TOLEROGENIC SYNTHETIC NANOCARRIERS FOR REGULATING INNATE IMMUNE RESPONSES

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ABSTRACT

Disclosed are synthetic nanocarrier methods, and related compositions, comprising administering B cell and/or MHC Class II-restricted epitopes of an antigen and immunosuppressants in order to reduce antigen-specific activation of innate immune cells.
Fig. 1

Fig. 2
**RELATED APPLICATIONS**


**FIELD OF THE INVENTION**

[0002] This invention relates to methods of administering synthetic nanocarrier compositions with immunosuppressants and B cell and/or MHC Class II-restricted epitopes of an antigen that reduce antigen-specific innate immune responses, and related compositions.

**BACKGROUND OF THE INVENTION**

[0003] Conventional strategies for generating immunosuppression associated with an undesired immune response are based on broad-acting immunosuppressive drugs. Additionally, in order to maintain immunosuppression, immunosuppressant drug therapy is generally a life-long proposition. Unfortunately, the use of broad-acting immunosuppressants are associated with a risk of severe side effects, such as tumors, infections, nephrotoxicity and metabolic disorders. Accordingly, new immunosuppressant therapies would be beneficial.

**SUMMARY OF THE INVENTION**

[0004] In one aspect, a method comprising administering to a subject a composition according to a protocol that was previously shown to suppress antigen-specific activation of innate immune cells in one or more test subjects; wherein the composition comprises:

[0005] (i) a first population of synthetic nanocarriers coupled to immunosuppressants; and

[0006] (ii) a second population of synthetic nanocarriers coupled to B cell and/or MHC Class II-restricted epitopes of an antigen is provided. In another aspect, a method comprising: suppressing antigen-specific activation of innate immune cells in a subject by administering to the subject a composition that comprises: (i) a first population of synthetic nanocarriers coupled to immunosuppressants, and (ii) a second population of synthetic nanocarriers coupled to B cell and/or MHC Class II-restricted epitopes of an antigen is provided. In another aspect, a method comprising: administering to a subject a composition that comprises: (i) a first population of synthetic nanocarriers coupled to immunosuppressants, and (ii) a second population of synthetic nanocarriers coupled to B cell and/or MHC Class II-restricted epitopes of an antigen is provided. In one embodiment, the composition is in an amount effective to suppress antigen-specific activation of innate immune cells in the subject. In another embodiment, the composition is administered in an amount effective to suppress antigen-specific activation of innate immune cells in the subject.

[0007] In another embodiment, the first population and the second population are the same population. In another embodiment, the first population and the second population are different populations.

[0008] In another embodiment, the B cell and/or MHC Class II-restricted epitopes are bound by antibodies and form complexes with the antibodies.

[0009] In another embodiment, the method further comprises providing or identifying the subject.

[0010] In another embodiment, the antigen is a therapeutic protein, an autoantigen, an allergen, or is associated with an inflammatory disease, an autoimmune disease, organ or tissue rejection or graft versus host disease.

[0011] In another embodiment, the method further comprises assessing antigen-specific activation of innate immune cells in the subject prior to and/or after the administration of the composition. In another embodiment, the assessment is performed by obtaining a sample from the subject and determining antigen-specific activation of innate immune cells in the sample.

[0012] In another embodiment, the subject has or is at risk of having an inflammatory disease, an autoimmune disease, an allergy, organ or tissue rejection or graft versus host disease. In another embodiment, the subject has undergone or will undergo transplantation. In another embodiment, the subject has or is at risk of having an undesired innate immune response against a therapeutic protein that is being administered or will be administered to the subject.

[0013] In another embodiment, one or more maintenance doses of the composition comprising the first population and second population of synthetic nanocarriers are administered to the subject.

[0014] In another embodiment, the administering is by intravenous, intraperitoneal, transmucosal, oral, subcutaneous, pulmonary, intranasal, intradermal or intramuscular administration. In another embodiment, the administering is by inhalation or intravenous, subcutaneous or transmucosal administration.

[0015] In another embodiment, the method further comprises administering a transplantable graft or therapeutic protein. In another embodiment, the administering of the transplantable graft or therapeutic protein, when the therapeutic protein is provided as one or more cells, is by parenteral, intraarterial, intranasal or intravenous administration or by injection to lymph nodes or anterior chamber of the eye or by local administration to an organ or tissue of interest.

[0016] In another embodiment, the immunosuppressants comprise a statin, an mTOR inhibitor, a TGF-β signaling agent, a corticosteroid, an inhibitor of mitochondrial function, a P38 inhibitor, an NF-κB inhibitor, an adenosine receptor agonist, a prostaglandin E2 agonist, a phosphodiesterase 4 inhibitor, an HDAC inhibitor or a proteasome inhibitor. In another embodiment, the mTOR inhibitor is rapamycin or a rapamycin analog.

[0017] In another embodiment, the load of the immunosuppressants and/or antigens on average across the first and/or second population of synthetic nanocarriers is between 0.0001% and 50% (weight/weight). In another embodiment, the load of the immunosuppressants and/or antigens on average across the first and/or second population of synthetic nanocarriers is between 0.1% and 10%.
In another embodiment, the synthetic nanocarriers of the first population and/or second population comprise lipid nanoparticles, polymeric nanoparticles, metallic nanoparticles, surfactant-based emulsions, dendrimers, buckyballs, nanowires, virus-like particles or peptide or protein particles. In another embodiment, the synthetic nanocarriers of the first population and/or second population comprise lipid nanoparticles. In another embodiment, the synthetic nanocarriers of the first population and/or second population comprise liposomes. In another embodiment, the synthetic nanocarriers of the first population and/or second population comprise metallic nanoparticles. In another embodiment, the metallic nanoparticles comprise gold nanoparticles. In another embodiment, the polymeric nanoparticles comprise a polyester, a polyester coupled to a polyether, polyamino acid, polycarbonate, polyacetal, polyketel, polysaccharide, polyethyleneoxide or polyethyleneamidine. In another embodiment, the polyelectrolyte comprises poly(lactic acid), poly(glycolic acid), poly(lactic-co-glycolic acid) or polycaprolactone. In another embodiment, the polymeric nanoparticles comprise a polyester and a polyester coupled to a polyether. In another embodiment, the polyelectrolyte comprises polyethylene glycol or polypropylene glycol.

In another embodiment, the mean of a particle size distribution obtained using dynamic light scattering of the synthetic nanocarriers of the first and/or second population is a diameter greater than 100 nm. In another embodiment, the diameter is greater than 150 nm. In another embodiment, the diameter is greater than 200 nm. In another embodiment, the diameter is greater than 250 nm. In another embodiment, the diameter is greater than 300 nm. In another embodiment, the aspect ratio of the synthetic nanocarriers of the first population and/or second population is greater than 1:1, 1:1.5, 1:2, 1:3, 1:5, 1:7 or 1:10.

In another aspect, a composition comprising: (i) a first population of synthetic nanocarriers coupled to immunosuppressants; (ii) a second population of synthetic nanocarriers coupled to B cell and/or MHC Class II-restricted epitopes of an antigen; and a pharmaceutically acceptable excipient is provided. In another aspect, a composition comprising: (i) a first population of synthetic nanocarriers coupled to immunosuppressants; (ii) a second population of synthetic nanocarriers coupled to B cell and/or MHC Class II-restricted epitopes of an antigen; and (iii) a transplanted graft or therapeutic protein; and optionally (iv) a pharmaceutically acceptable excipient is provided. In another aspect, a composition comprising: (i) a first population of synthetic nanocarriers coupled to immunosuppressants; and (ii) a second population of synthetic nanocarriers coupled to B cell and/or MHC Class II-restricted epitopes of an antigen; for use in therapy or prophylaxis is provided. In another aspect, a composition comprising: (i) a first population of synthetic nanocarriers coupled to immunosuppressants; and (ii) a second population of synthetic nanocarriers coupled to B cell and/or MHC Class II-restricted epitopes of an antigen, for use in a method of:

- a treatment, comprising the step of administering said composition to a subject and assessing the antigen-specific activation of innate immune cells in the subject prior to and/or after the administration of the composition;
peptides that comprise the aforementioned epitopes but additional amino acids that flank one or both ends of the epitope(s) can be coupled to the synthetic nanocarriers. In another embodiment, the epitopes themselves are coupled to the synthetic nanocarriers.

**BRIEF DESCRIPTION OF FIGURES**

[0036] FIG. 1 shows results from a flow cytometric analysis of Treg cells.

[0037] FIG. 2 demonstrates a reduction in the number of eosinophils in lavage samples from animal subjects treated with synthetic nanocarriers comprising OVA_{323-335} and immunosuppressant.

**DETAILED DESCRIPTION OF THE INVENTION**

[0038] Before describing the present invention in detail, it is to be understood that this invention is not limited to particularly exemplified materials or process parameters as such may, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments of the invention only, and is not intended to be limiting of the use of alternative terminology to describe the present invention.

[0039] All publications, patents and patent applications cited herein, whether supra or infra, are hereby incorporated by reference in their entirety for all purposes.

[0040] As used in this specification and the appended claims, the singular forms "a," "an" and "the" include plural references unless the content clearly dictates otherwise. For example, reference to "a polymer" includes a mixture of two or more such molecules or a mixture of differing molecular weights of a single polymer species, reference to "a synthetic nanocarrier" includes a mixture of two or more such synthetic nanocarriers or a plurality of such synthetic nanocarriers, reference to "a DNA molecule" includes a mixture of two or more such DNA molecules or a plurality of such DNA molecules, reference to "an immunosuppressant" includes a mixture of two or more such materials or a plurality of immunosuppressant molecules, and the like.

