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(54) Title: PEPTIDES DERIVED FROM ACINETOBACTER BAUMANNII AND THEIR USE IN VACCINATION

(57) Abstract: The present invention relates to proteins derived from Acinetobacter Baumannii, nucleic acids encoding the proteins, antibodies specific for the proteins as well as methods of therapy, prophylaxis, and diagnosis that utilise the proteins, nucleic acids, and antibodies.



PEPTIDES DERIVED FROM ACINETOBACTER BAUMANNII AND THEIR USE IN VACCINATION

FIELD OF THE INVENTION

The present invention relates to the field of antimicrobial prophylaxis and therapy. In particular the present invention relates to novel proteins and polynucleotides derived from *Acinetobacter baumannii*. The invention further relates to vectors comprising the polynucleotides, transformed host organisms expressing the polynucleotides, antibodies (mono- or polyclonal) specific for the polypeptides as well as diagnostic, prophylactic and therapeutic uses and methods. Finally, also methods of preparation are part of the invention.

BACKGROUND OF THE INVENTION

Antibiotic resistance is recognized as one of the greatest threats to human health on the planet (2009; Choffnes et al., *Antibiotic Resistance: Implications for Global Health and Novel Intervention Strategies*, The National Academic Press, Washington, D.C., (2010); Smolinski et al., *Microbial Threats to Health: Emergence, Detection, and Response*, The Institute of Medicine, Washington D.C., (2003); Spellberg et al., *Clin Infect Dis* 52(55):397-428 (2011); Spellberg et al., *Clin Infect Dis* 46:155-164 (2008); Walker et al., *Science* 325-1345-1346 (2009). In the last decade, *Acinetobacter baumannii* has emerged as one of the most common and highly antibiotic-resistant pathogens in the United States (US) and throughout the world (Doi et al., *Emerg Infect Dis* 15:980-982 (2009); Higgins et al., *J Antimicrob Chemother* 65-233-238 (2010); Perez et al., *Antimicrob Agents Chemother* 51:3471-3484 (2007). Indeed, 50-70% of *A. baumannii* clinical isolates are now extensively drug resistant (XDR; i.e. resistant to carbapenems and all other antibiotics except colistin or tigecycline), reflecting a >15-fold increase in just the past 10 years (Dizbay et al., *Scand J Infect Dis* (2010); Hidron et al., *Infect Control Hosp Epidemiol* 29:996-1011 (2008); Hoffmann et al., *Infect Control Hosp Epidemiol* 31:196-197 (2010); Kallen et al., *Infect Control Hosp Epidemiol* 31:528-531 (2010); Lautenbach et al., *Infect Control Hosp Epidemiol* 30:1186-1192 (2009); Mera et al., *Drug Resist* 16:209-215 (2010); Perez et al., *Am J Infect Control* 38:63-65 (2010); Rosenthal et al., *Am J Infect Control* 38:95-104 e102 (2010). Infections caused by carbapenem-resistant, XDR *A. baumannii* are associated with prolonged hospitalization, tremendous health care costs, and high rates of death despite treatment (Doi et al., *Emerg Infect Dis* 15:980-982 (2009); Falagas et al., *Int J Antimicrob Agents* 32:450-454 (2008); Gordon and Wareham, *J Antimicrob Chemother* 63:775-780 (2009); Lautenbach et al., *Infect Control Hosp Epidemiol* 30:1186-1192 (2009); Metan et al., *Eur J Intern Med* 20:540-544 (2009); Park et al., *Diagn Microbiol Infect Dis* 64:43-51 (2009); Perez et al., *Am J Infect Control* 38:63-65 (2007); Sunenshine et al., *Emerg Infect Dis* 13:97-103

(2007). Indeed, bloodstream infections caused by XDR *A. baumannii* cause >50-60% mortality rates despite antibiotic therapy (Gordon and Wareham, *J Antimicrob Chemother* 63:775-780 (2009); Metan et al., *Eur J Intern Med* 20:540-544 (2009); Munoz-Price et al., *Infect Control Hosp Epidemiol* 1(10):1057-62 (2010); Park et al., *Diagn Microbiol Infect Dis* 64:43-51 (2009); Tseng et al., *Diagn Microbiol Infect Dis* 59:181-190 (2007). A major reason for these high mortality rates is that XDR *A. baumannii* infections are treatable only with suboptimal second-line antibacterial agents, such as tigecycline and colistin. Even more concerning is the increasing resistance of *A. baumannii* to both colistin and tigecycline (Adams et al., *Antimicrob Agents Chemother* 53:3628-3634 (2009); Doi et al., *Emerg Infect Dis* 15:980-982 (2009); Falagas et al., *Int J Antimicrob Agents* 32:450-454 (2008); Hernan et al., *Diagn Microbiol Infect Dis* 65:188-191 (2009); Livermore et al., *Int J Antimicrob Agents* 35:19-24 (2010); Park et al., *Diagn Microbiol Infect Dis* 64:43-51 (2009); Valencia et al., *Infect Control Hosp Epidemiol* 30:257-263 (2009); Wang and Dowzicky, *Diagn Microbiol Infect Dis* 68:73-79 (2010). Such pan-drug resistant (PDR) *A. baumannii* infections are resistant to every FDA approved antibiotic, and are hence untreatable.

New methods to prevent and treat *A. baumannii* infections are critically needed, especially since no new drugs to treat these infections are in the antibacterial pipeline for the coming decade (Boucher et al., *Clin Infect Dis* 48:1-12 (2009); Spellberg et al., *Clin Infect Dis* 46:155-164 (2008). Since risk factors for *A. baumannii* infections are understood (Beavers et al., 2009; Caricato et al., *Intensive Care Med* 35:1964-1969 (2009); D'Agata et al., *Infect Control Hosp Epidemiol* 21:588-591 (2000); Furniss et al., *J Burn Care Rehabil* 26:405-408 (2005); Metan et al., *Eur J Intern Med* 20:540-544 (2009); Zakuan et al., *Trop Biomed* 26:123-129 (2009), vaccination of acutely at-risk patients is a promising method to prevent such infections, and antibody-based immunotherapy has promise to improve outcomes from infection.

The first full-genome sequence of *A. baumannii* was performed in 2007 (strain ATCC 17978) with a chromosome of 3976747 base pairs

Vaccination is considered to be a very effective method of preventing infectious diseases in human and veterinary health care. Vaccination is the administration of immunogenically effective amounts of antigenic material (the vaccine) to produce immunity to a disease/disease-causing pathogenic agent. Vaccines have contributed to the eradication of smallpox, the near eradication of polio, and the control of a variety of diseases, including rubella, measles, mumps, chickenpox, typhoid fever.

Before "the genomic era", vaccines were based on killed or live attenuated, microorganisms, or parts purified from them. Subunit vaccines are considered as a modern upgrade of these

types of vaccine, as the subunit vaccines contain one or more protective antigens, which are more or less the weak spot of the pathogen. Hence, in order to develop subunit vaccines, it is critical to identify the proteins, which are important for inducing protection and to eliminate others.

- 5 An antigen is said to be protective if it is able to induce protection from subsequent challenge by a disease-causing infectious agent in an appropriate animal model following immunization.

The empirical approach to subunit vaccine development, which includes several steps, begins with pathogen cultivation, followed by purification into components, and then testing of antigens for protection. Apart from being time and labour consuming, this approach has
10 several limitations that can lead to failure. It is not possible to develop vaccines using this approach for microorganisms, which cannot easily be cultured and only allows for the identification of the antigens, which can be obtained in sufficient quantities. The empirical approach has a tendency to focus on the most abundant proteins, which in some cases are not immuno-protective. In other cases, the antigen expressed during *in vivo* infection is not
15 expressed during *in vitro* cultivation. Furthermore, antigen discovery by use of the empirical approach demands an extreme amount of proteins in order to discover the protective antigens, which are like finding needles in the haystack. This renders it a very expensive approach, and it limits the vaccine development around diseases, which is caused by pathogens with a large genome or disease areas, which perform badly in a cost-effective
20 perspective.

OBJECT OF THE INVENTION

It is an object of embodiments of the invention to provide *A. baumannii* derived antigenic polypeptides that may serve as constituents in vaccines against *A. baumannii* infections and in diagnosis of *A. baumannii* infections. It is also an object to provide nucleic acids, vectors,
25 transformed cells, vaccine compositions, and other useful means for molecular cloning as well as for therapy and diagnosis with relevance for *A. baumannii*.

SUMMARY OF THE INVENTION

It has been found by the present inventor(s) that *A. baumannii*, expresses a number of hitherto unknown putatively surface exposed proteins which are candidates as vaccine
30 targets as well as candidates as immunizing agents for preparation of antibodies that target *A. baumannii*.

So, in a first aspect the present invention relates to a polypeptide comprising

- a) an amino acid sequence selected from the group consisting of any one of SEQ ID NOs: 1-30, or
- b) an amino acid sequence consisting of at least 5 contiguous amino acid residues from any one of SEQ ID NOs: 1-30, or
- c) an amino acid sequence having a sequence identity of at least 60% with the amino acid sequence of a),
- d) an amino acid sequence having a sequence identity of at least 60% with the amino acid sequence of b), or
- e) an assembly of amino acids derived from any one of SEQ ID NOs: 1-30 which has essentially the same 3D conformation as in the protein from which said assembly is derived so as to constitute a B-cell epitope, said polypeptide being antigenic in a mammal.

In another aspect, the invention relates to an isolated nucleic acid fragment, which comprises

- i) a nucleotide sequence encoding a polypeptide of the invention, or
- ii) a nucleotide sequence consisting of any one of SEQ ID NOs: 31-60.
- iii) a nucleotide sequence consisting of at least 10 consecutive nucleotides in any one of SEQ ID NOs: 31-60,
- iv) a nucleotide sequence having a sequence identity of at least 60% with the nucleotide sequence in i) or ii),
- v) a nucleotide sequence having a sequence identity of at least 60% with the nucleotide sequence in iii),
- vi) a nucleotide sequence complementary to the nucleotide sequence in i)-v), or
- vii) a nucleotide sequence which hybridizes under stringent conditions with the nucleotide sequence in i)-vi).

- In a third aspect, the invention relates to a vector comprising the nucleic acid of the invention, such as a cloning vector or an expression vector.

In fourth aspect, the invention relates to a cell which is transformed so as to carry the vector of the invention.

- In a fifth aspect, the invention relates to a pharmaceutical composition comprising a polypeptide of the invention, a nucleic acid fragment of the invention, a vector of the invention, or a transformed cell of the invention, and a pharmaceutically acceptable carrier, vehicle or diluent.

In a sixth aspect, the invention relates to a method for inducing immunity in an animal by administering at least once an immunogenically effective amount of a polypeptide of the

invention, a nucleic acid fragment of the invention, a vector of the invention, a transformed cell of the invention, or a pharmaceutical composition of the fifth aspect of the invention so as to induce adaptive immunity against *A. baumannii* in humans or animals.

5 In a seventh and eighth aspect, the invention relates to 1) a polyclonal antibody in which the antibodies specifically bind to at least one polypeptide of the invention, and which is essentially free from antibodies binding specifically to other *A. baumannii* polypeptides, and to 2) an isolated monoclonal antibody or antibody analogue which binds specifically to a polypeptide of the invention. In a related ninth aspect, the invention relates to a pharmaceutical composition comprising such a polyclonal or monoclonal antibody and a
10 pharmaceutically acceptable carrier, vehicle or diluent.

In a 10th aspect, the invention relates to a method for prophylaxis, treatment or amelioration of infection with *A. baumannii*, comprising administering a therapeutically effective amount of an antibody of the 7th or 8th aspect of the invention or a pharmaceutical composition of the eighth aspect to an individual in need thereof.

15 In an 11th aspect, the invention relates to a method for determining, quantitatively or qualitatively, the presence of *A. baumannii*, in particular the presence of multi-resistant *A. baumannii*, in a sample, the method comprising contacting the sample with an antibody of aspects 8 or 9 of the invention and detecting the presence of antibody bound to material in the sample.

20 In an 12th aspect of the invention is provided a method for determining, quantitatively or qualitatively, the presence of antibodies specific for *A. baumannii*, in particular the presence of antibodies specific for multi-resistant *A. baumannii*, in a sample, the method comprising contacting the sample with a polypeptide of the invention and detecting the presence of antibody that specifically bind said polypeptide.

25 In a 13th aspect, the invention relates to a method for determining, quantitatively or qualitatively, the presence of a nucleic acid characteristic of *A. baumannii*, in particular the presence of a nucleic acid characteristic of multi-resistant *A. baumannii*, in a sample, the method comprising contacting the sample with a nucleic acid fragment of the invention and detecting the presence of nucleic acid in the sample that hybridizes to said nucleic acid
30 fragment.

In a 14th aspect, the invention relates to a method for the preparation of the polypeptide of the invention, comprising

- culturing a transformed cell of the present invention, which is capable of expressing the

nucleic acid of the invention, under conditions that facilitate that the transformed cell expresses the nucleic acid fragment of the invention, which encodes a polypeptide of the invention, and subsequently recovering said polypeptide, or

- preparing said polypeptide by means of solid or liquid phase peptide synthesis.

- 5 In a 15th aspect, the invention relates to a method for determining whether a substance, such as an antibody, is potentially useful for treating infection with *A. baumannii*, the method comprising contacting the polypeptide of the invention with the substance and subsequently establishing whether the substance has at least one of the following characteristics:
- 1) the ability to bind specifically to said polypeptide,
 - 10 2) the ability to compete with said polypeptide for specific binding to a ligand/receptor, and
 - 3) the ability to specifically inactivate said polypeptide.

- Finally, in a 16th aspect, the invention relates to a method for determining whether a substance, such as a nucleic acid, is potentially useful for treating infection with *A. baumannii*, the method comprising contacting the substance with the nucleic acid fragment of
- 15 claim of the invention and subsequently establishing whether the substance has either the ability to
- 1) bind specifically to the nucleic acid fragment, or
 - 2) bind specifically to a nucleic acid that hybridizes specifically with the nucleic acid fragment.

20 DETAILED DISCLOSURE OF THE INVENTION

Definitions

- The term "polypeptide" is in the present context intended to mean both short peptides of from 2 to 10 amino acid residues, oligopeptides of from 11 to 100 amino acid residues, and polypeptides of more than 100 amino acid residues. Further-more, the term is also intended
- 25 to include proteins, i.e. functional biomolecules comprising at least one polypeptide; when comprising at least two polypeptides, these may form complexes, be covalently linked, or may be non-covalently linked. The polypeptide (s) in a protein can be glycosylated and/or lipidated and/or comprise prosthetic groups.

- The term "subsequence" means any consecutive stretch of at least 3 amino acids or, when
- 30 relevant, of at least 3 nucleotides, derived directly from a naturally occurring amino acid sequence or nucleic acid sequence, respectively

The term "amino acid sequence" is the order in which amino acid residues, connected by peptide bonds, lie in the chain in peptides and proteins.

The term "adjuvant" has its usual meaning in the art of vaccine technology, i.e. a substance or a composition of matter which is 1) not in itself capable of mounting a specific immune response against the immunogen of the vaccine, but which is 2) nevertheless capable of enhancing the immune response against the immunogen. Or, in other words, vaccination with the adjuvant alone does not provide an immune response against the immunogen, vaccination with the immunogen may or may not give rise to an immune response against the immunogen, but the combined vaccination with immunogen and adjuvant induces an immune response against the immunogen which is stronger than that induced by the immunogen alone.

"Sequence identity" is in the context of the present invention determined by comparing 2 optimally aligned sequences of equal length (e.g. DNA, RNA or amino acid) according to the following formula: $(N_{\text{ref}} - N_{\text{dif}}) \cdot 100 / N_{\text{ref}}$, wherein N_{ref} is the number of residues in one of the 2 sequences and N_{dif} is the number of residues which are non-identical in the two sequences when they are aligned over their entire lengths and in the same direction. So, two sequences 5'-ATTCGGAACC-3' and 5'-ATACGGGACC-3' will provide the sequence identity 80% ($N_{\text{ref}}=10$ and $N_{\text{dif}}=2$).

An "assembly of amino acids" means two or more amino acids bound together by physical or chemical means.

The "3D conformation" is the 3 dimensional structure of a biomolecule such as a protein. In monomeric polypeptides/proteins, the 3D conformation is also termed "the tertiary structure" and denotes the relative locations in 3 dimensional space of the amino acid residues forming the polypeptide.

"An immunogenic carrier" is a molecule or moiety to which an immunogen or a hapten can be coupled in order to enhance or enable the elicitation of an immune response against the immunogen/hapten. Immunogenic carriers are in classical cases relatively large molecules (such as tetanus toxoid, KLH, diphtheria toxoid etc.) which can be fused or conjugated to an immunogen/hapten, which is not sufficiently immunogenic in its own right – typically, the immunogenic carrier is capable of eliciting a strong T-helper lymphocyte response against the combined substance constituted by the immunogen and the immunogenic carrier, and this in turn provides for improved responses against the immunogen by B-lymphocytes and cytotoxic lymphocytes. More recently, the large carrier molecules have to a certain extent been substituted by so-called promiscuous T-helper epitopes, i.e. shorter peptides that are

recognized by a large fraction of HLA haplotypes in a population, and which elicit T-helper lymphocyte responses.

A "T-helper lymphocyte response" is an immune response elicited on the basis of a peptide, which is able to bind to an MHC class II molecule (e.g. an HLA class II molecule) in an antigen-presenting cell and which stimulates T-helper lymphocytes in an animal species as a consequence of T-cell receptor recognition of the complex between the peptide and the MHC Class II molecule prese

An "immunogen" is a substance of matter which is capable of inducing an adaptive immune response in a host, whose immune system is confronted with the immunogen. As such, immunogens are a subset of the larger genus "antigens", which are substances that can be recognized specifically by the immune system (e.g. when bound by antibodies or, alternatively, when fragments of the are antigens bound to MHC molecules are being recognized by T-cell receptors) but which are not necessarily capable of inducing immunity - an antigen is, however, always capable of *eliciting* immunity, meaning that a host that has an established memory immunity against the antigen will mount a specific immune response against the antigen.

A "hapten" is a small molecule, which can neither induce or elicit an immune response, but if conjugated to an immunogenic carrier, antibodies or TCRs that recognize the hapten can be induced upon confrontation of the immune system with the hapten carrier conjugate.

An "adaptive immune response" is an immune response in response to confrontation with an antigen or immunogen, where the immune response is specific for antigenic determinants of the antigen/immunogen - examples of adaptive immune responses are induction of antigen specific antibody production or antigen specific induction/activation of T helper lymphocytes or cytotoxic lymphocytes.

A "protective, adaptive immune response" is an antigen-specific immune response induced in a subject as a reaction to immunization (artificial or natural) with an antigen, where the immune response is capable of protecting the subject against subsequent challenges with the antigen or a pathology-related agent that includes the antigen. Typically, prophylactic vaccination aims at establishing a protective adaptive immune response against one or several pathogens.

"Stimulation of the immune system" means that a substance or composition of matter exhibits a general, non-specific immunostimulatory effect. A number of adjuvants and putative adjuvants (such as certain cytokines) share the ability to stimulate the immune

system. The result of using an immunostimulating agent is an increased "alertness" of the immune system meaning that simultaneous or subsequent immunization with an immunogen induces a significantly more effective immune response compared to isolated use of the immunogen.

5 Hybridization under "stringent conditions" is herein defined as hybridization performed under conditions by which a probe will hybridize to its target sequence, to a detectably greater degree than to other sequences. Stringent conditions are target-sequence-dependent and will differ depending on the structure of the polynucleotide. By controlling the stringency of the hybridization and/or washing conditions, target sequences can be identified which are 100%
10 complementary to a probe (homologous probing). Alternatively, stringency conditions can be adjusted to allow some mismatching in sequences so that lower degrees of similarity are detected (heterologous probing). Specificity is typically the function of post-hybridization washes, the critical factors being the ionic strength and temperature of the final wash solution. Generally, stringent wash temperature conditions are selected to be about 5°C to
15 about 2°C lower than the melting point (T_m) for the specific sequence at a defined ionic strength and pH. The melting point, or denaturation, of DNA occurs over a narrow temperature range and represents the disruption of the double helix into its complementary single strands. The process is described by the temperature of the midpoint of transition, T_m , which is also called the melting temperature. Formulas are available in the art for the
20 determination of melting temperatures.

The term "animal" is in the present context in general intended to denote an animal species (preferably mammalian), such as *Homo sapiens*, *Canis domesticus*, etc. and not just one single animal. However, the term also denotes a population of such an animal species, since it is important that the individuals immunized according to the method of the invention
25 substantially all will mount an immune response against the immunogen of the present invention.

As used herein, the term "antibody" refers to a polypeptide or group of polypeptides composed of at least one antibody combining site. An "antibody combining site" is the three-dimensional binding space with an internal surface shape and charge distribution
30 complementary to the features of an epitope of an antigen, which allows a binding of the antibody with the antigen. "Antibody" includes, for example, vertebrate antibodies, hybrid antibodies, chimeric antibodies, humanised antibodies, altered antibodies, univalent antibodies, Fab proteins, and single domain antibodies.

"Specific binding" denotes binding between two substances which goes beyond binding of
35 either substance to randomly chosen substances and also goes beyond simple association

between substances that tend to aggregate because they share the same overall hydrophobicity or hydrophilicity. As such, specific binding usually involves a combination of electrostatic and other interactions between two conformationally complementary areas on the two substances, meaning that the substances can "recognize" each other in a complex mixture.

The term "vector" is used to refer to a carrier nucleic acid molecule into which a heterologous nucleic acid sequence can be inserted for introduction into a cell where it can be replicated and expressed. The term further denotes certain biological vehicles useful for the same purpose, e.g. viral vectors and phage – both these infectious agents are capable of introducing a heterologous nucleic acid sequence

The term "expression vector" refers to a vector containing a nucleic acid sequence coding for at least part of a gene product capable of being transcribed. In some cases, when the transcription product is an mRNA molecule, this is in turn translated into a protein, polypeptide, or peptide.

Specific embodiments of the invention

The polypeptides of the invention

In some embodiments the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention may preferably constitute at least or exactly or at most 6, such as at least or exactly or at most 7, at least or exactly or at most 8, at least or exactly or at most 9, at least or exactly or at most 10, at least or exactly or at most 11, at least or exactly or at most 12, at least or exactly or at most 13, at least or exactly or at most 14, at least or exactly or at most 15, at least or exactly or at most 16, at least or exactly or at most 17, at least or exactly or at most 18, at least or exactly or at most 19, at least or exactly or at most 20, at least or exactly or at most 21, at least or exactly or at most 22, at least or exactly or at most 23, at least or exactly or at most 24, at least or exactly or at most 25, at least or exactly or at most 26, at least or exactly or at most 27 at least or exactly or at most 28, at least or exactly or at most 29, at least or exactly or at most 30, at least or exactly or at most 31, at least or exactly or at most 32, at least or exactly or at most 33, at least or exactly or at most 34, at least or exactly or at most 35 and at least or exactly or at most 36, at least or exactly or at most 37, at least or exactly or at most 38, at least or exactly or at most 39, at least or exactly or at most 40, at least or exactly or at most 41, at least or exactly or at most 42, at least or exactly or at most 43, at least or exactly or at most 44, at least or exactly or at most 45, at least or exactly or at most 46, at least or exactly or at most 47, at least or exactly or at most 48, at least or exactly or at most 49, at least or

exactly or at most 50, at least or exactly or at most 51, at least or exactly or at most 52, at least or exactly or at most 53, at least or exactly or at most 54, at least or exactly or at most 55 and at least or exactly or at most 56, at least or exactly or at most 57, at least or exactly or at most 58, at least or exactly or at most 59, or at least or exactly or at most 60

5 contiguous amino acid residues.

The number may, where applicable, be higher. Another way to phrase this is that for each of SEQ ID NOs: 1-30, the number of the contiguous amino acid residues is at least $N-n$, where N is the length of the sequence ID in question and n is any integer between 6 and $N-1$; that is, the at least 5 contiguous amino acids can be at least any number between 5 and the length of the reference sequence minus one, in increments of one. Consequently:

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Insofar as embodiment b relates to SEQ ID NO: 2-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably constitute at least or exactly or at most 61, at least or exactly or at most 62, at least or exactly or at most 63, at least or exactly or at most 64, at least or exactly or at most 65, at least or exactly or at most 66 contiguous amino acid residues.

