Gln	Phe	Thr	Gly	Asn	Lys	Pro	Arg	Leu
			595					600					605			
	Arg	Leu	Ser	Leu	Asp	Lys	Val	Ala	Gly	Thr	Gly	Val	Phe	Tyr	Phe	Asp
		610					615					620				
30	Lys	Ile	Glu	Phe	Ile	Pro	Val	Asp	Val	Asn	Tyr	Asp	Glu	Arg	Val	Gln
		625				630						635				640
	Leu	Glu	Lys	Ala	Gln	Lys	Ser	Val	Asn	Ala	Leu	Phe	Thr	Ala	Gly	Arg
					645					650					655	
	His	Ala	Leu	Gln	Thr	Asp	Val	Thr	Asp	Phe	Lys	Val	Asp	Gln	Val	Ser
				660					665					670		
35	Ile	Leu	Val	Asp	Cys	Val	Ser	Gly	Glu	Leu	Tyr	Pro	Asn	Glu	Lys	Arg
			675					680					685			
	Glu	Leu	Leu	Ser	Leu	Val	Lys	Tyr	Ala	Lys	Arg	Leu	Ser	Tyr	Ser	Arg
		690					695					700				
40	Asn	Leu	Leu	Leu	Asp	Pro	Thr	Phe	Asp	Ser	Ile	Asn	Ser	Ser	Glu	Glu
		705				710						715				720
	Asn	Gly	Trp	His	Gly	Ser	Asn	Gly	Ile	Val	Ile	Gly	Asn	Gly	Asn	Phe
					725					730					735	
	Val	Phe	Lys	Gly	Asn	Tyr	Leu	Ile	Phe	Ser	Gly	Thr	Asn	Asp	Thr	Gln
				740					745					750		
45	Tyr	Pro	Thr	Tyr	Leu	Tyr	Gln	Lys	Ile	Asp	Glu	Ser	Lys	Leu	Lys	Glu
			755					760					765			
	Tyr	Thr	Arg	Tyr	Lys	Leu	Arg	Gly	Phe	Ile	Glu	Asn	Ser	Gln	Asp	Leu
		770					775						780			
	Glu	Ala	Tyr	Val	Val	Arg	Tyr	Asp	Ala	Lys	His	Glu	Thr	Leu	Asp	Val
						790					795					800
50	Ser	Asp	Asn	Leu	Tyr	Pro	Asp	Ile	Ser	Pro	Val	Asn	Ala	Cys	Gly	Glu
					805					810					815	
	Pro	Asn	Arg	Cys	Ala	Ala	Leu	Pro	Tyr	Leu	Asp	Glu	Asn	Pro	Arg	Leu
				820					825					830		
	Glu	Cys	Ser	Ser	Ile	Gln	Asp	Gly	Ile	Leu	Ser	Asp	Ser	His	Ser	Phe
			835					840					845			
55	Ser	Leu	Asn	Ile	Asp	Thr	Gly	Ser	Ile	Asp	Ser	Asn	Glu	Asn	Val	Gly
		850					855					860				
	Ile	Trp	Val	Leu	Phe	Lys	Ile	Ser	Thr	Pro	Glu	Gly	Tyr	Ala	Lys	Phe

EP 2 728 007 B1

	865		870		875		880
	Gly Asn Leu Glu Val	Ile Glu Asp Gly Pro Val Ile Gly Glu Ala Leu					
		885		890			895
5	Ala Arg Val Lys Arg	Gln Glu Thr Lys Trp Arg Asn Lys Leu Ala Gln					
		900		905			910
	Leu Arg Thr Glu Thr	Gln Ala Ile Tyr Thr Arg Ala Lys Gln Ala Ile					
		915		920			925
	Asp Asn Leu Phe Thr	Asn Ala Gln Asp Ser His Leu Lys Ile Gly Ala					
		930		935			940
10	Thr Phe Ala Ser Ile	Val Ala Ala Arg Lys Ile Val Gln Ser Ile Arg					
		945		950			955
	Glu Ala Tyr Met Ser	Trp Leu Ser Ile Val Pro Gly Val Asn Tyr Pro					
		965		970			975
	Ile Phe Thr Glu Leu	Asn Glu Arg Val Gln Gln Ala Phe Gln Leu Tyr					
		980		985			990
15	Asp Val Arg Asn Val	Val Arg Asn Gly Arg Phe Leu Asn Gly Val Ser					
		995		1000			1005
	Asp Trp Ile Val Thr	Ser Asp Val Lys Val Gln Glu Asn Gly Asn					
		1010		1015			1020
	Asn Val Leu Val Leu	Ser Asn Trp Asp Ala Gln Val Leu Gln Cys Leu					
20		1025		1030			1035
	Lys Leu Tyr Gln Asp	Arg Gly Tyr Ile Leu Arg Val Thr Ala Arg Lys					
		1045		1050			1055
	Glu Gly Leu Gly Glu	Gly Tyr Ile Thr Ile Thr Asp Glu Ala Gly His					
		1060		1065			1070
25	Thr Asp Gln Leu Thr	Phe Gly Thr Cys Glu Glu Ile Asp Ala Ser Asn					
		1075		1080			1085
	Thr Phe Val Ser Thr	Gly Tyr Met Thr Lys Glu Leu Glu Phe Phe Pro					
		1090		1095			1100
	Asp Thr Glu Lys Val	Arg Ile Glu Ile Gly Glu Thr Glu Gly Ile Phe					
		1105		1110			1115
30	Gln Val Glu Ser Val	Glu Leu Phe Leu Met Glu Asp Leu Cys					
		1125		1130			

<210> 47

<211> 1144

35 <212> PRT

<213> Bacillus thuringiensis

<400> 47

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

	Ala	Ala	Asn	Leu	His	Leu	Val	Leu	Leu	Arg	Asp	Ala	Thr	Leu	Phe	Gly
			195					200					205			
	Ala	Gly	Trp	Gly	Phe	Thr	Glu	Thr	Asn	Ile	Asn	Asp	Arg	Tyr	Asn	Glu
		210					215					220				
5	Gln	Val	Arg	Val	Thr	Asn	Gly	Tyr	Ile	Asp	His	Cys	Thr	Lys	Trp	Tyr
	225					230					235					240
	Asn	Glu	Gly	Leu	Thr	Arg	Leu	Lys	Asn	Asn	Trp	Ser	Lys	Tyr	His	Gln
					245					250					255	
	Phe	Arg	Arg	Glu	Met	Thr	Leu	Met	Val	Leu	Asp	Leu	Ile	Ala	Leu	Phe
				260					265					270		
10	Pro	Ser	His	Asp	Ala	Arg	Arg	Tyr	Pro	Met	Glu	Thr	Ser	Ala	Gln	Leu
			275					280					285			
	Thr	Arg	Asp	Val	Tyr	Thr	Asp	Pro	Ile	Gly	Tyr	Arg	Gly	Asn	Ala	Asn
		290					295					300				
	Phe	Ser	Asp	Pro	Trp	Thr	Asn	His	Val	Ser	Phe	Ser	Lys	Ala	Glu	Ser
	305					310					315					320
15	Glu	Thr	Ile	Arg	Pro	His	Leu	Phe	Asp	Thr	Leu	Glu	Ser	Val	Glu	
					325				330					335		
	Ile	Asn	Thr	Ala	Lys	Ala	Met	Leu	Pro	Leu	Asn	Asp	Lys	Ser	Tyr	Met
				340					345					350		
	Tyr	Tyr	Trp	Ala	Gly	His	Thr	Val	Thr	Ser	Arg	Leu	Leu	Asp	Ser	Ser
			355					360					365			
20	Gly	Asn	Pro	Leu	Lys	Tyr	Thr	Tyr	Gly	Ser	Met	Thr	Ser	Glu	Lys	Asn
		370					375					380				
	Leu	Val	Ser	Leu	Pro	Gly	Lys	Asp	Val	Tyr	Arg	Ile	Asn	Ser	Val	Ala
	385					390					395					400
	Ser	Gly	Phe	Ser	Asn	Tyr	Tyr	Ala	Lys	Leu	Tyr	Gly	Val	Ser	Lys	Val
					405					410					415	
25	Asp	Phe	Ser	Ile	Val	Asp	Arg	Asn	Asn	Ser	Asn	Lys	Thr	Thr	Tyr	Ser
				420				425						430		
	Tyr	Ser	Lys	Ser	Ser	Thr	Val	Pro	Ser	Asp	Asn	Lys	Glu	Asn	Arg	Asp
			435					440					445			
	Ser	Glu	Asn	Glu	Leu	Pro	Gln	Thr	Thr	Thr	Asp	Gln	Pro	Asp	Tyr	Lys
		450					455					460				
30	Gly	Tyr	Ser	His	Arg	Leu	Ser	His	Ile	Thr	Phe	Ile	Ser	Ser	Ala	Ile
	465					470					475					480
	Pro	Thr	Tyr	Val	Trp	Thr	Arg	Lys	Ser	Ala	Asp	Leu	Thr	Asn	Thr	Ile
					485					490					495	
	Tyr	Pro	Asp	Lys	Ile	Thr	Gln	Ile	Pro	Ala	Val	Lys	Met	Tyr	Glu	Leu
				500					505					510		
35	Gly	Ser	Ser	Ala	Val	Val	Val	Lys	Gly	Pro	Gly	Phe	Thr	Gly	Gly	Asp
		515						520					525			
	Leu	Val	Lys	Arg	Thr	Asn	Asn	Gly	Ser	Leu	Gly	Arg	Phe	Lys	Ile	Thr
		530				535						540				
	Ile	Asp	Ser	Pro	Gly	Ala	His	Arg	Tyr	Arg	Leu	Arg	Val	Arg	Tyr	His
40		545				550					555					560
	Ser	Asp	Val	Ser	Gly	Val	Phe	His	Met	Gln	Ile	Asn	Asn	Val	Glu	Thr
					565					570					575	
	Ile	Gln	Gly	Glu	Phe	Lys	Ser	Thr	Val	Asp	Ser	Thr	Ser	Thr	Met	Ser
				580				585						590		
45	Asn	Asp	Ser	Phe	Gln	Leu	Arg	Glu	Phe	Thr	Thr	Thr	Phe	Arg	Phe	Pro
		595						600					605			
	Ser	Asn	Val	Thr	Asp	Ile	Lys	Val	Ser	Leu	Gly	Ala	Ile	Asn	Gly	Gln
		610					615					620				
	Gly	Asn	Phe	Tyr	Leu	Asp	Arg	Ile	Glu	Phe	Ala	Pro	Val	Asp	Thr	Asn
		625				630					635					640
50	Tyr	Asp	Glu	Arg	Ile	Thr	Leu	Glu	Lys	Ala	Gln	Lys	Ala	Val	Asn	Ala
					645					650					655	
	Leu	Phe	Thr	Glu	Gly	Arg	Asn	Ala	Leu	Gln	Thr	Asp	Met	Thr	Asp	Tyr
				660					665					670		
	Lys	Val	Asp	Gln	Val	Ser	Ile	Leu	Val	Asp	Cys	Val	Ser	Gly	Glu	Val
			675					680					685			
55	Tyr	Pro	Asn	Glu	Lys	Arg	Glu	Leu	Leu	Asn	Leu	Val	Lys	Tyr	Ala	Lys
		690					695					700				
	Arg	Leu	Ser	Ile	Ala	Arg	Asn	Leu	Leu	Val	Asp	Pro	Asn	Phe	Thr	Ser

EP 2 728 007 B1

	705				710					715				720
	Ile	His	Ala	Ser	Met	Tyr	Ser	Glu	Asp	Val	Lys	Gly	Trp	Tyr
					725					730				Gly
5	Asn	Gly	Ile	Ala	Thr	Gly	Ser	Gly	Asp	Val	Val	Leu	Lys	Glu
				740					745					750
	Val	Ser	Leu	Pro	Ser	Thr	Ser	Asp	Ala	Gln	Tyr	Pro	Thr	Tyr
			755					760					765	Leu
	Gln	Lys	Ile	Asp	Glu	Ser	Lys	Leu	Lys	Ala	Tyr	Thr	Arg	Tyr
		770					775					780		Lys
10	Arg	Gly	Phe	Ile	Glu	Asn	Ser	Gln	Asp	Leu	Glu	Ala	Tyr	Val
	785					790					795			Val
	Tyr	Asp	Ala	Lys	His	Glu	Thr	Leu	Asp	Val	Ser	Asn	Asn	Leu
				805						810				Leu
	Asp	Val	Leu	Pro	Val	Asn	Ala	Cys	Gly	Glu	Pro	Asp	Arg	Cys
			820						825					Ala
15	Leu	Gln	Tyr	Leu	Asp	Glu	Asn	Pro	Arg	Leu	Glu	Cys	Ser	Ser
		835						840					845	Ile
	Asp	Gly	Ile	Leu	Ser	Asp	Ser	His	Ser	Phe	Ser	Leu	Asn	Ile
		850				855						860		Asp
20	Gly	Ser	Met	Asp	Leu	Asn	Glu	Asn	Leu	Gly	Ile	Trp	Val	Leu
	865					870					875			Phe
	Ile	Ser	Thr	Pro	Glu	Gly	Tyr	Ala	Lys	Phe	Gly	Asn	Leu	Glu
				885						890				Val
	Glu	Asp	Gly	Thr	Val	Ser	Gly	Glu	Ala	Leu	Ala	Arg	Val	Lys
			900					905					910	Arg
25	Glu	Thr	Lys	Trp	Arg	Asn	Lys	Leu	Ala	Gln	Leu	Arg	Thr	Glu
		915						920					925	Thr
	Ala	Ile	Tyr	Thr	Arg	Ala	Lys	Gln	Ala	Leu	Asp	Asn	Leu	Phe
		930				935					940			Thr
	Ala	Gln	Asp	Ser	Tyr	Leu	Lys	Ile	Gly	Ala	Thr	Phe	Ala	Ala
	945					950				955				Ile
30	Ala	Ala	Arg	Lys	Ile	Val	Gln	Ser	Ile	Arg	Glu	Ala	Tyr	Met
				965						970				Ser
	Leu	Ser	Val	Val	Pro	Gly	Val	Asn	Tyr	Pro	Ile	Phe	Thr	Glu
			980					985						Leu
	Glu	Arg	Val	Gln	Arg	Ala	Phe	Gln	Leu	Tyr	Asp	Gly	Arg	Asn
35		995						1000					1005	Val
	Arg	Asn	Gly	Arg	Phe	Leu	Asn	Gly	Val	Leu	Asp	Trp	Ile	Val
		1010				1015						1020		Thr
	Asp	Val	Ser	Val	Gln	Glu	Glu	Asn	Gly	Asn	Asn	Val	Leu	Val
	1025					1030				1035				Leu
40	Asn	Trp	Asp	Ala	Gln	Val	Leu	Gln	Cys	Leu	Lys	Leu	Tyr	Gln
				1045						1050				Asp
	Gly	Tyr	Ile	Leu	Arg	Val	Thr	Ala	Arg	Lys	Glu	Gly	Leu	Gly
			1060						1065				1070	Glu
	Tyr	Ile	Thr	Ile	Thr	Asp	Glu	Glu	Gly	Asn	Thr	Asp	Gln	Leu
		1075				1080						1085		Thr
45	Gly	Ser	Cys	Glu	Glu	Ile	Asp	Thr	Ser	Asn	Ser	Phe	Val	Ser
		1090				1095					1100			Thr
	Tyr	Met	Thr	Lys	Glu	Leu	Glu	Phe	Phe	Pro	Asp	Thr	Glu	Lys
	1105					1110				1115				Val
	Ile	Glu	Ile	Glu	Glu	Thr	Glu	Gly	Thr	Phe	Lys	Val	Glu	Ser
50				1125						1130				Val
	Leu	Phe	Leu	Met	Glu	Asp	Leu	Cys						Glu
				1140										

<210> 48

<211> 1196

<212> PRT

<213> Bacillus thuringiensis

EP 2 728 007 B1

<400> 48

5	Met	Ser	Pro	Asn	Asn	Gln	Asn	Glu	Tyr	Glu	Ile	Ile	Asp	Thr	Pro	Ser
	1				5					10					15	
10																
15																
20																
25																
30																
35																
40																
45																
50																
55																

EP 2 728 007 B1

	Ser	Asn	Ser	Leu	Asp	Asn	Gln	Phe	Val	Arg	Tyr	Pro	Leu	Ala	Lys	Glu
			20					25						30		
	Pro	Thr	Gln	Val	Arg	Gln	Asn	Leu	Asn	Tyr	Lys	Asp	Trp	Leu	Asn	Ser
			35					40					45			
5	Leu	Asp	Glu	Asn	Asn	Asn	Gln	Ser	Phe	Gly	Val	Thr	Pro	Arg	Arg	Ala
		50					55					60				
	Ser	Val	Val	Gly	Ala	Val	Gly	Ser	Ile	Leu	Gly	Ala	Thr	Leu	Gly	Thr
	65					70					75				80	
	Ile	Pro	Tyr	Val	Gly	Asp	Ile	Leu	Ala	Leu	Ile	Val	Gly	Ile	Phe	Trp
				85						90					95	
10	Pro	Glu	Gly	Ser	Asp	Pro	Glu	Asp	Tyr	Ser	Glu	Leu	Ile	Asn	Ala	Ile
				100					105					110		
	Met	Glu	Gln	Val	Glu	Leu	Leu	Ile	Asp	Gln	Lys	Ile	Ser	Glu	Gln	Val
			115					120					125			
	Arg	Asn	Asp	Ala	Leu	Ala	Thr	Leu	Glu	Ser	Ser	Gly	Ile	Ala	Leu	Gln
		130					135					140				
15	Ala	Tyr	Leu	Asn	Ala	Leu	Glu	Asp	Trp	Lys	Ile	Asn	Pro	Asn	Asn	Ala
	145					150					155					160
	Arg	Ser	Thr	Gln	Leu	Val	Arg	Glu	Arg	Phe	Thr	Phe	Ala	Glu	Ala	Gln
				165						170					175	
	Val	Arg	Thr	Asn	Ile	Ala	Tyr	Val	Ser	Arg	Lys	Asp	Tyr	Glu	Ile	Leu
				180					185					190		
20	Leu	Leu	Pro	Ile	Tyr	Ala	Gln	Val	Ala	Asn	Ile	His	Leu	Leu	Leu	Leu
			195					200					205			
	Lys	Gln	Val	Gln	Leu	Tyr	Gly	Thr	Lys	Leu	Gly	Tyr	Thr	Gln	Asn	Asp
		210					215					220				
	Ile	Asp	Leu	Ile	Tyr	Glu	Glu	Gln	Lys	Lys	Phe	Thr	Ala	Gln	Tyr	Thr
	225					230					235					240
25	Asn	His	Cys	Thr	Asn	Trp	Tyr	Asn	Ile	Gly	Leu	Asn	Asn	Ile	Trp	Glu
				245						250					255	
	Ser	Ile	Ala	Gly	Thr	Ser	Tyr	Ser	Gly	Ser	Arg	Trp	Asp	Glu	Phe	Asn
			260						265					270		
	Asp	Phe	Arg	Arg	Asp	Leu	Thr	Leu	Thr	Val	Leu	Asp	Ile	Val	Ser	Thr
			275					280					285			
30	Phe	Pro	Ile	His	Asp	Thr	Arg	Leu	Tyr	Pro	Glu	Lys	Val	Asn	Gly	Gln
		290					295					300				
	Leu	Thr	Arg	Glu	Ile	Tyr	Thr	Arg	Ser	Ile	Asn	Val	Asn	Tyr	Phe	Asn
						310					315					320
	Gln	Val	Ser	Ala	Arg	Thr	Ile	Glu	Asp	Ala	Glu	Arg	Leu	Leu	Thr	Asn
				325						330					335	
35	Pro	Pro	Arg	Leu	Leu	Pro	Trp	Ile	Glu	Gln	Leu	Glu	Phe	Asn	Thr	Asn
				340					345					350		
	Val	Asn	Phe	Ser	Val	Asn	Trp	Lys	Phe	Leu	Thr	Ser	Thr	Arg	Arg	Arg
			355					360					365			
	Phe	Ile	Tyr	Thr	Asn	Ser	Ser	Asp	Leu	Asn	Tyr	Asp	Gly	Tyr	Ala	Gly
		370					375					380				
40	Tyr	His	Leu	Asp	Gly	Thr	Ser	Asn	Ser	Phe	Leu	Tyr	Pro	Ser	Asn	Asn
		385				390					395					400
	Glu	Arg	Ile	Tyr	Thr	Ile	Thr	Ala	Gln	Arg	Phe	Gly	Glu	Gln	Arg	Asn
					405					410					415	
	Ile	Pro	Gln	Ala	Ile	Thr	Gly	Leu	Thr	Phe	Ser	Met	Asn	Thr	Gly	Arg
				420					425					430		
45	Thr	Tyr	Arg	Tyr	Ser	Ser	Asn	Thr	Pro	Ala	Gly	Pro	Ser	Ile	Ile	Thr
			435					440					445			
	Glu	Asp	Tyr	His	Leu	Pro	Gly	Leu	Asn	Gly	Glu	Glu	Val	Pro	Asn	Ser
		450					455					460				
	Asn	Asn	Phe	Ser	His	Phe	Leu	Arg	Ser	Ile	Asn	Gly	Tyr	Ser	Asn	Gly
		465				470					475					480
	Asn	Gln	Arg	Ile	Phe	His	Ser	Phe	Gly	Trp	Thr	His	Ala	Ser	Val	Asp
					485					490					495	
	Phe	Glu	Asn	Lys	Ile	Tyr	Pro	Thr	Ile	Ile	Thr	Gln	Ile	Pro	Ala	Val
				500					505					510		
55	Lys	Ala	Ile	Gln	Gly	Thr	Met	Pro	Tyr	Pro	Val	Val	Lys	Gly	Pro	Gly
		515					520						525			
	Phe	Thr	Gly	Gly	Asp	Ile	Ala	Arg	Leu	Pro	Asn	Asn	Pro	Thr	Leu	Gly

EP 2 728 007 B1

					530													535																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																		</
--	--	--	--	--	-----	--	--	--	--	--	--	--	--	--	--	--	--	-----	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	----

EP 2 728 007 B1

	Ser	Gln	Val	Ser	Gln	Gln	Ile	Thr	Val	Gln	Pro	Asn	Arg	Arg	Tyr	Val
				1060					1065					1070		
	Leu	Arg	Val	Thr	Ala	Arg	Lys	Glu	Gly	Ser	Gly	Asp	Gly	Tyr	Val	Thr
			1075					1080					1085			
5	Ile	Arg	Asp	Gly	Ala	Lys	Tyr	Thr	Glu	Thr	Leu	Thr	Phe	Asn	Thr	Cys
			1090				1095					1100				
	Asp	Tyr	Asn	Gly	Ser	Asn	Val	Tyr	Gln	Glu	Gln	Ala	Leu	Tyr	Thr	Asn
	1105					1110					1115					1120
	Asp	Val	Tyr	Asn	Thr	Gln	Ser	Ala	Asn	Ile	His	Gly	Ser	Asn	Ser	Ala
					1125					1130					1135	
10	Tyr	His	Thr	Gln	Ala	Ser	Asn	Thr	Asp	Arg	Tyr	Asn	Met	Asn	Gly	Met
				1140					1145					1150		
	Tyr	Asn	Asp	Gln	Thr	Ser	Tyr	Val	Thr	Lys	Thr	Val	Glu	Phe	Ile	Pro
			1155					1160					1165			
	Asn	Thr	Glu	Gln	Val	Trp	Ile	Glu	Met	Ser	Glu	Thr	Glu	Gly	Val	Phe
		1170				1175					1180					
15	Tyr	Ile	Glu	Ser	Val	Glu	Leu	Ile	Val	Glu	Glu	Asn				
	1185					1190					1195					