[0041] As used herein, the term "comprise" or variations thereof such as "comprises" or "comprising" are to be read to indicate the inclusion of any recited integer (e.g. a feature, element, characteristic, property, method/process step or limitation) or group of integers (e.g. features, element, characteristics, properties, method/process steps or limitations) but not the exclusion of any other integer or group of integers. Thus, as used herein, the term "comprising" is inclusive and does not exclude additional, unrecited integers or method/process steps.

[0042] In embodiments of any of the compositions and methods provided herein, "comprising" may be replaced with "consisting essentially of or of consisting of." The phrase "consisting essentially of is used herein to require the specified integer(s) or steps as well as those which do not materially affect the character or function of the claimed invention. As used herein, the term "consisting of" is used to indicate the presence of the recited integer (e.g. a feature, element, characteristic, property, method/process step or limitation) or group of integers (e.g. features, element, characteristics, properties, method/process steps or limitations) alone.

**A. INTRODUCTION**

[0043] Generally, antibody responses mediate the clearance of dangerous pathogens using several systems including direct recognition and opsonization of the target leading to complement activation, enhancement of phagocytosis and activation of cells of the innate immune system. Exacerbated antibody responses to certain targets, however, may lead to serious disorders like allergies and autoimmune disorders. It is believed that delivering immunosuppressants and B cell epitopes that are recognized by antibodies can reduce antigen-specific activation of innate immune cells and result in beneficial tolerogenic immune responses specific to the antigens. Generally, and without wishing to be bound by any particular theory, antibodies recognize and bind antigen. The Fe regions of these antibodies can then be recognized and bound to receptors on innate immune cells leading to their activation. With the compositions provided herein, the innate immune cells can recognize the Fe regions of the antibodies in an immunosuppressive environment and, thus, activation of the innate immune cells can be reduced. In addition, the compositions and methods provided herein can also allow for more targeted immune effects by, for example, allowing for the targeted delivery to immune cells of interest. Thus, the compositions and methods can achieve immune suppression in a more directed manner. Thus, the compositions provided herein can reduce off-target effects and toxicity that usually occur with the use of broader acting immunosuppressive therapies. Further, it has been found that compositions of the invention that comprise immunosuppressant and MHC Class II-restricted epitopes of an antigen can also be used to reduce innate immune responses. As shown below in the examples, synthetic nanocarrier compositions comprising immunosuppressant and antigen were effective in reducing the number of eosinophils in lavage samples in an allergic asthma animal model.

[0044] Thus, the compositions of the invention can be used to treat or prevent a number of diseases, disorders or conditions where a reduction in the number and/or activity of innate immune cells would provide a benefit. Such subjects include those who have or are at risk of having an allergy, autoimmune disease, an inflammatory disease, organ or tissue rejection or graft versus host disease. Such subjects also include those who have undergone or will undergo transplantation. Such subjects also include those that have received, are receiving or will receive a therapeutic protein against which the undesired immune responses are generated or are expected to be generated. The compositions of the invention can effectively target immune cells of interest and lead to immune suppression. In some embodiments, this occurs through the production of tolerogenic cytokines or a reduction in the production of undesired cytokines.

[0045] The inventors have unexpectedly and surprisingly discovered that the problems and limitations noted above can be overcome by practicing the invention disclosed herein. In particular, the inventors have unexpectedly discovered that it is possible to provide synthetic nanocarrier compositions, and related methods, that induce a tolerogenic immune response (e.g., the reduction or inhibition of antigen-specific activation of innate immune cells). The method described herein includes administering to a subject a composition that comprises (i) a first population of synthetic nanocarriers coupled to immunosuppressants, and (ii) a second population of synthetic nanocarriers coupled to B cell and/or MHC Class II-restricted epitopes of an antigen. Preferably, the composition is in an amount effective to reduce antigen-specific activation of innate immune cells in the subject to the antigen. In another aspect, a method comprising reducing antigen-specific acti-
viation of innate immune cells in a subject by administering a composition that comprises (i) a first population of synthetic nanocarriers coupled to immunosuppressants, and (ii) a second population of synthetic nanocarriers coupled to B cell and/or MHC Class II-restricted epitopes of an antigen is provided. In another aspect, a method comprising administering to a subject a composition according to a protocol that was previously shown to reduce antigen-specific activation of innate immune cells in one or more test subjects wherein the composition comprises (i) a first population of synthetic nanocarriers that are coupled to immunosuppressants, and (ii) a second population of synthetic nanocarriers coupled to B cell and/or MHC Class II-restricted epitopes of an antigen is provided.

In embodiments, the compositions provided may also be administered as one or more maintenance doses to a subject. In such embodiments, the compositions provided are administered such that the generation of an undesired immune response (e.g., antigen-specific innate immune cell activation) is reduced for a certain length of time. Examples of such lengths of time are provided elsewhere herein.

In yet another aspect, the compositions comprising the first population and second population of synthetic nanocarriers are also provided. In embodiments, the compositions further comprise a transplanted graft or a therapeutic protein that may or may not be coupled to the first or second population of synthetic nanocarriers or another population of synthetic nanocarriers.

In another aspect, dosage forms of any of the compositions herein are provided. Such dosage forms may be administered to a subject, such as one in need of a reduction in antigen-specific activation of innate immune cells.

In yet another aspect, a method of (i) producing a first population of synthetic nanocarriers coupled to immunosuppressants, and (ii) producing a second population of synthetic nanocarriers coupled to B cell and/or MHC Class II-restricted epitopes of an antigen is provided. In one embodiment, the method further comprises producing a dosage form comprising the first and second populations of synthetic nanocarriers. In another embodiment, the method further comprises ensuring the second population of synthetic nanocarriers comprises B cell and/or MHC Class II-restricted epitopes that result in desired tolerogenic immune responses. In still another embodiment, the method further comprises assessing the reduction in antigen-specific activation of innate immune cells with a composition or dosage form comprising the first population and second population of synthetic nanocarriers. Such assessing may be performed in vitro or in vivo. In yet another embodiment, the method further comprises making a composition comprising the first population and second population of synthetic nanocarriers or the dosage form available to a subject for administration.

In embodiments, to ensure that a composition comprises the desired epitopes, antigens are selected that comprise the desired epitopes for coupling to the synthetic nanocarriers as provided herein. In other embodiments, to ensure that a composition comprises such antigens, tolerogenic synthetic nanocarriers coupled to an antigen are produced and tested for immune responses, such as the inhibition in innate immune cell proliferation and/or activation. The appropriate synthetic nanocarriers may then be selected.

In another aspect, the compositions or dosage forms produced by any of the methods provided herein are also provided.

The invention will now be described in more detail below.

B. DEFINITIONS

“Administering” or “administration” means providing a material to a subject in a manner that is pharmacologically useful.

“Allergens” are any substances that can cause an undesired (e.g., a Type 1 hypersensitive) immune response (i.e., an allergic response or reaction) in a subject. Allergens include, but are not limited to, plant allergens (e.g., pollen, ragweed allergen), insect allergens, insect sting allergens (e.g., bee sting allergens), animal allergens (e.g., pet allergens, such as animal dander or cat Fel d 1 antigen), latex allergens, mold allergens, fungal allergens, cosmetic allergens, drug allergens, food allergens, dust, insect venom, viruses, bacteria, etc. Food allergens include, but are not limited to milk allergens, egg allergens, nut allergens (e.g., peanut or tree nut allergens, etc. (e.g., walnuts, cashews, etc.)), fish allergens, shellfish allergens, soy allergens, legume allergens, seed allergens and wheat allergens. Insect sting allergens include allergens that are or are associated with bee stings, wasp stings, hornet stings, yellow jacket stings, etc. Insect allergens also include house dust mite allergens (e.g., Der P1 antigen) and cockroach allergens. Drug allergens include allergens that are or are associated with antibiotics, NSAIDs, anaesthetics, etc. Pollen allergens include grass allergens, tree allergens, weed allergens, flower allergens, etc. Subjects that develop or are at risk of developing an undesired immune response to any of the allergens provided herein may be treated with any of the compositions and methods provided herein. Subjects that may be treated with any of the compositions and methods provided also include those who have or are at risk of having an allergy to any of the allergens provided.

An “allergy” also referred to herein as an “allergic condition,” is any condition where there is an undesired (e.g., a Type 1 hypersensitive) immune response (i.e., allergic response or reaction) to a substance. Such substances are referred to herein as allergens. Allergies or allergic conditions include, but are not limited to, allergic asthma, hay fever, hives, eczema, plant allergies, bee sting allergies, pet allergies, latex allergies, mold allergies, cosmetic allergies, food allergies, allergic rhinitis or coryza, topical allergic reactions, anaphylaxis, atopic dermatitis, hypersensitivity reactions and other allergic conditions. The allergic reaction may be the result of an immune reaction to any allergen. In some embodiments, the allergy is a food allergy. Food allergies include, but are not limited to, milk allergies, egg allergies, nut allergies, fish allergies, shellfish allergies, soy allergies or wheat allergies.

“Amount effective” in the context of a composition or dosage form for administration to a subject refers to an amount of the composition or dosage form that produces one or more desired immune responses in the subject, for example, the reduction or inhibition of antigen-specific activation of innate immune cells. Therefore, in some embodiments, an amount effective is any amount of a composition provided herein that produces one or more of these desired immune responses. This amount can be for in vitro or in vivo purposes. For in vivo purposes, the amount can be one that a clinician would believe may have a clinical benefit for a subject in need of tolerization. Such subjects include those that have or are at risk of having an inflammatory disease, an
autoimmune disease, an allergy, organ or tissue rejection or graft versus host disease. Such subjects also include those that have undergone or will undergo transplantation. Such subjects further include those that have experienced, are experi-
encing or are expected to experience an undesired immune response against a therapeutic protein.