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Insofar as embodiment b relates to SEQ ID NO: 4-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably constitute at least or exactly or at most 67, at least or exactly or at most 68, at least or exactly or at most 69, at least or exactly or at most 70, at least or exactly or at most 71, at least or exactly or at most 72, at least or exactly or at most 73 contiguous amino acid residues.

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Insofar as embodiment b relates to SEQ ID NO: 5-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably constitute at least or exactly or at most 74, at least or exactly or at most 75, at least or exactly or at most 76, at least or exactly or at most 77, at least or exactly or at most 78, at least or exactly or at most 79, at least or exactly or at most 80, at least or exactly or at most 81, at least or exactly or at most 82, at least or exactly or at most 83, at least or exactly or at most 84, at least or exactly or at most 85, at least or exactly or at most 86, at least or exactly or at most 87, at least or exactly or at most 88, at least or exactly or at most 89, at least or exactly or at most 90, at least or exactly or at most 91, at least or exactly or at most 92, at least or exactly or at most 93, at least or exactly or at most 94, at least or exactly or at most 95, at least or exactly or at most 96, at least or exactly or at most 97, at least or exactly or at most 98, at least or exactly or at most 99, at least or exactly or at most 100, at least or exactly or at most 101, at least or exactly or at most 102, at least or exactly or at most 103, at least or exactly or at most 104, at least or exactly or at most 105, at least or

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exactly or at most 106, at least or exactly or at most 107, at least or exactly or at most 108 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 6-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably
5 constitute at least or exactly or at most 109, at least or exactly or at most 110, at least or exactly or at most 111, at least or exactly or at most 112, at least or exactly or at most 113, at least or exactly or at most 114 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 7-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably
10 constitute at least or exactly or at most 115, at least or exactly or at most 116, at least or exactly or at most 117, at least or exactly or at most 118, at least or exactly or at most 119, at least or exactly or at most 120, at least or exactly or at most 121, at least or exactly or at most 122, at least or exactly or at most 123, at least or exactly or at most 124, at least or exactly or at most 125, at least or exactly or at most 126 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 8-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably
15 constitute at least or exactly or at most 127, at least or exactly or at most 128, at least or exactly or at most 129, at least or exactly or at most 130, at least or exactly or at most 131, at least or exactly or at most 132, at least or exactly or at most 133, at least or exactly or at
20 most 134, at least or exactly or at most 135, at least or exactly or at most 136, at least or exactly or at most 137, at least or exactly or at most 138, at least or exactly or at most 139 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 9-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably
25 constitute at least or exactly or at most 140, at least or exactly or at most 141, at least or exactly or at most 142, at least or exactly or at most 143, at least or exactly or at most 144, at least or exactly or at most 145, at least or exactly or at most 146, at least or exactly or at most 147, at least or exactly or at most 148, at least or exactly or at most 149, at least or exactly or at most 150, at least or exactly or at most 151, at least or exactly or at most 152,
30 at least or exactly or at most 153, at least or exactly or at most 154, at least or exactly or at most 155, at least or exactly or at most 156, at least or exactly or at most 157, at least or exactly or at most 158, at least or exactly or at most 159 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 10-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably

constitute at least or exactly or at most 160, at least or exactly or at most 161, at least or exactly or at most 162 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 11-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably
5 constitute at least or exactly or at most 163, at least or exactly or at most 164, at least or exactly or at most 165, at least or exactly or at most 166 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 12-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably
10 constitute at least or exactly or at most 167, at least or exactly or at most 168, at least or exactly or at most 169, at least or exactly or at most 170, at least or exactly or at most 171, at least or exactly or at most 172, at least or exactly or at most 173, at least or exactly or at most 174, at least or exactly or at most 175, at least or exactly or at most 176, at least or exactly or at most 177, at least or exactly or at most 178, at least or exactly or at most 179, at least or exactly or at most 180, at least or exactly or at most 181, at least or exactly or at
15 most 182, at least or exactly or at most 183, at least or exactly or at most 184, at least or exactly or at most 185, at least or exactly or at most 186, at least or exactly or at most 187, at least or exactly or at most 188, at least or exactly or at most 189, at least or exactly or at most 190, at least or exactly or at most 191, at least or exactly or at most 192, at least or exactly or at most 193, at least or exactly or at most 194, at least or exactly or at most 195, at least or exactly or at most 196, at least or exactly or at most 197, at least or exactly or at
20 most 198, at least or exactly or at most 199, at least or exactly or at most 200, at least or exactly or at most 201, at least or exactly or at most 202, at least or exactly or at most 203, at least or exactly or at most 204, at least or exactly or at most 205, at least or exactly or at most 206, at least or exactly or at most 207, at least or exactly or at most 208, at least or exactly or at most 209, at least or exactly or at most 210, at least or exactly or at most 211, at least or exactly or at most 212, at least or exactly or at most 213, at least or exactly or at most 214, at least or exactly or at most 215, at least or exactly or at most 216, at least or exactly or at most 217, at least or exactly or at most 218, at least or exactly or at most 219, at least or exactly or at most 220, at least or exactly or at most 221, at least or exactly or at
25 most 222, at least or exactly or at most 223, at least or exactly or at most 224, at least or exactly or at most 225, at least or exactly or at most 226, at least or exactly or at most 227, at least or exactly or at most 228, at least or exactly or at most 229, at least or exactly or at most 230 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 13-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably
35 constitute at least or exactly or at most 231, at least or exactly or at most 232, at least or

exactly or at most 233, at least or exactly or at most 234, at least or exactly or at most 235, at least or exactly or at most 236, at least or exactly or at most 237, at least or exactly or at most 238 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 14-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably consist of at least or exactly or at most 239, at least or exactly or at most 240, at least or exactly or at most 241, at least or exactly or at most 242, at least or exactly or at most 243, at least or exactly or at most 244, at least or exactly or at most 245, at least or exactly or at most 246, at least or exactly or at most 247, at least or exactly or at most 248, at least or exactly or at most 249, at least or exactly or at most 250, at least or exactly or at most 251, at least or exactly or at most 252, at least or exactly or at most 253 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 15-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably consist of at least or exactly or at most 254, at least or exactly or at most 255, at least or exactly or at most 256, at least or exactly or at most 257, at least or exactly or at most 258, at least or exactly or at most 259, at least or exactly or at most 260, at least or exactly or at most 261, at least or exactly or at most 262, at least or exactly or at most 263, at least or exactly or at most 264, at least or exactly or at most 265, at least or exactly or at most 266, at least or exactly or at most 267, at least or exactly or at most 268, at least or exactly or at most 269, at least or exactly or at most 270, at least or exactly or at most 271, at least or exactly or at most 272, at least or exactly or at most 273, at least or exactly or at most 274, at least or exactly or at most 275, at least or exactly or at most 276, at least or exactly or at most 277, at least or exactly or at most 278, at least or exactly or at most 279, at least or exactly or at most 280, at least or exactly or at most 281, at least or exactly or at most 282, at least or exactly or at most 283, at least or exactly or at most 284, at least or exactly or at most 285, at least or exactly or at most 286, at least or exactly or at most 287, at least or exactly or at most 288, at least or exactly or at most 289, at least or exactly or at most 290, at least or exactly or at most 291, at least or exactly or at most 292, at least or exactly or at most 293, at least or exactly or at most 294 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 16-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably consist of at least or exactly or at most 295, at least or exactly or at most 296, at least or exactly or at most 297, at least or exactly or at most 298, at least or exactly or at most 299, at least or exactly or at most 300, at least or exactly or at most 301, at least or exactly or at most 302, at least or exactly or at most 303, at least or exactly or at most 304, at least or

exactly or at most 305, at least or exactly or at most 306, at least or exactly or at most 307,
at least or exactly or at most 308, at least or exactly or at most 309, at least or exactly or at
most 310, at least or exactly or at most 311, at least or exactly or at most 312, at least or
exactly or at most 313, at least or exactly or at most 314, at least or exactly or at most 315,
5 at least or exactly or at most 316, at least or exactly or at most 317, at least or exactly or at
most 318, at least or exactly or at most 319, at least or exactly or at most 320, at least or
exactly or at most 321, at least or exactly or at most 322, at least or exactly or at most 323,
at least or exactly or at most 324, at least or exactly or at most 325, at least or exactly or at
most 326, at least or exactly or at most 327, at least or exactly or at most 328, at least or
10 exactly or at most 329, at least or exactly or at most 330, at least or exactly or at most 331,
at least or exactly or at most 332, at least or exactly or at most 333, at least or exactly or at
most 334, at least or exactly or at most 335, at least or exactly or at most 336, at least or
exactly or at most 337, at least or exactly or at most 338, at least or exactly or at most 339,
at least or exactly or at most 340, at least or exactly or at most 341, at least or exactly or at
15 most 342, at least or exactly or at most 343, at least or exactly or at most 344, at least or
exactly or at most 345, at least or exactly or at most 346, at least or exactly or at most 347,
at least or exactly or at most 348, at least or exactly or at most 349, at least or exactly or at
most 350, at least or exactly or at most 351, at least or exactly or at most 352, at least or
exactly or at most 353, at least or exactly or at most 354, at least or exactly or at most 355,
20 at least or exactly or at most 356 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 17-30, the at least 5 contiguous amino acids
referred to in option b) in the definition of the first aspect of the invention will preferably
constitute at least or exactly or at most 357, at least or exactly or at most 358, at least or
exactly or at most 359, at least or exactly or at most 360, at least or exactly or at most 361,
25 at least or exactly or at most 362, at least or exactly or at most 363, at least or exactly or at
most 364, at least or exactly or at most 365, at least or exactly or at most 366, at least or
exactly or at most 367 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 18-30, the at least 5 contiguous amino acids
referred to in option b) in the definition of the first aspect of the invention will preferably
30 constitute at least or exactly or at most 368, at least or exactly or at most 369, at least or
exactly or at most 370, at least or exactly or at most 371, at least or exactly or at most 372,
at least or exactly or at most 373, at least or exactly or at most 374, at least or exactly or at
most 375, at least or exactly or at most 376, at least or exactly or at most 377, at least or
exactly or at most 378, at least or exactly or at most 379, at least or exactly or at most 380,
35 at least or exactly or at most 381, at least or exactly or at most 382, at least or exactly or at
most 383, at least or exactly or at most 384, at least or exactly or at most 385, at least or
exactly or at most 386, at least or exactly or at most 387, at least or exactly or at most 388,

at least or exactly or at most 389, at least or exactly or at most 390, at least or exactly or at most 391, at least or exactly or at most 392, at least or exactly or at most 393, at least or exactly or at most 394, at least or exactly or at most 395, at least or exactly or at most 396, at least or exactly or at most 397, at least or exactly or at most 398, at least or exactly or at most 399, at least or exactly or at most 400, at least or exactly or at most 401, at least or exactly or at most 402, at least or exactly or at most 403, at least or exactly or at most 404, at least or exactly or at most 405, at least or exactly or at most 406, at least or exactly or at most 407, at least or exactly or at most 408, at least or exactly or at most 409, at least or exactly or at most 410, at least or exactly or at most 411, at least or exactly or at most 412, at least or exactly or at most 413, at least or exactly or at most 414, at least or exactly or at most 415, at least or exactly or at most 416, at least or exactly or at most 417, at least or exactly or at most 418, at least or exactly or at most 419, at least or exactly or at most 420 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 19-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably constitute at least or exactly or at most 421, at least or exactly or at most 422, at least or exactly or at most 423, at least or exactly or at most 424, at least or exactly or at most 425, at least or exactly or at most 426, at least or exactly or at most 427, at least or exactly or at most 428, at least or exactly or at most 429, at least or exactly or at most 430, at least or exactly or at most 431, at least or exactly or at most 432, at least or exactly or at most 433, at least or exactly or at most 434, at least or exactly or at most 435, at least or exactly or at most 436, at least or exactly or at most 437, at least or exactly or at most 438, at least or exactly or at most 439, at least or exactly or at most 440, at least or exactly or at most 441, at least or exactly or at most 442, at least or exactly or at most 443, at least or exactly or at most 444, at least or exactly or at most 445 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 20-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably constitute at least or exactly or at most 446, at least or exactly or at most 447, at least or exactly or at most 448, at least or exactly or at most 449, at least or exactly or at most 450, at least or exactly or at most 451, at least or exactly or at most 452, at least or exactly or at most 453, at least or exactly or at most 454, at least or exactly or at most 455, at least or exactly or at most 456, at least or exactly or at most 457, at least or exactly or at most 458, at least or exactly or at most 459, at least or exactly or at most 460, at least or exactly or at most 461, at least or exactly or at most 462, at least or exactly or at most 463, at least or exactly or at most 464, at least or exactly or at most 465, at least or exactly or at most 466, at least or exactly or at most 467, at least or exactly or at most 468, at least or exactly or at most 469, at least or exactly or at most 470, at least or exactly or at most 471, at least or

[illegible]

[illegible]

exactly or at most 680, at least or exactly or at most 681, at least or exactly or at most 682, at least or exactly or at most 683, at least or exactly or at most 684, at least or exactly or at most 685, at least or exactly or at most 686, at least or exactly or at most 687, at least or exactly or at most 688, at least or exactly or at most 689, at least or exactly or at most 690, at least or exactly or at most 691, at least or exactly or at most 692, at least or exactly or at most 693, at least or exactly or at most 694, at least or exactly or at most 695, at least or exactly or at most 696, at least or exactly or at most 697, at least or exactly or at most 698, at least or exactly or at most 699, at least or exactly or at most 700, at least or exactly or at most 701, at least or exactly or at most 702, at least or exactly or at most 703, at least or exactly or at most 704, at least or exactly or at most 705, at least or exactly or at most 706, at least or exactly or at most 707, at least or exactly or at most 708, at least or exactly or at most 709, at least or exactly or at most 710, at least or exactly or at most 711 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 21-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably constitute at least or exactly or at most 712, at least or exactly or at most 713, at least or exactly or at most 714, at least or exactly or at most 715, at least or exactly or at most 716, at least or exactly or at most 717, at least or exactly or at most 718, at least or exactly or at most 719, at least or exactly or at most 720, at least or exactly or at most 721, at least or exactly or at most 722, at least or exactly or at most 723, at least or exactly or at most 724, at least or exactly or at most 725, at least or exactly or at most 726, at least or exactly or at most 727 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 22-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably constitute at least or exactly or at most 728 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 23-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably constitute at least or exactly or at most 729, at least or exactly or at most 730, at least or exactly or at most 731, at least or exactly or at most 732, at least or exactly or at most 733, at least or exactly or at most 734, at least or exactly or at most 735, at least or exactly or at most 736, at least or exactly or at most 737, at least or exactly or at most 738, at least or exactly or at most 739, at least or exactly or at most 740, at least or exactly or at most 741, at least or exactly or at most 742, at least or exactly or at most 743, at least or exactly or at most 744, at least or exactly or at most 745, at least or exactly or at most 746, at least or exactly or at most 747, at least or exactly or at most 748, at least or exactly or at most 749, at least or exactly or at most 750, at least or exactly or at most 751, at least or exactly or at

most 752, at least or exactly or at most 753, at least or exactly or at most 754 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 24-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably

5 constitute at least or exactly or at most 755, at least or exactly or at most 756, at least or exactly or at most 757, at least or exactly or at most 758, at least or exactly or at most 759, at least or exactly or at most 760, at least or exactly or at most 761, at least or exactly or at most 762, at least or exactly or at most 763, at least or exactly or at most 764, at least or exactly or at most 765, at least or exactly or at most 766, at least or exactly or at most 767,
10 at least or exactly or at most 768, at least or exactly or at most 769, at least or exactly or at most 770, at least or exactly or at most 771, at least or exactly or at most 772, at least or exactly or at most 773, at least or exactly or at most 774, at least or exactly or at most 775, at least or exactly or at most 776, at least or exactly or at most 777, at least or exactly or at most 778, at least or exactly or at most 779, at least or exactly or at most 780, at least or exactly or at most 781, at least or exactly or at most 782, at least or exactly or at most 783, at least or exactly or at most 784, at least or exactly or at most 785, at least or exactly or at most 786, at least or exactly or at most 787, at least or exactly or at most 788, at least or exactly or at most 789, at least or exactly or at most 790, at least or exactly or at most 791, at least or exactly or at most 792, at least or exactly or at most 793, at least or exactly or at most 794, at least or exactly or at most 795, at least or exactly or at most 796, at least or exactly or at most 797, at least or exactly or at most 798, at least or exactly or at most 799, at least or exactly or at most 800, at least or exactly or at most 801, at least or exactly or at most 802, at least or exactly or at most 803, at least or exactly or at most 804, at least or exactly or at most 805, at least or exactly or at most 806, at least or exactly or at most 807, at least or exactly or at most 808, at least or exactly or at most 809, at least or exactly or at most 810, at least or exactly or at most 811, at least or exactly or at most 812, at least or exactly or at most 813, at least or exactly or at most 814, at least or exactly or at most 815, at least or exactly or at most 816, at least or exactly or at most 817, at least or exactly or at most 818, at least or exactly or at most 819, at least or exactly or at most 820, at least or exactly or at most 821, at least or exactly or at most 822, at least or exactly or at most 823, at least or exactly or at most 824, at least or exactly or at most 825, at least or exactly or at most 826, at least or exactly or at most 827, at least or exactly or at most 828, at least or exactly or at most 829, at least or exactly or at most 830, at least or exactly or at most 831, at least or exactly or at most 832, at least or exactly or at most 833, at least or exactly or at most 834, at least or exactly or at most 835, at least or exactly or at most 836, at least or exactly or at most 837, at least or exactly or at most 838, at least or exactly or at most 839, at least or exactly or at most 840, at least or exactly or at most 841, at least or exactly or at most 842, at least or exactly or at most 843, at least or exactly or at most 844, at least or

exactly or at most 845, at least or exactly or at most 846, at least or exactly or at most 847, at least or exactly or at most 848, at least or exactly or at most 849, at least or exactly or at most 850, at least or exactly or at most 851, at least or exactly or at most 852, at least or exactly or at most 853, at least or exactly or at most 854, at least or exactly or at most 855, at least or exactly or at most 856, at least or exactly or at most 857, at least or exactly or at most 858, at least or exactly or at most 859, at least or exactly or at most 860, at least or exactly or at most 861, at least or exactly or at most 862, at least or exactly or at most 863, at least or exactly or at most 864, at least or exactly or at most 865, at least or exactly or at most 866, at least or exactly or at most 867, at least or exactly or at most 868, at least or exactly or at most 869, at least or exactly or at most 870, at least or exactly or at most 871, at least or exactly or at most 872, at least or exactly or at most 873, at least or exactly or at most 874, at least or exactly or at most 875, at least or exactly or at most 876, at least or exactly or at most 877, at least or exactly or at most 878, at least or exactly or at most 879, at least or exactly or at most 880, at least or exactly or at most 881, at least or exactly or at most 882, at least or exactly or at most 883, at least or exactly or at most 884, at least or exactly or at most 885, at least or exactly or at most 886, at least or exactly or at most 887, at least or exactly or at most 888, at least or exactly or at most 889, at least or exactly or at most 890, at least or exactly or at most 891, at least or exactly or at most 892, at least or exactly or at most 893, at least or exactly or at most 894, at least or exactly or at most 895, at least or exactly or at most 896, at least or exactly or at most 897, at least or exactly or at most 898, at least or exactly or at most 899, at least or exactly or at most 900, at least or exactly or at most 901, at least or exactly or at most 902, at least or exactly or at most 903, at least or exactly or at most 904, at least or exactly or at most 905, at least or exactly or at most 906 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 25-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably constitute at least or exactly or at most 907, at least or exactly or at most 908, at least or exactly or at most 909, at least or exactly or at most 910, at least or exactly or at most 911, at least or exactly or at most 912, at least or exactly or at most 913, at least or exactly or at most 914, at least or exactly or at most 915, at least or exactly or at most 916, at least or exactly or at most 917, at least or exactly or at most 918, at least or exactly or at most 919, at least or exactly or at most 920, at least or exactly or at most 921, at least or exactly or at most 922, at least or exactly or at most 923, at least or exactly or at most 924, at least or exactly or at most 925, at least or exactly or at most 926, at least or exactly or at most 927, at least or exactly or at most 928, at least or exactly or at most 929, at least or exactly or at most 930, at least or exactly or at most 931, at least or exactly or at most 932, at least or exactly or at most 933, at least or exactly or at most 934, at least or exactly or at most 935, at least or exactly or at most 936, at least or exactly or at most 937, at least or exactly or at

most 938, at least or exactly or at most 939, at least or exactly or at most 940, at least or exactly or at most 941, at least or exactly or at most 942, at least or exactly or at most 943, at least or exactly or at most 944, at least or exactly or at most 945, at least or exactly or at most 946, at least or exactly or at most 947, at least or exactly or at most 948, at least or exactly or at most 949, at least or exactly or at most 950, at least or exactly or at most 951, at least or exactly or at most 952, at least or exactly or at most 953, at least or exactly or at most 954, at least or exactly or at most 955, at least or exactly or at most 956, at least or exactly or at most 957, at least or exactly or at most 958, at least or exactly or at most 959, at least or exactly or at most 960, at least or exactly or at most 961, at least or exactly or at most 962, at least or exactly or at most 963, at least or exactly or at most 964, at least or exactly or at most 965, at least or exactly or at most 966, at least or exactly or at most 967, at least or exactly or at most 968, at least or exactly or at most 969, at least or exactly or at most 970, at least or exactly or at most 971, at least or exactly or at most 972, at least or exactly or at most 973, at least or exactly or at most 974 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 26-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably constitute at least or exactly or at most 975, at least or exactly or at most 976, at least or exactly or at most 977, at least or exactly or at most 978, at least or exactly or at most 979, at least or exactly or at most 980, at least or exactly or at most 981, at least or exactly or at most 982, at least or exactly or at most 983, at least or exactly or at most 984, at least or exactly or at most 985, at least or exactly or at most 986, at least or exactly or at most 987, at least or exactly or at most 988, at least or exactly or at most 989, at least or exactly or at most 990, at least or exactly or at most 991, at least or exactly or at most 992, at least or exactly or at most 993, at least or exactly or at most 994, at least or exactly or at most 995, at least or exactly or at most 996, at least or exactly or at most 997, at least or exactly or at most 998, at least or exactly or at most 999, at least or exactly or at most 1000, at least or exactly or at most 1001, at least or exactly or at most 1002, at least or exactly or at most 1003, at least or exactly or at most 1004, at least or exactly or at most 1005, at least or exactly or at most 1006, at least or exactly or at most 1007, at least or exactly or at most 1008, at least or exactly or at most 1009, at least or exactly or at most 1010, at least or exactly or at most 1011, at least or exactly or at most 1012, at least or exactly or at most 1013, at least or exactly or at most 1014, at least or exactly or at most 1015, at least or exactly or at most 1016, at least or exactly or at most 1017, at least or exactly or at most 1018, at least or exactly or at most 1019, at least or exactly or at most 1020, at least or exactly or at most 1021, at least or exactly or at most 1022, at least or exactly or at most 1023, at least or exactly or at most 1024, at least or exactly or at most 1025, at least or exactly or at most 1026, at least or exactly or at most 1027, at least or exactly or at most 1028, at least or exactly or at most 1029, at least or exactly or at most 1030, at least or

exactly or at most 1031, at least or exactly or at most 1032, at least or exactly or at most 1033, at least or exactly or at most 1034, at least or exactly or at most 1035, at least or exactly or at most 1036, at least or exactly or at most 1037, at least or exactly or at most 1038, at least or exactly or at most 1039, at least or exactly or at most 1040, at least or exactly or at most 1041, at least or exactly or at most 1042, at least or exactly or at most 1043, at least or exactly or at most 1044, at least or exactly or at most 1045, at least or exactly or at most 1046, at least or exactly or at most 1047, at least or exactly or at most 1048, at least or exactly or at most 1049, at least or exactly or at most 1050, at least or exactly or at most 1051, at least or exactly or at most 1052, at least or exactly or at most 1053, at least or exactly or at most 1054, at least or exactly or at most 1055, at least or exactly or at most 1056, at least or exactly or at most 1057, at least or exactly or at most 1058, at least or exactly or at most 1059, at least or exactly or at most 1060, at least or exactly or at most 1061, at least or exactly or at most 1062, at least or exactly or at most 1063, at least or exactly or at most 1064, at least or exactly or at most 1065, at least or exactly or at most 1066, at least or exactly or at most 1067, at least or exactly or at most 1068, at least or exactly or at most 1069, at least or exactly or at most 1070, at least or exactly or at most 1071 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 27-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably constitute at least or exactly or at most 1072, at least or exactly or at most 1073, at least or exactly or at most 1074, at least or exactly or at most 1075, at least or exactly or at most 1076, at least or exactly or at most 1077, at least or exactly or at most 1078, at least or exactly or at most 1079, at least or exactly or at most 1080, at least or exactly or at most 1081, at least or exactly or at most 1082, at least or exactly or at most 1083, at least or exactly or at most 1084, at least or exactly or at most 1085, at least or exactly or at most 1086, at least or exactly or at most 1087, at least or exactly or at most 1088, at least or exactly or at most 1089, at least or exactly or at most 1090, at least or exactly or at most 1091, at least or exactly or at most 1092, at least or exactly or at most 1093, at least or exactly or at most 1094, at least or exactly or at most 1095, at least or exactly or at most 1096, at least or exactly or at most 1097, at least or exactly or at most 1098, at least or exactly or at most 1099, at least or exactly or at most 1100, at least or exactly or at most 1101, at least or exactly or at most 1102, at least or exactly or at most 1103, at least or exactly or at most 1104, at least or exactly or at most 1105, at least or exactly or at most 1106, at least or exactly or at most 1107, at least or exactly or at most 1108, at least or exactly or at most 1109, at least or exactly or at most 1110 contiguous amino acid residues.