20

<210> 49
<211> 1226
<212> PRT
<213> Bacillus thuringiensis

<400> 49

EP 2 728 007 B1

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

EP 2 728 007 B1

5																
10																
15																
20																
25																
30																
35																
40																
45																
50																
55																

EP 2 728 007 B1

	Ser	Ser	Gln	Asp	Leu	Glu	Ile	Tyr	Val	Leu	Arg	His	Gln	Ala	Tyr	Arg
			835					840					845			
	Val	Ile	Lys	Asn	Val	Ser	Asp	Asn	Leu	Leu	Pro	Asn	Ile	Arg	Pro	Ile
		850					855					860				
5	Asn	Ala	Cys	Gly	Gly	Val	Asp	Arg	Cys	Ser	Gln	Gln	Lys	Tyr	Val	Asn
	865					870					875					880
	Asn	Ser	Leu	Glu	Val	Asn	Ser	Gly	Leu	Ser	Asn	Gly	Ile	Gly	Ala	Ser
					885					890						895
	Asp	Ser	His	Glu	Phe	Ser	Ile	His	Val	Asp	Thr	Gly	Glu	Leu	Asn	Tyr
10				900					905					910		
	Asn	Glu	Asn	Thr	Gly	Ile	Trp	Val	Val	Phe	Lys	Ile	Ala	Thr	Thr	Asn
			915					920					925			
	Gly	Tyr	Ala	Thr	Leu	Gly	Asn	Leu	Glu	Leu	Val	Glu	Glu	Gly	Pro	Leu
	930					935						940				
15	Ser	Gly	Asp	Ala	Leu	Glu	Arg	Val	Lys	Asn	Gln	Glu	Lys	Gln	Trp	Gln
	945					950					955					960
	Asp	Gln	Met	Thr	Arg	Arg	Arg	Ala	Glu	Thr	Glu	Asn	Arg	Tyr	Gly	Leu
					965					970						975
	Ala	Lys	Gln	Ala	Val	Asp	Arg	Leu	Phe	Val	Asp	Tyr	Gln	Asp	Gln	Gln
				980					985					990		
20	Val	Ser	Pro	Ile	Ile	Glu	Ile	Ser	Asp	Leu	Thr	Ala	Ala	Gln	Asn	Val
			995					1000					1005			
	Val	Gln	Ser	Ile	Pro	Tyr	Val	Tyr	Asn	Asp	Met	Leu	Pro	Glu	Ile	Pro
	1010						1015					1020				
	Gly	Met	Asn	Tyr	Thr	Ser	Val	Thr	Glu	Leu	Thr	Asn	Arg	Leu	Gln	Gln
25	1025					1030					1035					1040
	Ala	Trp	Asp	Leu	Tyr	Asp	Gln	Arg	Asn	Ser	Ile	Gln	Asn	Gly	Asp	Phe
					1045					1050					1055	
	Arg	Asn	Asp	Val	Ser	Asn	Trp	Asn	Val	Thr	Pro	Glu	Val	Asn	Ile	Gln
				1060				1065						1070		
30	Gln	Met	Asn	Asp	Thr	Ser	Val	Leu	Val	Ile	Pro	Asn	Trp	Asp	Ser	Gln
			1075					1080					1085			
	Ala	Ser	Gln	Gln	Ile	Thr	Val	Gln	Pro	Asn	Arg	Arg	Tyr	Val	Leu	Arg
	1090						1095					1100				
	Val	Thr	Ala	Arg	Lys	Glu	Gly	Ser	Gly	Asp	Gly	Tyr	Val	Thr	Ile	Arg
	1105					1110					1115					1120
35	Asp	Gly	Ala	Lys	Tyr	Thr	Glu	Thr	Leu	Thr	Phe	Asn	Thr	Cys	Asp	Tyr
					1125					1130					1135	
	Asn	Gly	Ser	Ser	Val	Tyr	Gln	Glu	Gln	Ala	Leu	Tyr	Thr	Asn	Asp	Val
				1140				1145						1150		
	Tyr	Asn	Thr	Gln	Ser	Ala	Asn	Ile	His	Gly	Ser	Asn	Ser	Ala	Tyr	His
40			1155					1160					1165			
	Thr	Gln	Ala	Ser	Asn	Thr	Asp	Arg	Tyr	Asn	Met	Asn	Gly	Met	Tyr	Asn
	1170						1175					1180				
	Asp	Gln	Thr	Ser	Tyr	Val	Thr	Lys	Thr	Val	Glu	Phe	Ile	Pro	Asn	Thr
	1185					1190					1195					1200
45	Glu	Gln	Val	Trp	Ile	Glu	Met	Ser	Glu	Thr	Glu	Gly	Val	Phe	Tyr	Ile
					1205					1210					1215	
	Glu	Ser	Val	Glu	Leu	Ile	Val	Glu	Glu	Asn						
				1220					1225							

<210> 50

50 <211> 1169

<212> PRT

<213> Bacillus thuringiensis

<400> 50

55

EP 2 728 007 B1

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

10

15

20

25

30

35

40

45

50

55

EP 2 728 007 B1

	50		55		60														
	Ala	Pro	Gly	Gly	Ile	Thr	Thr	Gly	Ile	Thr	Ile	Val	Thr	Lys	Leu	Leu			
	65					70					75					80			
5	Gly	Trp	Leu	Gly	Leu	Pro	Phe	Ala	Gly	Glu	Thr	Gly	Met	Ala	Leu	Asn			
					85					90					95				
	Phe	Ile	Leu	Gly	Leu	Leu	Trp	Pro	Thr	Ser	Gly	Asn	Pro	Trp	Ala	Glu			
				100					105					110					
	Leu	Met	Ile	Leu	Val	Glu	Glu	Leu	Ile	Asn	Gln	Lys	Ile	Glu	Glu	Ala			
			115					120					125						
10	Val	Arg	Asn	Lys	Ala	Leu	Ala	Asp	Leu	Ala	Asn	Ser	Gly	Arg	Ala	Leu			
		130						135					140						
	Gln	Ser	Tyr	Leu	Asn	Ala	Phe	Glu	Asp	Trp	Gln	Lys	Asn	Pro	Asn	Ile			
	145				150						155				160				
	Phe	Arg	Ser	Lys	Glu	Leu	Val	Arg	Glu	Arg	Phe	Ala	Asn	Ala	Glu	His			
				165					170						175				
15	Ser	Leu	Arg	Thr	Glu	Met	Ser	Ser	Phe	Ala	Ile	Arg	Gly	Phe	Glu	Ile			
				180					185					190					
	Pro	Leu	Leu	Ala	Thr	Tyr	Ala	Gln	Ala	Ala	Asn	Leu	His	Leu	Phe	Leu			
			195					200					205						
	Ile	Lys	Asp	Val	Gln	Ile	Tyr	Gly	Lys	Glu	Trp	Gly	Tyr	Thr	Gln	Ala			
		210					215					220							
20	Asp	Ile	Asp	Leu	Phe	Tyr	Arg	Glu	Gln	Val	Glu	Phe	Thr	Lys	Glu	Tyr			
	225				230						235				240				
	Thr	Glu	His	Cys	Ile	Asn	Ile	Tyr	Asn	Asp	Gly	Leu	Asn	Gln	Leu	Lys			
				245					250					255					
	Gly	Ser	Asn	Ala	Lys	Gln	Trp	Ile	Ala	Phe	Asn	Arg	Phe	Arg	Arg	Glu			
			260					265					270						
25	Met	Thr	Leu	Thr	Val	Leu	Asp	Val	Val	Ala	Leu	Phe	Ser	Asn	Tyr	Asp			
		275					280						285						
	Val	Arg	Met	Tyr	Pro	Ile	Lys	Thr	Thr	Thr	Glu	Leu	Thr	Arg	Thr	Ile			
		290					295					300							
	Tyr	Thr	Asp	Pro	Leu	Gly	Tyr	Thr	Lys	Thr	Gly	Ser	Ser	Ser	Thr	Pro			
	305				310						315				320				
30	Pro	Trp	Tyr	Asn	Tyr	Gly	Ser	Ser	Phe	Ser	Tyr	Ile	Glu	Ser	Val	Ala			
				325					330					335					
	Ile	Pro	Ala	Pro	Ser	Leu	Val	Lys	Trp	Leu	Ser	Gln	Ile	Glu	Ile	Tyr			
			340					345					350						
	Ser	Lys	Ser	Ala	Lys	Ala	Thr	Pro	Gln	Ser	Ala	Asp	Tyr	Trp	Ala	Gly			
		355					360					365							
35	His	Thr	Ile	Thr	Tyr	His	Tyr	Gly	Gly	Asp	Asn	Gly	Gln	Ala	Val	Ala			
		370				375					380								
	Asn	Tyr	Gly	Asp	Arg	Thr	Asn	Pro	Val	Ala	Val	Asp	Arg	Tyr	Asn	Phe			
	385				390						395				400				
	Glu	Gln	Ala	Asp	Ile	Tyr	Arg	Val	Ser	Ser	Ser	Val	Ala	Ser	Ser	Thr			
				405					410					415					
40	Thr	Ser	Gly	Val	Lys	Leu	Leu	Thr	Thr	Lys	Ala	Ile	Phe	Asp	Gly	Ile			
				420				425					430						
	Asn	Thr	Lys	Asn	Gly	Leu	Val	Ser	Tyr	Arg	Tyr	Glu	Lys	Ser	Ser	Asn			
		435					440					445							
	Phe	Phe	Asn	Glu	Leu	Lys	Asp	Thr	Ile	Thr	Glu	Leu	Pro	Val	Gln	Leu			
		450				455					460								
45	Ser	Ser	Pro	Pro	Thr	Tyr	Gly	Asp	Ala	Glu	Gln	Tyr	Ser	His	Arg	Leu			
	465				470						475				480				
	Ser	Tyr	Val	Ser	Asn	Ala	Pro	Thr	Glu	Tyr	Ser	Ser	Gly	Gly	His	Leu			
				485					490					495					
	Ile	Leu	Gly	Leu	Ile	Pro	Val	Leu	Gly	Trp	Thr	His	Thr	Ser	Leu	Thr			
			500					505					510						
50	Gln	Thr	Asn	Gln	Ile	His	Ser	Asp	Ser	Ile	Thr	Gln	Ile	Pro	Ala	Val			
		515						520				525							
	Lys	Val	Ser	Asn	Leu	Glu	Ser	Gly	Thr	Ser	Val	Val	Ala	Asn	Pro	Gly			
		530				535					540								
	Phe	Thr	Gly	Gly	Asp	Leu	Leu	Lys	Arg	Thr	Ser	Thr	Gly	Arg	Met	Gly			
	545				550						555				560				
55	Thr	Leu	Lys	Leu	Thr	Val	Ala	Gly	Ile	Leu	Ser	Arg	Glu	Met	Thr	Ile			
				565					570					575					

EP 2 728 007 B1

	Arg	Ile	Arg	Tyr	Ala	Ala	Thr	Thr	Asp	Phe	Lys	Leu	Gln	Val	Ile	Tyr
				580					585					590		
	Lys	Gly	Ile	Leu	Gln	Ser	Ser	Tyr	Asn	Ser	Asn	Lys	Thr	Met	Asn	Lys
			595					600					605			
5	Gly	Glu	Asn	Leu	Thr	Tyr	Gly	Lys	Phe	Lys	Phe	Ala	Asn	Phe	Thr	Leu
		610					615					620				
	Pro	Ile	Ser	Leu	Leu	Ile	Pro	Ser	Asp	Leu	Ser	Ile	Asp	Val	Gln	Asn
		625				630					635				640	
	Leu	Ser	Ser	Gly	Glu	Glu	Val	Tyr	Ile	Asp	Arg	Ile	Glu	Phe	Ile	Pro
				645						650					655	
10	Val	Gly	Ala	Thr	Tyr	Glu	Ala	Glu	Gln	Asp	Leu	Glu	Asn	Ala	Lys	Lys
				660					665					670		
	Ala	Val	Asn	Ala	Leu	Phe	Thr	Asn	Thr	Lys	Asp	Gly	Leu	Arg	Pro	Gly
			675					680					685			
	Val	Thr	Asp	Tyr	Glu	Val	Asn	Gln	Ala	Ala	Asn	Leu	Val	Glu	Cys	Leu
		690					695					700				
15	Ser	Asp	Asp	Leu	Tyr	Pro	Asn	Glu	Lys	Arg	Leu	Leu	Phe	Asp	Ala	Val
		705			710						715				720	
	Arg	Glu	Ala	Lys	Arg	Leu	Ser	Glu	Ala	Arg	Asn	Leu	Leu	Gln	Asp	Pro
				725						730					735	
	Asp	Phe	Gln	Glu	Ile	Asn	Gly	Glu	Asn	Gly	Trp	Thr	Ala	Ser	Thr	Gly
			740					745						750		
20	Ile	Glu	Val	Ile	Glu	Gly	Asp	Ala	Val	Phe	Lys	Gly	Arg	Tyr	Leu	His
			755					760					765			
	Leu	Pro	Gly	Ala	Arg	Glu	Ile	Asp	Thr	Glu	Thr	Tyr	Pro	Thr	Tyr	Leu
		770				775						780				
	Tyr	Gln	Lys	Val	Glu	Glu	Gly	Val	Leu	Lys	Pro	Tyr	Thr	Arg	Tyr	Arg
		785			790						795				800	
25	Leu	Arg	Gly	Phe	Val	Gly	Ser	Ser	Gln	Gly	Leu	Glu	Ile	Tyr	Thr	Ile
				805						810					815	
	Arg	His	Gln	Thr	Asn	Arg	Ile	Val	Lys	Asn	Val	Pro	Asp	Asp	Leu	Leu
			820						825					830		
	Pro	Asp	Val	Pro	Pro	Val	Asn	Asn	Asp	Gly	Arg	Ile	Asn	Arg	Cys	Ser
			835					840					845			
30	Glu	Gln	Lys	Tyr	Val	Asn	Ser	Arg	Leu	Glu	Val	Glu	Asn	Arg	Ser	Gly
			850				855					860				
	Glu	Ala	His	Glu	Phe	Ser	Ile	Pro	Ile	Asp	Thr	Gly	Glu	Ile	Asp	Tyr
					870						875				880	
	Asn	Glu	Asn	Ala	Gly	Ile	Trp	Val	Gly	Phe	Lys	Ile	Thr	Asp	Pro	Glu
				885						890					895	
35	Gly	Tyr	Ala	Thr	Leu	Gly	Asn	Leu	Glu	Leu	Val	Glu	Glu	Gly	Pro	Leu
				900					905					910		
	Ser	Gly	Asp	Ala	Leu	Glu	Arg	Leu	Gln	Arg	Glu	Glu	Gln	Gln	Trp	Lys
			915					920					925			
	Ile	Gln	Met	Thr	Lys	Arg	Arg	Glu	Glu	Thr	Asp	Arg	Lys	Tyr	Met	Ile
		930					935					940				
40	Ala	Lys	Gln	Ala	Val	Asp	Arg	Leu	Tyr	Ala	Asp	Tyr	Gln	Asp	Gln	Gln
					950						955				960	
	Leu	Asn	Pro	Asn	Val	Glu	Ile	Thr	Asp	Ile	Thr	Ala	Ala	Gln	Asn	Val
				965						970					975	
	Ile	Gln	Ser	Ile	Pro	Tyr	Val	Tyr	Asn	Asp	Ala	Phe	Pro	Gly	Leu	Pro
				980					985					990		
45	Gly	Met	Asn	Tyr	Thr	Lys	Phe	Thr	Glu	Leu	Thr	Asp	Arg	Leu	Gln	Gln
		995						1000					1005			
	Ala	Trp	Ser	Leu	Tyr	Asp	Gln	Arg	Asn	Ala	Ile	Pro	Asn	Gly	Asp	Phe
		1010					1015					1020				
50	Arg	Asn	Glu	Leu	Ser	Asn	Trp	Asn	Thr	Thr	Ala	Gly	Val	Asn	Val	Gln
		1025				1030						1035			1040	
	Gln	Leu	Asn	Gly	Thr	Ser	Val	Leu	Val	Ile	Pro	Asn	Trp	Asp	Ala	Gln
					1045					1050					1055	
	Val	Ser	Gln	Gln	Phe	Thr	Val	Gln	Pro	Asn	Gln	Arg	Tyr	Val	Leu	Arg
				1060					1065					1070		
55	Val	Thr	Ala	Arg	Lys	Glu	Gly	Val	Gly	Asn	Gly	Tyr	Val	Ser	Ile	Arg
			1075					1080					1085			
	Asp	Gly	Gly	Asn	Gln	Thr	Glu	Thr	Leu	Thr	Phe	Ser	Ala	Ser	Asp	Tyr

EP 2 728 007 B1

		1090				1095					1100						
		Asp	Thr	Asn	Gly	Val	Tyr	Asn	Ile	Gln	Ala	Ser	Asn	Thr	Asn	Gly	Tyr
		1105						1110				1115				1120	
5		Asn	Thr	Asn	Gly	Val	Tyr	Asn	Asp	Gln	Thr	Gly	Tyr	Ile	Thr	Lys	Thr
						1125						1130				1135	
		Ala	Glu	Phe	Ile	Pro	His	Thr	Asn	Gln	Val	Trp	Ile	Glu	Met	Ser	Glu
					1140					1145				1150			
		Thr	Glu	Gly	Thr	Phe	Tyr	Ile	Glu	Ser	Val	Glu	Leu	Ile	Val	Asp	Val
				1155					1160					1165			
10		Glu															

<210> 51
 <211> 1212
 <212> PRT
 15 <213> Bacillus thuringiensis

 <400> 51

20

25

30

35

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

	Met	Gln	Ile	Tyr	Thr	Lys	Phe	Val	Arg	His	Ala	Pro	Gln	Glu	Ser	His
	370						375					380				
	Tyr	Trp	Ala	Ala	His	Thr	Phe	Ser	Phe	His	His	Thr	Arg	Asp	Asn	Thr
	385					390					395					400
5	Lys	Thr	Thr	Leu	Thr	Tyr	Gly	Asp	Thr	Ser	Asn	Pro	Ile	Ser	Val	Gly
					405					410					415	
	Thr	Ala	Asp	Leu	Ser	Asp	Leu	Asp	Ile	Tyr	Lys	Val	Ser	Ser	Leu	Val
				420					425					430		
	Ala	Ser	Ser	Trp	Gly	Ser	Gly	Val	Arg	Leu	Leu	Val	Thr	Lys	Ala	Lys
			435					440					445			
10	Phe	Glu	Val	Ile	Tyr	Thr	Phe	Asn	Gln	Leu	Trp	Glu	Phe	Asn	Tyr	Glu
	450						455					460				
	Pro	Pro	Gly	Ile	Ser	Asn	Phe	Phe	Asn	Gln	Trp	Lys	Asn	Thr	Asp	Thr
	465					470					475					480
	Glu	Leu	Pro	Ile	Gln	Ile	Val	Asp	Pro	Pro	Thr	Phe	Gly	Asp	Pro	Asn
					485					490					495	
15	Gln	Tyr	Ser	His	Arg	Val	Ala	Tyr	Ile	Ser	His	Ala	Pro	Ile	Gln	Pro
				500					505					510		
	Tyr	Ser	Gly	Ala	Phe	Arg	Asn	Tyr	Gly	Leu	Val	Pro	Val	Phe	Gly	Trp
			515					520					525			
	Ser	His	Val	Ser	Val	Asp	Arg	Asn	Asn	Thr	Leu	Tyr	Ala	Asp	Arg	Ile
			530				535					540				
20	Thr	Gln	Ile	Pro	Ala	Val	Lys	Ala	Val	Gln	Leu	Ser	Gly	Glu	Pro	Tyr
	545					550					555					560
	Pro	Val	Val	Arg	Gly	Pro	Gly	Phe	Thr	Gly	Gly	Asp	Ile	Ala	Arg	Leu
					565					570					575	
	Pro	Asn	Asn	Pro	Asn	Val	Gly	Leu	Leu	Phe	Asn	Ser	Lys	Val	Glu	Ser
				580					585					590		
25	Pro	Ser	Glu	Asn	Lys	Arg	Tyr	Arg	Val	Arg	Ile	Arg	Tyr	Ala	Cys	Ala
			595					600					605			
	Ser	Gly	Ala	Arg	Ala	Ile	Phe	Gly	Gly	Leu	Tyr	Leu	Pro	Ile	Thr	Val
		610					615					620				
	Gln	Phe	Asn	Gln	Thr	Met	Ser	Thr	Thr	Thr	Pro	Thr	Arg	Tyr	Glu	Asp
	625					630					635					640
30	Phe	Gln	Tyr	Val	Asp	Val	Ser	Gly	Thr	Phe	Ile	Leu	Gly	Asn	Thr	Asn
					645					650					655	
	Val	Ser	Phe	Ser	Leu	Val	Pro	Gln	Ser	Ala	Asn	Gln	Thr	Asn	Asn	Leu
				660					665					670		
	Phe	Ile	Asp	Lys	Ile	Glu	Phe	Ile	Pro	Glu	Asn	Pro	Ala	Leu	Glu	Ala
			675					680					685			
35	Glu	Ser	Asp	Leu	Glu	Ala	Ala	Lys	Lys	Ala	Val	Asn	Ala	Leu	Phe	Thr
		690					695					700				
	Asn	Ser	Lys	Asp	Thr	Leu	Gln	Ile	Gly	Val	Thr	Asp	Tyr	Gln	Ile	Asn
		705				710					715					720
	Gln	Ala	Ala	Asn	Leu	Ile	Glu	Cys	Val	Ser	Asp	Glu	Val	Tyr	Pro	Asn
				725						730					735	
40	Glu	Lys	Arg	Leu	Leu	Phe	Asp	Ala	Val	Lys	Glu	Ala	Lys	Arg	Leu	Ser
				740				745						750		
	Thr	Ala	Arg	Asn	Leu	Leu	Glu	Asp	Thr	Asp	Phe	His	Thr	Ile	Asn	Gly
			755					760					765			
45	Gly	Asn	Gly	Trp	Thr	Gly	Ser	Thr	Gly	Ile	Glu	Ile	Val	Glu	Gly	Asp
		770					775					780				
	Ile	Leu	Phe	Lys	Asp	Arg	Ser	Leu	Arg	Leu	Pro	Ser	Ala	Arg	Glu	Ile
		785				790					795					800
	Glu	Arg	Glu	Thr	Tyr	Pro	Thr	Tyr	Ile	Tyr	Gln	Lys	Ile	Glu	Glu	Ser
				805						810					815	
50	Arg	Leu	Lys	Pro	Asn	Thr	Arg	Tyr	Ser	Leu	Arg	Gly	Phe	Ile	Gly	Ser
				820				825						830		
	Ser	Gln	Asp	Leu	Glu	Ile	Tyr	Val	Leu	Arg	His	Gln	Ala	Tyr	Arg	Val
			835					840					845			
	Ile	Lys	Asn	Val	Ser	Asp	Asn	Leu	Leu	Pro	Asn	Met	Arg	Pro	Ile	Asn
			850				855					860				
55	Ala	Cys	Gly	Gly	Val	Asp	Arg	Cys	Ser	Gln	Gln	Lys	Tyr	Val	Asn	Asn
						870					875					880
	Ser	Leu	Glu	Val	Asn	Ser	Gly	Leu	Ser	Asn	Gly	Ile	Gly	Ala	Ala	Asp