Amounts effective can involve only reducing the level of an undesired immune response, although in some embodiments, it involves preventing an undesired immune response altogether. Amounts effective can also involve delaying the occurrence of an undesired immune response. An amount that is effective can also be an amount of a compos-
ition provided herein that produces a desired therapeutic endpoint or a desired therapeutic result. Amounts effective, preferably, result in a tolerogenic immune response in a subject to an antigen. The achievement of any of the foregoing can be monitored by routine methods.

In some embodiments of any of the compositions and methods provided, the amount effective is one in which the desired immune response persists in the subject for at least 1 week, at least 2 weeks, at least 1 month, at least 2 months, at least 3 months, at least 4 months, at least 5 months, at least 6 months, at least 9 months, at least 1 year, at least 2 years, at least 3 years, or longer. In other embodiments of any of the compositions and methods provided, the amount effective is one which produces a measurable desired immune response, for example, a measurable decrease in an immune response (e.g., to a specific antigen), for at least 1 week, at least 2 weeks, at least 1 month, at least 2 months, at least 3 months, at least 4 months, at least 5 months, at least 6 months, at least 9 months, at least 1 year, at least 2 years, at least 3 years, or longer.

Amounts effective will depend, of course, on the particular subject being treated; the severity of a condition, disease or disorder; the individual patient parameters including age, physical condition, size and weight; the duration of the treatment; the nature of concurrent therapy (if any); the specific route of administration and like factors within the knowledge and expertise of the health practitioner. These factors are well known to those of ordinary skill in the art and can be addressed with no more than routine experimentation. It is generally preferred that a maximum dose be used, that is, the highest safe dose according to sound medical judgment. It will be understood by those of ordinary skill in the art, however, that a patient may insist upon a lower dose or tolerable dose for medical reasons, psychological reasons or for virtually any other reason.

In general, doses of the immunosuppressants and/or antigens in the compositions of the invention can range from about 10 μg/kg to about 100,000 μg/kg. In some embodiments, the doses can range from about 0.1 mg/kg to about 100 mg/kg. In still other embodiments, the doses can range from about 0.1 mg/kg to about 25 mg/kg, about 25 mg/kg to about 50 mg/kg, about 50 mg/kg to about 75 mg/kg or about 75 mg/kg to about 100 mg/kg. Alternatively, the dose can be administered based on the number of synthetic nanocarriers that provide the desired amount of immunosuppressants and/or epitopes. For example, useful doses include greater than 10⁶, 10⁷, 10⁸, 10⁹ or 10¹⁰ synthetic nanocarriers per dose. Other examples of useful doses include from about 1x10⁸ to about 1x10¹⁰, from about 1x10⁸×1x10⁸ to about 1x10¹⁰ or about 1x10¹⁰ to about 1x10¹⁰ synthetic nanocarriers per dose.

“Antigen” means a B cell antigen or T cell antigen. “Type(s) of antigens” means molecules that share the same, or substantially the same, antigenic characteristics. In some embodiments, antigens may be proteins, polypeptides, peptides, lipoproteins, glycolipids, polynucleotides, polysaccharides or are contained or expressed in cells. In some embodiments, such as when the antigens are not well defined or characterized, the antigens may be contained within a cell or tissue preparation, cell debris, cell exosomes, conditioned media, etc. An antigen can be combined with the synthetic nanocarriers in the same form as what a subject is exposed to that causes an undesired immune response but may also be a fragment or derivative thereof. When a fragment or derivative, however, a desired immune response to the form encountered by such a subject is the preferable result with the compositions and methods provided. Preferably, the antigens as provided herein comprise B cells and/or MHC Class II-restricted epitopes. The B cell epitopes may be recognized by antibodies, the Fc regions of which bind receptors on innate immune cells. In embodiments, such epitopes in the context of the compositions provided, result in the reduction or inhibition of innate immune cell activation in response to the recognition of the epitopes in an immunosuppressive environ-
ment. Whether or not this occurs can be established through measurement of macrophage activation reduction or inhibition, natural killer (NK) cell activation reduction or inhibition, mast cell, eosinophil, basophil, etc. activation reduction or inhibition, etc. using conventional techniques.

“Antigen-specific” refers to any immune response that results from the presence of the antigen, or portion thereof, or that generates molecules that specifically recognize or bind the antigen. For example, where the immune response is antigen-specific antibody production, antibodies are produced that specifically bind the antigen. As another example, where the immune response is antigen-specific innate immune cell proliferation and/or activity.

“Antigens associated” with a disease, disorder or condition provided herein are antigens that can generate an undesired immune response against, as a result of, or in con-
junction with the disease, disorder or condition; the cause of the disease, disorder or condition (or a symptom or effect thereof); and/or can generate an undesired immune response that is a symptom, result or effect of the disease, disorder or condition. Preferably, in some embodiments, the use of an antigen associated with a disease, disorder or condition, etc., in the compositions and methods provided herein will lead to a tolerogenic immune response against the antigen and/or the cells, by, on or in which the antigen is expressed. The antigens can be in the same form as expressed in a subject with the disease, disorder or condition but may also be a fragment or derivative thereof. When a fragment or derivative, however, a desired immune response to the form expressed in such a subject is the preferable result with the compositions and methods provided.

In one embodiment, the antigen is an antigen associated with an inflammatory disease, autoimmune disease, organ or tissue rejection or graft versus host disease. Such antigens include autoantigens, such as myelin basic protein, collagen (e.g., collagen type 11), human cartilage gp 39, chromogranin A, gp130-RAPS, proteolipid protein, fibril-
larin, nuclear proteins, molecular proteins (e.g., small nucle-
lar protein), thyroid stimulating factor receptor, histones, glycoprotein gp 70, ribosomal proteins, pyruvate dehydroge-

nase dehydrolipopamide acetyltransferase, hair follicle anti-
gens, human tropomyosin isoform 5, mitochondrial proteins, pancreatic β-cell proteins, myelin oligodendrocyte glycopro-


tein, insulin, glutamic acid decarboxylase (GAD), gluten, and fragments or derivatives thereof. Other autoantigens are provided in Table 1 below.

[0065] Antigens also include those associated with organ or tissue rejection. Examples of such antigens include, but are not limited to, antigens from allogeneic cells, e.g., antigens from an allogeneic cell extract and antigens from other cells, such as endothelial cell antigens.

[0066] Antigens also include those associated with an allergy. Such antigens include the allergens described elsewhere herein.

[0067] Antigens also include those associated with a transplantable graft. Such antigens are associated with a transplantable graft, or an undesired immune response in a recipient of a transplantable graft that is generated as a result of the introduction of the transplantable graft in the recipient, that can be presented for recognition by cells of the immune system and that can generate an undesired immune response. Transplant antigens include those associated with organ or tissue rejection or graft versus host disease. Transplant antigens may be obtained or derived from cells of a biological material or from information related to a transplantable graft. Transplant antigens generally include proteins, polypeptides, peptides, lipoproteins, glycolipids, nucleotides or are contained or expressed in cells. Information related to a transplantable graft is any information about a transplantable graft that can be used to obtain or derive transplant antigens. Such information includes information about antigens that would be expected to be present in or on cells of a transplantable graft such as, for example, sequence information, types or classes of antigens and/or their MHC Class I, MHC Class II or B cell presentation restrictions. Such information may also include information about the type of transplantable graft (e.g., autograft, allograft, xenograft), the molecular and cellular composition of the graft, the bodily location from which the graft is derived or to which the graft is to be transplanted (e.g., whole or partial organ, skin, bone, nerves, tendon, neurons, blood vessels, fat, cornea, etc.).

[0068] Antigens also include antigens associated with a therapeutic protein that can be presented for recognition by cells of the immune system and that can generate an undesired immune response against the therapeutic protein. Therapeutic protein antigens generally include proteins, polypeptides, peptides, lipoproteins, or are contained or expressed in, or on cells.

[0069] Antigens, can be antigens that are fully defined or characterized. However, in some embodiments, an antigen is not fully defined or characterized. Therefore, antigens, also include those that are contained within a cell or tissue preparation, cell debris, cell exosome or conditioned media and can be delivered in such form in some embodiments.

[0070] “Assessing an immune response” refers to any measurement or determination of the level, presence or absence, reduction, increase in, etc. of an immune response in vitro or in vivo. Such measurements or determinations may be performed on one or more samples obtained from a subject. Such assessing can be performed with any of the methods provided herein or otherwise known in the art.

[0071] An “at risk” subject is one in which a health practitioner believes has a chance of having a disease, disorder or condition as provided herein or is one a health practitioner believes has a chance of experiencing an undesired immune response as provided herein.

[0072] An “autoimmune disease” is any disease where the immune system mounts an undesired immune response against self (e.g., one or more autoantigens). In some embodiments, an autoimmune disease comprises an aberrant destruction of cells of the body as part of the self-targeted immune response. In some embodiments, the destruction of self manifests in the malfunction of an organ, for example, the colon or pancreas. Examples of autoimmune diseases are described elsewhere herein. Additional autoimmune diseases will be known to those of skill in the art and the invention is not limited in this respect.

[0073] “Average”, as used herein, refers to the arithmetic mean unless otherwise noted.

[0074] “B cell antigen” means any antigen that triggers an immune response in a B cell (e.g., an antigen that is specifically recognized by a B cell or a receptor thereof). In some embodiments, an antigen that is a T cell antigen is also a B cell antigen. In other embodiments, the T cell antigen is not also a B cell antigen. B cell antigens include, but are not limited to proteins, peptides, small molecules, and carbohydrates. In some embodiments, the B cell antigen comprises a non-protein antigen (i.e., not a protein or peptide antigen). In some embodiments, the B cell antigen comprises a autoantigen. In other embodiments, the B cell antigen is obtained or derived from an allergen, autoantigen, therapeutic protein, or transplantable graft.