Insofar as embodiment b relates to SEQ ID NO: 28-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably

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exactly or at most 1208, at least or exactly or at most 1209, at least or exactly or at most 1210, at least or exactly or at most 1211, at least or exactly or at most 1212, at least or exactly or at most 1213, at least or exactly or at most 1214, at least or exactly or at most 1215, at least or exactly or at most 1216, at least or exactly or at most 1217, at least or
5 exactly or at most 1218, at least or exactly or at most 1219, at least or exactly or at most 1220, at least or exactly or at most 1221, at least or exactly or at most 1222, at least or exactly or at most 1223, at least or exactly or at most 1224, at least or exactly or at most 1225, at least or exactly or at most 1226, at least or exactly or at most 1227, at least or exactly or at most 1228 contiguous amino acid residues.

10 Insofar as embodiment b relates to SEQ ID NO: 29-30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably constitute at least or exactly or at most 1229, at least or exactly or at most 1230, at least or exactly or at most 1231, at least or exactly or at most 1232, at least or exactly or at most 1233, at least or exactly or at most 1234, at least or exactly or at most 1235, at least or
15 exactly or at most 1236, at least or exactly or at most 1237, at least or exactly or at most 1238, at least or exactly or at most 1239, at least or exactly or at most 1240, at least or exactly or at most 1241, at least or exactly or at most 1242, at least or exactly or at most 1243, at least or exactly or at most 1244, at least or exactly or at most 1245, at least or exactly or at most 1246, at least or exactly or at most 1247, at least or exactly or at most
20 1248, at least or exactly or at most 1249, at least or exactly or at most 1250, at least or exactly or at most 1251, at least or exactly or at most 1252, at least or exactly or at most 1253, at least or exactly or at most 1254, at least or exactly or at most 1255, at least or exactly or at most 1256, at least or exactly or at most 1257, at least or exactly or at most 1258, at least or exactly or at most 1259, at least or exactly or at most 1260, at least or
25 exactly or at most 1261, at least or exactly or at most 1262, at least or exactly or at most 1263, at least or exactly or at most 1264, at least or exactly or at most 1265, at least or exactly or at most 1266, at least or exactly or at most 1267, at least or exactly or at most 1268, at least or exactly or at most 1269, at least or exactly or at most 1270, at least or exactly or at most 1271, at least or exactly or at most 1272, at least or exactly or at most
30 1273, at least or exactly or at most 1274, at least or exactly or at most 1275, at least or exactly or at most 1276, at least or exactly or at most 1277, at least or exactly or at most 1278, at least or exactly or at most 1279, at least or exactly or at most 1280, at least or exactly or at most 1281, at least or exactly or at most 1282, at least or exactly or at most 1283, at least or exactly or at most 1284 contiguous amino acid residues.

35 Insofar as embodiment b relates to SEQ ID NO: 30, the at least 5 contiguous amino acids referred to in option b) in the definition of the first aspect of the invention will preferably constitute at least or exactly or at most 1285, at least or exactly or at most 1286, at least or

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exactly or at most 3042, at least or exactly or at most 3043, at least or exactly or at most 3044, at least or exactly or at most 3045, at least or exactly or at most 3046, at least or exactly or at most 3047 contiguous amino acid residues.

In some embodiments, the polypeptide of the invention also has a sequence identity with the amino acid sequence of a) defined above of at least 65%, such as at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, and at least 99%.

Similarly, the polypeptide of the invention in some embodiments also has a sequence identity with the amino acid sequence of b) defined above of at least 60%, such as at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, and at least 99%.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, and 56 in any one of SEQ ID NOs: 1-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than N-L+1, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b).

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 57, 58, 59, 60, 61 and 62 in any one of SEQ ID NOs: 2-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than N-L+1, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b).

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 63, 64, 65, 66, 67, 68, and 69 in any one of SEQ ID NOs: 4-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-

terminal first residue will not be higher numbered than $N-L+1$, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, and 104 in any one of SEQ ID NOs: 5-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than $N-L+1$, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 105, 106, 107, 108, 109, 110, and 110 in any one of SEQ ID NOs: 6-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than $N-L+1$, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, and 122 in any one of SEQ ID NOs: 7-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than $N-L+1$, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, and 135 in any one of SEQ ID NOs: 8-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than

N-L+1, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, and 155 in any one of SEQ ID NOs: 9-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than N-L+1, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 156, 157, and 158 in any one of SEQ ID NOs: 10-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than N-L+1, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 159, 160, 161, and 162 in any one of SEQ ID NOs: 11-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than N-L+1, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, and 226 in any one of SEQ ID NOs: 12-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than N-L+1,

where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 227, 228, 229, 230, 231, 232, 233, and 234 in any one of SEQ ID NOs: 13-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than N-L+1, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, and 249 in SEQ ID NOs: 14-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than N-L+1, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, and 290 in any one of SEQ ID NOs: 15-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than N-L+1, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, and 352 in any one of SEQ ID NOs: 16-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher

than 5, the N-terminal first residue will not be higher numbered than $N-L+1$, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues In the

embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 353, 354, 355,

356, 357, 358, 359, 360, 361, 362, and 363 in any one of SEQ ID NOs: 17-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than $N-L+1$, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-

terminal amino acid residue corresponding to any one of amino acid residues 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, and 416 in any one of SEQ ID NOs: 18-30, if the length of the at least 5 amino acid residues so permit – if the

length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than $N-L+1$, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has

its N-terminal amino acid residue corresponding to any one of amino acid residues In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-

terminal amino acid residue corresponding to any one of amino acid residues 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, and 441 in any one of SEQ ID NOs: 19-30, if the length of the at least 5

amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5,

the N-terminal first residue will not be higher numbered than $N-L+1$, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b).

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues In the

embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 442, 443, 444,

445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, and 707 in any one of SEQ ID NOs: 20-

30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than $N-L+1$, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b).

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues In the

embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 708, 709, 710,

711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722 and 723 in any one of SEQ ID NOs: 21-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher

numbered than $N-L+1$, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b).

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to amino acid residue 724 in any one of SEQ ID NOs: 22-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than $N-L+1$, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b).

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, and 750 in any one of SEQ ID NOs: 23-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than $N-L+1$, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b).

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833, 834, 835, 836, 837, 838, 839, 840, 841, 842, 843, 844, 845, 846, 847, 848, 849, 850, 851, 852, 853, 854, 855, 856, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, 873, 874, 875, 876, 877, 878, 879, 880, 881, 882, 883, 884, 885, 886, 887, 888, 889, 890, 891, 892, 893, 894, 895, 896, 897, 898, 899, 900, 901, and 902 in any one of SEQ ID NOs: 24-30, if the length of the at least 5

amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than $N-L+1$, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

- 5 In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues In the
- embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-
- 10 terminal amino acid residue corresponding to any one of amino acid residues 903, 904, 905, 906, 907, 908, 909, 910, 911, 912, 913, 914, 915, 916, 917, 918, 919, 920, 921, 922, 923, 924, 925, 926, 927, 928, 929, 930, 931, 932, 933, 934, 935, 936, 937, 938, 939, 940, 941, 942, 943, 944, 945, 946, 947, 948, 949, 950, 951, 952, 953, 954, 955, 956, 957, 958, 959, 960, 961, 962, 963, 964, 965, 966, 967, 968, 969, and 970 in any one of SEQ ID NOs: 25-
- 15 30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than $N-L+1$, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

- In the embodiments defined by option b) above, the polypeptide of the invention is also one
- 20 that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues In the
- embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-
- terminal amino acid residue corresponding to any one of amino acid residues 971, 972, 973,
- 25 974, 975, 976, 977, 978, 979, 980, 981, 982, 983, 984, 985, 986, 987, 988, 989, 990, 991, 992, 993, 994, 995, 996, 997, 998, 999, 1000, 1001, 1002, 1003, 1004, 1005, 1006, 1007, 1008, 1009, 1010, 1011, 1012, 1013, 1014, 1015, 1016, 1017, 1018, 1019, 1020, 1021, 1022, 1023, 1024, 1025, 1026, 1027, 1028, 1029, 1030, 1031, 1032, 1033, 1034, 1035, 1036, 1037, 1038, 1039, 1040, 1041, 1042, 1043, 1044, 1045, 1046, 1047, 1048, 1049,
- 30 1050, 1051, 1052, 1053, 1054, 1055, 1056, 1057, 1058, 1059, 1060, 1061, 1062, 1063, 1064, 1065, 1066, and 1067 in any one of SEQ ID NOs: 26-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than $N-L+1$, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined
- 35 for option b.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues In the embodiments defined by option b) above, the polypeptide of the invention is also one that

5 has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 1068, 1069, 1070, 1071, 1072, 1073, 1074, 1075, 1076, 1077, 1078, 1079, 1080, 1081, 1082, 1083, 1084, 1085, 1086, 1087, 1088, 1089, 1090, 1091, 1092, 1093, 1094, 1095, 1096, 1097, 1098, 1099, 1100, 1101, 1102, 1103, 1104, 1105, and 1106 in any one of SEQ ID NOs: 27-

10 30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than $N-L+1$, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 1107, 1108,

20 1109, 1110, 1111, 1112, 1113, 1114, 1115, 1116, 1117, 1118, 1119, 1120, 1121, 1122, 1123, 1124, 1125, 1126, 1127, 1128, 1129, 1130, 1131, 1132, 1133, 1134, 1135, 1136, 1137, 1138, 1139, 1140, 1141, 1142, 1143, 1144, 1145, 1146, 1147, 1148, 1149, 1150, 1151, 1152, 1153, 1154, 1155, 1156, 1157, 1158, 1159, 1160, 1161, 1162, 1163, 1164, 1165, 1166, 1167, 1168, 1169, 1170, 1171, 1172, 1173, 1174, 1175, 1176, 1177, 1178,

25 1179, 1180, 1181, 1182, 1183, 1184, 1185, 1186, 1187, 1188, 1189, 1190, 1191, 1192, 1193, 1194, 1195, 1196, 1197, 1198, 1199, 1200, 1201, 1202, 1203, 1204, 1205, 1206, 1207, 1208, 1209, 1210, 1211, 1212, 1213, 1214, 1215, 1216, 1217, 1218, 1219, 1220, 1221, 1222, 1223, and 1224 in any one of SEQ ID NOs: 28-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5,

30 the N-terminal first residue will not be higher numbered than $N-L+1$, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-

terminal amino acid residue corresponding to any one of amino acid residues 1225, 1226, 1227, 1228, 1229, 1230, 1231, 1232, 1233, 1234, 1235, 1236, 1237, 1238, 1239, 1240, 1241, 1242, 1243, 1244, 1245, 1246, 1247, 1248, 1249, 1250, 1251, 1252, 1253, 1254, 1255, 1256, 1257, 1258, 1259, 1260, 1261, 1262, 1263, 1264, 1265, 1266, 1267, 1268, 1269, 1270, 1271, 1272, 1273, 1274, 1275, 1276, 1277, 1278, 1279, and 1280 in any one of SEQ ID NOs: 29-30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than N-L+1, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

10 In the embodiments defined by option b) above, the polypeptide of the invention is also one that has at least 5 contiguous amino acid residues defined for option b) above and also has its N-terminal amino acid residue corresponding to any one of amino acid residues 1281, 1282, 1283, 1284, 1285, 1286, 1287, 1288, 1289, 1290, 1291, 1292, 1293, 1294, 1295, 1296, 1297, 1298, 1299, 1300, 1301, 1302, 1303, 1304, 1305, 1306, 1307, 1308, 1309, 1310, 1311, 1312, 1313, 1314, 1315, 1316, 1317, 1318, 1319, 1320, 1321, 1322, 1323, 1324, 1325, 1326, 1327, 1328, 1329, 1330, 1331, 1332, 1333, 1334, 1335, 1336, 1337, 1338, 1339, 1340, 1341, 1342, 1343, 1344, 1345, 1346, 1347, 1348, 1349, 1350, 1351, 1352, 1353, 1354, 1355, 1356, 1357, 1358, 1359, 1360, 1361, 1362, 1363, 1364, 1365, 1366, 1367, 1368, 1369, 1370, 1371, 1372, 1373, 1374, 1375, 1376, 1377, 1378, 1379, 1380, 1381, 1382, 1383, 1384, 1385, 1386, 1387, 1388, 1389, 1390, 1391, 1392, 1393, 1394, 1395, 1396, 1397, 1398, 1399, 1400, 1401, 1402, 1403, 1404, 1405, 1406, 1407, 1408, 1409, 1410, 1411, 1412, 1413, 1414, 1415, 1416, 1417, 1418, 1419, 1420, 1421, 1422, 1423, 1424, 1425, 1426, 1427, 1428, 1429, 1430, 1431, 1432, 1433, 1434, 1435, 1436, 1437, 1438, 1439, 1440, 1441, 1442, 1443, 1444, 1445, 1446, 1447, 1448, 1449, 1450, 1451, 1452, 1453, 1454, 1455, 1456, 1457, 1458, 1459, 1460, 1461, 1462, 1463, 1464, 1465, 1466, 1467, 1468, 1469, 1470, 1471, 1472, 1473, 1474, 1475, 1476, 1477, 1478, 1479, 1480, 1481, 1482, 1483, 1484, 1485, 1486, 1487, 1488, 1489, 1490, 1491, 1492, 1493, 1494, 1495, 1496, 1497, 1498, 1499, 1500, 1501, 1502, 1503, 1504, 1505, 1506, 1507, 1508, 1509, 1510, 1511, 1512, 1513, 1514, 1515, 1516, 1517, 1518, 1519, 1520, 1521, 1522, 1523, 1524, 1525, 1526, 1527, 1528, 1529, 1530, 1531, 1532, 1533, 1534, 1535, 1536, 1537, 1538, 1539, 1540, 1541, 1542, 1543, 1544, 1545, 1546, 1547, 1548, 1549, 1550, 1551, 1552, 1553, 1554, 1555, 1556, 1557, 1558, 1559, 1560, 1561, 1562, 1563, 1564, 1565, 1566, 1567, 1568, 1569, 1570, 1571, 1572, 1573, 1574, 1575, 1576, 1577, 1578, 1579, 1580, 1581, 1582, 1583, 1584, 1585, 1586, 1587, 1588, 1589, 1590, 1591, 1592, 1593, 1594, 1595, 1596, 1597, 1598, 1599, 1600, 1601, 1602, 1603, 1604, 1605, 1606, 1607, 1608, 1609, 1610, 1611, 1612, 1613, 1614, 1615, 1616, 1617, 1618, 1619, 1620, 1621, 1622, 1623, 1624, 1625, 1626, 1627, 1628, 1629, 1630, 1631, 1632, 1633, 1634, 1635, 1636, 1637, 1638, 1639, 1640, 1641, 1642, 1643, 1644, 1645,

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5 2257, 2258, 2259, 2260, 2271, 2272, 2273, 2274, 2275, 2276, 2277, 2278, 2279, 2280,
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35 2687, 2688, 2689, 2690, 2691, 2692, 2693, 2694, 2695, 2696, 2697, 2698, 2699, 2700,
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2729, 2730, 2731, 2732, 2733, 2734, 2735, 2736, 2737, 2738, 2739, 2740, 2741, 2742,
2743, 2744, 2745, 2746, 2747, 2748, 2749, 2750, 2751, 2752, 2753, 2754, 2755, 2756,

2757, 2758, 2759, 2760, 2761, 2762, 2763, 2764, 2765, 2766, 2767, 2768, 2769, 2770, 2771, 2772, 2773, 2774, 2775, 2776, 2777, 2778, 2779, 2780, 2781, 2782, 2783, 2784, 2785, 2786, 2787, 2788, 2789, 2790, 2791, 2792, 2793, 2794, 2795, 2796, 2797, 2798, 2799, 2800, 2801, 2802, 2803, 2804, 2805, 2806, 2807, 2808, 2809, 2810, 2811, 2812, 2813, 2814, 2815, 2816, 2817, 2818, 2819, 2820, 2821, 2822, 2823, 2824, 2825, 2826, 2827, 2828, 2829, 2830, 2831, 2832, 2833, 2834, 2835, 2836, 2837, 2838, 2839, 2840, 2841, 2842, 2843, 2844, 2845, 2846, 2847, 2848, 2849, 2850, 2851, 2852, 2853, 2854, 2855, 2856, 2857, 2858, 2859, 2860, 2861, 2862, 2863, 2864, 2865, 2866, 2867, 2868, 2869, 2870, 2871, 2872, 2873, 2874, 2875, 2876, 2877, 2878, 2879, 2880, 2881, 2882, 2883, 2884, 2885, 2886, 2887, 2888, 2889, 2890, 2891, 2892, 2893, 2894, 2895, 2896, 2897, 2898, 2899, 2900, 2901, 2902, 2903, 2904, 2905, 2906, 2907, 2908, 2909, 2910, 2911, 2912, 2913, 2914, 2915, 2916, 2917, 2918, 2919, 2920, 2921, 2922, 2923, 2924, 2925, 2926, 2927, 2928, 2929, 2930, 2931, 2932, 2933, 2934, 2935, 2936, 2937, 2938, 2939, 2940, 2941, 2942, 2943, 2944, 2945, 2946, 2947, 2948, 2949, 2950, 2951, 2952, 2953, 2954, 2955, 2956, 2957, 2958, 2959, 2960, 2961, 2962, 2963, 2964, 2965, 2966, 2967, 2968, 2969, 2970, 2971, 2972, 2973, 2974, 2975, 2976, 2977, 2978, 2979, 2980, 2981, 2982, 2983, 2984, 2985, 2986, 2987, 2988, 2989, 2990, 2991, 2992, 2993, 2994, 2995, 2996, 2997, 2998, 2999, 3000, 3001, 3002, 3003, 3004, 3005, 3006, 3007, 3008, 3009, 3010, 3011, 3012, 3013, 3014, 3015, 3016, 3017, 3018, 3019, 3020, 3021, 3022, 3023, 3024, 3025, 3026, 3027, 3028, 3029, 3030, 3031, 3032, 3033, 3034, 3035, 3036, 3037, 3038, 3039, 3040, 3042, and 3043 in any one of SEQ ID NOs: 30, if the length of the at least 5 amino acid residues so permit – if the length of the at least 5 amino acids are higher than 5, the N-terminal first residue will not be higher numbered than N-L+1, where N is the number of amino acid residues of the reference sequence and L is the number of amino acids defined for option b.

The polypeptide of the invention is in certain embodiments also fused or conjugated to an immunogenic carrier molecule; or, phrased otherwise, the polypeptide of the invention also includes such an immunogenic carrier molecule in addition to the material derived from SEQ ID NOs. 1-30. The immunogenic carrier molecule is a typically polypeptide that induces T-helper lymphocyte responses in a majority of humans, such as immunogenic carrier proteins selected from the group consisting of keyhole limpet hemocyanino or a fragment thereof, tetanus toxoid or a fragment thereof, diphtheria toxoid or a fragment thereof. Other suitable carrier molecules are discussed infra. One further fusion partner, which is preferably incorporated is a "His tag", i.e. a stretch of amino acids, which is rich or only consists of histidyl residues so as to facilitate protein purification.

In preferred embodiments, the polypeptide of the invention detailed above is capable of inducing an adaptive immune response against the polypeptide in a mammal, in particular in

a human being. Preferably, the adaptive immune response is a protective adaptive immune response against infection with *A baumannii*. The polypeptide may in these cases induce a humeral and/or a cellular immune response.

Epitopes

- 5 SEQ ID NOs: 1-30 include antigenic determinants (epitopes) that are as such recognized by antibodies and/or when bound to MHC molecules by T-cell receptors. For the purposes of the present invention, B-cell epitopes (*i.e.* antibody binding epitopes) are of particular relevance.

10 It is relatively uncomplicated to identify linear B-cell epitopes – one very simple approach entails that antibodies raised against *A. baumannii* or *A. baumannii* derived proteins disclosed herein are tested for binding to overlapping oligomeric peptides derived from any one of SEQ ID NO: 1-30. Thereby, the regions of the *A. baumannii* polypeptide which are responsible for or contribute to binding to the antibodies can be identified.

15 Alternatively, or additionally, one can produce mutated versions of the polypeptides of the invention, e.g. version where each single non-alanine residue in SEQ ID NOs.: 1-30 are point mutated to alanine – this method also assists in identifying complex assembled B-cell epitopes; this is the case when binding of the same antibody is modified by exchanging amino acids in different areas of the full-length polypeptide.

20 Also, in silico methods for B-cell epitope prediction can be employed: useful state-of-the-art systems for β -turn prediction is provided in Petersen B et al. (November 2010), Plos One **5**(11): e15079; prediction of linear B-cell epitopes, cf: Larsen J E P et al. (April 2006), Immunome Research, **2**:2; prediction of solvent exposed amino acids: Petersen B et al (July 2009), BMC Structural Biology, **9**:51.

The nucleic acid fragments of the invention

25 The nucleic acid fragment of the invention referred to above is preferably is a DNA fragment (such as SEQ ID NOs: 31-60) or an RNA fragment (such as SEQ ID NOs 61-90).

The nucleic acid fragment of the invention typically consists of at least or exactly or at most 11, such as at least or exactly or at most 12, at least or exactly or at most 13, at least or exactly or at most 14, at least or exactly or at most 15, at least or exactly or at most 16, at least or exactly or at most 17 at least or exactly or at most 18, at least or exactly or at most 19, at least or exactly or at most 20, at least or exactly or at most 21, at least or exactly or at most 22, at least or exactly or at most 23, at least or exactly or at most 24, at least or

[illegible]

most 131, at least or exactly or at most 132, at least or exactly or at most 133, at least or exactly or at most 134, at least or exactly or at most 135, at least or exactly or at most 136, at least or exactly or at most 137, at least or exactly or at most 138, at least or exactly or at most 139, at least or exactly or at most 140, at least or exactly or at most 141, at least or exactly or at most 142, at least or exactly or at most 143, at least or exactly or at most 144, at least or exactly or at most 145, at least or exactly or at most 146, at least or exactly or at most 147, at least or exactly or at most 148, at least or exactly or at most 149, at least or exactly or at most 150, at least or exactly or at most 151, at least or exactly or at most 152, at least or exactly or at most 153, at least or exactly or at most 154, at least or exactly or at most 155, at least or exactly or at most 156, at least or exactly or at most 157, at least or exactly or at most 158, at least or exactly or at most 159, at least or exactly or at most 160, at least or exactly or at most 161, at least or exactly or at most 162, at least or exactly or at most 163, at least or exactly or at most 164, at least or exactly or at most 165, at least or exactly or at most 166, at least or exactly or at most 167, at least or exactly or at most 168, at least or exactly or at most 169, at least or exactly or at most 170, at least or exactly or at most 171, at least or exactly or at most 172, at least or exactly or at most 173, at least or exactly or at most 174, at least or exactly or at most 175, at least or exactly or at most 176, at least or exactly or at most 177, at least or exactly or at most 178, at least or exactly or at most 179, at least or exactly or at most 180, at least or exactly or at most 181, at least or exactly or at most 182 and at least or exactly or at most 183 consecutive nucleotides in any one of SEQ ID NOs: 31-90. Longer fragments are contemplated, *i.e.* fragments having at least or exactly or at most 200, at least or exactly or at most 300 at least or exactly or at most 400, at least or exactly or at most 500, at least or exactly or at most 600, at least or exactly or at most 700, at least or exactly or at most 800, at least or exactly or at most 900, at least or exactly or at most 1000, at least or exactly or at most 1500, at least or exactly or at most 2000, at least or exactly or at most 2500, at least or exactly or at most 3000, at least or exactly or at most 3500, and at least or exactly or at most 4000 nucleotides from those of SEQ ID NOs: 31-90 that encompass fragments of such lengths.