EP 2 728 007 B1

				885					890					895		
	Ser	His	Glu	Phe	Ser	Ile	His	Val	Asp	Thr	Gly	Glu	Leu	Asn	Tyr	Asn
				900					905					910		
5	Glu	Asp	Met	Gly	Ile	Trp	Val	Val	Phe	Lys	Ile	Thr	Thr	Thr	Asp	Gly
			915					920					925			
	Tyr	Ala	Thr	Val	Gly	Asn	Ile	Glu	Leu	Val	Glu	Val	Glu	Thr	Leu	Ser
			930				935					940				
	Gly	Glu	Ala	Leu	Glu	Arg	Val	Gln	Arg	Gln	Glu	Lys	Gln	Trp	Gln	Gly
	945					950					955					960
10	Gln	Leu	Ala	Thr	Arg	Arg	Lys	Glu	Thr	Glu	Thr	Arg	Tyr	Gly	Pro	Ala
					965					970					975	
	Lys	Gln	Ala	Ile	Asp	Arg	Leu	Phe	Val	Asp	Phe	Gln	Asp	Gln	Gln	Leu
				980					985					990		
	Ser	Arg	Ser	Thr	Glu	Ile	Ser	Asp	Leu	Thr	Glu	Ala	Gln	Asn	Leu	Val
			995					1000					1005			
15	Gln	Ser	Ile	Pro	Tyr	Val	Tyr	Asn	Asp	Met	Leu	Pro	Glu	Ile	Pro	Gly
			1010					1015					1020			
	Met	Asn	Tyr	Thr	Ser	Val	Thr	Glu	Leu	Thr	Asn	Arg	Leu	Gln	Gln	Ala
	1025					1030					1035					1040
	Trp	Asn	Leu	Tyr	Asp	Gln	Arg	Asn	Ser	Ile	Gln	Asn	Gly	Asp	Phe	Arg
20					1045						1050				1055	
	Asn	Asp	Val	Ser	Asn	Trp	Asn	Val	Thr	Thr	Glu	Val	Asn	Ile	Gln	Gln
				1060					1065					1070		
	Met	Asn	Asp	Thr	Ser	Val	Leu	Val	Ile	Pro	Asn	Trp	Asp	Ser	Gln	Val
			1075					1080					1085			
25	Ser	Gln	Gln	Ile	Thr	Val	Gln	Pro	Asn	Arg	Arg	Tyr	Val	Leu	Arg	Val
			1090				1095					1100				
	Thr	Ala	Arg	Lys	Glu	Gly	Asn	Gly	Asp	Gly	Tyr	Val	Thr	Ile	Arg	Asp
	1105					1110					1115					1120
	Gly	Ala	Asn	His	Thr	Glu	Thr	Leu	Thr	Phe	Asn	Thr	Cys	Asp	Tyr	Asp
					1125						1130					1135
30	Gly	Asn	Ser	Val	Tyr	Asn	Asn	Gln	Pro	Leu	Asn	Ala	Asn	Asn	Asn	Val
				1140					1145					1150		
	Tyr	Thr	Thr	Lys	Ser	Ser	Asn	Thr	Asn	Ser	Tyr	His	Thr	Asn	Gly	Val
			1155					1160					1165			
	Tyr	His	Asp	Gln	Thr	Ser	Tyr	Val	Thr	Lys	Thr	Met	Glu	Phe	Thr	Pro
35			1170				1175					1180				
	Tyr	Thr	Glu	Gln	Val	Trp	Val	Glu	Met	Ser	Glu	Thr	Glu	Gly	Val	Phe
	1185					1190					1195					1200
	Tyr	Ile	Asp	Ser	Val	Glu	Leu	Ile	Val	Glu	Glu	Met				
				1205						1210						

<210> 52

<211> 1231

<212> PRT

<213> Bacillus thuringiensis

<400> 52

EP 2 728 007 B1

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

20

25

30

35

40

45

50

55

EP 2 728 007 B1

	Gln	Val	Gln	Gly	Leu	Ile	Asp	Gln	Ser	Ile	Thr	Ala	Asn	Val	Arg	Ser
	130						135					140				
	Gln	Ala	Ile	Ala	Lys	Leu	Glu	Gly	Leu	Gly	Arg	Gly	Leu	Glu	Ala	Tyr
	145					150					155					160
5	Gln	Glu	Leu	Leu	Val	Ala	Trp	Leu	Glu	Asn	Arg	Asn	Asn	Ala	Arg	Thr
					165					170					175	
	Arg	Ser	Leu	Ile	Lys	Gln	Gln	Tyr	Val	Ala	Leu	Glu	Gln	Ile	Phe	Thr
					180				185					190		
	Thr	Gly	Leu	Pro	Glu	Phe	Ser	Val	Gln	Asn	Gln	Glu	Val	Pro	Leu	Leu
			195					200					205			
10	Gly	Val	Tyr	Ala	Gln	Ala	Ala	Asn	Leu	His	Leu	Leu	Leu	Leu	Arg	Asp
	210					215						220				
	Val	Ser	Ile	Phe	Gly	Ala	Glu	Trp	Gly	Phe	Glu	Asp	Tyr	Glu	Ile	Asp
	225					230					235					240
	Val	Phe	Tyr	Asn	Arg	Gln	Met	Arg	Tyr	Thr	Ala	Glu	Tyr	Ala	Asn	Tyr
					245					250					255	
15	Cys	Val	Glu	Trp	Tyr	Asn	Lys	Gly	Leu	Asp	Arg	Leu	Lys	Gly	Thr	Asp
				260				265						270		
	Arg	Ile	Ser	Trp	Met	Lys	Tyr	His	Gln	Phe	Arg	Arg	Glu	Met	Thr	Leu
			275					280					285			
	Leu	Val	Leu	Asp	Ile	Val	Ala	Leu	Phe	Pro	Asn	Tyr	Asp	Ala	Arg	Arg
	290					295						300				
20	Tyr	Pro	Leu	Glu	Thr	Glu	Ala	Gln	Leu	Thr	Arg	Glu	Val	Tyr	Thr	Asp
	305					310					315					320
	Pro	Ile	Val	Tyr	Asn	Pro	Glu	Glu	Phe	Leu	Gly	Gly	Phe	Cys	Asn	Ser
					325					330					335	
	Trp	Thr	Ser	Asp	Asn	Gln	Ser	Asp	Phe	Ser	Gln	Ile	Glu	Asn	Ala	Val
				340					345					350		
25	Ile	Arg	Pro	His	Val	Phe	Asp	Thr	Ile	Ala	Ser	Leu	Glu	Ile	Asn	
			355				360					365				
	Thr	Ala	Arg	Gly	Arg	Ile	Ala	Leu	Asn	Asn	Thr	Ala	Tyr	Ile	Asp	Phe
	370					375						380				
	Trp	Ala	Gly	His	Ser	Leu	Thr	Phe	Arg	Tyr	Pro	Asn	Asp	Ser	Ala	Arg
	385					390					395					400
30	His	Gln	Val	Gln	Tyr	Gly	Thr	Ile	Thr	Ser	Glu	Lys	Asn	Ser	Phe	Pro
					405					410					415	
	Phe	Glu	Val	Thr	Asp	Val	Val	Gln	Val	Asn	Thr	Thr	Ala	Ala	Asn	Leu
				420				425					430			
	Ala	Asn	Ala	Tyr	Gln	Gln	Ala	Tyr	Gly	Ala	Pro	Arg	Ala	Val	Phe	Gln
	435						440					445				
35	Leu	Val	Asn	Arg	Leu	Asn	Gly	Ala	Val	Gly	Ser	Leu	Thr	Tyr	Ser	Lys
	450					455					460					
	Thr	His	Thr	Ala	Ile	Gln	Ala	Cys	Thr	Gln	Ser	Leu	Asn	Thr	Asn	Ser
	465				470					475						480
	Glu	Ile	Pro	Arg	Leu	Pro	Val	Ser	Pro	Gly	Val	Thr	Asn	Leu	Ser	Thr
40					485					490					495	
	Leu	Tyr	Thr	His	Arg	Ile	Ser	His	Ile	Thr	Ser	Tyr	Asn	Phe	Ser	Asn
				500				505						510		
	Asn	Leu	Ala	Gly	Asn	Arg	Asn	Arg	Tyr	Gly	Asn	Phe	Pro	Val	Phe	Val
			515				520					525				
45	Trp	Thr	His	Arg	Ser	Ala	Glu	Ile	Asp	Asn	Lys	Ile	Tyr	Ala	Asn	Lys
	530					535						540				
	Ile	Thr	Gln	Ile	Pro	Ala	Val	Lys	Ala	Leu	Trp	Ala	Ser	Ser	Glu	Pro
	545				550						555					560
	Tyr	Pro	Val	Val	Arg	Gly	Pro	Gly	Phe	Thr	Gly	Gly	Asp	Ile	Ala	Arg
					565					570					575	
50	Leu	Pro	Asn	Asn	Pro	Asn	Ile	Gly	Leu	Arg	Phe	Leu	Leu	Asp	Pro	Glu
				580				585						590		
	Pro	Gly	Val	Leu	Phe	Asn	Arg	Arg	Phe	Arg	Val	Arg	Ile	Arg	Phe	Ala
			595				600						605			
	Cys	Asp	Ser	Gly	Ala	Arg	Val	Ile	Leu	Thr	Asp	Glu	Thr	Gly	Ile	Asn
	610					615						620				
55	Ser	Glu	Thr	Ile	Val	Leu	Asn	Gln	Thr	Met	Thr	Thr	Glu	Asn	Pro	Arg
	625				630						635					640
	Lys	Tyr	Asp	Asp	Phe	Gln	Tyr	Ile	Glu	Ser	Arg	Asn	Val	Tyr	Thr	Leu

EP 2 728 007 B1

	Thr	Arg	Phe	Pro	Gly	Pro	Trp	Ile	Trp	Arg	Leu	Gly	Ala	Gln	Ser	Ala	
				660					665					670			
5	Asp	Gln	Thr	Arg	Asn	Val	Tyr	Ile	Asp	Arg	Ile	Glu	Phe	Ile	Pro	Leu	
			675					680					685				
	Asn	Pro	Ala	Leu	Glu	Ala	Glu	Asn	Asp	Leu	Glu	Thr	Ala	Lys	Lys	Ala	
			690				695					700					
	Val	Asn	Ala	Leu	Phe	Thr	Asn	Arg	Lys	Asp	Thr	Leu	Gln	Ile	Ser	Val	
	705					710					715					720	
10	Thr	Asp	Tyr	Gln	Ile	Asn	Gln	Ala	Ala	Asn	Leu	Ile	Glu	Cys	Val	Ser	
				725						730					735		
	Asp	Glu	Val	Tyr	Pro	Asn	Glu	Lys	Arg	Leu	Leu	Phe	Asp	Ala	Val	Lys	
				740					745					750			
	Glu	Ala	Lys	Arg	Leu	Ser	Thr	Ala	Arg	Asn	Leu	Leu	Glu	Asp	Thr	Asp	
			755					760					765				
15	Phe	His	Ala	Ile	Asn	Gly	Gly	Asn	Gly	Trp	Thr	Gly	Ser	Thr	Gly	Ile	
	770						775					780					
	Glu	Ile	Val	Glu	Gly	Asp	Leu	Leu	Phe	Lys	Asp	Arg	Ser	Leu	Arg	Leu	
	785					790					795					800	
	Pro	Ser	Ala	Arg	Glu	Ile	Glu	Arg	Glu	Thr	Tyr	Pro	Thr	Tyr	Ile	Tyr	
				805						810					815		
20	Gln	Lys	Ile	Glu	Glu	Ser	Arg	Leu	Lys	Pro	Asn	Thr	Arg	Tyr	Ser	Leu	
				820					825					830			
	Arg	Gly	Phe	Ile	Gly	Ser	Ser	Gln	Asp	Leu	Glu	Ile	Tyr	Val	Leu	Arg	
			835					840					845				
	His	Gln	Ala	Tyr	Arg	Val	Ile	Lys	Asn	Val	Ser	Asp	Asn	Leu	Leu	Pro	
	850						855					860					
25	Asn	Met	Arg	Pro	Ile	Asn	Ala	Cys	Gly	Gly	Val	Asp	Arg	Cys	Ser	Gln	
	865				870						875					880	
	Gln	Lys	Tyr	Val	Asn	Asn	Ser	Leu	Glu	Leu	Asn	Ser	Ser	Leu	Ser	Asn	
				885						890					895		
	Gly	Ile	Gly	Ala	Ala	Asp	Ser	His	Glu	Phe	Ser	Ile	His	Met	Asp	Thr	
			900						905				910				
30	Gly	Glu	Leu	Asn	Tyr	Asn	Glu	Asp	Thr	Gly	Ile	Trp	Val	Val	Phe	Lys	
			915					920					925				
	Ile	Thr	Thr	Thr	Asp	Gly	Tyr	Ala	Thr	Leu	Gly	Asn	Leu	Glu	Leu	Val	
	930						935					940					
	Glu	Glu	Gly	Pro	Leu	Ser	Gly	Asp	Thr	Leu	Glu	Arg	Val	Arg	Lys	Gln	
	945				950						955					960	
35	Glu	Lys	Gln	Trp	Gln	Asp	Gln	Met	Ala	Arg	Arg	Arg	Ala	Glu	Thr	Glu	
				965						970					975		
	Thr	Arg	Tyr	Gly	Ala	Ala	Lys	Gln	Ala	Ile	Asp	Arg	Leu	Phe	Ile	Asp	
				980					985					990			
	Tyr	Gln	Asp	Gln	Gln	Leu	Ser	Pro	Gly	Thr	Asp	Ile	Ser	Asp	Leu	Thr	
			995					1000					1005				
40	Ala	Ala	Gln	Asn	Val	Val	Gln	Ser	Ile	Pro	Tyr	Val	Tyr	Asn	Asp	Met	
			1010					1015					1020				
	Leu	Pro	Glu	Ile	Pro	Gly	Met	Asn	Tyr	Thr	Ser	Val	Thr	Glu	Leu	Thr	
	1025					1030						1035				1040	
	Asn	Arg	Leu	Gln	Gln	Ala	Trp	Asp	Leu	Tyr	Asp	Gln	Arg	Asn	Ser	Ile	
				1045						1050					1055		
45	Pro	Asn	Gly	Asp	Phe	Arg	Tyr	Gly	Leu	Asn	Asp	Trp	Asn	Ala	Lys	Ser	
			1060						1065					1070			
	Gly	Ala	Asn	Val	Gln	Gln	Val	Asn	His	Thr	Ser	Val	Leu	Val	Ile	Pro	
			1075					1080					1085				
	Asn	Trp	Asp	Ser	Gln	Ala	Ser	Gln	Glu	Ile	Thr	Val	Gln	Pro	Asn	Arg	
	1090						1095						1100				
50	Arg	Tyr	Val	Leu	Arg	Val	Thr	Ala	Arg	Lys	Glu	Gly	Ser	Gly	Asp	Gly	
	1105					1110						1115				1120	
	Tyr	Val	Thr	Ile	Arg	Asp	Gly	Ala	Lys	Tyr	Thr	Glu	Thr	Leu	Thr	Phe	
				1125						1130					1135		
	Asn	Thr	Cys	Asp	Tyr	Asn	Gly	Ser	Asn	Val	Tyr	Gln	Glu	Gln	Ala	Leu	
			1140						1145					1150			
55	Tyr	Thr	Asn	Asp	Val	Tyr	Asn	Thr	Gln	Ser	Ala	Asn	Ile	Gln	Gly	Ser	
			1155					1160					1165				

EP 2 728 007 B1

	Asn	Ser	Ala	Tyr	His	Thr	Gln	Ala	Ser	Asn	Thr	Asp	Arg	Tyr	Asn	Met	
	1170					1175					1180						
	Asn	Gly	Met	Tyr	Asn	Asp	Gln	Thr	Ser	Tyr	Val	Thr	Lys	Thr	Val	Glu	
	1185					1190					1195					1200	
5	Phe	Ile	Pro	His	Thr	Glu	Gln	Val	Trp	Ile	Glu	Met	Ser	Glu	Thr	Glu	
					1205					1210					1215		
	Gly	Val	Phe	Tyr	Ile	Glu	Ser	Val	Glu	Leu	Ile	Val	Lys	Glu	Asn		
				1220					1225					1230			

10 <210> 53
 <211> 1168
 <212> PRT
 <213> Bacillus thuringiensis

15 <400> 53

20

25

30

35

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

5																
10																
15																
20																
25																
30																
35																
40																
45																
50																
55																
		</														

EP 2 728 007 B1

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

<210> 54

<211> 1204

<212> PRT

35 <213> Bacillus thuringiensis

<400> 54

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

		195				200				205					
		Gln Met	Pro Ser	Phe Ala	Val Ser	Gly Phe	Glu Ile	Leu Leu	Leu Ser						
		210			215			220							
5		Val Tyr	Thr Gln	Ala Ala	Asn Leu	His Leu	Asn Leu	Leu Arg	Asp Ile						
		225			230			235							240
		Thr Val	His Gly	Thr Gly	Trp Gly	Tyr Ser	Glu Gly	Thr Val	Glu Arg						
				245			250								255
		Tyr Asn	Gln Leu	Gln Arg	Cys Leu	Ile Thr	Ala Tyr	Val Asp	Tyr Cys						
			260			265									270
10		Val Asp	Gln Tyr	Asn Leu	Glu Leu	Glu Lys	Leu Pro	Lys Glu	Thr Leu						
			275			280									
		Lys Asn	Trp Val	Asp Tyr	Asn Arg	Tyr Arg	Arg Glu	Met Thr	Leu Ser						
			290			295									
		Val Leu	Asp Ile	Val Ser	Leu Phe	Pro Asn	Tyr Asp	Ala Ser	Val Tyr						
		305			310			315							320
15		Asp Leu	Pro Ile	Asn Ala	Glu Leu	Ser Arg	Gln Val	Tyr Thr	Asp Pro						
				325			330								335
		Leu Gly	Ser Tyr	Leu Pro	Tyr Asn	Thr Ala	Asn Pro	Ile Ser	Trp Tyr						
			340			345									
		Asp Met	Lys Ser	Tyr Ile	His Pro	Asn Phe	Trp Gln	Ile Asp	Lys Tyr						
			355			360									
20		Phe Ile	Lys Pro	Pro Asn	Leu Phe	Thr Phe	Ala Glu	Lys Leu	Ile Met						
			370			375									
		Tyr Ser	Gly Tyr	Arg Thr	Asp Val	Asp Pro	Ile Phe	Tyr Tyr	Tyr Trp						
		385			390			395							400
		Ser Gly	Ser Lys	Leu Glu	Ser Arg	Arg Val	His Gly	Asn Glu	Ile Ile						
				405			410								
25		Thr Thr	Ile Ser	Gly Asp	Ile Ser	Gln Ser	Ile Thr	Leu Val	Asn Val						
			420			425									
		Asp Phe	Lys Asp	Ser Asp	Ile Tyr	Lys Ile	Thr Thr	Asn Tyr	Ile Gly						
			435			440									
		Gln Tyr	Thr Gly	Ser Leu	Leu Gly	Thr Asn	Pro Ile	Thr Phe	Ser Leu						
			450			455									
30		Thr Asn	Ser Asn	Gly Gln	Thr Glu	Arg Lys	Tyr Glu	Tyr Ser	Lys Leu						
		465			470			475							480
		Leu Met	Pro Gly	Lys Glu	Lys Ile	Tyr Tyr	Ser Gln	Asp Glu	Ile Pro						
				485			490								495
		Pro Asn	Ile Glu	Thr Gly	Glu Pro	Asp Tyr	Val Ala	Tyr Ser	His Arg						
			500			505									
35		Leu Ser	Tyr Val	Ser Ala	Phe Asn	Pro Asn	Phe Thr	Ser Gly	Lys Lys						
			515			520									
		Ile Gly	Thr Val	Pro Ile	Tyr Gly	Trp Thr	His Thr	Ser Val	Ser Arg						
			530			535									
		Asp Asn	Leu Ile	Tyr Pro	Asp Lys	Ile Thr	Gln Ile	Pro Ile	Val Lys						
		545			550			555							560
40		Ser Tyr	Glu Ile	Gly Glu	Tyr Tyr	Lys Val	Met Gln	Gly Pro	Gly Phe						
				565			570								575
		Thr Gly	Gly Asp	Ile Leu	Thr Lys	Thr Tyr	Pro Val	Gln Asn	Pro Ser						
				580			585								590
		Gly Ser	Thr Leu	Ala Ala	Arg Ile	Arg Val	Ser Thr	Ala Gly	Ile His						
			595			600									
45		Leu Asn	Gln Arg	Tyr Thr	Leu Arg	Met His	Tyr Ala	Ala Ser	Gly Ser						
			610			615									
		Val Tyr	Asp Ala	Met Ile	Ile Lys	Pro Gly	Gln Ser	Glu Gly	Gly Tyr						
		625			630			635							640
		His Met	Arg Leu	Asn Pro	Thr Met	Glu Asn	Gly Glu	Thr Leu	Thr Phe						
				645			650								655
50		Asn Ser	Phe Thr	Ser Ile	Gly Met	Asn Ser	Gln Val	Leu Thr	Ser Ser						
				660			665								670
		Gln Thr	Asp Leu	Thr Leu	Tyr Ile	Lys Ser	Met Ser	Pro Ser	Thr Pro						
			675			680									
		Gly Thr	Ile Tyr	Ile Asp	Arg Ile	Glu Phe	Ile Pro	Val Asp	Asn Asn						
			690			695									
55		Tyr Glu	Ala Glu	Gln Asn	Leu Glu	Lys Ala	Gln Lys	Ala Val	Asn Ala						
		705			710			715							720