[0075] “Concomitantly” means administering two or more substances to a subject in a manner that is correlated in time, preferably sufficiently correlated in time so as to provide a modulation in an immune response. In embodiments, concomitant administration may occur through administration of two or more substances in the same dosage form. In other embodiments, concomitant administration may encompass administration of two or more substances in different dosage forms, but within a specified period of time, preferably within 1 month, more preferably within 1 week, still more preferably within 1 day, and even more preferably within 1 hour.

[0076] “Couple” or “Coupied” or “Couples” (and the like) means to chemically associate one entity (for example a moiety) with another. In some embodiments, the coupling is covalent, meaning that the coupling occurs in the context of the presence of a covalent bond between the two entities. In non-covalent embodiments, the non-covalent coupling is mediated by non-covalent interactions including but not limited to charge interactions, affinity interactions, metal coordination, physical adsorption, host-guest interactions, hydrophobic interactions, TT stacking interactions, hydrogen bonding interactions, van der Waals interactions, magnetic interactions, electrostatic interactions, dipole-dipole interactions, and/or combinations thereof. In embodiments, encapsulation is a form of coupling.

[0077] “Derived” means prepared from a material or information related to a material but is not “obtained” from the material. Such materials may be substantially modified or processed forms of materials taken directly from a biological material. Such materials also include materials produced from information related to a biological material.

[0078] “Dosage form” means a pharmacologically and/or immunologically active material in a medium, carrier, vehicle, or device suitable for administration to a subject.

[0079] “Encapsulate” means to enclose at least a portion of a substance within a synthetic nanocarrier. In some embodiments, a substance is enclosed completely within a synthetic nanocarrier. In other embodiments, most or all of a substance
that is encapsulated is not exposed to the local environment external to the synthetic nanocarrier. In other embodiments, no more than 50%, 40%, 30%, 20%, 10% or 5% (weight/weight) is exposed to the local environment. Encapsulation is distinct from absorption, which places most or all of a substance on a surface of a synthetic nanocarrier, and leaves the substance exposed to the local environment external to the synthetic nanocarrier.

[0080] “Epitope”, also known as an antigenic determinant, is the part of an antigen that is recognized by the immune system, specifically by, for example, antibodies, B cells, or T cells. As used herein, “MHC Class I-restricted epitopes” are epitopes that are presented to immune cells by MHC class I molecules found on nucleated cells. “MHC Class II-restricted epitopes” are epitopes that are presented to immune cells by nucleated cells that have exposed to the local environment external to the synthetic nanocarrier.

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[0082] Other examples of epitopes include any of the MHC Class I-restricted, MHC Class II-restricted and B cell epitopes as provided in SEQ ID NOs: 1-943. Without wishing to being bound by any particular theory, MHC Class I-restricted epitopes include those set forth in SEQ ID NOs: 1-186, MHC Class II-restricted epitopes include those set forth in SEQ ID NOs: 187-537, and B cell epitopes include those set forth in SEQ ID NOs: 538-943. These epitopes include MHC Class I-restricted antigens, MHC Class II-restricted epitopes of allergens and B cell epitopes of autoantigens and allergens.

[0083] “Generating” means causing an action, such as an immune response (e.g., a tolerogenic immune response) to occur, either directly oneself or indirectly, such as, but not limited to, an unrelated third party that takes an action through reliance on one’s words or deeds.

[0084] “Identifying” is any action or set of actions that allows a clinician to recognize a subject as one who may benefit from the methods and compositions provided herein. Preferably, the identified subject is one who is in need of a tolerogenic immune response as provided herein. The action or set of actions may be either directly oneself or indirectly, such as, but not limited to, an unrelated third party that takes an action through reliance on one’s words or deeds.

[0085] “Immunosuppressant” means a compound that causes an immune cell, such as an APC, to have an immunosuppressive (e.g., tolerogenic) effect. An immunosuppressive effect generally refers to the production or expression of cytokines or other factors by the immune cell that reduces, inhibits or prevents an undesired immune response. When the immune cell results in an immunosuppressive effect due to
the recognition of an antigen, the immunosuppressive effect is said to be specific to the presented antigen. Such effect is also referred to herein as a tolerogenic effect. Without being bound by any particular theory, it is thought that the immunosuppressive or tolerogenic effect is a result of the immunosuppressant being delivered to the immune cell, preferably in the presence of an antigen (e.g., an administered antigen or one that is already present in vivo). Accordingly, the immunosuppressant includes compounds that provide a tolerogenic immune response to an antigen that may or may not be provided in the same composition or a different composition. In one embodiment, the immunosuppressant is one that causes an immune cell to promote a regulatory phenotype in one or more immune effector cells. For example, the regulatory phenotype may be characterized by the inhibition of the production, induction, stimulation, or recruitment of antigen-specific innate immune cells, the inhibition of the production, induction, stimulation or recruitment of antigen-specific CD4+ T cells or B cells, the inhibition of the production of antigen-specific antibodies, the production, induction, stimulation or recruitment of Treg cells (e.g., CD4+CD25highFoxP3+ Treg cells), etc. This may be the result of the conversion of innate immune cells to a regulatory phenotype or downstream effects thereof. This may also be the result of induction of FoxP3 in other immune cells, such as CD8+ T cells, macrophages and iNKT cells. In one embodiment, the immunosuppressant is one that affects the response of an APC after it processes an antigen. In another embodiment, the immunosuppressant is not one that interferes with the processing of the antigen. In a further embodiment, the immunosuppressant is not an apoptotic-signaling molecule. In another embodiment, the immunosuppressant is not a phospholipid.

[0086] Immunosuppressants include, but are not limited to, statins; mTOR inhibitors, such as rapamycin or a rapamycin analog; TGF-β signaling agents; TGF-β receptor agonists; histone deacetylase inhibitors, such as Trichostatin A; corticosteroids; inhibitors of mitochondrial function, such as rotenone; P38 inhibitors; NF-κB inhibitors, such as 6.9.10, Dexamethasone, TCPA-1, IKK VII; adenosine receptor agonists; prostaglandin E2 agonists (PGE2), such as Misoprostol; phosphodiesterase inhibitors, such as phosphodiesterase 4 inhibitor (PDE4), such as Rolipram; proteasome inhibitors; kinase inhibitors; G-protein coupled receptor agonists; G-protein coupled receptor antagonists; glucocorticoids; retinoids; cytokine inhibitors; cytokine receptor inhibitors; cytokine receptor activators; peroxisome proliferator-activated receptor antagonists; peroxisome proliferator-activated receptor agonists; histone deacetylase inhibitors; calcineurin inhibitors; phosphatase inhibitors; P38KB inhibitors, such as TGX-221; autophagy inhibitors, such as 3-Methyladenine; aryl hydrocarbon receptor inhibitors; proteasome inhibitor I (PSI); and oxidized ATPs, such as P2X receptor blockers. Immunosuppressants also include IDO, vitamin D3, cyclosporins, such as cyclosporine A, aryl hydrocarbon receptor inhibitors, resveratrol, azathioprine (Aza), 6-mercaptothiopurine (6-MP), 6-thioguanine (6-TG), FK506, sanglifehrin A, sulmaterol, mycophenolate mofetil (MMF), aspirin and other COX inhibitors, niacinamide, estriol and triptolide. In embodiments, the immunosuppressant may comprise any of the agents provided herein.

[0087] The immunosuppressant can be a compound that directly provides the immunosuppressive (e.g., tolerogenic) effect or it can be a compound that provides the immunosuppressive (e.g., tolerogenic) effect indirectly (i.e., after being processed in some way after administration). Immunosuppressants, therefore, include prodrug forms of any of the compounds provided herein.

[0088] Immunosuppressants also include nucleic acids that encode the peptides, polypeptides or proteins provided herein that result in an immunosuppressive (e.g., tolerogenic) immune response. In embodiments, therefore, the immunosuppressant is a nucleic acid that encodes a peptide, polypeptide or protein that results in an immunosuppressive (e.g., tolerogenic) immune response, and it is the nucleic acid that is coupled to the synthetic nanocarrier.

[0089] The nucleic acid may be DNA or RNA, such as mRNA. In embodiments, the inventive compositions comprise a complement, such as a full-length complement, or a degenerate (due to degeneracy of the genetic code) of any of the nucleic acids provided herein. In embodiments, the nucleic acid is an expression vector that can be transcribed when transferred into a cell line. In embodiments, the expression vector may comprise a plasmid, retrovirus, or an adenovirus amongst others. Nucleic acids can be isolated or synthesized using standard molecular biology approaches, for example by using a polymerase chain reaction to produce a nucleic acid fragment, which is then purified and cloned into an expression vector. Additional techniques useful in the practice of this invention may be found in Current Protocols in Molecular Biology 2007 by John Wiley and Sons, Inc.; Molecular Cloning: A Laboratory Manual (Third Edition) Joseph Sumbrook, Peter MacCallum Cancer Institute, Melbourne, Australia; David Russell, University of Texas Southwestern Medical Center, Dallas, Cold Spring Harbor.

[0090] In embodiments, the immunosuppressants provided herein are coupled to synthetic nanocarriers. In preferable embodiments, the immunosuppressant is an element that is in addition to the material that makes up the structure of the synthetic nanocarrier. For example, in one embodiment, where the synthetic nanocarrier is made up of one or more polymers, the immunosuppressant is a compound that is in addition and coupled to the one or more polymers. As another example, in one embodiment, where the synthetic nanocarrier is made up of one or more lipids, the immunosuppressant is again in addition and coupled to the one or more lipids. In embodiments, such as where the material of the synthetic nanocarrier also results in an immunosuppressive (e.g., tolerogenic) effect, the immunosuppressant is an element present in addition to the material of the synthetic nanocarrier that results in an immunosuppressive (e.g., tolerogenic) effect.