Particularly preferred nucleic acid fragments (DNA or RNA) are those fragments of any one of SEQ ID NOs 31-90, which encode a polypeptide of the present invention discussed supra.

The nucleic acid fragment of the invention discussed above typically has a sequence identity with the nucleotide sequence defined for i) or ii) above, which is at least 65%, such as at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, and at least 99%.

The nucleic acid fragment of the invention discussed above may also have a sequence identity with the nucleotide sequence defined for iii) above, which is at least 65%, such as at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, and at least 99%.

The vectors of the invention

Vectors of the invention fall into several categories discussed *infra*. One preferred vector of the invention comprises in operable linkage and in the 5'-3' direction, an expression control region comprising an enhancer/promoter for driving expression of the nucleic acid fragment defined for option i) above, optionally a signal peptide coding sequence, a nucleotide sequence defined for option i), and optionally a terminator. Hence, such a vector constitutes an expression vector useful for effecting production in cells of the polypeptide of the invention. Since the polypeptides of the invention are bacterial of origin, recombinant production is conveniently effected in bacterial host cells, so here it is preferred that the expression control region drives expression in prokaryotic cell such as a bacterium, e.g. in *E. coli*. However, if the vector is to drive expression in mammalian cell (as would be the case for a DNA vaccine vector), the expression control region should be adapted to this particular use.

At any rate, certain vectors of the invention are capable of autonomous replication.

Also, the vector of the invention may be one that is capable of being integrated into the genome of a host cell – this is particularly useful if the vector is used in the production of stably transformed cells, where the progeny will also include the genetic information introduced via the vector. Alternatively, vectors incapable of being integrated into the genome of a mammalian host cell are useful in e.g. DNA vaccination.

Typically, the vector of the invention is selected from the group consisting of a virus, such as an attenuated virus (which may in itself be useful as a vaccine agent), a bacteriophage, a plasmid, a minichromosome, and a cosmid.

A more detailed discussion of vectors of the invention is provided in the following:

Polypeptides of the invention may be encoded by a nucleic acid molecule comprised in a vector. A nucleic acid sequence can be "heterologous," which means that it is in a context foreign to the cell in which the vector is being introduced, which includes a sequence homologous to a sequence in the cell but in a position within the host cell where it is ordinarily not found. Vectors include naked DNAs, RNAs, plasmids, cosmids, viruses

(bacteriophage, animal viruses, and plant viruses), and artificial chromosomes (e.g., YACs). One of skill in the art would be well equipped to construct a vector through standard recombinant techniques (for example Sambrook et al, 2001; Ausubel et al, 1996, both incorporated herein by reference). In addition to encoding the polypeptides of this invention, a vector of the present invention may encode polypeptide sequences such as a tag or immunogenicity enhancing peptide (e.g. an immunogenic carrier or a fusion partner that stimulates the immune system, such as a cytokine or active fragment thereof). Useful vectors encoding such fusion proteins include pIN vectors (Inouye et al, 1985), vectors encoding a stretch of histidines, and pGEX vectors, for use in generating glutathione S-transferase (GST) soluble fusion proteins for later purification and separation or cleavage.

Vectors of the invention may be used in a host cell to produce a polypeptide of the invention that may subsequently be purified for administration to a subject or the vector may be purified for direct administration to a subject for expression of the protein in the subject (as is the case when administering a nucleic acid vaccine).

Expression vectors can contain a variety of "control sequences," which refer to nucleic acid sequences necessary for the transcription and possibly translation of an operably linked coding sequence in a particular host organism. In addition to control sequences that govern transcription and translation, vectors and expression vectors may contain nucleic acid sequences that serve other functions as well and are described *infra*.

1. Promoters and Enhancers

A "promoter" is a control sequence. The promoter is typically a region of a nucleic acid sequence at which initiation and rate of transcription are controlled. It may contain genetic elements at which regulatory proteins and molecules may bind such as RNA polymerase and other transcription factors. The phrases "operatively positioned," "operatively linked," "under control," and "under transcriptional control" mean that a promoter is in a correct functional location and/or orientation in relation to a nucleic acid sequence to control transcriptional initiation and expression of that sequence. A promoter may or may not be used in conjunction with an "enhancer," which refers to a cis-acting regulatory sequence involved in the transcriptional activation of a nucleic acid sequence.

A promoter may be one naturally associated with a gene or sequence, as may be obtained by isolating the 5' non-coding sequences located upstream of the coding segment or exon. Such a promoter can be referred to as "endogenous." Similarly, an enhancer may be one naturally associated with a nucleic acid sequence, located either downstream or upstream of that sequence. Alternatively, certain advantages will be gained by positioning the coding nucleic

acid segment under the control of a recombinant or heterologous promoter, which refers to a promoter that is not normally associated with a nucleic acid sequence in its natural environment. A recombinant or heterologous enhancer refers also to an enhancer not normally associated with a nucleic acid sequence in its natural state. Such promoters or enhancers may include promoters or enhancers of other genes, and promoters or enhancers isolated from any other prokaryotic, viral, or eukaryotic cell, and promoters or enhancers not "naturally occurring," i.e., containing different elements of different transcriptional regulatory regions, and/or mutations that alter expression. In addition to producing nucleic acid sequences of promoters and enhancers synthetically, sequences may be produced using recombinant cloning and/or nucleic acid amplification technology, including PCR™, in connection with the compositions disclosed herein (see U.S. Patent 4,683,202, U.S. Patent 5,928,906, each incorporated herein by reference).

Naturally, it may be important to employ a promoter and/or enhancer that effectively direct(s) the expression of the DNA segment in the cell type or organism chosen for expression. Those of skill in the art of molecular biology generally know the use of promoters, enhancers, and cell type combinations for protein expression (see Sambrook et al, 2001, incorporated herein by reference). The promoters employed may be constitutive, tissue-specific, or inducible and in certain embodiments may direct high level expression of the introduced DNA segment under specified conditions, such as large-scale production of recombinant proteins or peptides.

Examples of inducible elements, which are regions of a nucleic acid sequence that can be activated in response to a specific stimulus, include but are not limited to Immunoglobulin Heavy Chain (Banerji et al, 1983; Gilles et al, 1983; Grosschedl et al, 1985; Atchinson et al, 1986, 1987; toiler et al, 1987; Weinberger et al, 1984; Kiledjian et al, 1988; Porton et al; 1990), Immunoglobulin Light Chain (Queen et al, 1983; Picard et al, 1984), T Cell Receptor (Luria et al, 1987; Winoto et al, 1989; Redondo et al; 1990), HLA DQ α and/or DQ β (Sullivan et al, 1987), β -Interferon (Goodbourn et al, 1986; Fujita et al, 1987; Goodbourn et al, 1988), Interleukin-2 (Greene et al, 1989), Interleukin-2 Receptor (Greene et al, 1989; Lin et al, 1990), MHC Class II 5 (Koch et al, 1989), MHC Class II HLA-DR α (Sherman et al, 1989), β -Actin (Kawamoto et al, 1988; Ng et al; 1989), Muscle Creatine Kinase (MCK) (Jaynes et al, 1988; Horlick et al, 1989; Johnson et al, 1989), Prealbumin (Transthyretin) (Costa et al, 1988), Elastase I (Omitz et al, 1987), Metallothionein (MTII) (Karin et al, 1987; Culotta et al, 1989), Collagenase (Pinkert et al, 1987; Angel et al, 1987), Albumin (Pinkert et al, 1987; Tranche et al, 1989, 1990), α -Fetoprotein (Godbout et al, 1988; Campere et al, 1989), γ -Globin (Bodine et al, 1987; Perez-Stable et al, 1990), β -Globin (Trudel et al, 1987), c-fos (Cohen et al, 1987), c-HA-ras (Triesman, 1986; Deschamps et al, 1985), Insulin (Edlund et al, 1985), Neural Cell Adhesion Molecule (NCAM) (Hirsh et al, 1990), α 1-Antitrypsin (Larimer

et al, 1990), H2B (TH2B) Histone (Hwang et al, 1990), Mouse and/or Type I Collagen (Ripe et al, 1989), Glucose-Regulated Proteins (GRP94 and GRP78) (Chang et al, 1989), Rat Growth Hormone (Larsen et al, 1986), Human Serum Amyloid A (SAA) (Edbrooke et al, 1989), Troponin I (TN I) (Yutzey et al, 1989), Platelet-Derived Growth Factor (PDGF) (Pech et al, 1989), Duchenne Muscular Dystrophy (Klamut et al, 1990), SV40 (Banerji et al, 1981; Moreau et al, 1981 ; Sleigh et al, 1985; Firak et al, 1986; Herr et al, 1986; Imbra et al, 1986; Kadesch et al, 1986; Wang et al, 1986; Ondek et al, 1987; Kuhl et al, 1987; Schaffner et al, 1988), Polyoma (Swartzendruber et al, 1975; Vasseur et al, 1980; Katinka et al, 1980, 1981; Tyndell et al, 1981 ; Dandolo et al, 1983; de Villiers et al, 1984; Hen et al, 1986; Satake et al, 1988; Campbell et al, 1988), Retroviruses (Kriegler et al, 1982, 1983; Levinson et al, 1982; Kriegler et al, 1983, 1984a, b, 1988; Bosze et al, 1986; Miksicek et al, 1986; Celander et al, 1987; Thiesen et al, 1988; Celander et al, 1988; Choi et al, 1988; Reisman et al, 1989), Papilloma Virus (Campo et al, 1983; Lusky et al, 1983; Spandidos and Wilkie, 1983; Spalholz et al, 1985; Lusky et al, 1986; Cripe et al, 1987; Gloss et al, 1987; Hirochika et al, 1987; Stephens et al, 1987), Hepatitis B Virus (Bulla et al, 1986; Jameel et al, 1986; Shaul et al, 1987; Spandau et al, 1988; Vannice et al, 1988), Human Immunodeficiency Virus (Muesing et al, 1987; Hauber et al, 1988; Jakobovits et al, 1988; Feng et al, 1988; Takebe et al, 1988; Rosen et al, 1988; Berkhout et al, 1989; Laspias et al, 1989; Sharp et al, 1989; Braddock et al, 1989), Cytomegalovirus (CMV) IE (Weber et al, 1984; Boshart et al, 1985; Foecking et al, 1986), Gibbon Ape Leukemia Virus (Holbrook et al, 1987; Quinn et al, 1989).

Inducible Elements include, but are not limited to MT II - Phorbol Ester (TFA)/Heavy metals (Palmiter et al, 1982; Haslinger et al, 1985; Searle et al, 1985; Stuart et al, 1985; Imagawa et al, 1987, Karin et al, 1987; Angel et al, 1987b; McNeall et al, 1989); MMTV (mouse mammary tumor virus) - Glucocorticoids (Huang et al, 1981; Lee et al, 1981; Majors et al, 1983; Chandler et al, 1983; Lee et al, 1984; Ponta et al, 1985; Sakai et al, 1988); β -Interferon - poly(rI)x/poly(rc) (Tavernier et al, 1983); Adenovirus 5 E2 - E1A (Imperiale et al, 1984); Collagenase - Phorbol Ester (TPA) (Angel et al, 1987a); Stromelysin - Phorbol Ester (TPA) (Angel et al, 1987b); SV40 - Phorbol Ester (TPA) (Angel et al, 1987b); Murine MX Gene - Interferon, Newcastle Disease Virus (Hug et al, 1988); GRP78 Gene - A23187 (Resendez et al, 1988); α -2-Macroglobulin - IL-6 (Kunz et al, 1989); Vimentin - Serum (Rittling et al, 1989); MHC Class I Gene H-2kb - Interferon (Blancar et al, 1989); HSP70 - E1A/SV40 Large T Antigen (Taylor et al, 1989, 1990a, 1990b); Proliferin - Phorbol Ester/TPA (Mordacq et al, 1989); Tumor Necrosis Factor - PMA (Hensel et al, 1989); and Thyroid Stimulating Hormone Gene - Thyroid Hormone (Chatterjee et al, 1989).

Also contemplated as useful in the present invention are the dectin-1 and dectin-2 promoters. Additionally any promoter/enhancer combination (as per the Eukaryotic Promoter

Data Base EPDB) could also be used to drive expression of structural genes encoding oligosaccharide processing enzymes, protein folding accessory proteins, selectable marker proteins or a heterologous protein of interest.

The particular promoter that is employed to control the expression of peptide or protein encoding polynucleotide of the invention is not believed to be critical, so long as it is capable of expressing the polynucleotide in a targeted cell, preferably a bacterial cell. Where a human cell is targeted, it is preferable to position the polynucleotide coding region adjacent to and under the control of a promoter that is capable of being expressed in a human cell. Generally speaking, such a promoter might include either a bacterial, human or viral promoter.

10 In various embodiments, the human cytomegalovirus (CMV) immediate early gene promoter, the SV40 early promoter, and the Rous sarcoma virus long terminal repeat can be used to obtain high level expression of a related polynucleotide to this invention. The use of other viral or mammalian cellular or bacterial phage promoters, which are well known in the art, to achieve expression of polynucleotides is contemplated as well.

15 In embodiments in which a vector is administered to a subject for expression of the protein, it is contemplated that a desirable promoter for use with the vector is one that is not down-regulated by cytokines or one that is strong enough that even if down-regulated, it produces an effective amount of the protein/polypeptide of the current invention in a subject to elicit an immune response. Non-limiting examples of these are CMV IE and RSV LTR. In other
20 embodiments, a promoter that is up-regulated in the presence of cytokines is employed. The MHC I promoter increases expression in the presence of IFN- γ .

Tissue specific promoters can be used, particularly if expression is in cells in which expression of an antigen is desirable, such as dendritic cells or macrophages. The mammalian MHC I and MHC II promoters are examples of such tissue-specific promoters. 2. Initiation Signals and

25 Internal Ribosome Binding Sites (IRES)

A specific initiation signal also may be required for efficient translation of coding sequences. These signals include the ATG initiation codon or adjacent sequences. Exogenous translational control signals, including the ATG initiation codon, may need to be provided. One of ordinary skill in the art would readily be capable of determining this and providing the
30 necessary signals. It is well known that the initiation codon must be "in-frame" with the reading frame of the desired coding sequence to ensure translation of the entire insert. The exogenous translational control signals and initiation codons can be either natural or synthetic and may be operable in bacteria or mammalian cells. The efficiency of expression may be enhanced by the inclusion of appropriate transcription enhancer elements.

In certain embodiments of the invention, the use of internal ribosome entry sites (IRES) elements are used to create multigene, or polycistronic, messages. IRES elements are able to bypass the ribosome scanning model of 5' methylated Cap dependent translation and begin translation at internal sites (Pelletier and Sonenberg, 1988). IRES elements from two members of the picornavirus family (polio and encephalomyocarditis) have been described (Pelletier and Sonenberg, 1988), as well an IRES from a mammalian message (Macejak and Sarnow, 1991). IRES elements can be linked to heterologous open reading frames. Multiple open reading frames can be transcribed together, each separated by an IRES, creating polycistronic messages. By virtue of the IRES element, each open reading frame is accessible to ribosomes for efficient translation. Multiple genes can be efficiently expressed using a single promoter/enhancer to transcribe a single message (see U.S. Patents 5,925,565 and 5,935,819, herein incorporated by reference).

2. Multiple Cloning Sites

Vectors can include a multiple cloning site (MCS), which is a nucleic acid region that contains multiple restriction enzyme sites, any of which can be used in conjunction with standard recombinant technology to digest the vector. (See Carbonelli et al, 1999, Levenson et al, 1998, and Cocea, 1997, incorporated herein by reference.) Frequently, a vector is linearized or fragmented using a restriction enzyme that cuts within the MCS to enable exogenous sequences to be ligated to the vector. Techniques involving restriction enzymes and ligation reactions are well known to those of skill in the art of recombinant technology.

3. Splicing Sites

Most transcribed eukaryotic RNA molecules will undergo RNA splicing to remove introns from the primary transcripts. If relevant in the context of vectors of the present invention, vectors containing genomic eukaryotic sequences may require donor and/or acceptor splicing sites to ensure proper processing of the transcript for protein expression. (See Chandler et al, 1997, incorporated herein by reference.)

4. Termination Signals

The vectors or constructs of the present invention will generally comprise at least one termination signal. A "termination signal" or "terminator" is comprised of the DNA sequences involved in specific termination of an RNA transcript by an RNA polymerase. Thus, in certain embodiments a termination signal that ends the production of an RNA transcript is contemplated. A terminator may be necessary in vivo to achieve desirable message levels.

In eukaryotic systems, the terminator region may also comprise specific DNA sequences that permit site-specific cleavage of the new transcript so as to expose a polyadenylation site. This signals a specialized endogenous polymerase to add a stretch of about 200 A residues (poly A) to the 3' end of the transcript. RNA molecules modified with this polyA tail appear to
5 more stable and are translated more efficiently. Thus, in other embodiments involving eukaryotes, it is preferred that that terminator comprises a signal for the cleavage of the RNA, and it is more preferred that the terminator signal promotes polyadenylation of the message.

Terminators contemplated for use in the invention include any known terminator of
10 transcription described herein or known to one of ordinary skill in the art, including but not limited to, for example, the bovine growth hormone terminator or viral termination sequences, such as the SV40 terminator. In certain embodiments, the termination signal may be a lack of transcribable or translatable sequence, such as due to a sequence truncation.

5. Polyadenylation Signals

15 In expression, particularly eukaryotic expression (as is relevant in nucleic acid vaccination), one will typically include a polyadenylation signal to effect proper polyadenylation of the transcript. The nature of the polyadenylation signal is not believed to be crucial to the successful practice of the invention, and/or any such sequence may be employed. Preferred
20 embodiments include the SV40 polyadenylation signal and/or the bovine growth hormone polyadenylation signal, convenient and/or known to function well in various target cells. Polyadenylation may increase the stability of the transcript or may facilitate cytoplasmic transport.

6. Origins of Replication

25 In order to propagate a vector in a host cell, it may contain one or more origins of replication sites (often termed "on"), which is a specific nucleic acid sequence at which replication is initiated. Alternatively an autonomously replicating sequence (ARS) can be employed if the host cell is yeast.

7. Selectable and Screenable Markers

30 In certain embodiments of the invention, cells containing a nucleic acid construct of the present invention may be identified in vitro or in vivo by encoding a screenable or selectable marker in the expression vector. When transcribed and translated, a marker confers an identifiable change to the cell permitting easy identification of cells containing the expression

vector. Generally, a selectable marker is one that confers a property that allows for selection. A positive selectable marker is one in which the presence of the marker allows for its selection, while a negative selectable marker is one in which its presence prevents its selection. An example of a positive selectable marker is a drug resistance marker.

- 5 Usually the inclusion of a drug selection marker aids in the cloning and identification of transformants, for example, markers that confer resistance to neomycin, puromycin, hygromycin, DHFR, GPT, zeocin or histidinol are useful selectable markers. In addition to markers conferring a phenotype that allows for the discrimination of transformants based on the implementation of conditions, other types of markers including screenable markers such as GFP for colorimetric analysis. Alternatively, screenable enzymes such as herpes simplex virus thymidine kinase (tk) or chloramphenicol acetyltransferase (CAT) may be utilized. One of skill in the art would also know how to employ immunologic markers that can be used in conjunction with FACS analysis. The marker used is not believed to be important, so long as it is capable of being expressed simultaneously with the nucleic acid encoding a protein of the invention. Further examples of selectable and screenable markers are well known to one of skill in the art.

The transformed cells of the invention

Transformed cells of the invention are useful as organisms for producing the polypeptide of the invention, but also as simple "containers" of nucleic acids and vectors of the invention.

- 20 Certain transformed cells of the invention are capable of replicating the nucleic acid fragment defined for option i) of the second aspect of the invention. Preferred transformed cells of the invention are capable of expressing the nucleic acid fragment defined for option i).

- For recombinant production it is convenient, but not a prerequisite that the transformed cell according is prokaryotic, such as a bacterium, but generally both prokaryotic cells and eukaryotic cells may be used.

Suitable prokaryotic cells are bacterial cells selected from the group consisting of Escherichia (such as E. coli.), Bacillus [e.g. Bacillus subtilis], Salmonella, and Mycobacterium [preferably non-pathogenic, e.g. M. bovis BCG].

- Eukaryotic cells can be in the form of yeasts (such as Saccharomyces cerevisiae) and protozoans. Alternatively, the transformed eukaryotic cells are derived from a multicellular organism such as a fungus, an insect cell, a plant cell, or a mammalian cell.

For production purposes, it is advantageous that the transformed cell of the invention is stably transformed by having the nucleic acid defined above for option i) stably integrated into its genome, and in certain embodiments it is also preferred that the transformed cell secretes or carries on its surface the polypeptide of the invention, since this facilitates recovery of the polypeptides produced. A particular version of this embodiment is one where the transformed cell is a bacterium and secretion of the polypeptide of the invention is into the periplasmic space.

As noted above, stably transformed cells are preferred – these i.a. allows that cell lines comprised of transformed cells as defined herein may be established – such cell lines are particularly preferred aspects of the invention.

Further details on cells and cell lines are presented in the following:

Suitable cells for recombinant nucleic acid expression of the nucleic acid fragments of the present invention are prokaryotes and eukaryotes. Examples of prokaryotic cells include *E. coli*; members of the *Staphylococcus* genus, such as *S. epidermidis*; members of the *Lactobacillus* genus, such as *L. plantarum*; members of the *Lactococcus* genus, such as *L. lactis*; members of the *Bacillus* genus, such as *B. subtilis*; members of the *Corynebacterium* genus such as *C. glutamicum*; and members of the *Pseudomonas* genus such as *Ps. fluorescens*. Examples of eukaryotic cells include mammalian cells; insect cells; yeast cells such as members of the *Saccharomyces* genus (e.g. *S. cerevisiae*), members of the *Pichia* genus (e.g. *P. pastoris*), members of the *Hansenula* genus (e.g. *H. polymorpha*), members of the *Kluyveromyces* genus (e.g. *K. lactis* or *K. fragilis*) and members of the *Schizosaccharomyces* genus (e.g. *S. pombe*).

Techniques for recombinant gene production, introduction into a cell, and recombinant gene expression are well known in the art. Examples of such techniques are provided in references such as Ausubel, Current Protocols in Molecular Biology, John Wiley, 1987-2002, and Sambrook et al., Molecular Cloning, A Laboratory Manual, 2 nd Edition, Cold Spring Harbor Laboratory Press, 1989.

As used herein, the terms "cell," "cell line," and "cell culture" may be used interchangeably. All of these terms also include their progeny, which is any and all subsequent generations. It is understood that all progeny may not be identical due to deliberate or inadvertent mutations. In the context of expressing a heterologous nucleic acid sequence, "host cell" refers to a prokaryotic or eukaryotic cell, and it includes any transformable organism that is capable of replicating a vector or expressing a heterologous gene encoded by a vector. A host cell can, and has been, used as a recipient for vectors or viruses. A host cell may be

"transfected" or "transformed," which refers to a process by which exogenous nucleic acid, such as a recombinant protein-encoding sequence, is transferred or introduced into the host cell. A transformed cell includes the primary subject cell and its progeny.