EP 2 728 007 B1

	Leu	Phe	Thr	Ala	Gly	Arg	Asn	Ala	Leu	Gln	Thr	Asp	Val	Thr	Asp	Tyr
					725					730					735	
	Lys	Val	Asp	Gln	Val	Ser	Ile	Val	Val	Asp	Cys	Val	Ser	Lys	Glu	Val
				740					745					750		
5	Tyr	Pro	Asn	Glu	Lys	Arg	Glu	Leu	Gln	Asn	Leu	Val	Lys	Tyr	Ala	Lys
			755					760					765			
	Arg	Leu	Thr	Asn	Ser	Arg	Asn	Leu	Leu	Val	Asp	Pro	Asn	Phe	Thr	Ser
			770				775					780				
	Ile	Asn	Ser	Glu	Gly	Val	Asn	Gly	Trp	Tyr	Gly	Ser	Asn	Gly	Ile	Val
						790					795					800
10	Ile	Gly	His	Gly	Asp	Asp	Val	Phe	Lys	Gly	Asn	Tyr	Ile	Gln	Leu	Ala
					805					810					815	
	Gly	Thr	Asn	Asp	Ala	Gln	Tyr	Pro	Thr	Tyr	Leu	Tyr	Gln	Lys	Ile	Asp
				820					825					830		
	Glu	Ser	Lys	Leu	Lys	Glu	Tyr	Thr	Arg	Tyr	Lys	Leu	Arg	Gly	Phe	Ile
15			835					840					845			
	Lys	Ser	Ser	Gln	Asp	Leu	Glu	Ala	Tyr	Val	Ile	Arg	Tyr	Asp	Ala	Lys
			850				855					860				
	His	Glu	Thr	Leu	Asp	Val	Ser	Asn	Asn	Leu	Phe	Pro	Asp	Ile	Ser	Pro
					870						875					880
20	Val	Asn	Ala	Cys	Gly	Glu	Pro	Asn	Arg	Cys	Gly	Ala	Leu	Gln	Tyr	Leu
					885					890					895	
	Asp	Glu	Asn	Pro	Arg	Leu	Glu	Cys	Ser	Ser	Ile	Gln	Asp	Gly	Ile	Leu
				900					905					910		
	Ser	Asp	Ser	His	Ser	Phe	Ser	Leu	Asn	Ile	Asp	Thr	Gly	Ser	Ile	Asp
			915					920					925			
25	Phe	Asn	Glu	Asn	Val	Gly	Ile	Trp	Val	Leu	Phe	Lys	Ile	Ser	Thr	Pro
			930				935					940				
	Glu	Gly	Tyr	Ala	Arg	Phe	Gly	Asn	Leu	Glu	Val	Ile	Glu	Asp	Asp	Thr
					950					955						960
	Val	Ile	Gly	Glu	Ala	Leu	Ala	Arg	Val	Lys	Arg	Gln	Glu	Thr	Lys	Trp
					965					970					975	
30	Arg	Asn	Lys	Leu	Thr	Gln	Leu	Arg	Thr	Glu	Thr	Gln	Ala	Ile	Tyr	Thr
				980					985					990		
	Arg	Ala	Lys	Gln	Ala	Ile	Asp	Asn	Leu	Phe	Thr	Asn	Ala	Gln	Asp	Ser
			995					1000					1005			
	His	Leu	Lys	Ile	Gly	Ala	Thr	Phe	Ala	Ser	Ile	Val	Ala	Ala	Arg	Lys
35			1010				1015					1020				
	Ile	Val	Gln	Ser	Ile	Arg	Glu	Ala	Tyr	Met	Pro	Trp	Leu	Ser	Ile	Val
					1030						1035					1040
	Pro	Gly	Val	Asn	Tyr	Pro	Ile	Phe	Thr	Glu	Leu	Asn	Glu	Arg	Val	Gln
					1045					1050					1055	
40	Arg	Ala	Phe	Gln	Leu	Tyr	Asp	Val	Arg	Asn	Val	Val	Arg	Asn	Gly	Arg
				1060					1065					1070		
	Phe	Leu	Ser	Gly	Val	Ser	Asp	Trp	Ile	Val	Thr	Ser	Asp	Val	Lys	Val
			1075					1080					1085			
	Gln	Glu	Glu	Asn	Gly	Asn	Asn	Val	Leu	Val	Leu	Ser	Asn	Trp	Asp	Ala
			1090				1095					1100				
45	Gln	Val	Leu	Gln	Cys	Leu	Lys	Leu	Tyr	Gln	Asp	His	Gly	Tyr	Ile	Leu
					1110						1115					1120
	Arg	Val	Thr	Ala	Arg	Lys	Glu	Gly	Leu	Gly	Glu	Gly	Tyr	Ile	Thr	Ile
					1125					1130					1135	
	Thr	Asp	Glu	Glu	Gly	His	Thr	Asp	Gln	Leu	Thr	Phe	Gly	Thr	Cys	Glu
				1140					1145					1150		
50	Glu	Ile	Asp	Ala	Ser	Asn	Met	Phe	Val	Thr	Thr	Gly	Tyr	Met	Thr	Lys
			1155					1160					1165			
	Glu	Leu	Glu	Phe	Phe	Pro	Asn	Thr	Glu	Lys	Val	Arg	Ile	Glu	Ile	Gly
			1170				1175					1180				
55	Glu	Thr	Glu	Gly	Thr	Phe	Gln	Val	Glu	Ser	Ile	Glu	Leu	Phe	Leu	Met
					1190						1195					1200
	Glu	Asp	Leu	Cys												

<210> 55
<211> 1131
<212> PRT
<213> Bacillus thuringiensis

5

<400> 55

10

15

20

25

30

35

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

	Ile	Tyr	Pro	Asp	Lys	Ile	Thr	Gln	Ile	Pro	Ala	Val	Lys	Ser	Ala	Ser
					485					490					495	
	Val	Glu	Gly	Gly	Thr	Trp	Lys	Asn	Val	Val	Lys	Gly	Pro	Gly	Phe	Thr
				500					505					510		
5	Gly	Gly	Asp	Val	Thr	Thr	Ala	Val	Ser	Pro	Ala	Asn	Leu	Ile	Asp	Val
			515					520					525			
	Ile	Lys	Ile	His	Val	Thr	Leu	Asp	Ser	Asn	Ser	Leu	Ser	Gln	Lys	Tyr
		530					535					540				
	Arg	Ala	Arg	Leu	Arg	Tyr	Ala	Ser	Asn	Ala	Tyr	Val	Ala	Ala	Thr	Leu
	545					550					555					560
10	Tyr	Thr	Asn	Thr	Ser	Ser	Asn	Tyr	His	Phe	Glu	Leu	Thr	Lys	Gly	Thr
					565					570					575	
	Thr	Glu	Gln	Phe	Ser	Thr	Tyr	Asn	Ser	Phe	Gln	Tyr	Val	Asp	Ile	Pro
				580					585					590		
	Gly	Ser	Ile	Gln	Phe	Asn	Asn	Thr	Ser	Asp	Thr	Val	Ser	Val	Tyr	Leu
			595					600					605			
15	His	Met	Asp	Ser	Thr	Thr	Asn	Ala	Ser	Val	Gln	Val	Asp	Arg	Ile	Glu
		610					615					620				
	Phe	Ile	Pro	Val	Asp	Ile	Asn	Tyr	Asp	Glu	Arg	Val	Gln	Leu	Glu	Lys
	625					630					635					640
	Thr	Gln	Lys	Ala	Val	Thr	Ala	Leu	Phe	Thr	Ala	Gly	Lys	His	Ala	Leu
					645					650					655	
20	Gln	Thr	Asp	Val	Thr	Asp	Tyr	Lys	Val	Asp	Gln	Val	Ser	Ile	Leu	Val
				660					665					670		
	Asp	Cys	Val	Ser	Ser	Glu	Leu	Tyr	Pro	Asn	Glu	Lys	Arg	Glu	Leu	Gln
			675					680					685			
	Asn	Leu	Val	Lys	Tyr	Ala	Lys	Arg	Leu	Ser	Tyr	Ser	Arg	Asn	Leu	Leu
		690					695					700				
25	Leu	Asp	Pro	Thr	Phe	Asp	Ser	Ile	Asn	Ser	Ser	Val	Glu	Asn	Gly	Trp
	705					710					715					720
	Tyr	Gly	Ser	Asn	Gly	Ile	Ala	Ile	Gly	Asn	Gly	Asp	Tyr	Val	Phe	Lys
					725				730						735	
	Gly	Asn	Tyr	Leu	Ile	Phe	Ser	Gly	Thr	Asn	Asp	Thr	Gln	Tyr	Pro	Thr
				740				745						750		
30	Tyr	Leu	Tyr	Gln	Lys	Ile	Asp	Glu	Ser	Lys	Leu	Lys	Glu	Tyr	Thr	Arg
			755					760					765			
	Tyr	Lys	Leu	Arg	Gly	Phe	Ile	Glu	Asn	Ser	Gln	Asp	Leu	Glu	Ala	Tyr
		770					775					780				
	Val	Val	Arg	Tyr	Asp	Ala	Lys	His	Glu	Thr	Leu	Asp	Val	Ser	Asn	Asn
						790					795					800
35	Leu	Leu	Pro	Asp	Val	Leu	Pro	Val	Asn	Ala	Cys	Gly	Glu	Pro	Asn	Arg
					805					810					815	
	Cys	Val	Ala	Leu	Gln	Tyr	Leu	Asp	Lys	Asn	Pro	Arg	Leu	Glu	Cys	Ser
				820					825					830		
	Ser	Ile	Gln	Asp	Gly	Ile	Leu	Ser	Asp	Ser	His	Ser	Phe	Ser	Leu	Asn
				835					840					845		
40	Ile	Asp	Thr	Gly	Ser	Ile	Asp	Leu	Asn	Glu	Asn	Val	Gly	Ile	Trp	Val
		850					855						860			
	Leu	Phe	Lys	Ile	Ser	Thr	Pro	Glu	Gly	Tyr	Ala	Lys	Phe	Gly	Asn	Leu
		865				870					875					880
	Glu	Val	Ile	Glu	Asp	Gly	Pro	Val	Ser	Gly	Glu	Ala	Leu	Ala	Arg	Val
					885					890					895	
45	Lys	Arg	Gln	Glu	Thr	Lys	Trp	Arg	Asn	Lys	Leu	Ala	Gln	Leu	Arg	Thr
				900					905					910		
	Glu	Thr	Gln	Ala	Ile	Tyr	Thr	Arg	Ala	Lys	Gln	Ala	Leu	Asp	Asn	Leu
				915				920						925		
	Phe	Thr	Asp	Ala	Gln	Asp	Ser	Tyr	Leu	Lys	Ile	Gly	Ala	Thr	Phe	Ala
		930					935						940			
	Ala	Ile	Val	Ala	Ala	Arg	Lys	Ile	Val	Gln	Ser	Ile	Arg	Glu	Ala	Tyr
						950					955					960
	Met	Ser	Trp	Leu	Ser	Val	Val	Pro	Gly	Val	Asn	Tyr	Pro	Ile	Phe	Thr
					965					970					975	
55	Glu	Leu	Asn	Glu	Arg	Val	Gln	Arg	Ala	Phe	Gln	Leu	Tyr	Asp	Gly	Arg
				980					985					990		
	Asn	Val	Val	Arg	Asn	Gly	Gln	Phe	Leu	Asn	Gly	Val	Leu	Asp	Trp	Ile

EP 2 728 007 B1

				995					1000					1005				
				Val Thr Ser Asp Val Ser Val Gln Glu Glu Asn Gly Asn Asn Val Leu														
				1010				1015				1020						
5				Val Leu Ser Asn Trp Asp Ala Gln Val Leu Gln Cys Leu Lys Leu Tyr														
				1025				1030				1035						1040
				Gln Asp Arg Gly Tyr Ile Leu Arg Val Thr Ala Arg Lys Glu Gly Leu														
				1045							1050							1055
				Gly Glu Gly Tyr Ile Thr Ile Thr Asp Glu Glu Gly Asn Thr Asp Gln														
				1060						1065					1070			
10				Leu Thr Phe Gly Ser Cys Glu Glu Ile Asp Thr Ser Asn Ser Phe Val														
				1075				1080						1085				
				Ser Thr Gly Tyr Met Thr Lys Glu Leu Glu Phe Phe Pro Asp Thr Glu														
				1090				1095					1100					
				Lys Val His Ile Glu Ile Gly Glu Thr Glu Gly Ile Phe Gln Val Glu														
				1105				1110				1115						1120
15				Ser Val Glu Leu Phe Leu Met Glu Asp Leu Cys														
				1125						1130								

<210> 56

<211> 775

<212> PRT

<213> *Bacillus thuringiensis*

<400> 56

EP 2 728 007 B1

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

EP 2 728 007 B1

	Glu	Arg	Leu	Ile	Val	Ser	Glu	Asn	Gln	Asn	Ile	Ser	Thr	Gly	Leu	Gly
					325					330					335	
	Arg	Thr	Val	Thr	Ala	Ser	Thr	Ser	Ala	Ser	Ser	Thr	Ala	Gly	Ile	Thr
				340					345					350		
5	Ala	Gly	Ile	Asp	Ala	Thr	Val	Gly	Ala	Ser	Leu	Leu	Gly	Pro	Ser	Gly
			355					360					365			
	Ser	Val	Thr	Ala	His	Phe	Ser	Tyr	Thr	Gly	Ser	Ser	Thr	Ala	Ala	Val
		370					375					380				
10	Glu	Asn	Ser	Ser	Ser	Asn	Asn	Trp	Ser	Asp	Asp	Leu	Gly	Ile	Asn	Thr
	385					390					395					400
	Ala	His	Ser	Ala	Tyr	Leu	Asn	Ala	Asn	Val	Arg	Tyr	Tyr	Asn	Thr	Gly
				405						410					415	
	Thr	Ala	Pro	Ile	Tyr	Asn	Val	Thr	Pro	Thr	Thr	Asn	Phe	Val	Leu	Asp
				420					425					430		
15	Ser	Glu	Thr	Ile	Val	Thr	Val	Arg	Ala	Lys	Glu	Asn	Gln	Leu	Gly	Asp
			435					440					445			
	Val	Leu	Lys	Ala	Gly	Gly	Thr	Tyr	Pro	Glu	Lys	His	Leu	Asn	Pro	Ile
		450					455					460				
	Ala	Leu	Asn	Thr	Leu	Asp	Asp	Phe	Gly	Ser	Gln	Leu	Ile	Pro	Ile	Asn
	465					470					475					480
20	Tyr	Asp	Gln	Thr	Lys	Arg	Leu	Glu	Asn	Gly	Asn	Lys	Leu	Gln	Leu	Gln
				485						490					495	
	Thr	Thr	Gln	Ala	Ser	Gly	Leu	Tyr	Gly	Lys	Met	Asn	Ser	Asn	Gly	Gly
			500						505					510		
25	Leu	Asn	Ile	His	Pro	Ser	Gln	Glu	Trp	Glu	Pro	Val	Arg	Ala	Gln	Ile
		515						520					525			
	Glu	Ser	Val	Ser	Ala	Gly	Ile	Val	Leu	Asp	Thr	Gly	Glu	Glu	Val	Leu
		530					535					540				
	Glu	Arg	Arg	Val	Ala	Thr	Arg	Asp	Asp	Arg	Asp	Pro	Glu	Asp	Leu	Thr
	545					550				555						560
30	Pro	Glu	Ile	Thr	Ile	Gly	Glu	Ala	Ile	Lys	Ile	Ala	Phe	Asp	Thr	Thr
				565						570					575	
	Glu	Gln	Gly	Gly	Lys	Leu	Gln	Tyr	Lys	Asp	Thr	Pro	Leu	Asn	Glu	Ser
			580						585					590		
	Leu	Val	Glu	Leu	Ile	Val	Asp	Glu	Ser	Thr	Ala	Arg	Glu	Ile	Lys	Ala
		595					600						605			
35	Gln	Leu	Asp	Gly	Asn	Pro	Gly	Leu	Glu	Lys	Lys	Ile	Tyr	Asn	Val	Lys
		610					615					620				
	Leu	Lys	Arg	Gly	Met	Asn	Ile	Met	Leu	Lys	Lys	Pro	Ile	Trp	Tyr	Ser
	625				630						635					640
40	Asp	Phe	Asp	Thr	His	Gln	His	Asn	Trp	Ser	Asn	Ile	Thr	Ile	Ala	Pro
				645						650					655	
	Glu	Glu	Gly	Ile	Thr	Gly	Asn	Ala	Gly	Lys	Ile	Ser	Gln	Gly	Ser	Val
			660						665					670		
	Gln	Pro	Ala	Phe	Leu	Arg	Tyr	Gln	Thr	Val	Glu	Asp	Phe	Lys	Asn	Leu
		675						680					685			
45	Lys	Pro	Asn	Thr	Arg	Tyr	Lys	Leu	Ser	Ala	Ser	Ile	Arg	Tyr	Leu	Asp
		690					695					700				
	Leu	Glu	Pro	Gly	Gly	Val	Thr	Gly	Ala	Tyr	Ile	Arg	Val	Asn	Asp	Leu
	705					710					715					720
	Pro	Asn	Asn	Glu	Tyr	Leu	Ile	Arg	Ser	Asn	Leu	Tyr	Glu	Arg	Ile	Glu
				725						730					735	
50	Ser	Thr	Phe	Thr	Thr	Gly	Ile	Ile	Pro	Ser	Gly	Ile	Thr	Asp	Phe	Arg
			740						745					750		
	Ile	Ala	Thr	Thr	Gly	Ser	Arg	Asp	Met	Leu	Leu	Asp	Asp	Ile	Thr	Leu
		755						760					765			
55	Val	Glu	Leu	Gly	Pro	Ser	Asn									
		770					775									

<210> 57

<211> 672

<212> PRT

<213> Bacillus thuringiensis

<400> 57

5

10

15

20

25

30

35

40

45

50

55

EP 2 728 007 B1

	Met	Lys	Asn	Met	Asn	Ser	Tyr	Gln	Asn	Lys	Asn	Lys	Asn	Glu	Tyr	Glu
	1				5					10					15	
	Ile	Leu	Asp	Thr	Ser	Arg	Ser	Ser	Ser	Thr	Met	Ser	Thr	Arg	Tyr	Pro
				20					25					30		
5	Arg	Tyr	Pro	Leu	Ala	Glu	Asn	Pro	Gln	Ile	Ser	Met	Gln	Asn	Thr	Asn
			35					40					45			
	Tyr	Lys	Asp	Trp	Ile	Asn	Met	Cys	Ala	Ser	Arg	Asn	Leu	Glu	Asp	Gly
		50				55						60				
	Ile	Tyr	Pro	Thr	Ser	Ala	Asn	Asp	Val	Ile	Thr	Asn	Ser	Ile	Asn	Ile
	65				70						75				80	
10	Ser	Ser	Tyr	Ile	Leu	Ser	Met	Leu	Gly	Met	Pro	Asn	Leu	Ser	Ser	Ile
				85						90					95	
	Ile	Ala	Ile	Trp	Gly	Val	Leu	Phe	Asn	Ala	Phe	Trp	Pro	Val	Ser	Gly
				100					105					110		
	Asn	Gln	Trp	Glu	His	Tyr	Met	Asn	His	Val	Gln	Ala	Leu	Ile	Lys	Arg
				115				120					125			
15	Glu	Leu	Gln	Ala	Phe	Ala	Arg	Glu	Gln	Ala	Leu	Arg	Gln	Leu	Glu	Gly
		130					135					140				
	Leu	Gly	Gly	Asn	Leu	Gly	Leu	Tyr	Lys	Glu	Ala	Leu	Ala	Glu	Trp	Glu
					150						155				160	
	Gln	Asp	Arg	Asp	Asn	Pro	Thr	Thr	Lys	Glu	Arg	Val	Arg	Asp	Arg	Phe
					165					170					175	
20	Arg	Ile	Leu	Asp	Gly	Phe	Phe	Thr	Gln	Tyr	Ile	Pro	Val	Phe	Arg	Ile
				180					185					190		
	Gln	Gly	Tyr	Glu	Val	Gln	Leu	Leu	Ser	Ile	Tyr	Ala	Lys	Val	Val	Asn
				195				200					205			
	Leu	His	Leu	Leu	Leu	Leu	Arg	Asp	Ala	Ser	Met	Phe	Gly	Ala	Asp	Trp
		210					215					220				
25	Gly	Met	Ser	Gln	Thr	Asn	Ile	Asn	Asp	Asn	Tyr	Asn	Arg	Gln	Met	Lys
		225				230					235				240	
	Leu	Thr	Ser	Leu	Tyr	Thr	Asn	His	Cys	Val	Asp	Phe	Tyr	Asn	Gln	Gly
				245						250					255	
	Leu	Asn	Glu	Ala	Arg	Ala	Leu	Ser	Asn	Ser	Ser	Trp	Asp	Ile	Phe	Asn
				260					265					270		
30	Asp	Tyr	Arg	Arg	Glu	Met	Thr	Leu	Thr	Val	Leu	Asp	Ile	Val	Ala	Leu
				275				280					285			
	Phe	Pro	Ala	Tyr	Asp	Tyr	Arg	Arg	Tyr	Pro	Ile	Thr	Thr	Lys	Val	Glu
		290				295						300				
35	Leu	Thr	Arg	Glu	Ile	Tyr	Thr	Pro	Ala	Ile	Ala	Ser	Gln	Thr	Trp	Ser
					310						315				320	
	Asn	His	Asn	His	Leu	Ser	Pro	Asn	Val	Asn	Phe	Gln	Phe	Tyr	Glu	Asn
					325					330					335	
	Asn	Leu	Val	Arg	Pro	Pro	Ala	Phe	Phe	Thr	Trp	Leu	Asp	Arg	Thr	Glu
				340				345					350			
40	Met	Phe	Ser	Arg	Asn	Leu	Ser	Ile	Glu	Val	Ser	Glu	Ala	Trp	Gly	Gly
				355				360					365			
	His	Ile	Asn	His	Phe	His	His	Thr	Gly	Glu	Gln	Pro	Leu	Ser	Ser	Arg
		370				375						380				
	Ser	Gly	Phe	Ile	Gly	Ser	Asp	Gln	Arg	Arg	Val	Ser	Tyr	Tyr	Asp	Phe
		385			390						395				400	
45	Asn	Phe	Val	Gly	Asn	Asp	Val	Phe	Arg	Ile	Tyr	Ser	Arg	Val	Met	Ser
				405						410					415	
	Asn	Gln	Val	Gly	Asn	Phe	Phe	Gly	Val	Gly	Gln	Gly	Asp	Phe	Phe	Leu
				420				425					430			
	Val	Asn	Ser	Asp	Asn	Ser	Asn	Thr	Lys	Thr	Ile	Ser	Phe	Thr	Thr	Arg
				435				440					445			
50	Ala	Thr	Asn	Ser	Asn	Gln	Arg	Ser	Ile	Phe	Ser	Gln	Phe	Pro	Gly	Glu
		450				455						460				
	Asn	Ser	Asp	Pro	Pro	Thr	Ser	Lys	Asp	Tyr	Ser	His	Arg	Leu	Ser	Trp
					470						475				480	
	Ile	Ser	Gly	Ala	Phe	Ile	Gly	Ser	Asp	Leu	Ala	Asn	Val	Leu	Ser	Tyr
					485					490					495	
55	Gly	Trp	Thr	His	Arg	Ser	Val	Asp	Pro	Asn	Asn	Thr	Ile	Tyr	Pro	Asp
				500					505					510		

EP 2 728 007 B1

	Arg	Ile	Thr	Gln	Val	Pro	Ala	Val	Lys	Ala	Ser	Ser	Ala	Pro	Asp	Cys
			515					520					525			
	Thr	Val	Ile	Leu	Gly	Pro	Gly	Ser	Thr	Gly	Gly	Asn	Leu	Val	Ser	Phe
		530					535					540				
5	Gly	Arg	Ser	Gly	Arg	Leu	Asn	Met	Gln	Phe	Lys	Phe	Thr	Asn	Ile	Gln
	545					550					555					560
	Thr	Glu	Tyr	Arg	Val	Arg	Ile	Arg	Tyr	Ala	Ser	Thr	Ala	Val	Asn	Thr
					565					570					575	
	Leu	Phe	Val	Ser	Phe	Ser	Asp	Tyr	Asn	Arg	Asp	Ile	Ala	Leu	Asn	Ser
10				580					585					590		
	Thr	Gly	Ala	Leu	Ser	Leu	Asn	Asn	Leu	Arg	Asn	Glu	Asn	Phe	Ala	Tyr
			595					600					605			
	Phe	Glu	Val	Pro	Gly	Gly	Ile	Phe	Arg	Pro	Ala	Leu	Gly	Asn	Thr	Leu
		610					615					620				
15	Ile	Ile	Ser	Asn	Trp	Thr	Thr	Val	Ala	Pro	Arg	Leu	Val	Ile	Asp	Lys
	625					630					635					640
	Ile	Glu	Phe	Ile	Pro	Ile	Asn	Ala	Thr	Thr	Ala	Arg	Tyr	Gly	Ser	Lys
					645					650					655	
	Gln	Glu	Leu	Glu	Lys	Ala	Thr	Lys	Val	Val	Asn	Asn	Leu	Phe	Ile	Asn
20				660					665					670		