[0091] Other exemplary immunosuppressants include, but are not limited to, small molecule drugs, natural products, antibodies (e.g., antibodies against CD20, CD3, CD4), biologics-based drugs, carbohydrate-based drugs, nanoparticles, liposomes, RNAi, antisense nucleic acids, aptamers, methotrexate, NSAIDs; fingolimod; natalizumab; alemtuzumab; anti-CD3; tacrolimus (FK506), etc. Further immunosuppressants, are known to those of skill in the art, and the invention is not limited in this respect.

[0092] “Inflammatory disease” means any disease, disorder or condition in which undesired inflammation occurs.

[0093] “Innate immune system cells” refers to any of the cells involved in the non-specific innate immune system which includes, for example, the recruitment of immune cells by, for example, the production of cytokines, activation of complement, the identification and removal of foreign substances, activation of the adaptive immune system, inflam-
mation, etc. Such cells include leukocytes (e.g., natural killer cells, mast cells, eosinophils, basophils and phagocytes (e.g., macrophages, neutrophils and dendritic cells)).

[0094] “Load” of the immunosuppressant or antigen is the amount of the immunosuppressant or antigen coupled to a synthetic nanocarrier based on the total weight of materials in an entire synthetic nanocarrier (weight/weight). Generally, the load is calculated as an average across a population of synthetic nanocarriers. In one embodiment, the load of the immunosuppressant on average across the first population of synthetic nanocarriers is between 0.001% and 50%. In another embodiment, the load of the antigen on average across the first and/or second population of synthetic nanocarriers is between 0.0001% and 50%. In yet another embodiment, the load of the immunosuppressant and/or antigen is between 0.01% and 20%. In a further embodiment, the load of the immunosuppressant and/or antigen is between 0.1% and 10%. In still a further embodiment, the load of the immunosuppressant and/or antigen is between 1% and 10%. In yet another embodiment, the load of the immunosuppressant and/or antigen is between 0.1% and 10%. At least 2%, at least 0.5%, at least 0.3%, at least 0.5%, at least 0.5%, at least 0.8%, at least 0.9%, at least 1%, at least 2%, at least 3%, at least 4%, at least 5%, at least 6%, at least 7%, at least 8%, at least 9%, at least 10%, at least 11%, at least 12%, at least 13%, at least 14%, at least 15%, at least 16%, at least 17%, at least 18%, at least 19%, at least 20%, on average across a population of synthetic nanocarriers. In yet another embodiment, the load of the immunosuppressant and/or antigen is no more than 25% on average across a population of synthetic nanocarriers. In embodiments of the above embodiments, the load of the immunosuppressant and/or antigen is no more than 50% on average across a population of synthetic nanocarriers. In embodiments, the load is calculated as described in the Examples.

[0095] In embodiments of any of the compositions and methods provided, the load may be calculated as follows: Approximately 3 mg of synthetic nanocarriers are collected and centrifuged to separate supernatant from synthetic nanocarrier pellet. Acetonitrile is added to the pellet, and the sample is sonicated and centrifuged to remove any insoluble material. The supernatant and pellet are injected on RPLC and absorbance is read at 278 nm. The µg found in the pellet is used to calculate % entrapped (load), µg in supernatant and pellet are used to calculate total µg recovered.

[0096] “Maintenance dose” refers to a dose that is administered to a subject, after an initial dose has resulted in an immunosuppressive (e.g., tolerogenic) response in a subject, to sustain a desired immunosuppressive (e.g., tolerogenic) response. A maintenance dose, for example, can be one that maintains the tolerogenic effect achieved after the initial dose, prevents an undesired immune response in the subject, or prevents the subject becoming a subject at risk of experiencing an undesired immune response, including an undesired level of an immune response. In some embodiments, the maintenance dose is one that is sufficient to sustain an appropriate level of (or no) innate immune cell activation.

[0097] “Maximum dimension of a synthetic nanocarrier” means the largest dimension of a nanocarrier measured along any axis of the synthetic nanocarrier. “Minimum dimension of a synthetic nanocarrier” means the smallest dimension of a synthetic nanocarrier measured along any axis of the synthetic nanocarrier. For example, for a spheroidal synthetic nanocarrier, the maximum and minimum dimension of a synthetic nanocarrier would be substantially identical, and would be the size of its diameter. Similarly, for a cuboidal synthetic nanocarrier, the minimum dimension of a synthetic nanocarrier would be the smallest of its height, width or length, while the maximum dimension of a synthetic nanocarrier would be the largest of its height, width or length. In an embodiment, a minimum dimension of at least 75%, preferably at least 80%, more preferably at least 90%, of the synthetic nanocarriers in the sample, based on the total number of synthetic nanocarriers in the sample, is equal to or greater than 100 nm. In an embodiment, a maximum dimension of at least 75%, preferably at least 80%, more preferably at least 90%, of the synthetic nanocarriers in a sample, based on the total number of synthetic nanocarriers in the sample, is equal to or greater than 100 nm. In an embodiment, a minimum dimension of at least 75%, preferably at least 80%, more preferably at least 90%, of the synthetic nanocarriers in a sample, based on the total number of synthetic nanocarriers in the sample, is greater than 110 nm, more preferably greater than 120 nm, more preferably greater than 130 nm, and more preferably still greater than 150 nm. Aspects ratios of the maximum and minimum dimensions of inventive synthetic nanocarriers may vary depending on the embodiment. For instance, aspect ratios of the maximum to minimum dimensions of the synthetic nanocarriers may vary from 1:1 to 1,000:1, preferably from 1:1 to 100,000:1, more preferably from 1:1 to 10,000:1, more preferably from 1:1 to 1000:1, still more preferably from 1:1 to 100:1, and yet more preferably from 1:1 to 10:1. Preferably, a maximum dimension of at least 75%, preferably at least 80%, more preferably at least 90%, of the synthetic nanocarriers in a sample, based on the total number of synthetic nanocarriers in the sample, is equal to or less than 3 µm, or more preferably equal to or less than 2 µm, more preferably equal to or less than 1 µm, more preferably equal to or less than 800 nm, more preferably equal to or less than 600 nm, and more preferably still equal to or less than 500 nm. In preferred embodiments, a minimum dimension of at least 75%, preferably at least 80%, more preferably at least 90%, of the synthetic nanocarriers in a sample, based on the total number of synthetic nanocarriers in the sample, is equal to or greater than 100 nm, more preferably equal to or greater than 120 nm, more preferably equal to or greater than 130 nm, more preferably equal to or greater than 140 nm, and more preferably still equal to or greater than 150 nm. Measurement of synthetic nanocarrier dimensions (e.g., diameter) is obtained by suspending the synthetic nanocarriers in a liquid (usually aqueous) medium and using dynamic light scattering (DLS) (e.g., using a Brookhaven ZetaPALS instrument). For example, a suspension of synthetic nanocarriers can be diluted from an aqueous buffer into purified water to achieve a final synthetic nanocarrier suspension concentration of approximately 0.01 to 0.1 mg/mL. The diluted suspension may be prepared directly inside, or transferred to, a suitable cuvette for DLS analysis. The cuvette may then be placed in the DLS allowed to equilibrate to the controlled temperature, and then scanned for sufficient time to acquire a stable and reproducible distribution based on appropriate inputs for viscosity of the medium and refractive indices of the sample. The effective diameter, or mean of the distribution, is then reported. “Dimension” or “size” or “diameter” of synthetic nanocarriers means the mean of a particle size distribution obtained using dynamic light scattering.
“MHC” refers to major histocompatibility complex, a large genomic region or gene family found in most vertebrates that encodes MHC molecules that display fragments or epitopes of processed proteins on the cell surface. The presentation of MHC:peptide on cell surfaces allows for surveillance by immune cells, usually a T cell. There are two general classes of MHC molecules: Class I and Class II. Generally, Class I MHC molecules are found on nucleated cells and present peptides to cytotoxic T cells. Class II MHC molecules are found on certain immune cells, chiefly macrophages, B cells and dendritic cells, collectively known as professional APCs. The best-known genes in the MHC region are the subset that encodes antigen-presenting proteins on the cell surface. In humans, these genes are referred to as human leukocyte antigen (HLA) genes.

“Non-methoxy-terminated polymer” means a polymer that has at least one terminus that ends with a moiety other than methoxy. In some embodiments, the polymer has at least two termini that ends with a moiety other than methoxy. In other embodiments, the polymer has no terminus that ends with methoxy. “Non-methoxy-terminated, pluronic polymer” means a polymer other than a linear pluronic polymer with methoxy at both termini Polymeric nanoparticles as provided herein can comprise non-methoxy-terminated polymers or non-methoxy-terminated, pluronic polymers.

“Obtained” means taken directly from a material and used with substantially no modification and/or processing.

“Pharmacologically acceptable excipient” means a pharmacologically inactive material used together with the recited synthetic nanocarriers to formulate the inventive compositions. Pharmacologically acceptable excipients comprise a variety of materials known in the art, including but not limited to saccharides (such as glucose, lactose, and the like), preservatives such as antimicrobial agents, reconstitution aids, colorants, saline (such as phosphate buffered saline), and buffers.

“Protocol” refers to any dosing regimen of one or more substances to a subject. A dosing regimen may include the amount, frequency, and/or mode of administration. In some embodiments, such a protocol may be used to administer one or more compositions of the invention to one or more test subjects. Immune responses in these test subject can then be assessed to determine whether or not the protocol was effective in reducing an undesired immune response or generating a desired immune response (e.g., the promotion of a tolerogenic effect). Any other therapeutic and/or prophylactic effect may also be assessed instead of or in addition to the aforementioned immune responses. Whether or not a protocol had a desired effect can be determined using any of the methods provided herein or otherwise known in the art. For example, a population of cells may be obtained from a subject to which a composition provided herein has been administered according to a specific protocol in order to determine whether or not specific immune cells, cytokines, antibodies, etc. were reduced, generated, activated, etc. Useful methods for detecting the presence and/or number of immune cells include, but are not limited to, flow cytometric methods (e.g., FACS) and immunohistochemistry methods. Antibodies and other binding agents for specific staining of immune cell markers, are commercially available. Such kits typically include staining reagents for multiple antigens that allow for FACS-based detection, separation and/or quantitation of a desired cell population from a heterogeneous population of cells.