Host cells may be derived from prokaryotes or eukaryotes, including bacteria, yeast cells, insect cells, and mammalian cells for replication of the vector or expression of part or all of the nucleic acid sequence(s). Numerous cell lines and cultures are available for use as a host cell, and they can be obtained through the American Type Culture Collection (ATCC), which is an organization that serves as an archive for living cultures and genetic materials (www.atcc.org) or from other depository institutions such as Deutsche Sammlung von Mikroorganismen und Zellkulturen (DSMZ). An appropriate host can be determined by one of skill in the art based on the vector backbone and the desired result. A plasmid or cosmid, for example, can be introduced into a prokaryote host cell for replication of many vectors or expression of encoded proteins. Bacterial cells used as host cells for vector replication and/or expression include *Staphylococcus* strains, DH5 α , JMI 09, and KC8, as well as a number of commercially available bacterial hosts such as SURE(R) Competent Cells and SOLOP ACK(TM) Gold Cells (STRATAGENE®, La Jolla, CA). Alternatively, bacterial cells such as *E. coli* LE392 could be used as host cells for phage viruses. Appropriate yeast cells include *Saccharomyces cerevisiae*, *Saccharomyces pombe*, and *Pichia pastoris*.

Examples of eukaryotic host cells for replication and/or expression of a vector include HeLa, NIH3T3, Jurkat, 293, Cos, CHO, Saos, and PC12. Many host cells from various cell types and organisms are available and would be known to one of skill in the art. Similarly, a viral vector may be used in conjunction with either a eukaryotic or prokaryotic host cell, particularly one that is permissive for replication or expression of the vector.

Some vectors may employ control sequences that allow it to be replicated and/or expressed in both prokaryotic and eukaryotic cells. One of skill in the art would further understand the conditions under which to incubate all of the above described host cells to maintain them and to permit replication of a vector. Also understood and known are techniques and conditions that would allow large-scale production of vectors, as well as production of the nucleic acids encoded by vectors and their cognate polypeptides, proteins, or peptides.

Expression Systems

Numerous expression systems exist that comprise at least a part or all of the compositions discussed above. Prokaryote- and/or eukaryote-based systems can be employed for use with the present invention to produce nucleic acid sequences, or their cognate polypeptides, proteins and peptides. Many such systems are commercially and widely available.

The insect cell/baculovirus system can produce a high level of protein expression of a heterologous nucleic acid segment, such as described in U.S. Patents 5,871,986, 4,879,236, both herein incorporated by reference, and which can be bought, for example, under the name MAXBAC® 2.0 from INVITROGEN® and BACPACK™ Baculovirus expression system
5 from CLONTECH®

In addition to the disclosed expression systems of the invention, other examples of expression systems include STRATAGENE®'s COMPLETE CONTROL™ Inducible Mammalian Expression System, which involves a synthetic ecdysone-inducible receptor, or its pET Expression System, an E. coli expression system. Another example of an inducible expression
10 system is available from INVITROGEN®, which carries the T-REX™ (tetracycline-regulated expression) System, an inducible mammalian expression system that uses the full-length CMV promoter. INVITROGEN® also provides a yeast expression system called the Pichia methanolica Expression System, which is designed for high-level production of recombinant proteins in the methylotrophic yeast Pichia methanolica. One of skill in the art would know
15 how to express a vector, such as an expression construct, to produce a nucleic acid sequence or its cognate polypeptide, protein, or peptide.

Amplification of Nucleic Acids

Nucleic acids used as a template for amplification may be isolated from cells, tissues or other samples according to standard methodologies (Sambrook et al, 2001). In certain
20 embodiments, analysis is performed on whole cell or tissue homogenates or biological fluid samples without substantial purification of the template nucleic acid. The nucleic acid may be genomic DNA or fractionated or whole cell RNA. Where RNA is used, it may be desired to first convert the RNA to a complementary DNA.

The term "primer," as used herein, is meant to encompass any nucleic acid that is capable of
25 priming the synthesis of a nascent nucleic acid in a template-dependent process. Typically, primers are oligonucleotides from ten to twenty and/or thirty base pairs in length, but longer sequences can be employed. Primers may be provided in double-stranded and/or single-stranded form, although the single-stranded form is preferred.

Pairs of primers designed to selectively hybridize to nucleic acids corresponding to sequences
30 of genes identified herein are contacted with the template nucleic acid under conditions that permit selective hybridization. Depending upon the desired application, high stringency hybridization conditions may be selected that will only allow hybridization to sequences that are completely complementary to the primers. In other embodiments, hybridization may occur under reduced stringency to allow for amplification of nucleic acids containing one or

more mismatches with the primer sequences. Once hybridized, the template-primer complex is contacted with one or more enzymes that facilitate template-dependent nucleic acid synthesis. Multiple rounds of amplification, also referred to as "cycles," are conducted until a sufficient amount of amplification product is produced.

- 5 The amplification product may be detected or quantified. In certain applications, the detection may be performed by visual means. Alternatively, the detection may involve indirect identification of the product via chemiluminescence, radioactive scintigraphy of incorporated radiolabel or fluorescent label or even via a system using electrical and/or thermal impulse signals (Bellus, 1994).
- 10 A number of template dependent processes are available to amplify the oligonucleotide sequences present in a given template sample. One of the best known amplification methods is the polymerase chain reaction (referred to as PCR(TM)) which is described in detail in U.S. Patents 4,683,195, 4,683,202 and 4,800,159, and in Innis et al., 1988, each of which is incorporated herein by reference in their entirety.
- 15 Alternative methods for amplification of target nucleic acid sequences that may be used in the practice of the present invention are disclosed in U.S. Patents 5,843,650, 5,846,709, 5,846,783, 5,849,546, 5,849,497, 5,849,547, 5,858,652, 5,866,366, 5,916,776, 5,922,574, 5,928,905, 5,928,906, 5,932,451, 5,935,825, 5,939,291 and 5,942,391, GB Application No. 2 202 328, and in PCT Application No. PCT/US89/01025, each of which is incorporated herein
- 20 by reference in its entirety.

Methods of Gene Transfer

- Suitable methods for nucleic acid delivery to effect expression of compositions of the present invention are believed to include virtually any method by which a nucleic acid (e.g., DNA, including viral and nonviral vectors) can be introduced into a cell, a tissue or an organism, as
- 25 described herein or as would be known to one of ordinary skill in the art. Such methods include, but are not limited to, direct delivery of DNA such as by injection (U.S. Patents 5,994,624, 5,981,274, 5,945,100, 5,780,448, 5,736,524, 5,702,932, 5,656,610, 5,589,466 and 5,580,859, each incorporated herein by reference), including microinjection (Harland and Weintraub, 1985; U.S. Patent 5,789,215, incorporated herein by reference); by
- 30 electroporation (U.S. Patent No. 5,384,253, incorporated herein by reference); by calcium phosphate precipitation (Graham and Van Der Eb, 1973; Chen and Okayama, 1987; Rippe et al., 1990); by using DEAE dextran followed by polyethylene glycol (Gopal, 1985); by direct sonic loading (Fechheimer et al, 1987); by liposome mediated transfection (Nicolau and Sene, 1982; Fraley et al, 1979; Nicolau et al, 1987; Wong et al, 1980; Kaneda et al, 1989;

Kato et al, 1991); by microprojectile bombardment (PCT Application Nos. WO 94/09699 and 95/06128; U.S. Patents 5,610,042; 5,322,783 5,563,055, 5,550,318, 5,538,877 and 5,538,880, and each incorporated herein by reference); by agitation with silicon carbide fibers (Kaepler et al, 1990; U.S. Patents 5,302,523 and 5,464,765, each incorporated herein
5 by reference); by Agrobacterium mediated transformation (U.S. Patents 5,591,616 and 5,563,055, each incorporated herein by reference); or by PEG mediated transformation of protoplasts (Omirulleh et al, 1993; U.S. Patents 4,684,611 and 4,952,500, each incorporated herein by reference); by desiccation/inhibition mediated DNA uptake (Potrykus et al, 1985).
10 Through the application of techniques such as these, organelle(s), cell(s), tissue(s) or organism(s) may be stably or transiently transformed.

The antibodies of the invention – and their production/isolation

Antibodies directed against the proteins of the invention are useful for affinity chromatography, immunoassays, and for distinguishing/identifying staphylococcus proteins as well as for passive immunisation and therapy.

15 Antibodies to the proteins of the invention, both polyclonal and monoclonal, may be prepared by conventional methods. In general, the protein is first used to immunize a suitable animal, preferably a mouse, rat, rabbit or goat. Rabbits and goats are preferred for the preparation of polyclonal sera due to the volume of serum obtainable, and the availability of labeled anti-rabbit and anti-goat antibodies. Immunization is generally performed by mixing or
20 emulsifying the protein in saline, preferably in an adjuvant such as Freund's complete adjuvant, and injecting the mixture or emulsion parenterally (generally subcutaneously or intramuscularly). A dose of 50-200 µg/injection is typically sufficient. Immunization is generally boosted 2-6 weeks later with one or more injections of the protein in saline, preferably using Freund's incomplete adjuvant. One may alternatively generate antibodies by
25 in vitro immunization using methods known in the art, which for the purposes of this invention is considered equivalent to *in vivo* immunization. Polyclonal antiserum is obtained by bleeding the immunized animal into a glass or plastic container, incubating the blood at 25 C for one hour, followed by incubating at 4 C for 2-18 hours. The serum is recovered by centrifugation (eg. 1,000 g for 10 minutes). About 20-50 ml per bleed may be obtained from
30 rabbits.

Monoclonal antibodies are prepared using the standard method of Kohler & Milstein [Nature (1975) 256 : 495-96], or a modification thereof. Typically, a mouse or rat is immunized as described above. However, rather than bleeding the animal to extract serum, the spleen (and optionally several large lymph nodes) is removed and dissociated into single cells. If desired,
35 the spleen cells may be screened (after removal of nonspecifically adherent cells) by applying

a cell suspension to a plate or well coated with the protein antigen. B-cells expressing membrane-bound immunoglobulin specific for the antigen bind to the plate, and are not rinsed away with the rest of the suspension. Resulting B-cells, or all dissociated spleen cells, are then induced to fuse with myeloma cells to form hybridomas, and are cultured in a selective medium (e.g. hypoxanthine, aminopterin, thymidine medium, "HAT"). The resulting hybridomas are plated by limiting dilution, and are assayed for production of antibodies, which bind specifically to the immunizing antigen (and which do not bind to unrelated antigens). The selected MAb-secreting hybridomas are then cultured either in vitro (e.g. in tissue culture bottles or hollow fiber reactors), or in vivo (as ascites in mice).

If desired, the antibodies (whether polyclonal or monoclonal) may be labeled using conventional techniques. Suitable labels include fluorophores, chromophores, radioactive atoms (particularly ^{32}P and ^{125}I), electron-dense reagents, enzymes, and ligands having specific binding partners. Enzymes are typically detected by their activity. For example, horseradish peroxidase is usually detected by its ability to convert 3,3', 5,5'-tetramethylbenzidine (TMB) to a blue pigment, quantifiable with a spectrophotometer. "Specific binding partner" refers to a protein capable of binding a ligand molecule with high specificity, as for example in the case of an antigen and a monoclonal antibody specific therefor. Other specific binding partners include biotin and avidin or streptavidin, IgG and protein A, and the numerous receptor-ligand couples known in the art. It should be understood that the above description is not meant to categorize the various labels into distinct classes, as the same label may serve in several different modes. For example, ^{115}I may serve as a radioactive label or as an electron-dense reagent. HRP may serve as enzyme or as antigen for a MAb. Further, one may combine various labels for desired effect. For example, MAbs and avidin also require labels in the practice of this invention: thus, one might label a MAb with biotin, and detect its presence with avidin labeled with ^{125}I , or with an anti-biotin MAb labeled with HRP. Other permutations and possibilities will be readily apparent to those of ordinary skill in the art, and are considered as equivalents within the scope of the instant invention.

According to the invention, the isolated monoclonal antibody or antibody analogue is preferably a monoclonal antibody selected from a multi-domain antibody such as a murine antibody, a chimeric antibody such as a humanized antibody, a fully human antibody, and single-domain antibody of a llama or a camel, or which is an antibody analogue selected from a fragment of an antibody such as an Fab or an F(ab')_2 , an scFV; cf. also the definition of the term "antibody" presented above.

Compositions of the invention; vaccines

Pharmaceutical compositions, in particular vaccines, according to the invention may either be prophylactic (ie. to prevent infection) or therapeutic (ie, to treat disease after infection).

Such vaccines comprise immunising antigen(s), immunogen(s), polypeptide(s), protein(s) or nucleic acid(s), usually in combination with "pharmaceutically acceptable carriers", which include any carrier that does not itself induce the production of antibodies harmful to the individual receiving the composition. Suitable carriers are typically large, slowly metabolized macromolecules such as proteins, polysaccharides, polylactic acids, polyglycolic acids, polymeric amino acids, amino acid copolymers, lipid aggregates (such as oil droplets or liposomes), and inactive virus particles.

Such carriers are well known to those of ordinary skill in the art. Additionally, these carriers may function as immunostimulating agents ("adjuvants"). Furthermore, the antigen or immunogen may be conjugated to a bacterial toxoid, such as a toxoid from diphtheria, tetanus, cholera, *H. pylori*, etc. pathogen, cf. the description of immunogenic carriers supra.

The pharmaceutical compositions of the invention thus typically contain an immunological adjuvant, which is commonly an aluminium based adjuvant or one of the other adjuvants described in the following:

Preferred adjuvants to enhance effectiveness of the composition include, but are not limited to : (1) aluminum salts (alum), such as aluminum hydroxide, aluminum phosphate, aluminum sulfate, etc; (2) oil-in-water emulsion formulations (with or without other specific immunostimulating agents such as muramyl peptides (see below) or bacterial cell wall components), such as for example (a) MF59 (WO 90/14837; Chapter 10 in Vaccine design: the subunit and adjuvant approach, eds. Powell & Newman, Plenum Press 1995), containing 5% Squalene, 0.5% Tween 80, and 0.5% Span 85 (optionally containing various amounts of MTP-PE (see below), although not required) formulated into submicron particles using a microfluidizer such as Model 110Y microfluidizer (Microfluidics, Newton, MA), (b) SAF, containing 10% Squalene, 0.4% Tween 80, 5% pluronic-blocked polymer L121, and thr-MDP (see below) either microfluidized into a submicron emulsion or vortexed to generate a larger particle size emulsion, and (c) Ribi adjuvant system (RAS), (Ribi Immunochem, Hamilton, MT) containing 2% Squalene, 0.2% Tween 80, and one or more bacterial cell wall components from the group consisting of monophosphoryl lipid A (MPL), trehalose dimycolate (TDM), and cell wall skeleton (CWS), preferably MPL + CWS (Detox™) ; (3) saponin adjuvants such as Stimulon™ (Cambridge Bioscience, Worcester, MA) may be used or particles generated therefrom such as ISCOMs (immunostimulating complexes); (4) Complete Freund's Adjuvant (CFA) and Incomplete Freund's Adjuvant (IFA); (5) cytokines, such as interleukins (eg. IL-1, IL-2, IL-4, IL-5, IL-6, IL-7, IL-12, etc.), interferons (eg.

gamma interferon), macrophage colony stimulating factor (M-CSF), tumor necrosis factor (TNF), etc.; and (6) other substances that act as immunostimulating agents to enhance the effectiveness of the composition. Alum and MF59TM adjuvants are preferred.

As mentioned above, muramyl peptides include, but are not limited to, N-acetyl-muramyl-L-threonyl-D-isoglutamine (thr-MDP), N-acetyl-normuramyl-L-alanyl-D-isoglutamine (nor-MDP), N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2"-2'-dipalmitoyl-sn-glycero-3-hydroxyphosphoryloxy)-ethylamine (MTP-PE), etc.

The immunogenic compositions (eg. the immunising antigen or immunogen or polypeptide or protein or nucleic acid, pharmaceutically acceptable carrier, and adjuvant) typically will contain diluents, such as water, saline, glycerol, ethanol, etc. Additionally, auxiliary substances, such as wetting or emulsifying agents, pH buffering substances, and the like, may be present in such vehicles.

Typically, the immunogenic compositions are prepared as injectables, either as liquid solutions or suspensions; solid forms suitable for solution in, or suspension in, liquid vehicles prior to injection may also be prepared. The preparation also may be emulsified or encapsulated in liposomes for enhanced adjuvant effect, as discussed above under pharmaceutically acceptable carriers.

Immunogenic compositions used as vaccines comprise an immunologically effective amount of the antigenic or immunogenic polypeptides, as well as any other of the above-mentioned components, as needed. By "immunologically effective amount", it is meant that the administration of that amount to an individual, either in a single dose or as part of a series, is effective for treatment or prevention. This amount varies depending upon the health and physical condition of the individual to be treated, the taxonomic group of individual to be treated (eg. nonhuman primate, primate, etc.), the capacity of the individual's immune system to synthesize antibodies or generally mount an immune response, the degree of protection desired, the formulation of the vaccine, the treating doctor's assessment of the medical situation, and other relevant factors. It is expected that the amount will fall in a relatively broad range that can be determined through routine trials. However, for the purposes of protein vaccination, the amount administered per immunization is typically in the range between 0.5 µg and 500 mg (however, often not higher than 5,000 µg), and very often in the range between 10 and 200 µg.

The immunogenic compositions are conventionally administered parenterally, eg, by injection, either subcutaneously, intramuscularly, or transdermally/transcutaneously (eg. WO 98/20734). Additional formulations suitable for other modes of administration include oral

and pulmonary formulations, suppositories, and transdermal applications. In the case of nucleic acid vaccination, also the intravenous or intraarterial routes may be applicable.

Dosage treatment may be a single dose schedule or a multiple dose schedule. The vaccine may be administered in conjunction with other immunoregulatory agents.

- 5 As an alternative to protein-based vaccines, DNA vaccination (also termed nucleic acid vaccination or gene vaccination) may be used [eg. Robinson & Torres (1997) Seminars in Immunol 9: 271-283; Donnelly et al. (1997) Annu Rev Immunol 15 : 617-648; later herein].

10 A further aspect of the invention is the recognition that combination vaccines can be provided, wherein 2 or more antigens disclosed herein are combined to enhance the immune response by the vaccinated animal, including to optimize initial immune response and duration of immunity. For the purposes of this aspect of the invention, multiple antigenic fragments derived from the same, longer protein can also be used, such as the use a combination of different lengths of polypeptide sequence fragments from one protein.

15 Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 1 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ
20 ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

25 Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 2 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

30 Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 3 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of

SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

5 Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 4 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23,
10 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein
15 wherein the first of said immunogens is SEQ ID NO: 5 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24,
20 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 6 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of
25 SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of)
30 comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 7 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ

ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein

5 wherein the first of said immunogens is SEQ ID NO: 8 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 10 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein

wherein the first of said immunogens is SEQ ID NO: 9 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 15 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of)

20 comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 10 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein

wherein the first of said immunogens is SEQ ID NO: 11 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 30 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 12 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of
5 SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 13 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of
10 SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ
15 ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 14 or a variant or fragment thereof
20 disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 15 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of
25 SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ
30 ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein
35 wherein the first of said immunogens is SEQ ID NO: 16 or a variant or fragment thereof

disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 17 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 18 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 19 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 20 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ

ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein

5 wherein the first of said immunogens is SEQ ID NO: 21 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 10 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein

wherein the first of said immunogens is SEQ ID NO: 22 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of 15 SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of)

20 comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 23 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ 25 ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein

wherein the first of said immunogens is SEQ ID NO: 24 or a variant or fragment thereof 30 disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 25 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of
5 SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 26 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of
10 SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ
15 ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 27 or a variant or fragment thereof
20 disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 28 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of
25 SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ
30 ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein
35 wherein the first of said immunogens is SEQ ID NO: 29 or a variant or fragment thereof

disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Thus, embodiments of the invention relate to a composition (or the use as a vaccine of) comprising 2 distinct (i.e. non-identical) proteinaceous immunogens disclosed herein wherein the first of said immunogens is SEQ ID NO: 30 or a variant or fragment thereof disclosed herein in combination with a proteinaceous immunogen selected from any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30, or a variant or fragment disclosed herein of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, and 30.

Treatment methods of the invention

The method of the sixth aspect of the invention generally relates to induction of immunity and as such also entails method that relate to treatment, prophylaxis and amelioration of disease.

When immunization methods entail that a polypeptide of the invention or a composition comprising such a polypeptide is administered the animal (e.g. the human) typically receives between 0.5 and 5,000 µg of the polypeptide of the invention per administration.

In preferred embodiments of the sixth aspect, the immunisation scheme includes that the animal (e.g. the human) receives a priming administration and one or more booster administrations.

Preferred embodiments of the 6th aspect of the invention comprise that the administration is for the purpose of inducing protective immunity against *A. baumannii*. In this embodiment it is particularly preferred that the protective immunity is effective in reducing the risk of attracting infection with *A. baumannii* or is effective in treating or ameliorating infection with *A. baumannii*.

As mentioned herein, the preferred vaccines of the invention induce humoral immunity, so it is preferred that the administration is for the purpose of inducing antibodies specific for *A. baumannii* and wherein said antibodies or B-lymphocytes producing said antibodies are subsequently recovered from the animal.

But, as also mentioned the method of the 6th aspect may also be useful in antibody production, so in other embodiments the administration is for the purpose of inducing antibodies specific for *A. baumannii* and wherein B-lymphocytes producing said antibodies are subsequently recovered from the animal and used for preparation of monoclonal antibodies.

Pharmaceutical compositions can as mentioned above comprise polypeptides, antibodies, or nucleic acids of the invention. The pharmaceutical compositions will comprise a therapeutically effective amount thereof.

The term "therapeutically effective amount" or "prophylactically effective amount" as used herein refers to an amount of a therapeutic agent to treat, ameliorate, or prevent a desired disease or condition, or to exhibit a detectable therapeutic or preventative effect. The effect can be detected by, for example, chemical markers or antigen levels. Therapeutic effects also include reduction in physical symptoms, such as decreased body temperature. The precise effective amount for a subject will depend upon the subject's size and health, the nature and extent of the condition, and the therapeutics or combination of therapeutics selected for administration. Thus, it is not useful to specify an exact effective amount in advance. Reference is however made to the ranges for dosages of immunologically effective amounts of polypeptides, cf. above.

However, the effective amount for a given situation can be determined by routine experimentation and is within the judgement of the clinician.

For purposes of the present invention, an effective dose will be from about 0.01 mg/kg to 50 mg/kg or 0.05 mg/kg to about 10 mg/kg of the DNA or RNA constructs in the individual to which it is administered.

A pharmaceutical composition can also contain a pharmaceutically acceptable carrier. The term "pharmaceutically acceptable carrier" refers to a carrier for administration of a therapeutic agent, such as antibodies or a polypeptide, genes, and other therapeutic agents. The term refers to any pharmaceutical carrier that does not itself induce the production of antibodies harmful to the individual receiving the composition, and which may be administered without undue toxicity. Suitable carriers may be large, slowly metabolized macromolecules such as proteins, polysaccharides, polylactic acids, polyglycolic acids, polymeric amino acids, amino acid copolymers, and inactive virus particles. Such carriers are well known to those of ordinary skill in the art.

Pharmaceutically acceptable salts can be used therein, for example, mineral acid salts such as hydrochlorides, hydrobromides, phosphates, sulfates, and the like; and the salts of organic acids such as acetates, propionates, malonates, benzoates, and the like. A thorough discussion of pharmaceutically acceptable excipients is available in Remington's

5 Pharmaceutical Sciences (Mack Pub. Co., N. J. 1991).

Pharmaceutically acceptable carriers in therapeutic compositions may contain liquids such as water, saline, glycerol and ethanol. Additionally, auxiliary substances, such as wetting or emulsifying agents, pH buffering substances, and the like, may be present in such vehicles. Typically, the therapeutic compositions are prepared as injectables, either as liquid solutions
10 or suspensions; solid forms suitable for solution in, or suspension in, liquid vehicles prior to injection may also be prepared. Liposomes are included within the definition of a pharmaceutically acceptable carrier.