<210> 58

<211> 1225

<212> PRT

<213> Bacillus thuringiensis

<400> 58

EP 2 728 007 B1

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

40

45

50

55

EP 2 728 007 B1

5																	
10																	
15																	
20																	
25																	
30																	
35																	
40																	
45																	

EP 2 728 007 B1

Tyr Arg Leu Arg Gly Phe Val Gly Ser Ser Gln Gly Leu Glu Ile Phe
 820 825 830
 Thr Ile Arg His Gln Thr Asn Arg Ile Val Lys Asn Val Pro Asp Asp
 835 840 845
 5 Leu Leu Pro Asp Val Pro Pro Val Asn Ser Asp Gly Arg Ile Asn Arg
 850 855 860
 Cys Ser Glu Gln Lys Tyr Val Asn Ser Arg Leu Glu Gly Glu Arg Gly
 865 870 875 880
 10 Leu Pro Asn Gly Asn Arg Ser Ala Glu Ala His Glu Phe Ser Leu Pro
 885 890 895
 Ile Asp Ile Gly Glu Leu Asp Tyr Asn Glu Asn Ala Gly Ile Trp Val
 900 905 910
 Gly Phe Lys Ile Thr Asp Pro Glu Gly Tyr Ala Thr Leu Gly Asn Leu
 915 920 925
 15 Glu Leu Val Glu Glu Gly Pro Leu Ser Gly Asp Ala Leu Glu Arg Leu
 930 935 940
 Gln Arg Glu Glu Gln Gln Trp Lys Leu Gln Met Thr Lys Arg Arg Glu
 945 950 955 960
 Glu Thr Asp Arg Lys Tyr Met Ala Ala Lys Gln Ala Val Asp Arg Leu
 965 970 975
 20 Tyr Ala Asp Tyr Gln Asp Gln Gln Leu Asn Pro Asn Val Glu Ile Thr
 980 985 990
 Asp Ile Thr Ala Ala Gln Asp Leu Ile Gln Ser Ile Pro Tyr Val Tyr
 995 1000 1005
 25 Asn Glu Ile Phe Pro Glu Ile Gln Gly Met Asn Tyr Ala Lys Phe Thr
 1010 1015 1020
 Glu Leu Ser Asn Arg Leu Gln Arg Ala Trp Gly Leu Tyr Asp Gln Arg
 1025 1030 1035 1040
 Asn Ala Ile Pro Asn Gly Asp Phe Arg Asn Gly Leu Ser Asn Trp Asn
 1045 1050 1055
 30 Thr Thr Pro Gly Val Glu Val Gln Gln Ile Asn Asp Thr Ser Val Leu
 1060 1065 1070
 Val Ile Pro Asn Trp Asp Glu Gln Val Ser Gln Gln Phe Thr Val Gln
 1075 1080 1085
 Pro Asn Gln Arg Tyr Val Leu Arg Val Thr Ala Arg Lys Glu Gly Val
 1090 1095 1100
 35 Gly Asn Gly Tyr Val Ser Ile Arg Asp Gly Gly Asn Gln Thr Glu Thr
 1105 1110 1115 1120
 Leu Thr Phe Ser Ala Ser Asp Tyr Asp Thr Asn Asn Val Tyr Asn Thr
 1125 1130 1135
 Gln Ala Ser Asn Thr Asn Gly Tyr Asn Thr Asn Asn Ala Tyr Asn Thr
 1140 1145 1150
 40 Gln Val Ser Asn Thr Asn Gly Tyr Asn Thr Asn Asn Ala Tyr Asn Thr
 1155 1160 1165
 Asn Gly Tyr Asn Thr Gln Ala Ser Asn Thr Asn Gly Leu Tyr Asn Glu
 1170 1175 1180
 45 Gln Thr Gly Tyr Ile Thr Lys Thr Val Thr Phe Ile Pro Tyr Thr Glu
 1185 1190 1195 1200
 Gln Val Trp Ile Glu Met Ser Glu Thr Glu Gly Thr Phe Tyr Ile Glu
 1205 1210 1215
 Ser Val Glu Leu Ile Val Asp Val Glu
 1220 1225

<210> 59

<211> 1184

<212> PRT

<213> Bacillus thuringiensis

<400> 59

EP 2 728 007 B1

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

10

15

20

25

30

35

40

45

50

55

EP 2 728 007 B1

[illegible]

EP 2 728 007 B1

	Lys	Gly	Pro	Gly	Ser	Thr	Gly	Gly	Asp	Leu	Val	Lys	Arg	Gly	Ser	Ser
				565						570					575	
	Gly	Asn	Ile	Gly	Ser	Met	Asn	Val	Thr	Val	Asn	Ser	Pro	Leu	Ser	Gln
				580						585					590	
5	Lys	Tyr	Arg	Val	Arg	Val	Arg	Tyr	Ala	Thr	Asn	Ala	Ser	Gly	Gln	Leu
			595					600					605			
	Asn	Val	Ser	Ile	Asn	Asp	Lys	Leu	Thr	Leu	Gln	Lys	Pro	Phe	Glu	Arg
		610					615					620				
	Thr	Gly	Thr	Thr	Ile	Gly	Glu	Gly	Thr	Asp	Leu	Ser	Tyr	Asp	Ser	Phe
		625				630						635				640
10	Gly	Tyr	Leu	Glu	Tyr	Ser	Thr	Thr	Ile	Gln	Phe	Pro	Asn	Glu	His	Pro
					645						650				655	
	Lys	Ile	Thr	Phe	Asn	Leu	Ser	His	Trp	Ser	Gly	Ser	Gly	Ala	Phe	Tyr
				660					665						670	
	Ile	Asp	Lys	Ile	Glu	Phe	Ile	Pro	Val	Asp	Glu	Asn	Tyr	Asp	Glu	Arg
			675					680					685			
15	Val	Thr	Leu	Glu	Lys	Ala	Gln	Lys	Ala	Val	Asn	Ala	Leu	Phe	Thr	Ala
							695					700				
	Gly	Arg	Asn	Ala	Leu	Gln	Lys	Asp	Val	Thr	Asp	Phe	Lys	Val	Asp	Gln
		705				710						715				720
	Val	Ser	Ile	Leu	Val	Asp	Cys	Ile	Pro	Gly	Glu	Leu	Tyr	Pro	Asn	Glu
					725					730					735	
20	Lys	Arg	Glu	Leu	Ser	Leu	Val	Lys	Tyr	Ala	Lys	Arg	Leu	Ser	Tyr	
				740					745					750		
	Ser	Arg	Asn	Leu	Leu	Leu	Asp	Pro	Thr	Phe	Asp	Ser	Ile	Asn	Ser	Pro
			755					760					765			
	Asp	Glu	Asn	Gly	Trp	Tyr	Gly	Ser	Asn	Gly	Ile	Ala	Ile	Gly	Asn	Gly
		770					775					780				
25	Asn	Phe	Val	Phe	Lys	Gly	Asn	Tyr	Leu	Ile	Phe	Ser	Gly	Thr	Asn	Asp
						790						795				800
	Thr	Gln	Tyr	Pro	Thr	Tyr	Leu	Tyr	Gln	Lys	Ile	Asp	Glu	Ser	Lys	Leu
					805					810					815	
	Lys	Glu	Tyr	Thr	Arg	Tyr	Lys	Leu	Arg	Gly	Phe	Ile	Glu	Ser	Ser	Gln
				820					825					830		
30	Asp	Leu	Glu	Ala	Tyr	Val	Ile	Arg	Tyr	Asp	Ala	Lys	His	Glu	Thr	Leu
			835					840					845			
	Asp	Val	Ser	Asn	Asn	Leu	Phe	Pro	Asp	Ile	Ser	Pro	Val	Asn	Ala	Cys
		850					855					860				
	Gly	Glu	Pro	Asn	Arg	Cys	Ala	Ala	Leu	Gln	Tyr	Leu	Asp	Glu	Asn	Pro
		865				870					875					880
35	Arg	Leu	Glu	Cys	Ser	Ser	Ile	Gln	Asp	Gly	Ile	Leu	Ser	Asp	Ser	His
					885					890					895	
	Ser	Phe	Ser	Leu	Asn	Ile	Asp	Thr	Gly	Ser	Ile	Asp	Tyr	Asp	Glu	Asn
				900					905					910		
40	Val	Gly	Ile	Trp	Val	Leu	Phe	Lys	Ile	Ser	Thr	Pro	Glu	Gly	Tyr	Ala
			915					920						925		
	Lys	Phe	Gly	Asn	Leu	Glu	Val	Ile	Glu	Asp	Gly	Leu	Val	Ile	Gly	Glu
		930					935					940				
	Ala	Leu	Ala	Arg	Val	Lys	Arg	Gln	Glu	Thr	Lys	Trp	Arg	Asn	Lys	Leu
		945				950						955				960
45	Thr	Gln	Leu	Arg	Thr	Glu	Thr	Gln	Ala	Ile	Tyr	Thr	Arg	Ala	Lys	Gln
					965					970					975	
	Ala	Ile	Asp	Asn	Leu	Phe	Thr	Asn	Ala	Gln	Asp	Ser	His	Leu	Lys	Ile
				980					985					990		
	Gly	Ala	Thr	Phe	Ala	Ser	Ile	Val	Ala	Ala	Arg	Lys	Ile	Val	Gln	Ser
			995					1000					1005			
50	Ile	Arg	Glu	Ala	Tyr	Met	Ser	Trp	Leu	Ser	Ile	Val	Pro	Ser	Val	Asn
		1010					1015					1020				
	Tyr	Pro	Ile	Phe	Thr	Glu	Leu	Asn	Glu	Arg	Val	Gln	Arg	Ala	Phe	Arg
		1025				1030					1035					1040
	Leu	Tyr	Asp	Val	Arg	Asn	Val	Val	Arg	Asn	Gly	Arg	Phe	Leu	Ser	Gly
					1045					1050					1055	
55	Val	Ser	Asp	Trp	Ile	Val	Thr	Ser	Asp	Val	Lys	Val	Gln	Glu	Glu	Asn
				1060					1065					1070		
	Gly	Asn	Asn	Val	Leu	Val	Leu	Ser	Asn	Trp	Asp	Ala	Gln	Val	Leu	Gln

EP 2 728 007 B1

[illegible]

15 <210> 60
 <211> 1102
 <212> PRT
 <213> Bacillus thuringiensis

20 <400> 60

25

30

35

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

	Gly	Asn	Ser	Ile	Tyr	Gln	Thr	Leu	Ser	Ala	Pro	Ser	Ala	Ile	Leu	Thr
			355					360					365			
	Pro	Asn	Tyr	Ile	Tyr	Tyr	Gly	Ile	Glu	Gln	Val	Glu	Phe	Tyr	Gly	Asn
		370					375					380				
5	Lys	Gly	Asn	Val	Tyr	Tyr	Arg	Gly	Gly	Asn	Lys	Tyr	Pro	Leu	Ser	Val
	385					390					395					400
	Asp	Ser	Ala	Asn	Gln	Leu	Pro	Pro	Asp	Val	Glu	Pro	Ile	Thr	Glu	Asn
				405						410					415	
	Tyr	Asn	His	Val	Leu	Cys	His	Ala	Thr	Ala	Val	Pro	Val	Lys	Asp	Gly
				420						425					430	
10	Gly	Thr	Val	Pro	Ile	Phe	Ser	Trp	Thr	His	Arg	Ser	Ala	Asp	Tyr	Tyr
			435					440					445			
	Asn	Thr	Ile	Tyr	Pro	Asp	Lys	Ile	Thr	Gln	Leu	Pro	Ala	Val	Lys	Ser
		450					455					460				
	Thr	Pro	Ser	Pro	Glu	Val	Glu	Gly	Leu	Lys	Val	Gln	Glu	Gly	Pro	Gly
	465					470					475					480
15	Phe	Thr	Gly	Gly	Asp	Leu	Val	Val	Ala	Lys	Ser	Ser	Asn	Gln	Thr	Ile
					485					490					495	
	Val	Arg	Leu	Lys	Val	Thr	Val	Asp	Ser	Pro	Gly	Thr	Gln	Lys	Tyr	Arg
				500					505					510		
	Ile	Arg	Leu	Lys	Tyr	Ala	Ala	Thr	Ser	Asn	Phe	Tyr	Leu	Gly	Ala	Tyr
			515					520					525			
20	Ala	Gly	Ser	Asn	Gly	Gly	Asn	Gly	Ile	Pro	Gly	Ile	Ser	Thr	Val	Pro
		530					535					540				
	Lys	Thr	Met	Asn	Ile	Glu	Asp	Pro	Leu	Ser	Tyr	Thr	Ser	Phe	Ala	Tyr
	545					550					555					560
	Ile	Asp	Leu	Pro	Asp	Ser	Tyr	Thr	Phe	Ser	Gln	Lys	Asp	Glu	Val	Ile
					565					570					575	
25	Arg	Phe	Thr	Ile	Asn	Ile	Tyr	Glu	Ser	Gly	Gly	Ala	Val	Tyr	Ala	Asp
				580					585					590		
	Lys	Val	Glu	Phe	Ile	Pro	Val	Asp	Ala	Asp	Tyr	Asp	Glu	Gly	Val	Gln
			595					600					605			
	Leu	Glu	Lys	Ala	Gln	Lys	Ala	Val	Asn	Ala	Leu	Phe	Thr	Ala	Gly	Arg
		610					615					620				
30	Asn	Ala	Leu	Gln	Thr	Asp	Val	Thr	Asp	Tyr	Lys	Val	Asp	Gln	Val	Ser
	625					630					635					640
	Ile	Leu	Val	Asp	Cys	Val	Ser	Gly	Glu	Leu	Tyr	Pro	Asn	Glu	Lys	Arg
				645						650					655	
	Glu	Leu	Gln	Asn	Leu	Ile	Lys	Tyr	Ala	Lys	Arg	Leu	Ser	Tyr	Ser	Arg
				660					665					670		
35	Asn	Leu	Leu	Leu	Asp	Pro	Thr	Phe	Asp	Ser	Ile	Asn	Ser	Ser	Asp	Glu
			675					680					685			
	Asn	Gly	Trp	Tyr	Gly	Ser	Asn	Gly	Ile	Ala	Ile	Gly	Ser	Gly	Asn	Ile
		690					695					700				
	Val	Phe	Lys	Gly	Asn	Tyr	Leu	Ile	Phe	Ser	Gly	Thr	Asn	Asp	Glu	Gln
	705					710					715					720
40	Tyr	Pro	Thr	Tyr	Leu	Tyr	Gln	Lys	Ile	Asp	Glu	Ser	Lys	Leu	Lys	Glu
					725					730					735	
	Tyr	Thr	Arg	Tyr	Lys	Leu	Arg	Gly	Phe	Ile	Glu	Ser	Ser	Gln	Asp	Leu
				740					745					750		
45	Glu	Ala	Tyr	Val	Ile	Arg	Tyr	Asp	Ala	Lys	His	Gln	Thr	Met	Asp	Val
			755					760					765			
	Ser	Asn	Asn	Leu	Phe	Ser	Asp	Ile	Thr	Pro	Val	Asn	Ala	Cys	Gly	Glu
		770					775					780				
	Pro	Asn	Arg	Cys	Ala	Ala	Leu	Pro	Tyr	Leu	Asp	Glu	Asn	Pro	Arg	Leu
	785					790					795					800
50	Glu	Cys	Ser	Ser	Ile	Gln	Asp	Gly	Ile	Leu	Ser	Asp	Ser	His	Ser	Phe
					805					810					815	
	Ser	Leu	His	Ile	Asp	Thr	Gly	Ser	Ile	Asp	Phe	Asn	Glu	Asn	Val	Gly
				820					825					830		
	Ile	Trp	Val	Leu	Phe	Lys	Ile	Ser	Thr	Leu	Glu	Gly	Tyr	Ala	Lys	Phe
			835					840					845			
55	Gly	Asn	Leu	Glu	Val	Ile	Glu	Asp	Gly	Pro	Val	Ile	Gly	Glu	Ala	Leu
		850					855					860				
	Ala	Arg	Val	Lys	Arg	Gln	Glu	Thr	Lys	Trp	Arg	Asn	Lys	Leu	Thr	Gln

EP 2 728 007 B1

	865		870		875		880
	Leu Arg Thr Glu Thr	Gln Ala Ile Tyr Thr	Arg Ala Lys Gln Ala Ile				
		885		890			895
5	Asp Asn Leu Phe Thr	Asn Glu Gln Asp Ser	His Leu Lys Ile Gly Thr				
		900		905			910
	Thr Phe Ala Leu Ile	Val Ala Ala Arg Lys	Ile Val Gln Ser Ile Arg				
		915		920			925
	Glu Ala Tyr Met Ser	Trp Leu Ser Ile Val	Pro Gly Val Asn Tyr Pro				
		930		935			940
10	Ile Phe Thr Glu Leu	Asn Glu Arg Val Gln	Gln Ala Phe Gln Leu Tyr				
		945		950			955
	Asp Val Arg Asn Val	Val Arg Asn Gly Arg	Phe Gln Ser Gly Thr Ser				
		965		970			975
	Asp Trp Ile Val Thr	Ser Asp Val Lys Val	Gln Glu Glu Asn Gly Asn				
		980		985			990
15	Asn Val Leu Val Leu	Ser Asn Trp Asp Ala	Gln Val Leu Gln Cys Met				
		995		1000			1005
	Thr Leu Tyr Gln Asp	Arg Gly Tyr Ile Leu	Arg Val Thr Ala Arg Lys				
		1010		1015			1020
	Glu Gly Leu Gly Glu	Gly Tyr Val Thr Ile	Thr Asp Glu Glu Gly Asn				
20		1025		1030			1035
	Thr Asp Gln Leu Arg	Phe Gly Gly Cys Glu	Glu Ile Asp Ala Ser Asn				
		1045		1050			1055
	Ser Phe Val Ser Thr	Gly Tyr Val Thr Lys	Glu Leu Glu Phe Phe Pro				
		1060		1065			1070
25	Asp Thr Glu Lys Val	Arg Ile Glu Ile Gly	Glu Thr Glu Gly Ile Phe				
		1075		1080			1085
	Gln Val Gly Ser Val	Glu Leu Phe Leu Met	Glu Asp Leu Cys				
		1090		1095			1100

30 <210> 61
 <211> 1131
 <212> PRT
 <213> Bacillus thuringiensis

35 <400> 61

40

45

50

55

EP 2 728 007 B1

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

30

35

40

45

50

55

EP 2 728 007 B1

	Leu	Lys	Gly	Asn	Leu	Thr	Gly	Glu	Asn	Trp	Tyr	Thr	Tyr	Asn	Arg	Phe
	225					230					235					240
	Arg	Arg	Glu	Met	Thr	Leu	Met	Val	Leu	Asp	Val	Val	Ala	Leu	Phe	Pro
					245					250						255
5	Asn	Tyr	Asp	Thr	Arg	Met	Tyr	Pro	Ile	Gly	Thr	Ser	Ser	Glu	Leu	Thr
				260					265					270		
	Arg	Met	Ile	Tyr	Thr	Asp	Pro	Ile	Ala	Tyr	Thr	Gln	Ser	Asp	Pro	Trp
			275					280					285			
	Tyr	Lys	Ile	Thr	Ser	Leu	Ser	Phe	Ser	Asn	Ile	Glu	Asn	Ser	Ala	Ile
		290					295					300				
10	Pro	Ser	Pro	Ser	Phe	Phe	Arg	Trp	Leu	Lys	Ser	Val	Ser	Ile	Asn	Ser
						310						315				320
	Gln	Trp	Trp	Gly	Ser	Gly	Pro	Ser	Gln	Thr	Tyr	Tyr	Trp	Val	Gly	His
					325					330					335	
	Glu	Leu	Val	Tyr	Ser	Asn	Ser	Asn	Ser	Asn	Gln	Ser	Leu	Lys	Val	Lys
				340				345						350		
15	Tyr	Gly	Asp	Pro	Asn	Ser	Phe	Ile	Glu	Pro	Pro	Asp	Ser	Phe	Ser	Phe
			355					360					365			
	Ser	Ser	Thr	Asp	Val	Tyr	Arg	Thr	Ile	Ser	Val	Val	Arg	Asn	Ser	Val
			370				375					380				
	Ser	Asn	Tyr	Ile	Val	Ser	Glu	Val	Arg	Phe	Asn	Ser	Ile	Ser	Ser	Thr
						390					395					400
20	Asn	Gln	Ile	Ser	Glu	Ile	Tyr	Lys	His	Gln	Ser	Asn	Trp	Ser	Arg	
					405				410						415	
	Gln	Glu	Thr	Lys	Asp	Ser	Ile	Thr	Glu	Leu	Ser	Leu	Ala	Ala	Asn	Pro
				420					425					430		
	Pro	Thr	Thr	Phe	Gly	Asn	Val	Ala	Glu	Tyr	Ser	His	Arg	Leu	Ala	Tyr
			435					440					445			
25	Ile	Ser	Glu	Ala	Tyr	Gln	Ser	His	Asn	Pro	Ser	Lys	Tyr	Pro	Thr	Tyr
			450				455					460				
	Ile	Pro	Val	Phe	Gly	Trp	Thr	His	Thr	Ser	Val	Arg	Tyr	Asp	Asn	Lys
					470						475					480
	Ile	Phe	Pro	Asp	Lys	Ile	Thr	Gln	Ile	Pro	Ala	Val	Lys	Ser	Ser	Ser
					485					490					495	
30	Ala	Gln	Gly	Gly	Ser	Trp	Lys	Asn	Ile	Val	Lys	Gly	Pro	Gly	Phe	Thr
				500					505					510		
	Gly	Gly	Asp	Val	Thr	Thr	Ala	Val	Ser	Pro	Ala	Thr	Val	Thr	Asp	Ile
			515					520					525			
	Ile	Lys	Ile	Gln	Val	Thr	Leu	Asp	Pro	Asn	Ser	Leu	Ser	Gln	Lys	Tyr
		530					535					540				
35	Arg	Ala	Arg	Leu	Arg	Tyr	Ala	Ser	Asn	Ala	Phe	Val	Pro	Ala	Thr	Leu
						550					555					560
	Tyr	Thr	Asn	Thr	Ser	Ser	Asn	Tyr	Asn	Phe	Glu	Leu	Lys	Lys	Gly	Thr
					565					570					575	
	Thr	Glu	Gln	Phe	Thr	Thr	Tyr	Asn	Ser	Tyr	Gln	Tyr	Val	Asp	Ile	Pro
					580				585					590		
40	Gly	Ser	Ile	Gln	Phe	Asn	Asn	Thr	Ser	Asp	Thr	Val	Ser	Val	Tyr	Leu
			595					600					605			
	His	Met	Asp	Ser	Thr	Ser	Asn	Val	Asn	Val	His	Val	Asp	Arg	Ile	Glu
							615					620				
45	Phe	Ile	Pro	Ile	Asp	Glu	Asn	Tyr	Asp	Glu	Arg	Phe	Gln	Leu	Glu	Lys
						630					635					640
	Ala	Gln	Lys	Ala	Val	Asn	Ala	Leu	Phe	Thr	Ala	Gly	Arg	Asn	Ala	Leu
					645					650					655	
	Gln	Thr	Asp	Val	Thr	Asp	Tyr	Lys	Val	Asp	Gln	Val	Ser	Ile	Leu	Val
				660					665					670		
50	Asp	Cys	Val	Ser	Gly	Glu	Leu	Tyr	Pro	Asn	Glu	Lys	Arg	Glu	Leu	Leu
			675					680					685			
	Ser	Leu	Val	Lys	Tyr	Ala	Lys	Arg	Leu	Ser	Tyr	Ser	Arg	Asn	Leu	Leu
			690				695					700				
	Leu	Asp	Pro	Thr	Phe	Asp	Ser	Ile	Asn	Ser	Pro	Glu	Glu	Asn	Gly	Trp
						710					715					720
55	Tyr	Gly	Ser	Asn	Gly	Ile	Ala	Ile	Gly	Ser	Gly	Asn	Ile	Val	Phe	Lys
					725					730					735	
	Gly	Asn	Tyr	Leu	Ile	Phe	Ser	Gly	Thr	Asn	Asp	Glu	Gln	Tyr	Pro	Thr