“Providing a subject” is any action or set of actions that causes a clinician to come in contact with a subject and administer a composition provided herein thereto or to perform a method provided herein thereupon. Preferably, the subject is one who is in need of a tolerogenic immune response as provided herein. The action or set of actions may be either directly oneself or indirectly, such as, but not limited to, an unrelated third party that takes an action through reliance on one’s words or deeds.

“Subject” means animals, including warm blooded mammals such as humans and primates; avians; domestic household or farm animals such as cats, dogs, sheep, goats, cattle, horses and pigs; laboratory animals such as mice, rats and guinea pigs; fish; reptiles; zoo and wild animals; and the like.

“Substantially no MHC Class I-restricted epitopes” refers to the absence of MHC Class I-restricted epitopes in an amount (by itself, within the context of the antigen, in conjunction with a carrier or in conjunction with an inventive composition) that promotes substantial activation of an immune response specific to the epitopes presented in the class I context. In embodiments, a composition with substantially no MHC Class I-restricted epitopes does not contain a measurable amount of MHC Class I-restricted epitopes of an antigen. In other embodiments, such a composition may comprise a measurable amount of MHC Class I-restricted epitopes of an antigen but said amount is not effective to generate a measurable cytotoxic T cell immune response (by itself, within the context of the antigen, in conjunction with a carrier or in conjunction with an inventive composition) or is not effective to generate a significant measurable cytotoxic T cell immune response (by itself, within the context of the antigen, in conjunction with a carrier or in conjunction with an inventive composition). In some embodiments, a significant measurable cytotoxic T cell immune response is one that produces or would be expected to produce an adverse clinical result in a subject. In other embodiments, a significant measurable cytotoxic T cell immune response is one that is greater than the level of the same type of immune response produced by a control antigen (e.g., one known not to comprise MHC Class I-restricted epitopes or to stimulate cytotoxic T cell immune responses).

In embodiments, the compositions do not comprise MHC Class I-restricted epitopes that (by itself, within the context of the antigen, in conjunction with a carrier or in conjunction with an inventive composition) generate antigen-specific cytotoxic T cell immune responses or an undesired level thereof. In some embodiments, to ensure that a composition does not comprise such epitopes, antigens are selected such that they do not comprise MHC Class I-restricted epitopes for coupling to the synthetic nanocarriers as provided herein. In other embodiments, to ensure that a composition does not comprise such epitopes, synthetic nanocarriers coupled to an antigen are produced and tested for cytotoxic T cell immune responses. The appropriate synthetic nanocarriers may then be selected.

“Substantially no MHC Class II-restricted epitopes” refers to the absence of MHC Class II-restricted epitopes in an amount that (by itself, within the context of the antigen, in conjunction with a carrier or in conjunction with an inventive composition) stimulates substantial activation of
a CD4+ T cell immune response specific to the antigen. In embodiments, a composition with substantially no MHC Class II-restricted epitopes does not contain a measurable amount of MHC Class II-restricted epitopes of an antigen. In other embodiments, such a composition may comprise a measurable amount of MHC Class II-restricted epitopes of an antigen but said amount is not effective to generate a measurable CD4+ T cell immune response (by itself, within the context of the antigen, in conjunction with a carrier or in conjunction with an inventive composition) or is not effective to generate a significant measurable CD4+ T cell immune response (by itself, within the context of the antigen, in conjunction with a carrier or in conjunction with an inventive composition). In some embodiments, a significant measurable CD4+ T cell immune response is one that produces or would be expected to produce an adverse clinical result in a subject. In other embodiments, a significant measurable CD4+ T cell immune response is one that is greater than the level of the same type of immune response produced by a control antigen (e.g., one known not to comprise MHC Class II-restricted epitopes or to stimulate CD4+ T cell immune responses).

[0108] In embodiments, the compositions do not comprise MHC Class II-restricted epitopes (by itself, within the context of the antigen, in conjunction with a carrier or in conjunction with an inventive composition) that generate antigen-specific CD4+ T cell immune responses or an undesired level thereof. In some embodiments, to ensure that a composition does not comprise such epitopes, antibodies are selected such that they do not comprise MHC Class II-restricted epitopes for coupling to the synthetic nanocarriers as provided herein. In other embodiments, to ensure that a composition does not comprise such epitopes, synthetic nanocarriers coupled to an antigen are produced and tested for CD4+ T cell immune responses. The appropriate synthetic nanocarriers may then be selected.

[0109] “Synthetic nanocarrier(s)” means a discrete object that is not found in nature, and that possesses at least one dimension that is less than or equal to 5 microns in size. Albumin nanoparticles are generally included as synthetic nanocarriers, however in certain embodiments the synthetic nanocarriers do not comprise albumin nanoparticles. In embodiments, inventive synthetic nanocarriers do not comprise a phospholipid. In other embodiments, inventive synthetic nanocarriers are not lipid-based nanoparticles. In further embodiments, inventive synthetic nanocarriers do not comprise a phospholipid.

[0110] A synthetic nanocarrier can be, but is not limited to, one or a plurality of lipid-based nanoparticles (also referred to herein as lipid nanoparticles, i.e., nanoparticles where the majority of the material that makes up their structure are lipids), polymeric nanoparticles, metallic nanoparticles, surfactant-based emulsions, dendrimers, buckyballs, nanowires, virus-like particles (i.e., particles that are primarily made up of viral structural proteins but that are not infectious or have low infectivity), peptide or protein-based particles (also referred to herein as protein particles, i.e., particles where the majority of the material that makes up their structure are peptides or proteins) (such as albumin nanoparticles) and/or nanoparticles that are developed using a combination of nanomaterials such as lipid-polymer nanoparticles. Synthetic nanocarriers may be a variety of different shapes, including but not limited to spheroidal, cuboidal, pyramidal, oblong, cylindrical, toroidal, and the like. Synthetic nanocarriers according to the invention comprise one or more surfaces.

Exemplary synthetic nanocarriers that can be adapted for use in the practice of the present invention comprise: (1) the biodegradable nanoparticles disclosed in U.S. Pat. No. 5,543,158 to Gref et al., (2) the polymeric nanoparticles of Published US Patent Application 20060002852 to Saltzman et al., (3) the lithographically constructed nanoparticles of Published US Patent Application 20090028910 to DeSimone et al., (4) the disclosure of WO 2009/051837 to von Andrian et al., (5) the nanoparticles disclosed in Published US Patent Application 2008/0145441 to Penades et al., (6) the protein nanoparticles disclosed in Published US Patent Application 20090226525 to de los Rios et al., (7) the virus-like particles disclosed in published US Patent Application 20060222652 to Sebbel et al., (8) the nucleic acid coupled virus-like particles disclosed in published US Patent Application 20060251677 to Bachmann et al., (9) the virus-like particles disclosed in WO2010047839A1 or WO2009106999A2, (10) the nanoparticles disclosed in P. Paolicelli et al., “Surface-modified PLGA-based Nanoparticles that can Efficiently Associate and Deliver Virus-like Particles” Nano- medicine. 5(6):843-853 (2010), or (11) apoptotic cells, apoptotic bodies or the synthetic or semisynthetic mimics disclosed in U.S. Publication 2002/0086049. In embodiments, synthetic nanocarriers may possess an aspect ratio greater than 1:1, 1:1.2, 1:1.5, 1:2, 1:3, 1:5, 1:7, or greater than 1:10.

[0111] Synthetic nanocarriers according to the invention that have a minimum dimension of equal to or less than about 100 nm, preferably equal to or less than 100 nm, do not comprise a surface with hydroxyl groups that activate complement or alternatively comprise a surface that consists essentially of moieties that are not hydroxyl groups that activate complement. In a preferred embodiment, synthetic nanocarriers according to the invention that have a minimum dimension of equal to or less than about 100 nm, preferably equal to or less than 100 nm, do not comprise a surface that substantially activates complement or alternatively comprise a surface that consists essentially of moieties that do not substantially activate complement. In a more preferred embodiment, synthetic nanocarriers according to the invention that have a minimum dimension of equal to or less than about 100 nm, preferably equal to or less than 100 nm, do not comprise a surface that activates complement or alternatively comprise a surface that consists essentially of moieties that do not activate complement. In embodiments, synthetic nanocarriers exclude virus-like particles. In embodiments, synthetic nanocarriers may possess an aspect ratio greater than 1:1, 1:1.2, 1:1.5, 1:2, 1:3, 1:5, 1:7, or greater than 1:10.