As is apparent from the claims, the invention also relates to related embodiments to the treatment and prophylaxis disclosed herein: the invention also includes embodiments where

- 15 - the polypeptide of the invention is for use as a pharmaceutical, in particular for use as a pharmaceutical in the treatment, prophylaxis or amelioration of infection with *A. baumannii*;
- the nucleic acid fragment of the invention or the vector of the invention is for use as a pharmaceutical, in particular for use as a pharmaceutical in the treatment, prophylaxis or amelioration of infection with *A. baumannii*;
- 20 - the transformed cell of the invention is for use as a pharmaceutical, in particular for use as a pharmaceutical in the treatment, prophylaxis or amelioration of infection with *A. baumannii*.
- the antibody, antibody fragment or antibody analogue of the invention is for use as a pharmaceutical, in particular for use as a pharmaceutical in the treatment, prophylaxis or
25 amelioration of infection with *A. baumannii*.

EXAMPLE 1

*Immunization study*Experimental

16 individual proteins derived from *A. baumannii* (where 1 protein is a positive control) were tested. 16 mice were included in each group. The study was divided into 4 separate experiments comprising testing of 5 groups, that is 4 protein groups and 1 control group (adjuvant only). The 4 experiments are run in parallel, that is staggered with 7-14 days between each immunization. Hence the studies had a duration of 70-98 days (~2.3-3.3 months):

10 Challenge strain: *A. baumannii* AB5075.

Mouse strain: C57BL/6 (inbred).

Dose: 25 µg protein in each immunization.

Immunization route and interval: 3 x subcutaneous with 14 days intervals.

Inoculation route (challenge): intranasal.

15 End point: Lethal challenge.

Adjuvant: Priming immunization: Alum + incomplete Freund's adjuvant (IFA). 1st and second boost: Alum.

Bled and ELISA: Mice were bled 4 days prior to challenge and ELISAs were run.

20 Mouse Tag: Each mouse was tagged, hence making it possible to track the mouse-specific antibody titer with survival.

Trial type: Double blinded.

Number of mice per group: 16 mice.

Monitoring period: 7-10 days.

Experiment 1

Group 1 was immunized with the protein AB57_3582-22-253, i.e. SEQ ID NO: 14, amino acid residues 22-253.

Study Group 3 was immunized with the protein AB57_1088-22-159, i.e. SEQ ID NO: 9,
5 amino acid residues 22-159.

Group 5 (the negative control) received phosphate buffered saline (PBS).

Groups 2 and 4 were immunized with proteins irrelevant for the present invention and did not provide protection. Data are hence not shown.

Experiment 2

10 Group 1 was immunized with a protein consisting of amino acids 2-346 of the protein having ATCC accession number 17978.

Group 2 was immunized with a cocktail of AB57_2465-45-550, AB57_2465-551-906, AB57_1136-35-420, and AB57_1136-421-1071, i.e. 2 fragments of SEQ ID NO: 24 (amino acid residues 45 to 550 and 551 to 906, respectively) and 2 fragments of SEQ ID NO: 25
15 (amino acid residues 35 to 420 and 421 to 1071, respectively).

Group 3 was immunized with a cocktail of the proteins AB57_1893-26-711, AB57_1893-48-176, AB57_1893-478-711, and AB57_1893-26-477, i.e. 4 fragments of SEQ ID NO: 20 (amino acid residues 26-711, 48-176, 478-711, and 26-477, respectively).

Group 4 was immunized with the protein AB57_2233-22-162, i.e. a fragment of SEQ ID NO:
20 10 (amino acids 22-162).

Group 5 (the negative control) received phosphate buffered saline (PBS).

Experiment 3

Group 1 was immunized with the protein (AB57_3370-27-356), i.e. a fragment of SEQ ID NO: 16 (amino acid residues 27-356)

Group 2 was immunized with a cocktail of the proteins AB57_1059-1-754 + AB57_1059-25-754 + AB57_1059-25-466 + AB57_1059-58-177, i.e. the complete protein having SEQ ID NO: 23, as well as 3 fragments thereof (amino acid residues 25-754, 25-466, and 58-177, respectively).

- 5 Group 3 was immunized with the protein AB57_1621-1-367, i.e. SEQ ID NO: 17.

Group 4 was immunized with a cocktail of the proteins AB57_3396-23-691 + AB57_3396-306-691 + AB57_3396-23-305, i.e. 3 fragments of a positive control (the protein having accession number ACJ 41966).

Group 5 (the negative control) received phosphate buffered saline (PBS).

10 *Experiment 4*

Group 1 was immunized with a cocktail of the 4 proteins AB57_0478-1-550, AB57_0478-551-1110, AB57_2309-22-294, and AB57_2309-1-294, i.e. 2 fragments of SEQ ID NO: 27 (amino acids 1-550 and 551-1110, respectively) and a fragment (amino acids 22-294) and the full-length version of SEQ ID NO: 15.

- 15 Group 2 was immunized with a cocktail of the 4 proteins AB57_0053-19-108, AB57_1336-19-114, AB57_0830-1-166, and AB57_3389-22-126, i.e. amino acids 19-108 of SEQ ID NO: 5, amino acids 19-114 of SEQ ID NO: 6, the entire sequence SEQ ID NO: 11, and amino acids 22-126 of SEQ ID NO: 7.

- 20 Group 3 was immunized with a cocktail of the 3 proteins AB57_3081-2651-3047, AB57_0596-29-580, and AB57_0596-581-727, i.e. amino acids 2651-3047 of SEQ ID NO: 30, and 2 fragments of SEQ ID NO: 21 (amino acids 29-580 and 581-727, respectively).

Group 4 was immunized with a cocktail of the 2 proteins AB57_3778-23-230 and AB57_1830-35-238, i.e. amino acids 22-230 of SEQ ID NO: 12 and amino acids 35-238 of SEQ ID NO: 13.

- 25 Group 5 (the negative control) received phosphate buffered saline (PBS).

Results

| Experiment 1 | | | | | | | | | |
|--------------|--------------|-------|-------|-------|-------|-------|-------|-------|-------|
| Group | Survival | Day 0 | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 |
| 1 | # Mice alive | 13 | 13 | 2 | 2 | 2 | 2 | 2 | 2 |
| | % Survival | N/A | 100.0 | 15.4 | 15.4 | 15.4 | 15.4 | 15.4 | 15.4 |
| 3 | # Mice alive | 15 | 15 | 0 | 0 | 0 | 0 | 0 | 0 |
| | % Survival | N/A | 100 | 0 | 0 | 0 | 0 | 0 | 0 |
| 5 | # Mice alive | 12 | 12 | 0 | 0 | 0 | 0 | 0 | 0 |
| | % Survival | N/A | 100.0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Experiment 2 | | | | | | | | | |
| Group | Survival | Day 0 | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 |
| 1 | # Mice alive | 12 | 12 | 3 | 2 | 2 | 2 | 2 | 2 |
| | % Survival | N/A | 100.0 | 25.0 | 16.7 | 16.7 | 16.7 | 16.7 | 16.7 |
| 2 | # Mice alive | 10 | 10 | 5 | 4 | 4 | 4 | 4 | 3 |
| | % Survival | N/A | 100 | 50 | 40 | 40 | 40 | 40 | 30 |
| 3 | # Mice alive | 13 | 13 | 0 | 0 | 0 | 0 | 0 | 0 |
| | % Survival | N/A | 100 | 0 | 0 | 0 | 0 | 0 | 0 |
| 4 | # Mice alive | 9 | 9 | 0 | 0 | 0 | 0 | 0 | 0 |
| | % Survival | N/A | 100 | 0 | 0 | 0 | 0 | 0 | 0 |
| 5 | # Mice alive | 13 | 13 | 2 | 1 | 1 | 1 | 1 | 1 |
| | % Survival | | 100.0 | 15.4 | 7.7 | 7.7 | 7.7 | 7.7 | 7.7 |
| Experiment 3 | | | | | | | | | |
| Group | Survival | Day 0 | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 |
| 1 | # Mice alive | 15 | 11 | 3 | 3 | 3 | 3 | 3 | 3 |
| | % Survival | N/A | 73.3 | 20.0 | 20.0 | 20.0 | 20.0 | 20.0 | 20.0 |
| 2 | # Mice alive | 16 | 15 | 8 | 8 | 7 | 7 | 7 | 7 |
| | % Survival | N/A | 93.8 | 50.0 | 50.0 | 43.8 | 43.8 | 43.8 | 43.8 |
| 3 | # Mice alive | 16 | 13 | 0 | | | | | |
| | % Survival | N/A | 81.3 | 0.0 | | | | | |
| 4 | # Mice alive | 16 | 15 | 6 | 6 | 6 | 6 | 6 | 6 |
| | % Survival | N/A | 93.8 | 37.5 | 37.5 | 37.5 | 37.5 | 37.5 | 37.5 |
| 5 | # Mice alive | 15 | 13 | 1 | 0 | | | | |
| | % Survival | | 86.7 | 6.7 | 0.0 | | | | |

| Experiment 4 | | | | | | | | | |
|--------------|--------------|-------|-------|-------|-------|-------|-------|-------|-------|
| Group | Survival | Day 0 | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 |
| 1 | # Mice alive | 12 | 12 | 9 | 7 | 6 | 6 | 6 | 6 |
| | % Survival | N/A | 100 | 75 | 58 | 50 | 50 | 50 | 50 |
| 2 | # Mice alive | 13 | 13 | 5 | 2 | 2 | 2 | 2 | 2 |
| | % Survival | N/A | 100 | 38 | 15 | 15 | 15 | 15 | 15 |
| 3 | # Mice alive | 10 | 10 | 5 | 2 | 2 | 2 | 2 | 2 |
| | % Survival | N/A | 100 | 50 | 20 | 20 | 20 | 20 | 20 |
| 4 | # Mice alive | 13 | 13 | 4 | 0 | 0 | 0 | 0 | 0 |
| | % Survival | N/A | 100 | 31 | 0 | 0 | 0 | 0 | 0 |
| 5 | # Mice alive | 13 | 13 | 1 | 1 | 1 | 1 | 1 | 1 |
| | % Survival | | 100,0 | 7.7 | 7.7 | 7.7 | 7.7 | 7.7 | 7.7 |

The above observations has let the inventors to the following conclusions:

Proteins tested that provide significant protection against challenge:

1: AB57_1059-1-754, AB57_1059-25-754, AB57_1059-25-466, and AB57_1059-58-177;

2: AB57_3396-23-691 (positive control), AB57_3396-306-691 (positive controls, and

5 AB_3396-23-305 (positive control);

3: AB57_0478-1-550 and AB57_0478-551-1110;

4: AB57_2309-22-294 and AB57_2309-22-294.

A number of proteins tested are found to possibly provide protection against challenge infection:

10 1: AB57_3582-22-253;

2: AB57_2465-45-550 and AB57_2465-551-906;

3: AB57_1136-35-420 and AB57_1136-421-1071;

4. AB57_3370-27-356.

AMINO ACID SEQUENCES OF THE PROTEINS OF THE INVENTION:

15 In the present specification and claims, the amino acid sequences of the proteins are identified via the SEQ ID NOs. set forth in the sequence listing and the table below. However, alternative designations are used in the examples, according to the following table:

| Designation: | SEQ ID NO: | Designation: | SEQ ID NO: |
|--------------|------------|--------------|------------|
| AB57_1759 | 1 | AB57_3370 | 16 |
| AB57_1009 | 2 | AB57_1621 | 17 |
| AB57_1902 | 3 | AB57_0504 | 18 |
| AB57_1614 | 4 | AB57_0619 | 19 |
| AB57_0053 | 5 | AB57_1893 | 20 |
| AB57_1336 | 6 | AB57_0596 | 21 |
| AB57_3389 | 7 | AB57_2870 | 22 |
| AB57_3578 | 8 | AB57_1059 | 23 |
| AB57_1088 | 9 | AB57_2465 | 24 |
| AB57_2233 | 10 | AB57_0791 | 25 |
| AB57_0830 | 11 | AB57_1136 | 26 |
| AB57_3778 | 12 | AB57_0478 | 27 |
| AB57_1830 | 13 | AB57_1048 | 28 |
| AB57_3582 | 14 | AB57_3621 | 29 |
| AB57_2309 | 15 | AB57_3081 | 30 |

When designating a fragment of one of these proteins, this is done using the nomenclature AB57_XXXX-A-p1-p2, where XXXX is any of the 4 digit numbers following "AB57" in the table above, and p1 and p2 are the start and end amino acids relative to the entire sequence of the protein. For instance AB57_3081-50-200 is the fragment of AB57_3081 that has the amino acid sequence defined by residues 50 to 200 of AB57_3081.

SEQ ID NO: 1

MTQLINKGGFRERANRSRKYQQSENKQVALPSKKYQPQTKLQDNQSEMIQAKAGTAETSD

SEQ ID NO: 2

MKLAKTLLATTLALTAASTFAASKHDQAHNTAGEEKVVVSTQEQAANTANAASDAVGSASEAAPATR

10 SEQ ID NO: 3

MIDEEKPLNFEDDDDEPLDFEDEFIDDKKEDEMYNSITKDGSSVDPADDGTRHIRPEDGDPIEIDE

SEQ ID NO: 4

MSTTNNQANQRNNQQQQQQQNDNRNQQQHGNQQQNDQQQNNQQQQQNDNRGQQQGSNQKDSGQQNSNNNQQR

SEQ ID NO: 5

15 MSAKLVTLLATSLTVCVAYTDDPYRGGYGYHDHDDRYDRNDGRRYSEWERKRWEERKRLYEQQRKDIREQQKDR
REWEKRHREWEKKRLED RDHHRDYRHDD

SEQ ID NO: 6

MNKLVLALGLAATVALVGCNKDKAPETGATTGEHLENAAQQATADIKSAGDQAASDIATATDNASAKIDAAADHAADAT
AKAAAETEATARKATADTAQAVENAAADVKKDAQH

SEQ ID NO: 7

MKMTAKIALFSAAIVTMGSLAACQSTTQPPKPEHGMMQDGPDRDGHHRMKHREFTPEQKAWEQHRAERKARFEQIQKA
CEGKVVGQTVNVQVGDKTLEGTCNLRFEPKRPQPPVNAPAPVATQAK

SEQ ID NO: 8

5 MKAIKILCITSSILVSSSLFAETPQPQVNEATSKTMPYGDNP SLGRVLLYKTGKGIQNLGDSIQGASEKTSNKISEKW
KDTKEFTA EKA EVVQQKADTAKVFTEQKIEQAKQNITSSRNGENIPIEQGELSKSSTTAN

SEQ ID NO: 9

10 MKKSLLAIALMSTLLVACNKHENKTETTS DASTPVQTAQSNNEAVDTAHTAENSLDWDGKYKGTLP CADCEGIKTELE
LKDDKTYELTETYLKGKDANPFETHGKFTFDKDN TSVITLDDKAQNRKFFIGENTAT ALDMEGKKVEGSLAEHYVLKKE
D

SEQ ID NO: 10

MANKLLICA AIAAGLLLTACVKKETPKEEEQDKVETAVSEPQPQKPAKFESLESVDTQEAQVQEQQVEVHREETANT
TTEIRRETRPARSDESSQTQVAEQPKSETPKVEPKPEKKPEPKAEPKPEKAQSKPAAKATEPANTEDDAVAAAIAAATP
ALKN

15 SEQ ID NO: 11

MTTENKLDELKANAADAKVQGEKALDDLKENVKEKQTAGKEAIADKVDELKTKAADAKVQGEKALEDLKENVKEKQAAA
KEAVEDKASDLKGKLDDAQHSLQDKFDHLRTEAAHKLDDAKAKAAELKEEAATKFDELKTQATAKFDELKKTATEKLNK
LKNHDSAE

SEQ ID NO: 12

20 MHTRRILLAFSLAASAASVAFADYQNIQSTDSRLEQLSKTSLQGSYTHPDDLDPASAKVSVTLREKTVELNND SLA
KKYGT TTA KNSFKTSSSNPYSWLVSHPLPDTVRVSSNFGGR TMGGRAEHHGGLDMAAPSGTPIYATGPGIVTKSGWGTG
YGQYVEINHNGY LTRYAHASRLMVRVGDQVSAGDHIANVGCTGRCTGPHLHYEVVKDQQRKNPSTYLAML P

SEQ ID NO: 13

25 MGMTFTDIENKSAKRLIGIAAVIFLHLLVAYILMSGLANNIQKPAEKPVELQIIQDIKPPPPPKPEEPKPKEKPPEPPK
MVEKVAKVPEPPKEVEKVATPVQKTTPVAQTTKVATPAPAAPSTPSPSPVAAPAPVAAAAPALKPAGVTRGVSEGSAGC
EKPEYPREALMNEEQGTVRIRVLVDTS GKVIDAKVKKSSGSKTLDKAATKAYSLCTFKPAMKDGVPQQDWYEIEYPFVI
E

SEQ ID NO: 14

30 MKMMKTAIVTASVLASASIFAQSAGVNAGASAQVNVQPGGLVSGVANTVKNTAHTVGNTAKHAGHVAADTTVKATKKT
GKVTELSSKAATGTKHVASEAVTGTKHFATEAATGTKNLATKAATGTKNLAVEAKADTKAHLDAVKTKVAEKQADQKEF
TAEKQADAQARVDAVKARVAQNQAEQKEFVADTKADAQAKLN TAQPAHGVNAQTGVNVGVNVAGINANANVNAGA QAST
QKGEKKSF IKGLFGTN

SEQ ID NO: 15

MQMKKHSLLFIALMSTTSLYANIPIESRGLSQNDGSASNTSSSNISVPTNLNWELMQKNQOLENDIRTLRGQLEEQAND
IEQLKKDLANRYTDLDQRLELLHQKVDPSATQDDSSNATSDNTTPASAPAPQTTESNKVAAPATQTSEQQPSAPTTT
TQPAPAAAQNSNSLELEKAAAYTVALDAYKQGAKKAIAPMQNFIKNHPNSIYTGNAFWLAEFHLATDPVNYNEAKKN
5 YNVVANQYPNSSKAPRALYQLYSIAKDVKNTVSAHQYKNKLLSQYPKSEEAKFFNK

SEQ ID NO: 16

MSMNNKQRMGGVLLGGGVLLAALLLKGNIEIKQVDVQPQTSTSPKLQAKPKQSAQEGQMVLQPLAVDVETEKRLLE
EQRRSREKAVAEQEARAAEFAMQQQAEADAARKAAEYAAINARRAAQESSDNIPEVAGSENKAKGQQTDTTKKSVD
LAKADADKKAEEAKRLAEADKKAEEAKRQAEADKKAEEAKRQAEADKKAEEAKRQAEADKKAEEAKRQAEADKKAEEAK
10 RQAEADKKAEEAKRKAEEAKKAEAEKARELLENGDKKWMVQVALAANQANADAVVSKLRAKGYKVTTSPTSKGIRIMVG
PAKDRDTADTTRKKITSDASLNMKSAWVIDWVPLDQRKSD

SEQ ID NO: 17

MANTRYEDDNNSSGTSNRGFASMDPERVREIASKGGRAHASGNAHEFTSEEAREAGRAHASGNAHEFTSEEAREAGA
LSHKNDNRNGRGRSRYDDDEDDDRGRSSGGRGRGRSRYDDDEDDDRGRSGGRGRGRRDDDEDDDRGRSGGRGRGRSR
15 DDDDEDDDRGRSGGRGRGRSRRDDDEDDDRGRSGGRGRGRSRRDDDEDDDRGRSGGRGRGRSRYDDDEDDDRGRSG
GRGRGRSRRDDDEDDDRGRSGGRGRGRSRYDDDEDDDRGRSGGRGRGRSRRDDDEDDDRGRSGGRGRGRSRYDDDD
EDDDRGRSGGRGRGRSRRDDDDDDDRGRSDGRGQNSRNQKRDYGRFTS

SEQ ID NO: 18

MLYVIPFIIILLVAVILKKRENSQKQEATSPKNINRKSGKKASAKSSKSSREKIKAKVIEENIPAI PQSNPVPEALRHN
IQQLIQEKQFSAAEAQVNQALKKDNTQHLYLLLLLEIHIAQKDEFAIQQLISHIRSLGLNEIAAQAEATROKEYESSQP
20 DAIDFPQAQTYEPPKNTDTTAQFDELTTSSSEASFDLQKDYTPVKQEPALIEPLEFNFSFEQNSATENTNQPAQQPE
LSSTQETNELADLEFSFDLAPLHETEEKSQAVEVKADQENSINALDFNFDLNPSSSETKSVQQAPSLDEIKLIEQAPLE
ATSIAPLEFSLDEPALVPAPPELETQNHIDVVNEAATQTQIEDPLLEAFPELKQINENELDLKLAEQYIKFGANQAARNL
LQGDEQKFNTEQQQHAKNLLNRIAS

SEQ ID NO: 19

MPKIKPIKLVIIVVCIAIIAVLAWKFLPKPQQPQYITAETVRGDIENNVLATGTLDATKLISVGAQVSGQVKKMYVQL
GDQVKQGQLIAQIDSTTQENSLKTS DANIKNLEAQRLLQQLIASLNEKQLEYRRQQQMYAQDATPRADLESAAAYKTAQA
QVKALDAQIESAKITRSTAQTNIQYTRIVAPTGTVAIVTEEGQTVNANQSAPTIVKIAKLQNMTIKAQVSEADIMKV
EKGQOVYFTTLGDETKRYATLRQIEPAPDISSESNTSTSTSSAVYYNALFDVPNTDGKLRIIDMTAQVYIVLNSAKN
30 ALLVPSSALSSKQFSGQRKQGSADKASSTPSAERKHQGNQVRLERLNLTPQKQLIEQKATLSVVRVLQADGTTKPT
QILVGINNVRVAQVLGLKQGDQVVIADSSSENSAASANSNGNRRRGPMGM

SEQ ID NO: 20

MNIPRPFKLSVIAICAICYANLTYAQDAQVQALQTIQVKASNAEQSSEQTKAYNVKNSSSATKLNIEAKETPQTINVVT
RQQIEDFGLTSTRDVLNTPGVTVSNQETERTTYMARGFEISNILDGVGFPPLSGYNNNTNPDTYFYDRVEVVKGADS
35 LTNAFGDPSATINNIRKRPTQEFQASGGVSYGSDWTQRYEADVSGSILPSGKVRGRIMGYEQTGDSYLDRYSAEKNQFA
GIVEADLTDSTLLTAGYSQEQNKPNANNWGALPLLDANGKQISYDRSYNPNPDWAHWDNETQNAFVELKQKLNDQWNAK

LTNYLDTKHNSRLLYYYGYPKADGSGVSLTPWGGQEHQEKHAVDFNLEGTYKLFNREHEATLGYSYVRNHQQDKQSTG
TINDSNVIKSTTTDASWTPQSITWSDTFTEAANYKQNINSIYAATRLHLNEDLKLLLGANYVQAESKGESYSSPMSYSE
SKVSPYVGLTYNFTPEYTGYSYTSIFRPQTGIDKDTNQALKPIEGKSYEMGVKSSWLDDRLTGTLVSFKTEQNNYPLR
NSDGNPLNRKVPTSDLESQGEVGLSGQITDNVNLSFGYAQFSIKDTKNGGEARTYNPNQTLNLLTTYTPPVLPLKLVG
5 AGLQWQDGIKLYDSNVNGTIKQDAYALVNLMASYEVNDHITLQANGNNIFDKKYLNSFPDQAFYGAANYTVAVKFKY

SEQ ID NO: 21

MKLQTIACAVAIATGGLFFSHTMNEARAATNTAAVSQSIQPTQEALVARQLATLVDRQHLYLNMRLDANTSNRILDMYL
DSLDPDHSFLFLDAEVQNYKKLYGSNFGASLKAGNLTGPFATIHQQYRERLKQFYEFMLAELKKPQNLKQPNTFIEVDREK
APYFKTSAEQQNHWRKMLVSQLINLTISREEEQAKQKALKENPSLADGQDLTGPEDLTPAQTTLTKRYTRQLERISRVKS
10 DDVLDKTLNAMLATYDPHSNYPPIDAIELNRQTTLQLEGIGVSIRPERGNEDYTKIETIVEGGPASKSGQVKSGDRIV
GVAQEGGKMIDVVGWSSSEIVGLIRGKRGTKVTLKLLGAGASMSQARNVTLVDRDVIQEEEDAGVRSRTVEVTRDGKKHLL
GVIEIPSFYFDYRSRRAGQQYRSVSED TANAFEALKAKKVEGIIIDLRNDPGGSLEEVARMLGQVIKSGPVVQIRDNGG
NVSVFEDNDGGQQIYTGPLAVLVNLSASASEIYSAAIQDYERGIIGSTTTGKGTAQVQLD TLAYGQATLTQRKFYRV
TGGSTQNGVVPDIKLVDIYNEEFGERKSKNALKWDTIPTAPFKREGSVQPYVAKLSQLSEQRVAVDPPQFKYLNKRTAI
15 AKVTSQKQVVLIDIKRRAEALLSLEKQTLDAENERRIATGQKPPFNWESYQASLDALAESRAKMKANQRPALPEEETFV
NEAANVLM DYAKLQNR