EP 2 728 007 B1

				740				745				750				
	Tyr	Leu	Tyr	Gln	Lys	Ile	Asp	Glu	Thr	Lys	Leu	Lys	Glu	Tyr	Thr	Arg
			755					760					765			
5	Tyr	Lys	Leu	Arg	Gly	Phe	Ile	Glu	Ser	Ser	Gln	Asp	Leu	Glu	Ala	Tyr
		770					775					780				
	Val	Ile	Arg	Tyr	Asp	Ala	Lys	His	Gln	Thr	Met	Asp	Val	Ser	Asn	Asn
	785					790					795					800
	Leu	Phe	Ser	Asp	Ile	Thr	Pro	Val	Asn	Ala	Cys	Gly	Glu	Pro	Asn	Arg
				805						810					815	
10	Cys	Ala	Ala	Leu	Pro	Tyr	Leu	Asp	Glu	Asn	Pro	Arg	Leu	Glu	Cys	Ser
			820						825					830		
	Ser	Ile	Gln	Asp	Gly	Ile	Leu	Ser	Asp	Ser	His	Ser	Phe	Ser	Leu	His
		835						840					845			
	Ile	Asp	Thr	Gly	Ser	Ile	Asp	Phe	Asn	Glu	Asn	Val	Gly	Ile	Trp	Val
	850						855					860				
15	Leu	Phe	Lys	Ile	Ser	Thr	Pro	Glu	Gly	Tyr	Ala	Arg	Phe	Gly	Asn	Leu
	865					870					875					880
	Glu	Val	Ile	Glu	Asp	Gly	Pro	Val	Ile	Gly	Glu	Ala	Leu	Ala	Arg	Val
				885						890					895	
	Lys	Arg	Gln	Glu	Thr	Lys	Trp	Arg	Asn	Lys	Leu	Thr	Gln	Leu	Arg	Thr
20			900						905					910		
	Glu	Thr	Gln	Ala	Ile	Tyr	Thr	Arg	Ala	Lys	Gln	Ala	Ile	Asp	Asn	Leu
		915						920					925			
	Phe	Thr	Asn	Ala	Gln	Asp	Ser	His	Leu	Lys	Ile	Gly	Ala	Thr	Phe	Ala
	930					935						940				
25	Ser	Ile	Val	Ala	Ala	Arg	Lys	Ile	Val	Gln	Ser	Ile	Arg	Glu	Ala	Tyr
	945					950					955					960
	Met	Ser	Trp	Leu	Ser	Ile	Val	Pro	Gly	Val	Asn	Tyr	Pro	Ile	Val	Thr
				965						970					975	
	Glu	Leu	Asn	Glu	Arg	Ile	Gln	Gln	Ala	Phe	Gln	Leu	Tyr	Asp	Val	Arg
			980						985					990		
30	Asn	Val	Val	Arg	Asn	Gly	Arg	Phe	Gln	Ser	Gly	Thr	Ser	Asp	Trp	Ile
			995					1000						1005		
	Val	Thr	Ser	Asp	Val	Arg	Val	Gln	Glu	Glu	Asn	Gly	Asn	Asn	Val	Leu
		1010					1015					1020				
	Val	Leu	Ser	Asn	Trp	Asp	Ala	Gln	Val	Leu	Gln	Cys	Met	Thr	Leu	Tyr
35	1025					1030					1035					1040
	Gln	Asp	Arg	Gly	Tyr	Ile	Leu	Arg	Val	Thr	Ala	Arg	Lys	Glu	Gly	Leu
				1045						1050					1055	
	Gly	Glu	Gly	Tyr	Val	Thr	Ile	Thr	Asp	Glu	Glu	Gly	Asn	Thr	Asp	Gln
			1060						1065					1070		
40	Leu	Arg	Phe	Gly	Gly	Cys	Glu	Glu	Ile	Asp	Ala	Ser	Asn	Ser	Phe	Val
			1075						1080					1085		
	Ser	Thr	Gly	Tyr	Met	Thr	Lys	Glu	Leu	Glu	Phe	Phe	Pro	Asp	Thr	Glu
		1090					1095						1100			
	Lys	Val	Arg	Ile	Glu	Ile	Gly	Glu	Thr	Glu	Gly	Thr	Phe	Gln	Val	Glu
	1105					1110					1115					1120
45	Ser	Val	Glu	Leu	Phe	Leu	Met	Glu	Asp	Leu	Cys					
				1125						1130						

<210> 62

<211> 1206

50 <212> PRT

<213> *Bacillus thuringiensis*

<400> 62

55

EP 2 728 007 B1

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

EP 2 728 007 B1

	Ser	Gly	Gln	Asp	Ala	Ala	Lys	Ala	Ala	Ile	Asp	Ile	Val	Gly	Lys	Leu
	65				70					75						80
	Leu	Ser	Gly	Leu	Gly	Val	Pro	Phe	Val	Gly	Pro	Ile	Val	Ser	Leu	Tyr
				85						90					95	
5	Thr	Gln	Leu	Ile	Asp	Ile	Leu	Trp	Pro	Ser	Gly	Glu	Lys	Ser	Gln	Trp
				100					105						110	
	Glu	Ile	Phe	Met	Glu	Gln	Val	Glu	Glu	Leu	Ile	Asn	Gln	Lys	Ile	Ala
			115					120					125			
	Glu	Tyr	Ala	Arg	Asn	Lys	Ala	Leu	Ser	Glu	Leu	Glu	Gly	Leu	Gly	Asn
			130				135					140				
10	Asn	Tyr	Gln	Leu	Tyr	Leu	Thr	Ala	Leu	Glu	Glu	Trp	Glu	Glu	Asn	Pro
	145					150					155					160
	Asn	Gly	Ser	Arg	Ala	Leu	Arg	Asp	Val	Arg	Asn	Arg	Phe	Glu	Ile	Leu
					165					170					175	
	Asp	Ser	Leu	Phe	Thr	Gln	Tyr	Met	Pro	Ser	Phe	Arg	Val	Thr	Asn	Phe
				180					185					190		
15	Glu	Val	Pro	Phe	Leu	Thr	Val	Tyr	Ala	Met	Ala	Ala	Asn	Leu	His	Leu
			195					200					205			
	Leu	Leu	Leu	Lys	Asp	Ala	Ser	Ile	Phe	Gly	Glu	Glu	Trp	Gly	Trp	Ser
			210				215						220			
	Thr	Thr	Thr	Ile	Asn	Asn	Tyr	Tyr	Asp	Arg	Gln	Met	Lys	Leu	Thr	Ala
	225				230						235					240
20	Glu	Tyr	Ser	Asp	His	Cys	Val	Lys	Trp	Tyr	Glu	Thr	Gly	Leu	Ala	Lys
					245					250					255	
	Leu	Lys	Gly	Thr	Ser	Ala	Lys	Gln	Trp	Val	Asp	Tyr	Asn	Gln	Phe	Arg
				260					265					270		
	Arg	Glu	Met	Thr	Leu	Ala	Val	Leu	Asp	Val	Val	Ala	Leu	Phe	Pro	Asn
			275					280					285			
25	Tyr	Asp	Thr	Arg	Thr	Tyr	Pro	Met	Glu	Thr	Lys	Ala	Gln	Leu	Thr	Arg
			290				295					300				
	Glu	Val	Tyr	Thr	Asp	Pro	Leu	Gly	Ala	Val	Asn	Val	Ser	Ser	Ile	Gly
					310						315					320
	Ser	Trp	Tyr	Asp	Lys	Ala	Pro	Ser	Phe	Gly	Val	Ile	Glu	Ser	Ser	Val
					325					330					335	
30	Ile	Arg	Pro	Pro	His	Val	Phe	Asp	Tyr	Ile	Thr	Gly	Leu	Thr	Val	Tyr
				340					345					350		
	Thr	Gln	Ser	Arg	Ser	Ile	Ser	Ser	Ala	Arg	Tyr	Ile	Arg	His	Trp	Ala
			355					360					365			
	Gly	His	Gln	Ile	Ser	Tyr	His	Arg	Val	Ser	Arg	Gly	Ser	Asn	Leu	Gln
			370				375					380				
35	Gln	Met	Tyr	Gly	Thr	Asn	Gln	Asn	Leu	His	Ser	Thr	Ser	Thr	Phe	Asp
					390						395					400
	Phe	Thr	Asn	Tyr	Asp	Ile	Tyr	Lys	Thr	Leu	Ser	Lys	Asp	Ala	Val	Leu
					405					410					415	
	Leu	Asp	Ile	Val	Tyr	Pro	Gly	Tyr	Thr	Tyr	Ile	Phe	Phe	Gly	Met	Pro
				420					425					430		
40	Glu	Val	Glu	Phe	Phe	Met	Val	Asn	Gln	Leu	Asn	Asn	Thr	Arg	Lys	Thr
				435					440				445			
	Leu	Lys	Tyr	Asn	Pro	Val	Ser	Lys	Asp	Ile	Ile	Ala	Ser	Thr	Arg	Asp
			450				455					460				
45	Ser	Glu	Leu	Glu	Leu	Pro	Pro	Glu	Thr	Ser	Asp	Gln	Pro	Asn	Tyr	Glu
					470						475					480
	Ser	Tyr	Ser	His	Arg	Leu	Cys	His	Ile	Thr	Ser	Ile	Pro	Ala	Thr	Gly
					485					490					495	
	Asn	Thr	Thr	Gly	Leu	Val	Pro	Val	Phe	Ser	Trp	Thr	His	Arg	Ser	Ala
				500					505					510		
50	Asp	Leu	Asn	Asn	Thr	Ile	Tyr	Ser	Asp	Lys	Ile	Thr	Gln	Ile	Pro	Ala
			515					520					525			
	Val	Lys	Cys	Trp	Asp	Asn	Leu	Pro	Phe	Val	Pro	Val	Val	Lys	Gly	Pro
			530				535					540				
	Gly	His	Thr	Gly	Gly	Asp	Leu	Leu	Gln	Tyr	Asn	Arg	Ser	Thr	Gly	Ser
					550						555					560
55	Val	Gly	Thr	Leu	Phe	Leu	Ala	Arg	Tyr	Gly	Leu	Ala	Leu	Glu	Lys	Ala
					565					570					575	
	Gly	Lys	Tyr	Arg	Val	Arg	Leu	Arg	Tyr	Ala	Thr	Asp	Ala	Asp	Ile	Val

EP 2 728 007 B1

				580				585				590				
	Leu	His	Val	Asn	Asp	Ala	Gln	Ile	Gln	Met	Pro	Lys	Thr	Met	Asn	Pro
			595					600					605			
5	Gly	Glu	Asp	Leu	Thr	Ser	Lys	Thr	Phe	Lys	Val	Ala	Asp	Ala	Ile	Thr
		610					615					620				
	Thr	Leu	Asn	Leu	Ala	Thr	Asp	Ser	Ser	Leu	Ala	Leu	Lys	His	Asn	Leu
	625				630						635					640
	Gly	Glu	Asp	Pro	Asn	Ser	Thr	Leu	Ser	Gly	Ile	Val	Tyr	Val	Asp	Arg
				645						650					655	
10	Ile	Glu	Phe	Ile	Pro	Val	Asp	Glu	Thr	Tyr	Glu	Ala	Glu	Gln	Asp	Leu
				660					665					670		
	Glu	Ala	Ala	Lys	Lys	Ala	Val	Asn	Ala	Leu	Phe	Thr	Asn	Thr	Lys	Asp
			675					680					685			
	Gly	Leu	Arg	Pro	Gly	Val	Thr	Asp	Tyr	Glu	Val	Asn	Gln	Ala	Ala	Asn
	690						695					700				
15	Leu	Val	Glu	Cys	Leu	Ser	Asp	Asp	Leu	Tyr	Pro	Asn	Glu	Lys	Arg	Leu
	705					710					715					720
	Leu	Phe	Asp	Ala	Val	Arg	Glu	Ala	Lys	Arg	Leu	Ser	Glu	Ala	Arg	Asn
				725						730					735	
	Leu	Leu	Gln	Asp	Pro	Asp	Phe	Gln	Glu	Ile	Asn	Gly	Glu	Asn	Gly	Trp
				740					745					750		
20	Thr	Ala	Ser	Thr	Gly	Ile	Glu	Val	Ile	Glu	Gly	Asp	Ala	Leu	Phe	Lys
			755					760					765			
	Gly	Arg	Tyr	Leu	Arg	Leu	Pro	Gly	Ala	Arg	Glu	Ile	Asp	Thr	Glu	Thr
	770					775						780				
	Tyr	Pro	Thr	Tyr	Leu	Tyr	Gln	Lys	Val	Glu	Glu	Gly	Val	Leu	Lys	Pro
	785					790					795					800
25	Tyr	Thr	Arg	Tyr	Arg	Leu	Arg	Gly	Phe	Val	Gly	Ser	Ser	Gln	Gly	Leu
				805						810					815	
	Glu	Ile	Phe	Thr	Ile	Arg	His	Gln	Thr	Asn	Arg	Ile	Val	Lys	Asn	Val
				820					825					830		
	Pro	Asp	Asp	Leu	Leu	Pro	Asp	Val	Ser	Pro	Val	Asn	Ser	Asp	Gly	Ser
			835					840					845			
30	Ile	Asn	Arg	Cys	Ser	Glu	Gln	Lys	Tyr	Val	Asn	Ser	Arg	Leu	Glu	Val
	850						855					860				
	Glu	Asn	Arg	Ser	Gly	Glu	Ala	His	Glu	Phe	Ser	Ile	Pro	Ile	Asp	Thr
	865					870					875					880
	Gly	Glu	Ile	Asp	Tyr	Asn	Glu	Asn	Ala	Gly	Ile	Trp	Val	Gly	Phe	Lys
				885						890					895	
35	Ile	Thr	Asp	Pro	Glu	Gly	Tyr	Ala	Thr	Leu	Gly	Asn	Leu	Glu	Leu	Val
			900						905					910		
	Glu	Glu	Gly	Pro	Leu	Ser	Gly	Asp	Ala	Leu	Glu	Arg	Leu	Gln	Arg	Glu
			915					920					925			
	Glu	Gln	Gln	Trp	Lys	Ile	Gln	Met	Thr	Arg	Arg	Arg	Glu	Glu	Thr	Asp
	930						935					940				
40	Arg	Arg	Tyr	Met	Ala	Ser	Lys	Gln	Ala	Val	Asp	Arg	Leu	Tyr	Ala	Asp
	945					950					955					960
	Tyr	Gln	Asp	Gln	Gln	Leu	Asn	Pro	Asp	Val	Glu	Ile	Thr	Asp	Leu	Thr
				965						970					975	
	Ala	Ala	Gln	Asp	Leu	Ile	Gln	Ser	Ile	Pro	Tyr	Val	Tyr	Asn	Glu	Met
				980					985					990		
45	Phe	Pro	Glu	Ile	Pro	Gly	Met	Asn	Tyr	Thr	Lys	Phe	Thr	Glu	Leu	Thr
			995					1000					1005			
	Asp	Arg	Leu	Gln	Gln	Ala	Trp	Ser	Leu	Tyr	Asp	Gln	Arg	Asn	Ala	Ile
	1010						1015					1020				
	Pro	Asn	Gly	Asp	Phe	Arg	Asn	Gly	Leu	Ser	Asn	Trp	Asn	Ala	Thr	Pro
	1025					1030						1035				1040
50	Gly	Val	Glu	Val	Gln	Gln	Ile	Asn	His	Thr	Ser	Val	Leu	Val	Ile	Pro
				1045							1050				1055	
	Asn	Trp	Asp	Glu	Gln	Val	Ser	Gln	Gln	Phe	Thr	Val	Gln	Pro	Asn	Gln
			1060						1065					1070		
	Arg	Tyr	Val	Leu	Arg	Val	Thr	Ala	Arg	Lys	Glu	Gly	Val	Gly	Asn	Gly
			1075					1080					1085			
55	Tyr	Val	Ser	Ile	Arg	Asp	Gly	Gly	Asn	Gln	Thr	Glu	Thr	Leu	Thr	Phe
	1090						1095					1100				

EP 2 728 007 B1

	Ser	Ala	Ser	Asp	Tyr	Asp	Thr	Asn	Gly	Met	Tyr	Asn	Thr	Gln	Val	Ser
	1105					1110					1115					1120
	Asn	Thr	Asn	Gly	Tyr	Asn	Thr	Asn	Asn	Ala	Tyr	Asn	Thr	Gln	Ala	Ser
					1125					1130						1135
5	Ser	Thr	Asn	Gly	Tyr	Asn	Ala	Asn	Asn	Met	Tyr	Asn	Thr	Gln	Ala	Ser
					1140					1145						1150
	Asn	Thr	Asn	Gly	Tyr	Asn	Thr	Asn	Ser	Val	Tyr	Asn	Asp	Gln	Thr	Gly
					1155					1160						1165
	Tyr	Ile	Thr	Lys	Thr	Val	Thr	Phe	Ile	Pro	Tyr	Thr	Asp	Gln	Met	Trp
10					1170					1175						1180
	Ile	Glu	Met	Ser	Glu	Thr	Glu	Gly	Thr	Phe	Tyr	Ile	Glu	Ser	Val	Glu
	1185					1190					1195					1200
	Leu	Ile	Val	Asp	Val	Glu										
						1205										

15

<210> 63

<211> 1210

<212> PRT

<213> Bacillus thuringiensis

20

<400> 63

25

30

35

40

45

50

55

EP 2 728 007 B1

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

EP 2 728 007 B1

5																
10																
15																
20																
25																
30																
35																
40																
45																
50																
55																

Arg Leu Glu Val Glu Asn Arg Ser Gly Glu Ala His Glu Phe Ser Ile
 865 870 875 880
 Pro Ile Asp Thr Gly Glu Ile Asp Tyr Asn Glu Asn Ala Gly Ile Trp
 885 890 895
 5 Val Gly Phe Lys Ile Thr Asp Pro Glu Gly Tyr Ala Thr Leu Gly Asn
 900 905 910
 Leu Glu Leu Val Glu Glu Gly Pro Leu Ser Gly Asp Ala Leu Glu Arg
 915 920 925
 10 Leu Gln Arg Glu Glu Gln Gln Trp Lys Ile Gln Met Thr Arg Arg Arg
 930 935 940
 Glu Glu Thr Asp Arg Arg Tyr Met Ala Ser Lys Gln Ala Val Asp Arg
 945 950 955 960
 Leu Tyr Ala Asp Tyr Gln Asp Gln Gln Leu Asn Pro Asp Val Glu Ile
 965 970 975
 15 Thr Asp Leu Thr Ala Ala Gln Asp Leu Ile Gln Ser Ile Pro Tyr Val
 980 985 990
 Tyr Asn Glu Met Phe Pro Glu Ile Pro Gly Met Asn Tyr Thr Lys Phe
 995 1000 1005
 Thr Glu Leu Thr Asp Arg Leu Gln Gln Ala Trp Ser Leu Tyr Asp Gln
 1010 1015 1020
 20 Arg Asn Ala Ile Pro Asn Gly Asp Phe Arg Asn Gly Leu Ser Asn Trp
 1025 1030 1035 1040
 Asn Ala Thr Pro Gly Val Glu Val Gln Gln Ile Asn His Thr Ser Val
 1045 1050 1055
 25 Leu Val Ile Pro Asn Trp Asp Glu Gln Val Ser Gln Gln Phe Thr Val
 1060 1065 1070
 Gln Pro Asn Gln Arg Tyr Val Leu Arg Val Thr Ala Arg Lys Glu Gly
 1075 1080 1085
 Val Gly Asn Gly Tyr Val Ser Ile Arg Asp Gly Gly Asn Gln Thr Glu
 1090 1095 1100
 30 Thr Leu Thr Phe Ser Ala Ser Asp Tyr Asp Thr Asn Gly Met Tyr Asn
 1105 1110 1115 1120
 Thr Gln Val Ser Asn Thr Asn Gly Tyr Asn Thr Asn Asn Ala Tyr Asn
 1125 1130 1135
 Thr Gln Ala Ser Ser Thr Asn Gly Tyr Asn Ala Asn Asn Met Tyr Asn
 1140 1145 1150
 35 Thr Gln Ala Ser Asn Thr Asn Gly Tyr Asn Thr Asn Ser Val Tyr Asn
 1155 1160 1165
 Asp Gln Thr Gly Tyr Ile Thr Lys Thr Val Thr Phe Ile Pro Tyr Thr
 1170 1175 1180
 40 Asp Gln Met Trp Ile Glu Met Ser Glu Thr Glu Gly Thr Phe Tyr Ile
 1185 1190 1195 1200
 Glu Ser Val Glu Leu Ile Val Asp Val Glu
 1205 1210

<210> 64

<211> 1138

<212> PRT

<213> Bacillus thuringiensis

<400> 64

EP 2 728 007 B1

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

15

20

25

30

35

40

45

50

55

EP 2 728 007 B1

[illegible]