[0112] “T cell antigen” means a CD4+ T-cell antigen or CD8+ cell antigen. “CD4+ T-cell antigen” means any antigen that is recognized by and triggers an immune response in a CD4+ T-cell e.g., an antigen that is specifically recognized by a T-cell receptor on a CD4+ T cell via presentation of the antigen or portion thereof bound to a Class II major histocompatibility complex molecule (MHC). “CD8+ T-cell antigen” means any antigen that is recognized by and triggers an immune response in a CD8+ T-cell e.g., an antigen that is specifically recognized by a T-cell receptor on a CD8+ T cell via presentation of the antigen or portion thereof bound to a Class I major histocompatibility complex molecule (MHC). In some embodiments, an antigen that is a T cell antigen is also a B cell antigen. In other embodiments, the T cell antigen is not also a B cell antigen. T cell antigens generally are proteins or peptides.
A “therapeutic protein” refers to any protein or protein-based therapy that may be administered to a subject and have a therapeutic effect. Such therapies include protein replacement and protein supplementation therapies. Such therapies also include the administration of exogenous or foreign protein, antibody therapies, and cell or cell-based therapies. Therapeutic proteins include enzymes, enzyme cofactors, hormones, blood clotting factors, cytokines, growth factors, monoclonal antibodies and polyclonal antibodies. Examples of other therapeutic proteins are provided elsewhere herein. Therapeutic proteins may be produced in, or on by cells and may be obtained from such cells or administered in the form of such cells. In embodiments, the therapeutic protein is produced in, or on by mammalian cells, insect cells, yeast cells, bacteria cells, plant cells, transgenic animal cells, transgenic plant cells, etc. The therapeutic protein may be recombinantly produced in such cells. The therapeutic protein may be produced in, or on by a virally transformed cell. The therapeutic protein may also be produced in, or on by autologous cells that have been transfected, transduced or otherwise manipulated to express it. Alternatively, the therapeutic protein may be administered as a nucleic acid or by introducing a nucleic acid into a virus, VLP, liposome, etc. Alternatively, the therapeutic protein may be obtained from such forms and administered as the therapeutic protein itself. Subjects, therefore, include any subject that has received, is receiving or will receive any of the foregoing. Such subject includes subjects that have received, is receiving or will receive gene therapy, autologous cells that have been transfected, transduced or otherwise manipulated to express a therapeutic protein, polypeptide or peptide; or cells that express a therapeutic protein, polypeptide or peptide.

“Therapeutic protein antigen” means an antigen that is associated with a therapeutic protein that can be, or a portion of which can be, presented for recognition by cells of the immune system and can generate an undesired immune response (e.g., the production of therapeutic protein-specific antibodies) against the therapeutic protein. Therapeutic protein antigens generally include proteins, polypeptides, peptides, lipoproteins, or are contained or expressed in, or on by cells.

“Tolerogenic immune response” means any immune response that can lead to immune suppression specific to an antigen or a cell, tissue, organ, etc. that expresses such an antigen. Such immune responses include any reduction, delay or inhibition in an undesired immune response specific to the antigen or cell, tissue, organ, etc. that expresses such antigen. Such immune responses also include any stimulation, production, induction, promotion or recruitment in a desired immune response specific to the antigen or cell, tissue, organ, etc. that expresses such antigen. Tolerogenic immune responses, therefore, include the absence of or reduction in an undesired immune response to an antigen that can be mediated by antigen reactive cells as well as the presence or promotion of suppressive cells. Tolerogenic immune responses as provided herein include immunological tolerance. To “generate a tolerogenic immune response” refers to the generation of any of the foregoing immune responses specific to an antigen or cell, tissue, organ, etc. that expresses such antigen. The tolerogenic immune response can be the result of MHC Class II-restricted presentation and/or MHC Class I-restricted presentation and/or B cell presentation and/or presentation by CD1d, etc.

Tolerogenic immune responses include any reduction, delay or inhibition in CD4+ T cell, CD8+ T cell or B cell proliferation and/or activity. Tolerogenic immune responses also include a reduction in antigen-specific antibody production. Tolerogenic immune responses can also include any response that leads to the stimulation, induction, production or recruitment of regulatory cells, such as CD4+ Treg cells, CD8+ Treg cells, Breg cells, etc. In some embodiments, the tolerogenic immune response, is one that results in the conversion to a regulatory phenotype characterized by the production, induction, stimulation or recruitment of regulatory cells.

Tolerogenic immune responses also include any response that leads to the stimulation, production or recruitment of CD4+ Treg cells and/or CD8+ Treg cells. CD4+ Treg cells can express the transcription factor FoxP3 and inhibit inflammatory responses and auto-immune inflammatory diseases (Human regulatory T cells in autoimmune diseases. Cvetanovich G L, Hafer D A. Curr Opin Immunol. 2010 December; 22(6):753-60. Regulatory T cells and autoimmunity. Vila J, Isaacs J D, Anderson A E. Curr Opin Hematol. 2009 July; 16(4):274-9). Such cells also suppress T-cell help to B-cells and induce tolerance to both self and foreign antigens (Toleropathic approaches to allergy and autoimmunity based on FoxP3+regulatory T-cell activation and expansion. Miyara M, Wing K, Sakaguchi S. J Allergy Clin Immunol. 2009 April; 123(4):749-55). CD4+ Treg cells recognize antigen when presented by Class II proteins on APC’s. CD8+ Treg cells, which recognize antigen presented by Class I (and Qa-1), can also suppress T-cell help to B-cells and result in suppression of antigen-specific suppression inducing tolerance to both self and foreign antigens. Disruption of the interaction of Qa-1 with CD8+ Treg cells has been shown to dysregulate immune responses and results in the development of autoantibody formation and an autoimmune lethal systemic-lupus-erythematosus (Kim et al., Nature. 2010 Sep. 16, 467 (7313): 328-32). CD8+ Treg cells have also been shown to inhibit models of autoimmune inflammatory diseases including rheumatoid arthritis and colitis (CD4+CD25+regulatory T cells in autoimmune arthritis. Oh S, Rankin A L, Caton A J. Immunol Rev. 2010 January;233(1):97-111. Regulatory T cells in inflammatory bowel disease. Boden E K, Snapper S B. Curr Opin Gastroenterol. 2008 November; 24(6):733-41). In some embodiments, the compositions provided can effectively result in both types of responses (CD4+ Treg and CD8+ Treg). In other embodiments, FoxP3 can be induced in other immune cells, such as macrophages, iNKT cells, etc., and the compositions provided herein can result in one or more of these responses as well.

Tolerogenic immune responses also include, but are not limited to, the induction of regulatory cytokines, such as Treg cytokines; induction of inhibitory cytokines; the inhibition of inflammatory cytokines (e.g., IL-4, IL-10, TNF-α, IL-1β, IL-6, GM-CSF, IFN-γ, IL-2, IL-9, IL-12, IL-17, IL-18, IL-21, IL-22, IL-23, M-CSF, C reactive protein, acute phase protein, chemokines (e.g., MCP-1, RANTES, MIP-1α, MIP-1β, MIG, ITAC or IP-10), the production of anti-inflammatory cytokines (e.g., IL-4, IL-13, IL-10, etc.), chemokines (e.g., CCL-2, CXCL8), proteases (e.g., MMP-3, MMP-9), leukotrienes (e.g., CysLT-1, CysLT-2), prostaglandins (e.g., PGE2) or histamines; the inhibition of polarization to a Th17, Th1 or Th2 immune response; the inhibition of effector cell-specific cytokines: Th17 (e.g., IL-17, IL-25), Th1 (IFN-γ), Th2 (e.g., IL-4, IL-13); the inhibition of Th1-, Th2- or Th17-specific cytokines: Th17 (e.g., IL-17, IL-25), Th1 (IFN-γ), Th2 (e.g., IL-4, IL-13), the inhibition of Th1-, Th2- or Th17-specific cytokines.
specific transcription factors; the inhibition of proliferation of effecter T cells; the induction of apoptosis of effecter T cells; the induction of tolerogenic dendritic cell-specific genes; the induction of FoxP3 expression, the inhibition of IgE induction or IgE-mediated immune responses; the inhibition of antibody responses (e.g., antigen-specific antibody production); the inhibition of T helper cell response; the production of TGF-β and/or IL-10; the inhibition of effector function of autoantibodies (e.g., inhibition in the depletion of cells, cell or tissue damage or complement activation); etc.

Any of the foregoing may be measured in vivo in one or more animal models or may be measured in vitro. One of ordinary skill in the art is familiar with such in vivo or in vitro measurements. Undesired immune responses or tolero genic immune responses can be monitored using, for example, methods of assessing immune cell number and/or function, tetramer analysis, ELISPOT, flow cytometry-based analysis of cytokine expression, cytokine secretion, cytokine expression profiling, gene expression profiling, protein expression profiling, analysis of cell surface markers, PCR-based detection of immune cell receptor gene usage (see T. Clay et al., “Assays for Monitoring Cellular Immune Response to Active Immunotherapy of Cancer” Clinical Cancer Research 7:1127-1135 (2001)), etc. Undesired immune responses or tolerogenic immune responses may also be monitored using, for example, methods of assessing protein levels in plasma or serum, immune cell proliferation and/or functional assays, etc. In some embodiments, tolerogenic immune responses can be monitored by assessing the induction of FoxP3. In addition, specific methods are described in more detail in the Examples.

Preferably, tolerogenic immune responses lead to the inhibition of the development, progression or pathology of the diseases, disorders or conditions described herein. Whether or not the inventive compositions can lead to the inhibition of the development, progression or pathology of the diseases, disorders or conditions described herein can be measured with animal models of such diseases, disorders or conditions. In some embodiments, the reduction of an undesired immune response or generation of a tolerogenic immune response may be assessed by determining clinical endpoints, clinical efficacy, clinical symptoms, disease biomarkers and/or clinical scores. Undesired immune responses or tolerogenic immune responses can also be assessed with diagnostic tests to assess the presence or absence of a disease, disorder or condition as provided herein. Undesired immune responses can further be assessed by methods of measuring therapeutic proteins levels and/or function in a subject. In embodiments, methods for monitoring or assessing undesired allergic responses include assessing an allergic response in a subject by skin reactivity and/or allergen-specific antibody production.