SEQ ID NO: 22

MTRIIIVASKEGLDVLQDQGLNKVVLNQPTIIQIGVSQKDIASMEKQGGSLVIHLKNGETIVLENFFNEATNTTEHSLVF
PTEQGKFVEAQFDAQGKVIDYRGLNHVTDLAYTSTSPSAATMAVDNDPSFSMGNVLKAGLAVLAAEGLYLWAFDKDDKD
20 DSPSTPDLIAPAAPTATLADDTVTVTGKTEANAKIYIKDAAGNTVASGVADASGNITIKLDKPLVNGDKLVIAQDAAG
NNSKVTVTGKTDTIAPDVPQAQLSDDGSLTGKAEANAKITVYDATGKVLGTVFANKDGIYSLKLTPLPTSEAGGKVV
AEDAAGNKSEEVKIIAGKDTIPPASPFVEVNKEGSVIHGKTEANAKVQIKDADGKVI GSGTADAQGEFQITLSPALKEA
QKGTVVVEDAAGNVSKPVEITPGFDSIAPDKPTVQINTDGTSTGTAEANAKIEIKDTTGKVI GSGTADANGKFTISIS
PALTDNKHASVSAIDNAGNKSEVV DIVGTDKDTTPPAKPILNSVDDDVGAVKGAITAGSETDDARPKLTGSGEANATLTI
25 YDNGVAIGVVTVTSGRSWSTFDKDLALGKHTITLTQTDAAGLTSEASSPFTFYVVPKAASLSETSV DILSTEGPSLA
DSVGLHTLKVAQNTTTETNNPQKSVPLDDLLKSSTASESDPIAKLLSSTALKTTQASEPIEVNASVGQTTSNPNHPLPD
TTSSVLQNLDDQTYPPV

SEQ ID NO: 23

MSKRIIQSVLSVSVLASMMMAFAAQNEQEQAQTLEKPAEPVKLETIFVTAEQVKQSLGVS VITKEDLEKLPVRNDI
30 SDYVRRMPGVNLTGNSATGQRGNRQIDIRGMGPENTLILVDGKPINSRNSVRYGWKGERDTRGDSNWVPAEAIESIEV
LRGPAAARYGSGAAGGVNIITKKVTNETHGSVEFYTSQPEDSKEGSSNRVGFNVSGPLIKDVLSYRLYGNYNKTEADD
VDINKSIGSTAAGREGVKNKDISGRLAWQATDQQTVLLDISSSKQGNISGDSQLNANA EADAILSQ LIGKETNTMYRD
SYALTHEGDWSWGKSKLVAQYDKTHNKRLPEGLAGSVEGKINNLDKATSRLET LRFNGEANI PF EYLYLPQVLTVGTEW
VEDRFKDNVSTTQGDSSSGYGDQLAKGDRSKMESRIASAYIEDNLKVTDS TDVVLGLRFDDHKS GSNWSPSLNITQ
35 KLNDNFTLKGGAAYKAPNMYQNAEGYLLSTNGNGCPANIESRCLLQGNGLKPKETSVNKE LGIQFQRDIVNASLTWF
RNDYKDKIVAGTHVGTVDGSSSTNANTGAVTNTKWNILRWENTPKALIQGFEGSLGLDFGDIRWTNNFTYMMDSKDKQT
GNPLSLVPIYTINSIFDYDITDQLDVNFVFTQYGRQKSRQFAENRLESGIGSGGANSALKPSTVKSYSTAGINVGYKFS
DQISTRVGVSNFLDKQILRDSNSISQTYNEPGRAYYASLKYSF

SEQ ID NO: 24

MPSKIKFKQSTLSHSMHLILKMQSIPKLISSLLSLCVTPCYAQSSAETVIPEANQTVTDSLQQTNTNPNPSDVPITD
 VATLVTQAQQQQDSLAILQQEQFPNQIEEFKPITLDNLEDLPVMPVDQNMANEIYRVAAEEAKNEAQNFQNGTQKQPEM
 VVSDASQAELEHINQAPVNIQQLMHEIQSDSKIVVEANETGKTLPELTAAVEEPPEEKGFRRIFNKIRPPRVI PMEQI
 5 PRITAEVTGAPDDLAKNIKGKLSTFTQESFEDFNAALPQLRSLNQAAQAVGYNAEFRFEKLSASRVRVNVTNPNEPVR
 INEQNIEFTGAGAKQPQFQVIRLVPDQDVGDIFNHGLYETTKSRIVDAASDNGYFDAYWRLHDVKVSQPENKADINLKY
 ETGERYKLGKVEFRMSDPSKPLPLNMNILESMAPWKEGDDYAFWRVNVLANNLNNSRYFNITLVDSEIKPDPIEKPLELP
 PDLQALVDQQNVDDIDESKLLPLEQQQLAKARQLASSSKEVTQNVVDEKQFAGTESVQAAPASLKAATVQHHEEQESEQDR
 LQAQAREEKRIPVIVTLNADKLSLETGIGYGTDTGARLRSQYRRSIVNKYGHSDANLELSQIRQSIDGRYSIPYKHP
 10 LNDYFNIVGGYERETRDDIGPDVSLLTESAVLGGERVIKKPLGNWQHTIGVRYRLDRLTQKGNVDISELPDAFKTAASE
 QEALLFSYETSKTSSNTRLNPTKAFKQTYKLELGSESLSDANMAIATAGWRFIYSLGENDDHQFVGRSDFSIFTDEF
 DKVPYNLRFFFTGGDQTIIRGFYKSLSPEDNGYKIGGQALAVGSLEYNYQFKEGWRAAVFSDFGNAYDKSFSNPTAYSVG
 VGIRWKSPIGPIRLDVASGISDDNHPIRLHFFIGPQL

SEQ ID NO: 25

MFIKSILSSITSIIPLPENSNTSSNLGNGSGDGLLNGISSNGEHNIGYIGNGIADDASITAPITIPNLNSGNSITLIGN
 SSSSVNSSPTTSSNNVNDNDVTNNGNGSTIGSGTGNGSGDGLLNGAASNGEHNIGYIGNGIADDASITAPLSIPINLA
 GNSITLIGDSSSSSVNNSATNTSNTVNDNDTTYNGNGSGGGNGSGDGLLNGIGSGNGEQNYGIGNGIADDASITAPITL
 PINLSGNSITLIGNSSASSVNSSPTTSSNTVNDNDTTYNGNGTGDSGVSAALGGSGNGSGDGAGNGIASNGEHNIGIGN
 GNGDDVDITAPITGVNLISGNSFTLIGNSSSSSVNTAPTSTSSNTVNDNDTIDNGNSGGTGSGSGNGSGDGLLNGAASGN
 20 GEHNIGYIGNGNGDDVDITAPITGVNFSGNSFSIIGNSSSSSINTAPTSTTNTVNDNDVTDNGNDGGGLVGGSSGNGSG
 DGLLNGAASNGEHNIGYIGNGNGDDADFTFPLTGVLNFGNSLSGFGSSSSSDSVNVAPTATNTVNDNDTIDNANTGGL
 GDGSGNGSGDGLLNGAASNGEHNIGYIGNGNGDDADFTLPTGGLNIGNALSGIGGSSTDSINISPTTSSNTVNDNDT
 TNNGNTSGGVIGSGDSNGSGDGLLNGISSNGEHNIGYIGNGNGDDVDVAPITPLNLVGNFSFIGGEGTGDI LGPI
 TGIIGGIGGDGDI LSPITGIIGGIGGDGDI LSPITGIIGSIGGIGDLDGNPLTGIIQSGIDVLQNLKLTGLINTGI
 25 DTIAGTIIGVFPDAEHPVGDFADLGKLLFETSRSVNGTLEAISDLAGADLEGASGSITGVIDTLITNGSTASTIIQHI
 VGDDLVTENGGLLSITTIIGGVDSGDGGLLGGLDGLISINYGSDNSNSIDVEDILGNILGSVGSNQGIAGVGEPTPTG
 GSLIHTISLNTVNQLTDQLLHALPTV

SEQ ID NO: 26

MYKPTTFVWQPSAASLFKITVLSALAALGITTGCSSTPQSAKTSKTKQVSGAGYLDASSLDSLEDLLSATDMRAVEGD
 30 RLLILKHGVDVWKRMAVGFKMDLNHWDPRIEAQRSWFISRQPYLDRLSARASRYLYHTVKEAERRGLPTLALLPVISS
 YDPAATSSAAAAGLWQFIPSTGRIYGLQQTGMVDGRRDVVESTRAAYEFLGSLYNQFGSWELALAAYNAGPGRIQQAIN
 RNQAAGLPDYWSLKLPEQETMNYVPRFLAVAQIIKNPRAYGVSPLPIANRPHFREVTLAPLSLNEIASVTGLSRAELY
 ALNPGYRGETVDPASPMRILIPADISPSVDNKLKGMKAGSSGWWASVTSPSKPTTTTSTSVTVRTPSTPAQPVRPST
 PAKTSSSSVTVKTTTPRGS DALAAFAASADVPSAPRIPVAVTPAANIKPVRTEPPISATEREKILA AVRAEGEKETVDQ
 35 ALEPQATQA EKQVVAELKALAPQGTEIVDPYDGKIKLTAIQTSQSVAEQQKEVSKGFAYPKTLAEDATLANSEDAQR
 NKDKPYIKTDTDVVVVQPKGKRSTYTVQPGDTLAVIAMKNGVNWDRDAKWNQIDPEKTLFVGTSLYLYDAKPQEAETTA
 KSAAPKPDVYVQANDSLTG VANQFNLSVKQLAEYNDLSVTDGLFVGQKLQLKEPKGNRAAKVEPKAIQASTRRIATKSY
 TVKRGEYLKLIADRYALS NQELADLTPLSAGSNLIVGQKINVPAKEITVDEVDDSKASGKYEKLAAGPSYKTESYKVQ
 RGD TLSS IATKSKISLAELAE LNNL KANSHVQLGQTLKVPAGASVPDQYVVQSGDSLNAIAAKYNLQTSYLADLNLGR

TAGLRAGQRLKLTGEVETTSKVS AKNTKEETPETYTVKSGDSLGNIANRYHLQLDYLAALNGLSRNSNVRVQGRLKLTG
DLPTVETAKTDTAKSSPKAVVAGKNTKEYTVKAGESLNAIASRAGISVRELAEMNALKANANLQRGQNIVIPKTVVEYK
VKRGDTLIGLASKYGLETTLLAELNNLTPSTQLRIGDIIKVPNL

SEQ ID NO: 27

5 MKRMLINATHAEVRVALITGNRLYDFDLENRTREQKSNIYKGHVTRVEPSLEAVFVEYGAGRQGFLSMREIANSYFQ
ADPRQTSNIRELITEGTELLVQVEKEERGNGAALSTFISLAGRYLVMPNNPKGGISRQISGVSREELKEILASLNV
PRGMSVIVRTAGIGRTQEELQLDLQHLLDLWAQIQGTASSGPSMLVHQEAGVVTRAIRDYLRDDVAEILIDSEQAYNE
AYNFVKAVMPRQLDKLKYTLNEPLFAHFGIESQIQTAYEREVKLPSSGGSIVIDQTEALVSIDINSKSTRGHDVEETA
LNTNLEAAEEIARQLRLRDIGGLVVIDFIDMTKERNQRMVEAKLREATQSDRARIQFGQLSRFGLMEMSRQRLRPSLEE
10 ATGYVCPRCHGTGMVRDLRSLSLIMRKVEEIALRERHGEVQVEVPVEIAAFLNEKRHSLVYLEQTSGRVTVLPHPH
LETPHYEIAYNPDGFAPSSYERTEATRSSEKELGYESSEWHLEADHGHAVTATASTHAAAQKKANHATQPVAQPSAQ
KAASPCAWLENLFVQKQAQTVDDQSRSQAQNAIAEQMVNTGAVSRGQFGQVAVPAVAEAPVQSNNAISQSPVKQDVR
EHVEKDDKSQQQRQNNKKRKHKEQREQHHQSHEQQHQVHEEVVQLSRQEQRELKRQQRQQQDQHQHNDVQHTENAV
PRRDRNNQQRPNRPNRHRDPSVLNENQNTLVVVDEKQIKVDVIDAPKHDVMNTALIINVDQGGSEIVALTPERRHVERV
15 ETTSTEV AQEPTPAPVVAEKA AVVETKEEAQPSQEAQAPQIKRASNDPRMRRRQOREAKHAKAATPSIAPSQIPTLAQH
TIGSLIRHVYGEDCTVLIEQFGLVPTFNRLAQKFAEQYASTLVVEVTAETEEKKPVTRDAELPSHKPAEEAEAPVLPPL
TPPQAPAPRVANDPRERRRLAKLAAEQAFEQVKQHS AQEEVATPAPVAEETVAAPTAETQATVEPAQQPLELNQSTEV
VQPEAAPAEKATEETVAEAPAAKEPAPSKAASKAKAAAEETVAPTEATTDAESEDVKADKDKPSRPRRPRGRPPKKAN
PVAE

20 SEQ ID NO: 28

MSTLATLKALLAKRILIIDGAMGTMIQRHKLEEADYRGERFADWAHDLKGNNDLLVLTQPQIIQGIHEAYLDAGADIIE
TNSFNGTRVMSDYHMEDLVPEINREARLAKAAACEKYSTPDKPRFVAGVLGPTSRTCSISP DVNNPAFRNISFDELKE
NYIEATHALIEGGADII LIETVFDTLNCKAAIFAVKEVFKQIGRELPIMISGTITDASGRTLGTQTAEAFWNSVRHGLD
LSIGFNCALGADAMRPHVKTISDVADTFVSAHPNAGLPNAFGEYDETPEQTAAFLKEFAESGLINITGGCCGTTPDHIR
25 AIANAVKDIAPRQVPETVPACRLSGLEPFNIYDDSLFVNNGERTNVTGSKKFLRLIREENFAEAELEVAQQQVEAGAQII
DINMDEGMLDSQNAMVHFLNLVASEPDISRVPIMIDSSKWEIEAGLKCVQGKPVVNSISLKEGYDEFVEKARLCRQYG
AAIIVMAFDEVGQADTAERKREICKRSYDILVNEVGFP AEDIIFDPNVFAVATGIEEHNNYAVDFIEATGWIKQNLPHA
MISGGVSNVSFSFRGNEPVREAIHSVFLYHAIKQGMTMGIVNAGQMAIYDDIPTELKEAVEDVILNQNGESGQAATEK
LLEVAEKYRGQGGATKEAENLEWRNESVEKRLEYALVKGITTYIDQDTEEARLKSKRPLDVIEGPLMDGMNVVGD LFGS
30 GKMFLPQVVKSARVMKQAVAWLNPYIEAEKTEGQSKGKVLMA TVKGDVHDIGKNIVGVVLGCNGYDIVDLGVMVPCEKI
LQTAIDEKCDIIGLSGLITPSLDEMVFVAKEMQRKGFNIPL LIGGATTSKAHTAVKIDPQYQNDAVIYVADASRAVGVA
TTLLSKEMRGAFIEEHRAEYAKIRERLANKQPKAAKLTYKESVENGFKIDESYVPPKPNLLGTQVLKNYPLATLV DYFD
WTPFFISWSLTGKFPKILEDEVVGAAATDLYNQAQAMLKDIIDNNRFDARAVFGMFPAQRTDADTVSVFDEAGQNVTH T
FEHLRQQSDKVTGKPNLSLADYIRADREQQDYLGGFTVSIFGAEEELANEYKAKGDDYSAILVQSLADRFAEAF AEHLHE
35 RIRKEFWGYKADEQLSNEELIKEKYVGIRPAGYPACPEHSEKAVLFDWL GSTDKIGTKLTEHFAMPPSSVSGFY YSH
PQSEYFNVGKISQDQLEDYAKRKGWTLDEAKRWLAPNLDDSI V

SEQ ID NO: 29

MKLKLNKFNKPNNLWYAVCSSSMIFTWLMTSSVVQASDLQIYASPTAGKKTIVMMLDTSGSMTNNSYGENRLAMLKNGMN

AFLASNNPVLNDTRVGLGNFSANGDSRSQILVAAAPLGDASTLNTVGSQRYKQAVANLTAGGSTPSAHAYAEAAAY
 LMGTTTTYSETNYAIRKDSYIKRVRSDNRTEYSYCTNYRDSQIDTANLWQPCRSNSYSSWSTNNPGVDNATAYDTSSD
 WTYYYYTYYYTTFNYAVANADSGIPKSKSNDTASNPNIVDRNATNSNAVYQSPLPAVANRQSCDGGQIYFLSDGEPNNT
 TNTRSASVMSTALGSTFGADFNCSSGGLSNTTADSGWACMGFAKRLFDKTKNPAGVSIQTAFVFGSDFSSSLNSSDVKN
 5 ACRLSSRTQSDRKGDACS PNQSTNAVAAPGYGNGGFFPTQSSQGVTDSVIAFINNLDKVPLEPLTTGAISVPYDALNP
 KNLQEYGYLRAFEPNPANTYLTWRGNLKKYHVVLSGANAGAFEANSGLVYNASGAFTGTGKYWNSSTYTDGGKVFLG
 GSYANVPLPIAGQPETRAEGNITKYYYAVQSKIRNLFTDVSAAADGSLTKISTSGTNLLKI PAAPPEETNPFDTVAN
 TASYVLGKFDPSTGQNILKAFFISLKLKILNYLGYSTDINATTLPSLSVTSNEPYLSMGGSIHSLPVQLTYNGTLDNDG
 NLTSAEQSILYGTMEGGLHIVDASSGIEQMVFPADILNDSVASKALVVGQSDASAPAHGMDGAWSDPAYNITTVGS
 10 GSSAVSKVTAKQMNIYGGMRMGSSYYGLDVLSTSPKLLFRIGADQNDYSRMGQSWSKPVLANIRYNGSIRRVLIVGG
 GYDQCYEKPNIITLDACFTNGKAKGNAVYIIDAKTGQRLWWTSDTGSNTDNANMKHSIVSRISTLDRDADGLVDHLYFG
 DLGGQIFRVDLNNNQTKNSTYSSFGVRVRLANLATNDSTYDGTNDYTGGNAPRFYEPPTVTIHDYGIHTFITVGIAS
 GDRSTPLDVYPLTGREGMTPASALSGRPVNNVYGIIDRDFVKKNLMSLTDNQLETKDITRTGLRKNPQILRTGETRVAQ
 IFFPTTGVGKGGWYRSLSSSTSDGTEKANNSFRIGGLKAFFEPMAITGNLIILVYDPQGTGIVAADPCLPRVVGETDRQ
 15 TYCLPFGACLNDSGSDQNKENHSGFETQGTGNCVPGASECNKNVIGSGIRSVTFVPTEDNPPTTNSCGKLKLSGNEQG
 TGQWQCTSHLPTRWYERYR

SEQ ID NO: 30

MTDAAGNTSEQAVQKVVDTTAPQAGELTSLDLSDTGISATDQITQDKNFNLKLEGQESGSRVTVLVSTDEGKTWQETT
 IAQKDLTDGVYQYKAVVTDAGNTSETAVQKVVDTTTTQAGELTSLDLNDTGVSVDQITQDKNFNLKLEGQETGSRV
 20 TYLVSTDEGKTWQETTIAQKDLADGVYKYKAVVTDAGNTSETAVQKVVDTTAPQAGKLTSLDLNDTGVSATDQITQD
 NSFTLKLQAQPIVIGEQAALLDHYEVSKDEGKTWQETTADQKDLADGIYQYKAIVTDLAGNISESAIQKVVDNSLNVES
 TTVIVKPITEDNTISLVEKDQVISIRLEIANLPTDLNSSLTSVNTTLGNVTYNFHFDEVTQEWVTEIPAEFLWSVEPQT
 NISIEISLTDQAGNTAIKHTQNYNVDHPTNSPTLDSLTFNNIDGAIISGSAYKGSKVDIYNKNGDWLASTITNEEGKF
 TLQDLSINSNQEVYAVATYNGYSSSENSSIGLVTEVPAISITRISPEGVISGYATEGSHFIVKDQNGNLIQEFNSNVFDS
 25 SGITPFSVMALGEVRPFILSLDQPLEEGAQIIISIDKDNISGHPQYITADYTPAVFLETQFDISGETLSVHVNEPNSF
 IRAFSGEGNLIATGFTDEQGFASLQVFQFLKEGETVSVQVVDKNQNTSETLIEVPNFAYIPHVERITQEGLISGVAEDN
 STVIVRDADGNELGKVTGLDDNSWSDFSLSVNRPLIDGKISVQIIDNKGLMSPEQNIIVDLTPPPAPTELNFNDA
 GDLVYGHAEPFSEILVKDGQGNILNKWFNNWTDSEGSFISIELGTFLTNAETVYVTATDVNGNVSLAAQIQAPNYAFAP
 YVDSFTSDGVISGQAENNSTLVVKDAKGDVVAEIKVGEDNGWNGSSYFKLQLDRPLVDGEQFFLSIKDARGQVSADTVI
 30 TADTVAPTPASNLVFSSEDGSYLTGVAELNTTIQVFDHNGQLVNIWNNTINS DGTFTIYLGSSNNLHGEAFTVTVKDQAGN
 VSEAISINAPLDDIAPNPIKNILLDANGQNFTAQAEANSQIEVFDSLGNQGTGWGSTDSAGNVSGSFNQTYLHGEELTFV
 VIDRAGNRSIEFKQNALIDTIAPNPIANIIFNEDGQSFTAQAEAGSSIDVLDQTGNKIGFGYTDSSGNVSGYFQQVYLH
 GEELTFVVIDRAGNRSAEVKQSALNDDVVPNPIENIVLDLNGQNFTAQAEANSQIEIKNNNGDVVGYGSADSAGNVSGY
 LYQVHLHGEELTFIVVDRAGNRSTEVKQNALIDDIAPNPIENIVLDINGQNFTAQAEANTQIEVKNAVGEIVGLGYVDG
 35 AGNVSGYLYQVYLHGEELTFVVDVDRAGNRSTEVKQNALIDDIAPNPIENIVLDINGQNFTAQAEANTQIEVKNAVGEIV
 GLGYVDGAGNVSGYLYQVYLHGEELTFVVVDVDRAGNRSTEVKQNALIDDIAPNPIENILLDANGQNFTAQAEANTQIEVK
 NTAGEVIGSGSTDSMGNVSGYFYQVYLHGEELTFVVVDVDRAGNRSTEVKQNALIDDIAPNAIENIIFNENGQNFTAQAEA
 NSKVEVKNAAGEVVGSGYVDSVGNVSGYLNQVYLKGEELTFVVIDQAGNRSIEVKQTAFLDNTAPENATNLVFSSEDGSY
 LSGMAEPNATIQIFDQYQQLLNQWNNNVNWDGTFNIIYLSNSYMHGEVFKVVVDHAGNLSGEVTVKAPLDDIAPVAASD
 40 LVFNEDGSSLSGVAEPNTFIQIFDQNGQOMNTWSQSVNADGTFTIFFGTYNLHGEELTFVIVKDLAGNVSEAVSVKAPLD
 DIAPKPIKNIVFDANGQSFTAQAEANSQIEIFDSFGSQIGWGSTDSTGSVTGYFYQVYLHGEELTFVVIDRVGNRSDM

KLNALMDTIAPKPIENIIFNENGQNFTAQAEANSFISVKNAAGEFVGYGYVDSTGNVSGHFNQVYLKGEELTFIVIDKA
GNQSIYEKQNALTDDIAPNPIENIVLNKNGQNFTAQAEADSQIEVKNTAGEVVGSGYVDSIGNVSGSFNQVYLHGEELT
FVVVDRAGNRSTEVKQNALIDDIAPNQIENIVFDVNGQYFTGHAEADTRIEVLDDQFGNRAGWGYVDSQGNVIGYFNQVY
LHGEELTFIVVDIAGNRSVEVKQNALIDNVAPPAAANITLTS DGLLFGEAEPNSTVEIIDQYGAVITTTTVWYDGT FNQ
5 WINLSQYQTQNL SIVVKDQAGNRSEVVHELVPVFTNSPIAATELKLDDIDGHILT GKATVGMSVVVTSTDGQTINGGWNN
AVNEDGSFAIQ LNDYYLQGQTLQVRVYDQNTNQYSLISEIIAPLDNIAPVINEVVINNDGYGITGQTDSKAI IQVMDAD
GDLRAEFQADETG YFNASIYPPILRGEQLFITAI DLAKNISKPFNITFNADTNAPPSAEHIVVSENGFFIEGTAVAIST
VHIFDVHSNHVATNVADEAGNFNIQLYPPLASGQILRIVVEYNGYQSAYTEITAPIDTVAPNAATQLLLEDGNVLSGQA
EAYSIVNIFDANNNLVGQTNVGS DGAFLTHLWY EYWHGETLTVKVVDANQNVSVGTTIVAINDTVVPDVVTQLAIDEWG
10 SLTGRVESYATVELTYHFTDQPLSVTSTTALANGMFFIYLDRNATSLDLTVIDRAGNRSETISQIISDLPTVIIDHFKG
DATDNTYNIDTIDDFVQEYIVEPYAIYKDVWIDNSYMYSDWVIEGHYEQIWFVDGYYESQWATSGYSTVQNIYQNQNGI
TYIDNGTADSDYSRYEQYYDFVNGQWQEGYELTYIRSEEGWVDTSHYEDVYIDTSHYEEVWVDTSHYQDIWVENS YWE
SOLVESGRRDVDLGGHDKI ISSVNYSLVGLYQTVNDPTTVDSFLESGRYVEDLELVGSAHLNATGNALDNLLTGNSGNN
VLNGREGNDTYITNEGTD TIVFQLLNSQDATGGNGHDTVLDFTLGDIRTNLQADKIDLSELLIDYSKDV SALAKFITVE
15 QDAGNTTISLDRDGEGTMFNSVSLTLNQVNTTLD ELLNNQQIIIV

CLAIMS

1. A polypeptide comprising

a) an amino acid sequence selected from the group consisting of any one of SEQ ID NOs: 1-30, or

5 b) an amino acid sequence consisting of at least 5 contiguous amino acid residues from any one of SEQ ID NOs: 1-30, or

c) an amino acid sequence having a sequence identity of at least 60% with the amino acid sequence of a),

10 d) an amino acid sequence having a sequence identity of at least 60% with the amino acid sequence of b), or

e) an assembly of amino acids derived from any one of SEQ ID NOs: 1-30 which has essentially the same 3D conformation as in the protein from which said assembly is derived so as to constitute a B-cell epitope, said polypeptide being antigenic in a mammal.