EP 2 728 007 B1

	Ser	Phe	Tyr	Val	Asp	Ser	Ile	Glu	Phe	Ile	Pro	Val	Asp	Val	Asn	Tyr
	625					630					635				640	
	Ala	Glu	Lys	Glu	Lys	Leu	Glu	Lys	Ala	Gln	Lys	Ala	Val	Asn	Thr	Leu
					645					650					655	
5	Phe	Thr	Glu	Gly	Arg	Asn	Ala	Leu	Gln	Lys	Asp	Val	Thr	Asp	Tyr	Lys
				660					665					670		
	Val	Asp	Gln	Val	Ser	Ile	Leu	Val	Asp	Cys	Ile	Ser	Gly	Asp	Leu	Tyr
		675					680						685			
	Pro	Asn	Glu	Lys	Arg	Glu	Leu	Gln	Asn	Leu	Val	Lys	Tyr	Ala	Lys	Arg
		690					695					700				
10	Leu	Ser	Tyr	Ser	Arg	Asn	Leu	Leu	Asp	Pro	Thr	Phe	Asp	Ser	Ile	
	705					710				715					720	
	Asn	Ser	Ser	Glu	Glu	Asn	Gly	Trp	Tyr	Gly	Ser	Asn	Gly	Ile	Val	Ile
					725					730					735	
	Gly	Asn	Gly	Asp	Phe	Val	Phe	Lys	Gly	Asn	Tyr	Leu	Ile	Phe	Ser	Gly
				740					745					750		
15	Thr	Asn	Asp	Thr	Gln	Tyr	Pro	Thr	Tyr	Leu	Tyr	Gln	Lys	Ile	Asp	Glu
			755					760					765			
	Ser	Lys	Leu	Lys	Glu	Tyr	Thr	Arg	Tyr	Lys	Leu	Lys	Gly	Phe	Ile	Glu
		770					775					780				
	Ser	Ser	Gln	Asp	Leu	Glu	Ala	Tyr	Val	Ile	Arg	Tyr	Asp	Ala	Lys	His
	785					790					795					800
20	Arg	Thr	Leu	Asp	Val	Ser	Asp	Asn	Leu	Leu	Pro	Asp	Ile	Leu	Pro	Glu
					805					810					815	
	Asn	Thr	Cys	Gly	Glu	Pro	Asn	Arg	Cys	Ala	Ala	Gln	Gln	Tyr	Leu	Asp
				820					825					830		
	Glu	Asn	Pro	Ser	Pro	Glu	Cys	Ser	Ser	Met	Gln	Asp	Gly	Ile	Leu	Ser
		835						840					845			
25	Asp	Ser	His	Ser	Phe	Ser	Leu	Asn	Ile	Asp	Thr	Gly	Ser	Ile	Asn	His
		850					855					860				
	Asn	Glu	Asn	Leu	Gly	Ile	Trp	Val	Leu	Phe	Lys	Ile	Ser	Thr	Leu	Glu
	865				870						875					880
	Gly	Tyr	Ala	Lys	Phe	Gly	Asn	Leu	Glu	Val	Ile	Glu	Asp	Gly	Pro	Val
					885					890					895	
30	Ile	Gly	Glu	Ala	Leu	Ala	Arg	Val	Lys	Arg	Gln	Glu	Thr	Lys	Trp	Arg
				900					905					910		
	Asn	Lys	Leu	Ala	Gln	Leu	Thr	Thr	Glu	Thr	Gln	Ala	Ile	Tyr	Thr	Arg
			915					920					925			
	Ala	Lys	Gln	Ala	Leu	Asp	Asn	Leu	Phe	Ala	Asn	Ala	Gln	Asp	Ser	His
		930					935					940				
35	Leu	Lys	Arg	Asp	Val	Thr	Phe	Ala	Glu	Ile	Ala	Ala	Ala	Arg	Lys	Ile
	945					950					955					960
	Val	Gln	Ser	Ile	Arg	Glu	Ala	Tyr	Met	Ser	Trp	Leu	Ser	Val	Val	Pro
					965					970					975	
	Gly	Val	Asn	His	Pro	Ile	Phe	Thr	Glu	Leu	Ser	Gly	Arg	Val	Gln	Arg
				980					985					990		
40	Ala	Phe	Gln	Leu	Tyr	Asp	Val	Arg	Asn	Val	Val	Arg	Asn	Gly	Arg	Phe
			995					1000					1005			
	Leu	Asn	Gly	Leu	Ser	Asp	Trp	Ile	Val	Thr	Ser	Asp	Val	Lys	Val	Gln
		1010					1015					1020				
45	Glu	Glu	Asn	Gly	Asn	Asn	Val	Leu	Val	Leu	Asn	Asn	Trp	Asp	Ala	Gln
	1025					1030					1035				1040	
	Val	Leu	Gln	Asn	Val	Lys	Leu	Tyr	Gln	Asp	Arg	Gly	Tyr	Ile	Leu	His
					1045					1050					1055	
	Val	Thr	Ala	Arg	Lys	Ile	Gly	Ile	Gly	Glu	Gly	Tyr	Ile	Thr	Ile	Thr
				1060					1065					1070		
50	Asp	Glu	Glu	Gly	His	Thr	Asp	Gln	Leu	Arg	Phe	Thr	Ala	Cys	Glu	Glu
			1075					1080					1085			
	Ile	Asp	Ala	Ser	Asn	Ala	Phe	Ile	Ser	Gly	Tyr	Ile	Thr	Lys	Glu	Leu
		1090					1095					1100				
	Glu	Phe	Phe	Pro	Asp	Thr	Glu	Lys	Val	His	Ile	Glu	Ile	Gly	Glu	Thr
	1105					1110					1115					1120
55	Glu	Gly	Ile	Phe	Leu	Val	Glu	Ser	Ile	Glu	Leu	Phe	Leu	Met	Glu	Glu
					1125					1130					1135	
	Leu	Cys														

Claims

1. A recombinant nucleic acid molecule comprising a nucleotide sequence encoding a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID NO: 2.
2. The recombinant nucleic acid molecule of claim 1, wherein:
 - (a) said nucleotide sequence is a synthetic sequence that has been designed for expression in a plant; and/or
 - (b) said nucleotide sequence is operably linked to a promoter capable of directing expression of said nucleotide sequence in a plant cell.
3. The recombinant nucleic acid molecule of claim 1, wherein said variant comprises an amino acid sequence having at least 95% sequence identity to SEQ ID NO:15, 17, or 38.
4. The recombinant nucleic acid molecule of claim 1, wherein said variant comprises an amino acid sequence comprising SEQ ID NO: 15, 17, or 38
5. A vector comprising the nucleic acid molecule of any of claims 1 - 4, preferably further comprising a nucleic acid molecule encoding a heterologous polypeptide.
6. A host cell comprising the vector of claim 4, preferably that is a bacterial host cell or a plant host cell.
7. A transgenic plant comprising the plant host cell of claim 5, preferably wherein said plant is selected from the group consisting of maize, sorghum, wheat, cabbage, sunflower, tomato, crucifers, peppers, potato, cotton, rice, soybean, sugarbeet, sugarcane, tobacco, barley, and oilseed rape.
8. A seed comprising the nucleic acid molecule of any of claims 1 to 4.
9. A recombinant polypeptide comprising a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID No: 2, more preferably further comprising heterologous amino acid sequences.
10. The recombinant polypeptide of claim 9, wherein said variant comprises an amino acid sequence having at least 95% sequence identity to SEQ ID NO:15, 17, or 38.
11. The recombinant polypeptide of claim 9, wherein said variant comprises SEQ ID NO:15, 17, or 38.
12. A composition comprising the polypeptide of claim 9 - 11, preferably wherein said composition:
 - (a) is selected from the group consisting of a powder, dust, pellet, granule, spray, emulsion, colloid, and solution;
 - (b) is prepared by desiccation, lyophilization, homogenization, extraction, filtration, centrifugation, sedimentation, or concentration of a culture of *Bacillus thuringiensis* cells; and/or
 - (c) comprises from about 1% to about 99% by weight of said polypeptide.
13. A method for controlling or killing a coleopteran pest population comprising contacting said population with a pesticidally-effective amount of the polypeptide of any of claims 9 - 11.
14. A method for producing a polypeptide with pesticidal activity toward a coleopteran pest, comprising culturing a host cell comprising the vector of claim 5.

15. A plant having stably incorporated into its genome a DNA construct comprising nucleic acid molecule comprising a nucleotide sequence encoding a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID NO: 2.
16. The plant of claim 15, wherein said variant comprises an amino acid sequence having at least 95% sequence identity to SEQ ID NO:15, 17, or 38.
17. The plant of claim 15, wherein said variant comprises SEQ ID NO:15, 17, or 38.
18. A recombinant nucleic acid according to any one of claims 1 to 5, a recombinant polypeptide according to any one of claims 9 - 11 or a plant according to any one of claims 15 - 17, wherein said pesticidal activity is coleopteran activity or activity is against rootworm pests, preferably wherein said rootworm is Western corn rootworm or Southern corn rootworm.
19. The plant of claims 15 or 17, wherein said plant is a plant cell.
20. A method for protecting a plant from a pest, comprising expressing in a plant or cell thereof a nucleotide sequence encoding a variant Cry3 amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID NO:2 over the full length of SEQ ID NO:2, wherein said variant comprises a glutamic acid residue at the position corresponding to amino acid position 316 of SEQ ID NO: 2, a leucine residue at the position corresponding to amino acid position 482 of SEQ ID NO: 2, and a lysine residue at the position corresponding to amino acid position 483 of SEQ ID NO: 2, and wherein said variant has pesticidal activity which is improved relative to the pesticidal activity of SEQ ID No: 2.
21. The method of claim 20, wherein said variant comprises an amino acid sequence having at least 95% sequence identity to SEQ ID NO:15, 17, or 38.
22. The method of claim 20, wherein said variant comprises SEQ ID NO:15, 17, or 38.

Patentansprüche

1. Rekombinantes Nucleinsäuremolekül, das eine Nucleotidsequenz umfasst, die eine Varianten-Cry3-Aminosäuresequenz codiert, die wenigstens 95% Aminosäuresequenzidentität zu SEQ ID NO:2 über die volle Länge von SEQ ID NO:2 hat, wobei die Variante einen Glutaminsäurerest an der Position, die Aminosäureposition 316 von SEQ ID NO:2 entspricht, einen Leucinrest an der Position, die Aminosäureposition 482 von SEQ ID NO:2 entspricht, und einen Lysinrest an der Position, die Aminosäureposition 483 von SEQ ID NO:2 entspricht, hat und wobei die Variante pestizide Aktivität hat, die bezüglich der pestiziden Aktivität von SEQ ID NO:2 verbessert ist.
2. Rekombinantes Nucleinsäuremolekül gemäß Anspruch 1, wobei:
 - (a) die Nucleotidsequenz eine synthetische Sequenz ist, die zur Expression in einer Pflanze entwickelt wurde, und/oder
 - (b) die Nucleotidsequenz funktionell mit einem Promotor verknüpft ist, der fähig ist, eine Expression der Nucleotidsequenz in einer Pflanzenzelle zu steuern.
3. Rekombinantes Nucleinsäuremolekül gemäß Anspruch 1, wobei die Variante eine Aminosäuresequenz umfasst, die wenigstens 95% Sequenzidentität zu SEQ ID NO:15, 17 oder 38 hat.
4. Rekombinantes Nucleinsäuremolekül gemäß Anspruch 1, wobei die Variante eine Aminosäuresequenz umfasst, die SEQ ID NO:15, 17 oder 38 umfasst.
5. Vektor, umfassend das Nucleinsäuremolekül gemäß einem der Ansprüche 1 bis 4, der vorzugsweise außerdem ein Nucleinsäuremolekül umfasst, das ein heterologes Polypeptid codiert.

6. Wirtszelle, die den Vektor gemäß Anspruch 4 umfasst, die vorzugsweise eine bakterielle Wirtszelle oder eine Pflanzenwirtszelle ist.
7. Transgene Pflanze, die die Pflanzenwirtszelle gemäß Anspruch 5 umfasst, wobei die Pflanze vorzugsweise aus der Gruppe, bestehend aus Mais, Sorghum, Weizen, Kohl, Sonnenblume, Tomate, Kruzifere, Pfeffer bzw. Paprika, Kartoffel, Baumwolle, Reis, Sojabohne, Zuckerrübe, Zuckerrohr, Tabak, Gerste und Ölsamenraps, ausgewählt ist.
8. Samen, der das Nucleinsäuremolekül gemäß einem der Ansprüche 1 bis 4 umfasst.
9. Rekombinantes Polypeptid, das eine Varianten-Cry3-Aminosäuresequenz umfasst, die wenigstens 95% Aminosäuresequenzidentität zu SEQ ID NO:2 über die volle Länge von SEQ ID NO:2 hat, wobei die Variante einen Glutaminsäurerest an der Position, die Aminosäureposition 316 von SEQ ID NO:2 entspricht, einen Leucinrest an der Position, die Aminosäureposition 482 von SEQ ID NO:2 entspricht, und einen Lysinrest an der Position, die Aminosäureposition 483 von SEQ ID NO:2 entspricht, hat und wobei die Variante pestizide Aktivität hat, die bezüglich der pestiziden Aktivität von SEQ ID NO:2 verbessert ist, das vorzugsweise außerdem heterologe Aminosäuresequenzen umfasst.
10. Rekombinantes Polypeptid gemäß Anspruch 9, wobei die Variante eine Aminosäuresequenz umfasst, die wenigstens 95% Sequenzidentität zu SEQ ID NO:15, 17 oder 38 hat.
11. Rekombinantes Polypeptid gemäß Anspruch 9, wobei die Variante SEQ ID NO:15, 17 oder 38 umfasst.
12. Zusammensetzung, die das Polypeptid gemäß Anspruch 9 bis 11 umfasst, wobei die Zusammensetzung vorzugsweise:
 - (a) ausgewählt ist aus der Gruppe, bestehend aus einem/r Pulver, Stäubemittel, Pellet, Granulat, Spray, Emulsion, Kolloid und Lösung;
 - (b) hergestellt ist durch Trocknung, Lyophilisierung, Homogenisierung, Extraktion, Filtration, Zentrifugation, Sedimentation oder Konzentrierung einer Kultur von *Bacillus thuringiensis*-Zellen und/oder
 - (c) etwa 1 Gew.-% bis etwa 99 Gew.-% des Polypeptids umfasst.
13. Verfahren zur Bekämpfung oder Abtötung einer Coleoptera-Schädlingpopulation, umfassend Inkontaktbringen der Population mit einer pestizidwirksamen Menge des Polypeptids gemäß einem der Ansprüche 9 bis 11.
14. Verfahren zur Herstellung eines Polypeptids mit pestizider Aktivität gegen einen Coleoptera-Schädling, das Kultivieren einer Wirtszelle, die den Vektor gemäß Anspruch 5 umfasst, umfasst.
15. Pflanze, die stabil in ihr Genom ein DNA-Konstrukt eingebaut hat, das ein Nucleinsäuremolekül umfasst, welches eine Nucleotidsequenz umfasst, die eine Varianten-Cry3-Aminosäuresequenz codiert, die wenigstens 95% Aminosäuresequenzidentität zu SEQ ID NO:2 über die volle Länge von SEQ ID NO:2 hat, wobei die Variante einen Glutaminsäurerest an der Position, die Aminosäureposition 316 von SEQ ID NO:2 entspricht, einen Leucinrest an der Position, die Aminosäureposition 482 von SEQ ID NO:2 entspricht, und einen Lysinrest an der Position, die Aminosäureposition 483 von SEQ ID NO:2 entspricht, umfasst und wobei die Variante pestizide Aktivität hat, die bezüglich der pestiziden Aktivität von SEQ ID NO:2 verbessert ist.
16. Pflanze gemäß Anspruch 15, wobei die Variante eine Aminosäuresequenz umfasst, die wenigstens 95% Sequenzidentität zu SEQ ID NO:15, 17 oder 38 hat.
17. Pflanze gemäß Anspruch 15, wobei die Variante SEQ ID NO:15, 17 oder 38 umfasst.
18. Rekombinante Nucleinsäure gemäß einem der Ansprüche 1 bis 5, rekombinantes Polypeptid gemäß einem der Ansprüche 9 bis 11 oder Pflanze gemäß einem der Ansprüche 15 bis 17, wobei die pestizide Aktivität Coleoptera-Aktivität ist oder die Aktivität gegen Wurzelnematoden-Schädlinge ist, wobei die Wurzelnematode westlicher Maiswurzelbohrer oder südlicher Maiswurzelbohrer ist.
19. Pflanze gemäß Anspruch 15 oder 17, wobei die Pflanze eine Pflanzenzelle ist.
20. Verfahren zum Schützen einer Pflanze vor einem Schädling, umfassend Expressieren in einer Pflanze oder Zelle

davon einer Nucleotidsequenz, die eine Varianten-Cry3-Aminosäuresequenz codiert, die wenigstens 95% Aminosäuresequenzidentität zu SEQ ID NO:2 über die volle Länge von SEQ ID NO:2 hat, wobei die Variante einen Glutaminsäurerest an der Position, die Aminosäureposition 316 von SEQ ID NO:2 entspricht, einen Leucinrest an der Position, die Aminosäureposition 482 von SEQ ID NO:2 entspricht, und einen Lysinrest an der Position, die Aminosäureposition 483 von SEQ ID NO:2 entspricht, umfasst und wobei die Variante pestizide Aktivität hat, die bezüglich der pestiziden Aktivität von SEQ ID NO:2 verbessert ist.

21. Verfahren gemäß Anspruch 20, wobei die Variante eine Aminosäuresequenz umfasst, die wenigstens 95% Sequenzidentität zu SEQ ID NO:15, 17 oder 38 hat.

22. Verfahren gemäß Anspruch 20, wobei die Variante SEQ ID NO:15, 17 oder 38 umfasst.

Revendications

1. Molécule d'acide nucléique recombiné, comprenant une séquence de nucléotides qui code une variante de séquence d'acides aminés de Cry3 qui est identique, à un degré d'au moins 95 %, à la séquence d'acides aminés Séquence N° 2 sur toute la longueur de cette Séquence N° 2, laquelle variante comprend un résidu d'acide glutamique en la position correspondant au résidu d'acide aminé n° 316 de la Séquence N° 2, un résidu de leucine en la position correspondant au résidu d'acide aminé n° 482 de la Séquence N° 2, et un résidu de lysine en la position correspondant au résidu d'acide aminé n° 483 de la Séquence N° 2, et laquelle variante est dotée d'une activité de pesticide améliorée par rapport à l'activité de pesticide de la Séquence N°2.

2. Molécule d'acide nucléique recombiné, conforme à la revendication 1, dans laquelle

a) ladite séquence de nucléotides est une séquence synthétique qui a été conçue pour s'exprimer chez un végétal,

b) et/ou ladite séquence de nucléotides est opérationnellement raccordée à un promoteur capable de diriger l'expression de ladite séquence de nucléotides au sein d'une cellule végétale.

3. Molécule d'acide nucléique recombiné, conforme à la revendication 1, pour laquelle ladite variante comprend une séquence d'acides aminés qui est identique, à un degré d'au moins 95 %, à la Séquence N° 15, N° 17 ou N° 38.

4. Molécule d'acide nucléique recombiné, conforme à la revendication 1, pour laquelle ladite variante comprend une séquence d'acides aminés comportant la Séquence N° 15, N° 17 ou N° 38.

5. Vecteur comprenant une molécule d'acide nucléique conforme à l'une des revendications 1 à 4, et comprenant en outre, de préférence, une molécule d'acide nucléique codant un polypeptide hétérologue.

6. Cellule hôte comprenant un vecteur conforme à la revendication 4, qui est de préférence une cellule hôte bactérienne ou une cellule hôte végétale.

7. Végétal transgénique comprenant une cellule hôte végétale conforme à la revendication 5, lequel végétal est de préférence choisi dans l'ensemble formé par les suivants : maïs, sorgho, blé, chou, tournesol, tomate, crucifères, poivron et piment, pomme de terre, coton, riz, soja, betterave sucrière, canne à sucre, tabac, orge et navette.

8. Semence comprenant une molécule d'acide nucléique conforme à l'une des revendications 1 à 4.

9. Polypeptide recombinant, comprenant une variante de séquence d'acides aminés de Cry3 qui est identique, à un degré d'au moins 95 %, à la séquence d'acides aminés Séquence N° 2 sur toute la longueur de cette Séquence N° 2, laquelle variante comprend un résidu d'acide glutamique en la position correspondant au résidu d'acide aminé n° 316 de la Séquence N° 2, un résidu de leucine en la position correspondant au résidu d'acide aminé n° 482 de la Séquence N° 2, et un résidu de lysine en la position correspondant au résidu d'acide aminé n° 483 de la Séquence N° 2, et laquelle variante est dotée d'une activité de pesticide améliorée par rapport à l'activité de pesticide de la Séquence N°2, et comprenant en outre, de préférence, des séquences hétérologues d'acides aminés.

10. Polypeptide recombinant, conforme à la revendication 9, dans lequel ladite variante comprend une séquence d'acides aminés identique, à un degré d'au moins 95 %, à la Séquence N° 15, N° 17 ou N° 38.

11. Polypeptide recombinant, conforme à la revendication 9, dans lequel ladite variante comprend la Séquence N° 15, N° 17 ou N° 38.

12. Composition comprenant un polypeptide conforme à l'une des revendications 9 à 11, laquelle composition, de préférence :

a) est choisie dans l'ensemble formé par une poudre, une poudre fine, des comprimés, des granules, un liquide à pulvériser, une émulsion, une solution colloïdale et une solution;

b) est préparée par dessiccation, lyophilisation, homogénéisation, extraction, filtration, centrifugation, sédimentation ou concentration d'une culture de cellules de *Bacillus thuringiensis* ;

c) et/ou contient d'environ 1 % à environ 99 % en poids dudit polypeptide.

13. Procédé de lutte contre une population de coléoptères nuisibles ou de destruction d'une telle population, comportant le fait de mettre ladite population en contact avec un polypeptide conforme à l'une des revendications 9 à 11, employé en une quantité à effet de pesticide.

14. Procédé de production d'un polypeptide doté d'une activité de pesticide envers un coléoptère nuisible, comportant le fait de cultiver une cellule hôte comprenant un vecteur conforme à la revendication 5.

15. Végétal comportant, incorporée de façon stable dans son génome, une construction d'ADN comprenant une molécule d'acide nucléique qui comporte une séquence de nucléotides codant une variante de séquence d'acides aminés de Cry3 qui est identique, à un degré d'au moins 95 %, à la séquence d'acides aminés Séquence N° 2 sur toute la longueur de cette Séquence N° 2, laquelle variante comprend un résidu d'acide glutamique en la position correspondant au résidu d'acide aminé n° 316 de la Séquence N° 2, un résidu de leucine en la position correspondant au résidu d'acide aminé n° 482 de la Séquence N° 2, et un résidu de lysine en la position correspondant au résidu d'acide aminé n° 483 de la Séquence N° 2, et laquelle variante est dotée d'une activité de pesticide améliorée par rapport à l'activité de pesticide de la Séquence N°2.

16. Végétal conforme à la revendication 15, dans lequel ladite variante comprend une séquence d'acides aminés qui est identique, à un degré d'au moins 95 %, à la Séquence N° 15, N° 17 ou N° 38.

17. Végétal conforme à la revendication 15, dans lequel ladite variante comprend la Séquence N° 15, N° 17 ou N° 38.

18. Acide nucléique recombiné conforme à l'une des revendications 1 à 5, polypeptide recombinant conforme à l'une des revendications 9 à 11 ou végétal conforme à l'une des revendications 15 à 17, dont ou chez lequel l'activité de pesticide est une activité contre des coléoptères ou une activité contre des vers nuisibles pour les racines, le ver nuisible pour les racines étant de préférence la chrysomèle occidentale des racines du maïs ou la chrysomèle méridionale des racines du maïs.

19. Végétal conforme à la revendication 15 ou 17, lequel végétal est une cellule végétale.

20. Procédé de protection d'un végétal contre un nuisible, comprenant l'expression, chez un végétal ou dans une cellule d'un végétal, d'une séquence de nucléotides codant une variante de séquence d'acides aminés de Cry3 qui est identique, à un degré d'au moins 95 %, à la séquence d'acides aminés Séquence N° 2 sur toute la longueur de cette Séquence N° 2, laquelle variante comprend un résidu d'acide glutamique en la position correspondant au résidu d'acide aminé n° 316 de la Séquence N° 2, un résidu de leucine en la position correspondant au résidu d'acide aminé n° 482 de la Séquence N° 2, et un résidu de lysine en la position correspondant au résidu d'acide aminé n° 483 de la Séquence N° 2, et laquelle variante est dotée d'une activité de pesticide améliorée par rapport à l'activité de pesticide de la Séquence N°2.

21. Procédé conforme à la revendication 20, dans lequel ladite variante comprend une séquence d'acides aminés identique, à un degré d'au moins 95 %, à la Séquence N° 15, N° 17 ou N° 38.

22. Procédé conforme à la revendication 20 dans lequel ladite variante comprend la Séquence N° 15, N° 17 ou N° 38.

D I

MNPNNRSEHDTIKTTENNEVPTNHVQYPLAETPNPTLEDLNYKEFLRMTADNNTEALDSSTTKDVIQ

KGISVVGDLLGVVGFPFGGALVSYFTNFLTNTIWPSEDPWKAFMEQVEALMDQKIADYAKNKALÆL

QGLQNNVEDYVSALSSWQKNPVSSRNPHSQGRIRELFSQAESHFRNSMPSFAISGYEVLFTTAYQ

AANTHLFLLKDAQIYGEEWGYEKEDIAEFYKRQLKLTQEYTDHCVKWYNVGLDKLRGSSYESWW

FNRYRREMTLTVLDLIALFPLYDVRLYPKEVKTELTRDVLTDPIGVNNLRGYGTTFSNIENYRKPHL

FDYLHRIQFHTRFQPGYYGNDSFNYWSGNYVSTRPSIGSNDIITSPFYGNKSSEPQVQNLEFNGBKVY

RAVANTNLAVWPSAVYSGVTKVEFSQYNDQTDEASTQTYDSKRNVGAVSWDSIDQLPPETTDEFL

EKGYSHQLNHYVMCFLMQGSRGTIPVLTWTHKSVDDFFNMIDSKKITQLPLVKAYKLQSGASVVAQPR

FTGGDIIQCTENGSAATIIYVTPDVSYSQKYRARIHYASTSQITFTLSLDGAPFNQYYFDKTINKGDTLT

YNSFNLASFSTPFELSGNNLQIGVTGLSAGDKVYIDKIEFIPVN

Figure 1

	(187)	187	200	210	220	230	
Axmi164	(128)	--EYARNKALTEIKGLGDALDVYQESLEA	ML	ENRNDT	--RARSVVSK		
Axmi161	(118)	--ESFKNEAISKINGGLADLYTVYLSLEL	ML	EHHPDP	--SIIQSVRT		
Axmi152	(119)	--NYAREKAITIELEGLGDNMKDYKSKLQ	ML	DTND	--DTKRSLKH		
Axmi151	(119)	--KAVRSKAISELEGIHQVYRLYIEALNE	ML	DKDTPDNP	--FVQERVRT		
Axmi146	(126)	--EQVRNDALATLESSEGLALQAYLNAL	ED	WKINPNAR	--STQLVRE		
Axmi141	(128)	--EYARNLALTNIKGLENSYKLYLEAL	AD	WKQNP	TS--SSQERVRT		
Axmi129	(88)	--EAVRNKALADILANSGRALQSYLN	AFED	WKKNPIFR	--SKELVRE		
Axmi128	(127)	--EYARNLALTHLKGLENSYKLYLEAL	AD	WKQNP	TS--SSQERVRT		
Axmi127	(128)	--ANVRSQAIAKIEGLGRGLEAYQEL	LV	AMLENRNN	A--RTRSLIKQ		
Axmi120	(14)	--ESTRKDAIARLQGLGAASEVYQES	LES	ML	ENQNDAR	--AMSVVRQ	
Axmi116	(155)	--EAVKSKALSEIEGLQRIYSSYQSD	LER	ML	GDRDNP	--EYQEIIRQ	
Axmi114	(95)	PNDPVVIDADNKLIEGLKNTLDLYLE	ALKE	ML	KNDPQNP	--ASQERVRT	
Axmi101	(145)	--AYAKSRALTDIVSIGNAVERYQT	ALED	ML	EKPEN	--LKSLGLVIQ	
Axmi091	(129)	--AFAREQALRQLEGLGGLNLYGLY	KEAL	AE	ML	EQDRDNP	--TTKERVVD
Axmi087	(129)	--EYARNKALAEITGLGNAMDVYQ	QSLED	ML	MANPND	A--RTRSVVAT	
Axmi037	(146)	--EQVELDALTELEKIGEAVEAYY	IALDD	ML	EVPEDM	--FSLSEVIK	
Axmi029	(80)	--QQVIIDAETALESVKLNVDLYLN	AFEE	ML	EKRP	TNE--YSTELVYK	
Axmi028	(95)	PDDPVVKDANTILKGINGSLNLYLN	AL	IEI	ML	KKDPNNL	--TTIENVTD
Cy6Bb1	(129)	--EYARNKALSEIEGLGNNYQLYLT	ALEE	ML	WEENPNGS	--RALRDVRN	
Cy6Bc1	(129)	--EYARNKALSEIEGLGNNYQLYLT	ALEE	ML	WEENPNGS	--RALRDVRN	
Cy7Aa	(117)	--EYVRNKALAEILDGLGSALDKYQ	KAL	AD	ML	LKQDDP	--EAILSVAT
axmi-R1 permuP3c7	(123)	--DYAKNKALAEIQGLQNNVEDYV	SALSS	ML	QKNAKSSRN	M	HSQGRIRE
axmi-R1	(123)	--DYAKNKALAEIQGLQNNVEDYV	SALSS	ML	QKNPVSSRN	M	HSQGRIRE

Figure 2

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- US 5659123 A, Van Rie [0027] [0036]
- US 6023013 A, English [0027] [0034] [0036] [0037]
- US RE39580 E [0027]
- US 7030295 B, Chen [0028]
- US 5743477 A [0043] [0050] [0063] [0064]
- US 4196265 A [0066]
- US 5605793 A [0069]
- US 5837458 A [0069]
- US 5380831 A [0078] [0080]
- US 5436391 A [0078]
- US 20010026941 A [0088]
- US 4945050 A [0088]
- WO 9100915 A [0088]
- US 2002015066 A [0088]
- US 5039523 A [0102]
- EP 0480762 A2 [0102]
- US 6468523 B [0109]
- US 7351881 B [0120]
- WO 0138514 A [0159] [0160]
- US 5240842 A [0159]
- WO 61229567 A [0166]
- WO 61150309 A [0166]

Non-patent literature cited in the description

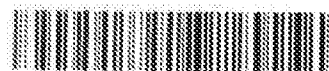
- FEITELSON. *Nemathelminthes, Platyhelminthes, and Sarcostigophora*, 1993 [0003]
- Advanced Engineered Pesticides. Marcel Dekker, Inc, [0003]
- CRICKMORE et al. *Microbiol. Mol. Biol. Rev.*, 1998, vol. 62, 807-813 [0004] [0024]
- HÖFTE ; WHITELEY. *Microbiol. Rev.*, 1989, vol. 53, 242-255 [0005]
- DE MAAGD et al. *Trends Genetics*, 2001, vol. 17, 193-199 [0006] [0053]
- HERRNSTADT et al. *Gene*, 1987, vol. 57, 37-46 [0007]
- HOFTE et al. *Nucleic acids Res.*, 1987, vol. 15, 7183 [0007]
- MCPHERSON et al. *BioTechnology*, 1988, vol. 6, 61-66 [0007]
- SEKAR et al. *Proc. Natl. Acad. Sci. USA*, 1987, vol. 84, 7036-7040 [0007]
- DONOVAN et al. *Mol Gen Genet.*, 1988, vol. 214 (3), 365-72 [0007]
- CRICKMORE et al. *Bacillus thuringiensis toxin nomenclature*, 2003, www.biol.susx.ac.uk/Home/Neil_Crickmore/Bt/index [0024]
- LI et al. *Nature*, 1991, vol. 353, 815-821 [0026] [0033] [0037] [0130]
- WU ; DEAN. *J.Mol. Biol.*, 1996, vol. 255, 628-640 [0027] [0036]
- WU et al. *Febs Letters*, 2000, vol. 473, 227-232 [0027] [0036]
- WALTERS et al. *Applied and Environ. Micro.*, 2008, vol. 74, 367-374 [0028]
- CARROLL et al. *Biochem J.*, 1989, vol. 261, 99-105 [0029]
- CARROLL et al. *J Invert. Biol.*, 1997, vol. 70, 41-49 [0029]
- CZAPLA ; LANG. *J. Econ. Entomol.*, 1990, vol. 83, 2480-2485 [0043] [0050] [0063] [0064]
- ANDREWS et al. *Biochem. J.*, 1988, vol. 252, 199-206 [0043] [0050] [0063] [0064]
- MARRONE et al. *J. of Economic Entomology*, 1985, vol. 78, 290-293 [0043] [0050] [0063] [0064] [0067] [0099]
- KARLIN ; ALTSCHUL. *Proc. Natl. Acad. Sci. USA*, 1990, vol. 87, 2264 [0047]
- KARLIN ; ALTSCHUL. *Proc. Natl. Acad. Sci. USA*, 1993, vol. 90, 5873-5877 [0047]
- ALTSCHUL et al. *J. Mol. Biol.*, 1990, vol. 215, 403 [0047]
- ALTSCHUL et al. *Nucleic Acids Res.*, 1997, vol. 25, 3389 [0047]
- HIGGINS et al. *Nucleic Acids Res.*, 1994, vol. 22, 4673-4680 [0048]
- MYERS ; MILLER. *CABIOS*, 1988, vol. 4, 11-17 [0048]
- NEEDLEMAN ; WUNSCH. *J. Mol. Biol.*, 1970, vol. 48 (3), 443-453 [0049]
- SAMBROOK ; RUSSELL. *Molecular Cloning: A Laboratory Manual*. Cold Spring Harbor Laboratory Press, 2001 [0056]
- INNIS et al. *PCR Protocols: A Guide to Methods and Applications*. Academic Press, 1990 [0056]
- SAMBROOK et al. *Molecular Cloning: A Laboratory Manual*. Cold Spring Harbor Laboratory Press, 1989 [0058] [0061]
- MEINKOTH ; WAHL. *Anal. Biochem.*, 1984, vol. 138, 267-284 [0061]

- **TIJSSEN.** Laboratory Techniques in Biochemistry and Molecular Biology-Hybridization with Nucleic Acid Probes. Elsevier, 1993 [0061]
- Current Protocols in Molecular Biology. Greene Publishing and Wiley-Interscience, 1995 [0061]
- **HARLOW ; LANE.** Antibodies: A Laboratory Manual. Cold Spring Harbor Laboratory, 1988 [0066]
- **SCHNEPF et al.** *Microbiol. Mol. Biol. Rev.*, 1998, vol. 62, 775-806 [0067]
- **STEMMER.** *Proc. Natl. Acad. Sci. USA*, 1994, vol. 91, 10747-10751 [0069]
- **STEMMER.** *Nature*, 1994, vol. 370, 389-391 [0069]
- **CRAMERI et al.** *Nature Biotech.*, 1997, vol. 15, 436-438 [0069]
- **MOORE et al.** *J. Mol. Biol.*, 1997, vol. 272, 336-347 [0069]
- **ZHANG et al.** *Proc. Natl. Acad. Sci. USA*, 1997, vol. 94, 4504-4509 [0069]
- **CRAMERI et al.** *Nature*, 1998, vol. 391, 288-291 [0069]
- **NAIMOV et al.** *Appl. Environ. Microbiol.*, 2001, vol. 67, 5328-5330 [0070]
- **DE MAAGD et al.** *Appl. Environ. Microbiol.*, 1996, vol. 62, 1537-1543 [0070]
- **GE et al.** *J. Biol. Chem.*, 1991, vol. 266, 17954-17958 [0070]
- **SCHNEPF et al.** *J. Biol. Chem.*, 1990, vol. 265, 20923-20930 [0070]
- **RANG et al.** *Appl. Environ. Microbiol.*, vol. 65, 2918-2925 [0070]
- **CHANG.** *Methods Enzymol.*, 1987, vol. 153, 507-516 [0072]
- **HELLENS ; MULLINEAUX.** *Trends in Plant Science*, 2000, vol. 5, 446-451 [0073] [0086]
- **GUERINEAU et al.** *Mol. Gen. Genet.*, 1991, vol. 262, 141-144 [0077]
- **PROUDFOOT.** *Cell*, 1991, vol. 64, 671-674 [0077]
- **SANFACON et al.** *Genes Dev.*, 1991, vol. 5, 141-149 [0077]
- **MOGEN et al.** *Plant Cell*, 1990, vol. 2, 1261-1272 [0077]
- **MUNROE et al.** *Gene*, 1990, vol. 91, 151-158 [0077]
- **BALLAS et al.** *Nucleic Acids Res.*, 1989, vol. 17, 7891-7903 [0077]
- **JOSHI et al.** *Nucleic Acid Res.*, 1987, vol. 15, 9627-9639 [0077]
- **CAMPBELL ; GOWRI.** *Plant Physiol.*, 1990, vol. 92, 1-11 [0078]
- **MURRAY et al.** *Nucleic Acids Res.*, 1989, vol. 17, 477-498 [0078]
- **VON HEIJNE et al.** *Plant Mol. Biol. Rep.*, 1991, vol. 9, 104-126 [0079]
- **CLARK et al.** *J. Biol. Chem.*, 1989, vol. 264, 17544-17550 [0079]
- **DELLA-CIOPPA et al.** *Plant Physiol.*, 1987, vol. 84, 965-968 [0079]
- **ROMER et al.** *Biochem. Biophys. Res. Commun.*, 1993, vol. 196, 1414-1421 [0079]
- **SHAH et al.** *Science*, 1986, vol. 233, 478-481 [0079]
- **HIEI et al.** *The Plant Journal*, 1994, vol. 6, 271-282 [0087]
- **ISHIDA et al.** *Nature Biotechnology*, 1996, vol. 14, 745-750 [0087]
- **AYRES ; PARK.** *Critical Reviews in Plant Science*, 1994, vol. 13, 219-239 [0087]
- **BOMMINENI ; JAUHAR.** *Maydica*, 1997, vol. 42, 107-120 [0087]
- **SVAB et al.** *Proc. Natl. Acad. Sci. USA*, 1990, vol. 87, 8526-8530 [0089]
- **SVAB ; MALIGA.** *Proc. Natl. Acad. Sci. USA*, 1993, vol. 90, 913-917 [0089]
- **SVAB ; MALIGA.** *EMBO J.*, 1993, vol. 12, 601-606 [0089]
- **MCBRIDE et al.** *Proc. Natl. Acad. Sci. USA*, 1994, vol. 91, 7301-7305 [0089]
- **MCCORMICK et al.** *Plant Cell Reports*, 1986, vol. 5, 81-84 [0091]
- **SAMBROOK ; RUSSELL.** Molecular Cloning: A Laboratory Manual. Cold Spring Harbor Laboratory Press, 2001 [0093]
- **STALKER et al.** *J. Biol. Chem.*, 1985, vol. 263, 6310-6314 [0098]
- **SATHASIVAN et al.** *Nucl. Acids Res.*, 1990, vol. 18, 2188 [0098]
- Pesticide bioassays with arthropods. CRC, 1992 [0152]
- **MILLER et al.** *Plant Physiology*, 2001, vol. 127, 594-606 [0155]

Variáns Axmi-R1 delta-endotoxin gének és eljárások azok alkalmazására

Szabadalmi igénypontok

1. Rekombináns nukleinsav molekula, mely egy variáns Cry3 aminosav-szekvenciát kódoló nukleotidszekvenciát tartalmaz, mely a 2. számú szekvenciával legalább 95%-os aminosavszekvencia azonosságot mutat a 2. számú szekvencia teljes hosszában, ahol a variáns egy glutaminsavgyököt tartalmaz a 2. számú szekvencia 316. aminosav-helyzetének megfelelő helyen, egy leucin gyököt tartalmaz a 2. számú szekvencia 482. aminosav-helyzetének megfelelő helyen, és egy lizin-gyököt tartalmaz a 2. számú szekvencia 483. aminosav-helyzetének megfelelő helyen, és ahol a variáns a 2. számú szekvencia peszticid aktivitásához viszonyítva fokozott peszticid aktivitással rendelkezik.
2. Az 1. igénypont szerinti rekombináns nukleinsav molekula, ahol:
 - (a) a nukleotidszekvencia egy növényben kifejeződésre szerkesztett szintetikus szekvencia; és/vagy
 - (b) a nukleotidszekvencia működőképesen kapcsolódik egy, a nukleotid-szekvencia növényi sejtben történő kifejeződésének irányítására képes promoterhez.
3. Az 1. igénypont szerinti rekombináns nukleinsav molekula, ahol a variáns a 15, 17, vagy 38. számú szekvenciával legalább 95%-os aminosavszekvencia azonosságot mutató aminosavszekvenciát tartalmaz.
4. Az 1. igénypont szerinti rekombináns nukleinsav molekula, ahol a variáns egy 15, 17, vagy 38. számú szekvenciával rendelkező aminosavszekvenciát tartalmaz.
5. Az 1-4. igénypontok bármelyike szerinti nukleinsav molekulát tartalmazó vektor, mely előnyösen továbbá egy heterológ polipeptidet kódoló nukleinsav molekulát is tartalmaz.
6. A 4. igénypont szerinti vektort tartalmazó gazdasejt, előnyösen amely egy baktérium gazdasejt vagy egy növényi gazdasejt.



SZTNH-100017916

7. Az 5. igénypont szerinti növényi gazdasejtet tartalmazó transzgenikus növény, előnyösen ahol a növény kukorica, citrom, búza, káposzta, napraforgó, paradicsom, keresztesvirágúak, bors illetve paprika, burgonya, gyapot, rizs, szója, cukorrépa, cukornád, dohány, árpa, és repce közül választott.

8. Az 1-4. igénypontok bármelyike szerinti nukleinsav molekulát tartalmazó mag.

9. Rekombináns nukleinsav molekula, mely egy variáns Cry3 aminosav-szekvenciát kódoló nukleotidszekvenciát tartalmaz, mely a 2. számú szekvenciával legalább 95%-os aminosavszekvencia azonosságot mutat a 2. számú szekvencia teljes hosszában, ahol a variáns egy glutaminsavgyököt tartalmaz a 2. számú szekvencia 316. aminosav-helyzetének megfelelő helyen, egy leucin gyököt tartalmaz a 2. számú szekvencia 482. aminosav-helyzetének megfelelő helyen, és egy lizin-gyököt tartalmaz a 2. számú szekvencia 483. aminosav-helyzetének megfelelő helyen, és ahol a variáns a 2. számú szekvencia peszticid aktivitásához viszonyítva fokozott peszticid aktivitással rendelkezik, és mely előnyösebben heterológ aminosavszekvenciákat tartalmaz.

10. A 9. igénypont szerinti rekombináns nukleinsav molekula, ahol a variáns a 15, 17, vagy 38. számú szekvenciával legalább 95%-os aminosavszekvencia azonosságot mutató aminosavszekvenciát tartalmaz.

11. A 9. igénypont szerinti rekombináns nukleinsav molekula, ahol a variáns egy 15, 17, vagy 38. számú szekvenciával rendelkező aminosavszekvenciát tartalmaz.

12. Készítmény, mely a 9-11. igénypontok bármelyike szerinti polipeptidet tartalmazza, előnyösen ahol a készítmény:

(a) formája por, hintőpor, pellet, granulátum, permet, emulzió, koloid és oldat közül választott;

(b) szárítással, liofilizálással, homogenizálással, extrakcióval, szüréssel, centrifugálással, vagy *Bacillus thuringiensis* sejtenyészet bekoncentráálásával kerül előállításra; és/vagy

(c) a polipeptidet körülbelül 1 tömeg% és körülbelül 99 tömeg% közötti mennyiségben tartalmazza.

13. Eljárás Coleoptera kártevő-populáció visszaszorítására vagy irtására, melynek során a populációt hatékony kártevőirtó mennyiségű 9-11. igénypontok bármelyike szerinti polipeptiddel hozzuk érintkezésbe.

14. Eljárás Coleoptera kártevőkkel szemben kártevőirtó hatású polipeptid előállítására, melynek során egy 5. igénypont szerinti vektort tartalmazó gazdasejtet tenyésztünk.

15. Növény, mely genomjába stabilan beépítve egy variáns Cry3 aminosav-szekvenciát kódoló nukleotidszekvenciát, mely a 2. számú szekvenciával legalább 95%-os aminosavszekvencia azonosságot mutat a 2. számú szekvencia teljes hosszában, ahol a variáns egy glutaminsavgyököt tartalmaz a 2. számú szekvencia 316. aminosav-helyzetének megfelelő helyen, egy leucin gyököt tartalmaz a 2. számú szekvencia 482. aminosav-helyzetének megfelelő helyen, és egy lizin-gyököt tartalmaz a 2. számú szekvencia 483. aminosav-helyzetének megfelelő helyen, és ahol a variáns a 2. számú szekvencia peszticid aktivitásához viszonyítva fokozott peszticid aktivitással rendelkezik, tartalmazó DNS konstruktot tartalmaz.

16. A 15. igénypont szerinti növény, ahol a variáns a 15, 17, vagy 38. számú szekvenciával legalább 95%-os aminosavszekvencia azonosságot mutató aminosavszekvenciát tartalmaz.

17. A 15. igénypont szerinti növény, ahol a variáns egy 15, 17, vagy 38. számú szekvenciával rendelkező aminosavszekvenciát tartalmaz.

18. Egy 1-5. igénypontok bármelyike szerinti rekombináns nukleinsav, egy 9-11. igénypontok bármelyike szerinti rekombináns polipeptid vagy egy 15-17. igénypontok bármelyike szerinti növény, ahol a kártevőirtó hatás Coleoptera-aktivitás, vagy gyökérkártevő nematódák elleni, előnyösen amerikai kukoricabogár vagy déli kukoricabogár elleni hatás.

19. A 15. vagy 17. igénypont szerinti növény, ahol a növény növényi sejt.

20. Eljárás növények kártevőktől történő védelmére, melynek során egy növényben vagy annak sejtjében egy variáns Cry3 aminosav-szekvenciát kódoló nukleotidszekvenciát fejezünk ki, mely a 2. számú szekvenciával legalább 95%-os aminosavszekvencia azonosságot mutat a 2. számú szekvencia teljes hosszában, ahol a variáns egy glutaminsavgyököt tartalmaz a 2. számú szekvencia 316. aminosav-helyzetének megfelelő helyen, egy leucin gyököt tartalmaz

a 2. számú szekvencia 482. aminosav-helyzetének megfelelő helyen, és egy lizin-gyököt tartalmaz a 2. számú szekvencia 483. aminosav-helyzetének megfelelő helyen, és ahol a variáns a 2. számú szekvencia peszticid aktivitásához viszonyítva fokozott peszticid aktivitással rendelkezik.

21. A 20. igénypont szerinti eljárás, ahol a variáns a 15, 17, vagy 38. számú szekvenciával legalább 95%-os aminosavszekvencia azonosságot mutató aminosavszekvenciát tartalmaz.

22. A 20. igénypont szerinti eljárás, ahol a variáns egy 15, 17, vagy 38. számú szekvenciával rendelkező aminosavszekvenciát tartalmaz.

Szentpéter Zsolt
szabadalmi ügyvéd
SOGK Szabadalmi Ügyvédi Iroda
H-1062 Budapest, Andrássy út 113.
Telefon: 461-1090 Fax: 461-1099
E-mail: szentpeter_zs@soqk.hu