15 2. The polypeptide according to claim 1, wherein the at least 5 contiguous amino acids

are at least or exactly or at most 6, such as at least or exactly or at most 7, at least or exactly or at most 8, at least or exactly or at most 9, at least or exactly or at most 10, at least or exactly or at most 11, at least or exactly or at most 12, at least or exactly or at most 13, at least or exactly or at most 14, at least or exactly or at most 15, at least or exactly or

20 at most 16, at least or exactly or at most 17, at least or exactly or at most 18, at least or exactly or at most 19, at least or exactly or at most 20, at least or exactly or at most 21, at least or exactly or at most 22, at least or exactly or at most 23, at least or exactly or at most 24, at least or exactly or at most 25, at least or exactly or at most 26, at least or exactly or at most 27 at least or exactly or at most 28, at least or exactly or at most 29, at least or

25 exactly or at most 30, at least or exactly or at most 31, at least or exactly or at most 32, at least or exactly or at most 33, at least or exactly or at most 34, at least or exactly or at most 35 and at least or exactly or at most 36, at least or exactly or at most 37, at least or exactly or at most 38, at least or exactly or at most 39, at least or exactly or at most 40, at least or exactly or at most 41, at least or exactly or at most 42, at least or exactly or at most 43, at

30 least or exactly or at most 44, at least or exactly or at most 45, at least or exactly or at most 46, at least or exactly or at most 47, at least or exactly or at most 48, at least or exactly or at most 49, at least or exactly or at most 50, at least or exactly or at most 51, at least or exactly or at most 52, at least or exactly or at most 53, at least or exactly or at most 54, at least or exactly or at most 55 and at least or exactly or at most 56, at least or exactly or at

35 most 57, at least or exactly or at most 58, at least or exactly or at most 59, or at least or exactly or at most 60 contiguous amino acid residues.

3. The polypeptide according to claim 1 or 2, wherein the sequence identity with the amino acid sequence of a) is at least 65%, such as at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, and at least 99%.

5 4. The polypeptide according to claim 1 or 2, wherein the sequence identity with the amino acid sequence of b) is at least 60%, such as at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, and at least 99%.

5. The polypeptide according to any one of the preceding claims, wherein the at least 5
10 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, and 56 in any one of SEQ ID NOs: 1-30.

6. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous
15 amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 57, 58, 59, 60, 61, and 62 in any one of SEQ ID NOs: 2-30.

7. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 63, 64, 65, 66, 67, 68, and 69 in any one of SEQ ID NOs: 4-30.

8. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, and 104 in any one of SEQ ID NOs: 5-30.

9. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 105, 106, 107, 108, 109, and 110 in any one of SEQ ID NOs: 6-30.

10. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121 and 122 in any one of
30 SEQ ID NOs: 7-30.

11. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, and 135 in any one of SEQ ID NOs: 8-30.

5 12. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acids 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, and 155 in any one of SEQ ID NOs: 9-30.

10 13. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 156, 157, and 158 in any one of SEQ ID NOs: 10-30.

14. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 159, 160, 161, and 162 in any one of SEQ ID NOs: 11-30.

15 15. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 20 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, and 226 in any one of SEQ ID NOs: 12-30.

16. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 227, 228, 229, 230, 231, 232, 233, and 234 in any one of SEQ ID NOs: 13-30.

25 17. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, and 249 in any one of SEQ ID NOs: 14-30.

30 18. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 271, 272, 273, 274,

275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, and 290 in any one of SEQ ID NOs: 15-30.

19. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, and 352 in any one of SEQ ID NOs: 16-30.

20. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, and 363 in any one of SEQ ID NOs: 17-30.

21. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, and 416 in any one of amino acid residues in any one of SEQ ID NOs: 18-30.

22. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, and 441 in any one of SEQ ID NOs: 19-30.

23. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600,

601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 5 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, and 707 in any one of SEQ ID NOs: 20-30.

24. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino 10 acid residues 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, and 723 in any one of SEQ ID NOs: 21-30.

25. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to amino acid residue 724 in any one of SEQ ID NOs: 22-30.

15 26. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, and 750 in any one of SEQ ID NOs: 23-30.

20 27. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 25 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833, 834, 835, 836, 837, 838, 839, 840, 841, 842, 843, 844, 845, 846, 847, 848, 849, 850, 851, 852, 853, 854, 855, 856, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, 873, 874, 875, 876, 877, 878, 879, 880, 881, 882, 883, 884, 885, 886, 887, 888, 889, 890, 891, 30 892, 893, 894, 895, 896, 897, 898, 899, 900, 901, and 902 in any one of SEQ ID NOs: 24-30.

28. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 903, 904, 905, 906, 907, 908, 909, 910, 911, 912, 913, 914, 915, 916, 917,

918, 919, 920, 921, 922, 923, 924, 925, 926, 927, 928, 929, 930, 931, 932, 933, 934, 935, 936, 937, 938, 939, 940, 941, 942, 943, 944, 945, 946, 947, 948, 949, 950, 951, 952, 953, 954, 955, 956, 957, 958, 959, 960, 961, 962, 963, 964, 965, 966, 967, 968, 969, and 970 in any one of SEQ ID NOs: 25-30.

5 29. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 971, 972, 973, 974, 975, 976, 977, 978, 979, 980, 981, 982, 983, 984, 985, 986, 987, 988, 989, 990, 991, 992, 993, 994, 995, 996, 997, 998, 999, 1000, 1001, 1002, 1003, 1004, 1005, 1006, 1007, 1008, 1009, 1010, 1011, 1012, 1013, 1014, 1015, 1016,
10 1017, 1018, 1019, 1020, 1021, 1022, 1023, 1024, 1025, 1026, 1027, 1028, 1029, 1030, 1031, 1032, 1033, 1034, 1035, 1036, 1037, 1038, 1039, 1040, 1041, 1042, 1043, 1044, 1045, 1046, 1047, 1048, 1049, 1050, 1051, 1052, 1053, 1054, 1055, 1056, 1057, 1058, 1059, 1060, 1061, 1062, 1063, 1064, 1065, 1066, and 1067 in any one of SEQ ID NOs: 26-30.

15 30. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 1068, 1069, 1070, 1071, 1072, 1073, 1074, 1075, 1076, 1077, 1078, 1079, 1080, 1081, 1082, 1083, 1084, 1085, 1086, 1087, 1088, 1089, 1090, 1091, 1092, 1093, 1094, 1095, 1096, 1097, 1098, 1099, 1100, 1101, 1102, 1103, 1104, 1105, and 1106 in any
20 one of SEQ ID NOs: 27-30.

31. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 1107, 1108, 1109, 1110, 1111, 1112, 1113, 1114, 1115, 1116, 1117, 1118, 1119, 1120, 1121, 1122, 1123, 1124, 1125, 1126, 1127, 1128, 1129, 1130, 1131, 1132,
25 1133, 1134, 1135, 1136, 1137, 1138, 1139, 1140, 1141, 1142, 1143, 1144, 1145, 1146, 1147, 1148, 1149, 1150, 1151, 1152, 1153, 1154, 1155, 1156, 1157, 1158, 1159, 1160, 1161, 1162, 1163, 1164, 1165, 1166, 1167, 1168, 1169, 1170, 1171, 1172, 1173, 1174, 1175, 1176, 1177, 1178, 1179, 1180, 1181, 1182, 1183, 1184, 1185, 1186, 1187, 1188, 1189, 1190, 1191, 1192, 1193, 1194, 1195, 1196, 1197, 1198, 1199, 1200, 1201, 1202,
30 1203, 1204, 1205, 1206, 1207, 1208, 1209, 1210, 1211, 1212, 1213, 1214, 1215, 1216, 1217, 1218, 1219, 1220, 1221, 1222, 1223, and 1224 in any one of SEQ ID NOs: 28-30.

32. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous amino acid residues has an N-terminal amino acid residue corresponding to any one of amino acid residues 1225, 1226, 1227, 1228, 1229, 1230, 1231, 1232, 1233, 1234, 1235, 1236,
35 1237, 1238, 1239, 1240, 1241, 1242, 1243, 1244, 1245, 1246, 1247, 1248, 1249, 1250,

1251, 1252, 1253, 1254, 1255, 1256, 1257, 1258, 1259, 1260, 1261, 1262, 1263, 1264, 1265, 1266, 1267, 1268, 1269, 1270, 1271, 1272, 1273, 1274, 1275, 1276, 1277, 1278, 1279, and 1280 in any one of SEQ ID NOs: 29-30.

33. The polypeptide according to any one of claims 1-4, wherein the at least 5 contiguous
5 amino acid residues has an N-terminal amino acid residue corresponding to any one of amino
acid residues 1281, 1282, 1283, 1284, 1285, 1286, 1287, 1288, 1289, 1290, 1291, 1292,
1293, 1294, 1295, 1296, 1297, 1298, 1299, 1300, 1301, 1302, 1303, 1304, 1305, 1306,
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20 2007, 2008, 2009, 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2017, 2018, 2019, 2020,
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34. The polypeptide according to any one of the preceding claims, which is fused or conjugated to an immunogenic carrier molecule.

35. The polypeptide according to claim 37, wherein the immunogenic carrier molecule is a polypeptide that induces T-helper lymphocyte responses in a majority of humans, such as immunogenic carrier proteins selected from the group consisting of keyhole limpet hemocyanin or a fragment thereof, tetanus toxoid or a fragment thereof, diphtheria toxoid or a fragment thereof.

36. The polypeptide according to any one of the preceding claims, which is capable of inducing an adaptive immune response against the polypeptide in a mammal, in particular in a human being.

37. The polypeptide according to claim 36, which is capable of inducing, in the mammal, a protective adaptive immune response against infection with *A. baumannii*.

38. The polypeptide according to claim 36 or 37, which induces a humoral and/or a cellular immune response.

39. An isolated nucleic acid fragment, which comprises

i) a nucleotide sequence encoding a polypeptide according to any one of the preceding claims, or

ii) a nucleotide sequence consisting of the amino acid encoding part of any one of SEQ ID NOs: 31-90.

iii) a nucleotide sequence consisting of at least 10 consecutive nucleotides in the amino acid encoding part of any one of SEQ ID NOs: 31-90,

iv) a nucleotide sequence having a sequence identity of at least 60% with the nucleotide sequence in i) or ii),

5 v) a nucleotide sequence having a sequence identity of at least 60% with the nucleotide sequence in iii),

vi) a nucleotide sequence complementary to the nucleotide sequence in i)-v), or

vii) a nucleotide sequence which hybridizes under stringent conditions with the nucleotide sequence in i)-vi).

10 40. The nucleic acid fragment according to claim 39, which is a DNA or an RNA fragment.

41. The nucleic acid fragment according to claim 39 or 40, wherein the nucleotide sequence consists of at least 11, such as at least or exactly or at most 12, at least or exactly or at most 13, at least or exactly or at most 14, at least or exactly or at most 15, at least or exactly or at most 16, at least or exactly or at most 17 at least or exactly or at most 18, at
15 least or exactly or at most 19, at least or exactly or at most 20, at least or exactly or at most 21, at least or exactly or at most 22, at least or exactly or at most 23, at least or exactly or at most 24, at least or exactly or at most 25, at least or exactly or at most 26, at least or exactly or at most 27, at least or exactly or at most 28, at least or exactly or at most 29, at least or exactly or at most 30, at least or exactly or at most 31, at least or exactly or at most
20 32, at least or exactly or at most 33, at least or exactly or at most 34, at least or exactly or at most 35, at least or exactly or at most 36, at least or exactly or at most 37, at least or exactly or at most 38, at least or exactly or at most 39, at least or exactly or at most 40, at least or exactly or at most 41, at least or exactly or at most 42, at least or exactly or at most 43, at least or exactly or at most 44, at least or exactly or at most 45, at least or exactly or at most 46, at least or exactly or at most 47, at least or exactly or at most 48, at least or exactly or at most 49, at least or exactly or at most 50, at least or exactly or at most 51, at least or exactly or at most 52, at least or exactly or at most 53, at least or exactly or at most 54, at least or exactly or at most 55, at least or exactly or at most 56, at least or exactly or at most 57, at least or exactly or at most 58, at least or exactly or at most 59, at least or
25 exactly or at most 60, at least or exactly or at most 61, at least or exactly or at most 62, at least or exactly or at most 63, at least or exactly or at most 64, at least or exactly or at most 65, at least or exactly or at most 66, at least or exactly or at most 67, at least or exactly or at most 68, at least or exactly or at most 69, at least or exactly or at most 70, at least or exactly or at most 71, at least or exactly or at most 72, at least or exactly or at most 73, at least or exactly or at most 74, at least or exactly or at most 75, at least or exactly or at most 76, at least or exactly or at most 77, at least or exactly or at most 78, at least or exactly or at most 79, at least or exactly or at most 80, at least or exactly or at most 81, at least or
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[illegible]

42. The nucleic acid fragment according to any one of claims 39-41, wherein the sequence identity with the nucleotide sequence in i) or ii) is at least 65%, such as at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, and at least 99%.
43. The nucleic acid fragment according to any one of claims 39-41, wherein the sequence identity with the nucleotide sequence in iii) is at least 65%, such as at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, and at least 99%.
44. A vector comprising the nucleic acid according to any one of claims 39-43, such as a cloning vector or an expression vector.
45. The vector according to claim 44, which comprises in operable linkage and in the 5'-3' direction, an expression control region comprising an enhancer/promoter for driving expression of the nucleic acid fragment defined in claim 39-i), optionally a signal peptide coding sequence, a nucleotide sequence defined in claim 39-i), and optionally a terminator.
46. The vector according to claim 44 or 45, wherein the expression control region drives expression in prokaryotic cell such as a bacterium, e.g. in E coli.
47. The vector according to claim any one of claims 44-46, which is capable of autonomous replication.
48. The vector according to any one of claims 44-47, which is capable of being integrated into the genome of a host cell.
49. The vector according to any one of claims 44-47, which is incapable of being integrated into the genome of a mammalian host cell.
50. The vector according to any one of claims 44-49, which is selected from the group consisting of a virus, such as a attenuated virus, a bacteriophage, a plasmid, a minichromosome, and a cosmid.
51. A cell which is transformed so as to carry the vector according to any one of claims 46-49.

52. The transformed cell according to claim 51, which is capable of replicating the nucleic acid fragment defined in claim 39-i).

53. The transformed cell according to claim 51, which is capable of expressing the nucleic acid fragment defined in claim 39-i).

5 54. The transformed cell according to any one of claims 51-53, which is selected from a prokaryotic cell and a eukaryotic cell.

55. The transformed cell according to any one of claims 51-53, which is a bacterial cell selected from the group consisting of Escherichia (such as E. coli.), Bacillus (e.g. Bacillus subtilis), Salmonella, and Mycobacterium, preferably non-pathogenic, e.g. M. bovis BCG.

10 56. The transformed cell according to any one of claims 51-55, which is stably transformed by having the nucleic acid defined in claim 39-i) stably integrated into its genome.

57. The transformed cell according to any one of claims 51-56, which secretes or carries on its surface the polypeptide according to any one of claims 1-38.

15 58. The transformed cell according to claim 57, wherein the cell is a bacterium and secretion is into the periplasmic space.

59. A cell line derived from a transformed cell according to any one of claims 51-58.

60. A pharmaceutical composition comprising a polypeptide according to any one of claims 1-38, a nucleic acid fragment according to any one of claims 39-43, a vector according to any
20 one of claims 44-50, or a cell according to any one of claims 51-58, and a pharmaceutically acceptable carrier, vehicle or diluent.

61. The pharmaceutical composition according to claim 60, which further comprises an immunological adjuvant.

62. The pharmaceutical composition according to claim 61, wherein the adjuvant is an
25 aluminium based adjuvant.

63. A method for inducing immunity in an animal by administering at least once an immunogenically effective amount of a polypeptide according to any one of claims 1-38, a

nucleic acid fragment according to any one of claims 39-43, a vector according to any one of claims 44-50, a cell according to any one of claims 51-58, or a pharmaceutical composition according to any one of claims 59-62 so as to induce adaptive immunity against *A. baumannii* in the animal.

5 64. The method according to claim 63, wherein, when the polypeptide according to any one of claim 1-38 or a composition comprising said polypeptide is administered, the animal receives between 0.5 and 5,000 µg of the polypeptide according to any one of claims 1-38 per administration.

10 65. The method according to claim 63 or 64, wherein the animal receives a priming administration and one or more booster administrations.

66. The method according to any one of claims 63-65, wherein the animal is a human being.

67. The method according to any one of claims 63-66, wherein the administration is for the purpose of inducing protective immunity against *A. baumannii*.

15 68. The method according to claim 67, wherein the protective immunity is effective in reducing the risk of attracting infection with *A. baumannii* or is effective in treating or ameliorating infection with *A. baumannii*.

20 69. The method according to claim 63, wherein the administration is for the purpose of inducing antibodies specific for *A. baumannii* and wherein said antibodies or B-lymphocytes producing said antibodies are subsequently recovered from the animal.

70. The method according to claim 63, wherein the administration is for the purpose of inducing antibodies specific for *A. baumannii* and wherein B-lymphocytes producing said antibodies are subsequently recovered from the animal and used for preparation of monoclonal antibodies.

25 71. A polyclonal antibody in which the antibodies specifically bind to at least one polypeptide according to any one of claims 1-38, and which is essentially free from antibodies binding specifically to other *A. baumannii* polypeptides.

72. An isolated monoclonal antibody or antibody analogue which binds specifically to a polypeptide according to any one of claims 1-38.

73. The isolated monoclonal antibody or antibody analogue according to claim 72, which is a monoclonal antibody selected from a multi-domain antibody such as a murine antibody, a chimeric antibody such as a humanized antibody, a fully human antibody, and single-domain antibody of a llama or a camel, or which is an antibody analogue selected from a fragment of an antibody such as an Fab or an F(ab')₂, and an scFV.

74. A pharmaceutical composition comprising an antibody according to any one of claims 71-73 and a pharmaceutically acceptable carrier, vehicle or diluent.

75. A method for prophylaxis, treatment or amelioration of infection with *A. baumannii*, in particular infection with multi-resistant *A. baumannii*, comprising administering a therapeutically effective amount of an antibody according to any one of claims 71-73 or a pharmaceutical composition according to claim 74 to an individual in need thereof.

76. A method for determining, quantitatively or qualitatively, the presence of *A. baumannii* in a sample, the method comprising contacting the sample with an antibody according to any one of claims 71-73 and detecting the presence of antibody bound to material in the sample.

77. A method for determining, quantitatively or qualitatively, the presence of antibodies specific for *A. baumannii*, in a sample, the method comprising contacting the sample with a polypeptide according to any one of claims 1-38 and detecting the presence of antibody said polypeptide.

78. A method for determining, quantitatively or qualitatively, the presence of a nucleic acid characteristic of *A. baumannii*, in particular the presence of a nucleic acid characteristic of multi-resistant *A. baumannii*, in a sample, the method comprising contacting the sample with a nucleic acid fragment according to any one of claims 39-43 and detecting the presence of nucleic acid in the sample that hybridized to said nucleic acid fragment.

79. The method according to claim 78, which includes at least one step of molecular amplification of the nucleic acid which is to be detected in the sample, for instance a step of PCR amplification.

80. A method for the preparation of the polypeptide according to any one of claims 1-38, comprising
- culturing a transformed cell according to claim 50-58, insofar as these depend on claim 56 under conditions that facilitate that the transformed cell expresses the nucleic acid fragment according to claim 39-i) and any one of claims 40-43 insofar as these depend on

claim 39-i) and subsequently recovering said polypeptide, or
- preparing said polypeptide by means of solid or liquid phase peptide synthesis.

81. A method for determining whether a substance, such as an antibody, is potentially useful for treating infection with *A. baumannii*, the method comprising contacting the polypeptide according to any one of claims 1-38 with the substance and subsequently establishing whether the substance has at least one of the following characteristics:

- 1) the ability to bind specifically to said polypeptide,
- 2) the ability to compete with said polypeptide for specific binding to a ligand/receptor,
- 3) the ability to specifically inactivate said polypeptide.

82. A method for determining whether a substance, such as a nucleic acid, is potentially useful for treating infection with *A. baumannii*, the method comprising contacting the substance with the nucleic acid fragment of any one of claims 39-43 and subsequently establishing whether the substance has either the ability to

- 1) bind specifically to the nucleic acid fragment, or
- 2) bind specifically to a nucleic acid that hybridizes specifically with the nucleic acid fragment.

83. The polypeptide according to any one of claims 1-38 for use as a pharmaceutical.

84. The polypeptide according to any one of claims 1-38 for use as a pharmaceutical in the treatment, prophylaxis or amelioration of infection with *A. baumannii*.

85. The nucleic acid fragment according to any one of claims 39-43 or the vector according to any one of claims 44-50 for use as a pharmaceutical.

86. The nucleic acid fragment according to any one of claims 39-43 or the vector according to any one of claims 44-50 for use as a pharmaceutical in the treatment, prophylaxis or amelioration of infection with *A. baumannii*.

87. The cell according to any one of claims 50-58 for use as a pharmaceutical.

88. The cell according to any one of claims 50-58 for use as a pharmaceutical in the treatment, prophylaxis or amelioration of infection with *A. baumannii*.

89. The antibody, antibody fragment or antibody analogue according to any one of claims 71-73 for use as a pharmaceutical.

90. The antibody, antibody fragment or antibody analogue according to any one of claims 71-73 for use as a pharmaceutical in the treatment, prophylaxis or amelioration of infection with *A. baumannii*.