In some embodiments, monitoring or assessing the generation of an undesired immune response or a tolerogenic immune response in a subject can be prior to the administration of a composition of synthetic nanocarriers provided herein and/or prior to administration of a transplantable graft or therapeutic protein or exposure to an allergen. In other embodiments, assessing the generation of an undesired immune response or tolerogenic immune response can be after administration of a composition of synthetic nanocarriers provided herein and/or after administration of a transplantable graft or therapeutic protein or exposure to an allergen. In some embodiments, the assessment is done after administration of the composition of synthetic nanocarriers, but prior to administration of a transplantable graft or therapeutic protein or exposure to an allergen. In other embodiments, the assessment is done after administration of a transplantable graft or therapeutic protein or exposure to an allergen, but prior to administration of the composition. In still other embodiments, the assessment is performed prior to both the administration of the synthetic nanocarriers and administration of a transplantable graft or therapeutic protein or exposure to an allergen, while in yet other embodiments the assessment is performed after both the administration of synthetic nanocarriers and the administration of a transplantable graft or therapeutic protein or exposure to an allergen. In further embodiments, the assessment is performed both prior to and after the administration of the synthetic nanocarriers and/or administration of a transplantable graft or therapeutic protein or exposure to an allergen. In still other embodiments, the assessment is performed more than once on the subject to determine that a desirable immune state is maintained in the subject, such as a subject that has or is at risk of having an inflammatory disease, an autoimmune disease, an allergy, organ or tissue rejection or graft versus host disease. Other subjects include those that have undergone or will undergo transplantation as well as those that have received, are receiving or will receive a therapeutic protein against which they have experienced, are experiencing or are expected to experience an undesired immune response.

An antibody response can be assessed by determining one or more antibody titers. “Antibody titer” means a measurable level of antibody production. Methods for measuring antibody titers are known in the art and include Enzyme-linked Immunosorbent Assay (ELISA). In embodiments, the antibody response can be quantitated, for example, as the number of antibodies, concentration of antibodies or titer. The values can be absolute or they can be relative. Assessments quantifying an antibody response include antibody capture assays, enzyme-linked immunosorbent assays (ELISAs), inhibition liquid phase absorption assays (IL-PAAs), rocket immunoelectrophoresis (RIE) assays and line immunoelectrophoresis (LIE) assays. When an antibody response is compared to another antibody response the same type of quantitative value (e.g., titer) and method of measurement (e.g., ELISA) is preferably used to make the comparison.

An ELISA method for measuring an antibody titer, for example, a typical sandwich ELISA, may consist of the following steps (i) preparing an ELISA-plate coating material such that the antibody target of interest is coupled to a substrate polymer or other suitable material (ii) preparing the coating material in an aqueous solution (such as PBS) and delivering the coating material solution to the wells of a multiwell plate for overnight deposition of the coating onto the multiwell plate (iii) thoroughly washing the multiwell plate with wash buffer (such as 0.05% Tween-20 in PBS) to remove excess coating material (iv) blocking the plate for nonspecific binding by applying a diluted solution (such as 10% fetal bovine serum in PBS), (v) washing the blocking/dilution solution from the plate with wash buffer (vi) diluting the serum sample(s) containing antibodies and appropriate standards (positive controls) with diluent as required to obtain a concentration that suitably saturates the ELISA response (vii) serially diluting the plasma samples on the multiwell plate such to cover a range of concentrations suitable for generating an ELISA response curve (viii) incubating the
plate to provide for antibody-target binding (ix) washing the plate with wash buffer to remove antibodies not bound to antigen (x) adding an appropriate concentration of a secondary detection antibody in same diluent such as a biotin-coupled detection antibody capable of binding the primary antibody (xi) incubating the plate with the applied detection antibody, followed by washing with wash buffer (xii) adding an enzyme such as streptavidin-HRP (horse radish peroxidase) that will bind to biotin found on biotinylated antibodies and incubating (xiii) washing the multiwell plate (xiv) adding substrate(s) (such as TMB solution) to the plate (xv) applying a stop solution (such as 2N sulfuric acid) when color development is complete (xvi) reading optical density of the plate wells at a specific wavelength for the substrate (450 nm with subtraction of readings at 570 nm) (xvii) applying a suitable multiparameter curve fit to the data and defining half-maximal effective concentration (EC50) as the concentration on the curve at which half the maximum OD value for the plate standards is achieved.

A “transplantable graft” refers to a biological material, such as cells, tissues and organs (in whole or in part) that can be administered to a subject. Transplantable grafts may be autografts, allografts, or xenografts of, for example, a biological material such as an organ, tissue, skin, bone, nerves, tendon, neurons, blood vessels, fat, cornea, pluripotent cells, differentiated cells (obtained or derived in vivo or in vitro), etc. In some embodiments, a transplantable graft is formed, for example, from cartilage, bone, extracellular matrix, or collagen matrices. Transplantable grafts may also be single cells, suspensions of cells and cells in tissues and organs that can be transplanted. Transplantable cells typically have a therapeutic function, for example, a function that is lacking or diminished in a recipient subject. Some non-limiting examples of transplantable cells are B cells, hepatocytes, hematopoietic stem cells, neuronal stem cells, neurons, glial cells, or myelinating cells. Transplantable cells can be cells that are unmodified, for example, cells obtained from a donor subject and usable in transplantation without any genetic or epigenetic modifications. In other embodiments, transplantable cells can be modified cells, for example, cells obtained from a subject having a genetic defect, in which the genetic defect has been corrected, or cells that are derived from reprogrammed cells, for example, differentiated cells derived from cells obtained from a subject.

“Transplantation” refers to the process of transferring (moving) a transplantable graft into a recipient subject (e.g., from a donor subject, from an in vitro source (e.g., differentiated autologous or heterologous native or induced pluripotent cells)) and/or from one bodily location to another bodily location in the same subject.

“Undesired immune response” refers to any undesired immune response, such as an innate immune response, that results from exposure to an antigen, promotes or exacerbates a disease, disorder or condition provided herein (or a symptom thereof), or is symptomatic of a disease, disorder or condition provided herein. Such immune responses generally have a negative impact on a subject’s health or is symptomatic of a negative impact on a subject’s health. Undesired immune responses include antigen-specific innate immune cell proliferation and/or activity.

C. INVENTIVE COMPOSITIONS

Provided herein are tolerogenic methods that include the administration of synthetic nanocarrier compositions comprising immunosuppressants and B cell and/or MHC Class II-restricted epitopes of an antigen, and related compositions. Such methods and compositions are useful for reducing or inhibiting antigen-specific activation of innate immune cells and promoting the generation of tolerogenic immune responses. The methods provided may also include the administration of therapeutic proteins and/or transplantable grafts. The compositions provided, therefore, may also include the therapeutic proteins and/or transplantable grafts. The compositions may be administered to subjects in which a tolerogenic immune response is desired. Such subjects include those that have or are at risk of having an inflammatory disease, an autoimmune disease, an allergy, organ or tissue rejection or graft versus host disease. Such subjects also include those that have been, are being or will be administered a therapeutic protein against which the subject has experienced or is expected to experience an undesired immune response. Such subjects also include those that have undergone or will undergo transplantation.

Preferably, the compositions of the invention result in the reduction or inhibition of innate immune cell number and/or activation. Such innate immune cells include macrophages, mast cells and NK cells. One hallmark of macrophages is the ability to produce and secrete IL-12 and TNF. Another hallmark of a reduction or inhibition of innate immune cells is the reduction of IFN-γ. Additional markers and cytokine or chemokine secretion profiles that can be used to identify innate immune cells are known to those of skill in the art. Based on the knowledge of such markers useful for the identification of various innate immune cell populations, those of skill in the art are able to identify and enumerate innate immune cells in a heterogeneous population of cells, for example, in a population of cells in culture or in a population of cells obtained from a subject.

As mentioned above, the synthetic nanocarriers are designed to comprise B cell epitopes and immunosuppressants. A wide variety of synthetic nanocarriers can be used according to the invention. In some embodiments, synthetic nanocarriers are spheres or spheroids. In some embodiments, synthetic nanocarriers are flat or plate-shaped. In some embodiments, synthetic nanocarriers are cubes or cubic. In some embodiments, synthetic nanocarriers are ovals or ellipses. In some embodiments, synthetic nanocarriers are cylinders, cones, or pyramids.

In some embodiments, it is desirable to use a population of synthetic nanocarriers that is relatively uniform in terms of size, shape, and/or composition so that each synthetic nanocarrier has similar properties. For example, at least 80%, at least 90%, or at least 95% of the synthetic nanocarriers, based on the total number of synthetic nanocarriers, may have a minimum dimension or maximum dimension that falls within 5%, 10%, or 20% of the average diameter or average dimension of the synthetic nanocarriers. In some embodiments, a population of synthetic nanocarriers may be heterogeneous with respect to size, shape, and/or composition.

Synthetic nanocarriers can be solid or hollow and can comprise one or more layers. In some embodiments, each layer has a unique composition and unique properties relative to the other layer(s). To give but one example, synthetic nanocarriers may have a core/shell structure, wherein the core is one layer (e.g. a polymeric core) and the shell is a second layer (e.g. a lipid bilayer or monolayer). Synthetic nanocarriers may comprise a plurality of different layers.
In some embodiments, synthetic nanocarriers may optionally comprise one or more lipids. In some embodiments, a synthetic nanocarrier may comprise a liposome. In some embodiments, a synthetic nanocarrier may comprise a lipid bilayer. In some embodiments, a synthetic nanocarrier may comprise a lipid monolayer. In some embodiments, a synthetic nanocarrier may comprise a micelle. In some embodiments, a synthetic nanocarrier may comprise a non-polymeric core (e.g., metal particle, quantum dot, ceramic particle, bone particle, viral particle, proteins, nucleic acids, carbohydrates, etc.) surrounded by a lipid layer (e.g., lipid bilayer, lipid monolayer, etc.).

In other embodiments, synthetic nanocarriers may comprise metal particles, quantum dots, ceramic particles, etc. In some embodiments, a non-polymeric synthetic nanocarrier is an aggregate of non-polymeric components, such as an aggregate of metal atoms (e.g., gold atoms).

In some embodiments, an amphiphilic entity can promote the production of synthetic nanocarriers with increased stability, improved uniformity, or increased viscosity. In some embodiments, amphiphilic entities can be associated with the interior surface of a lipid membrane (e.g., lipid bilayer, lipid monolayer, etc.). Many amphiphilic entities known in the art are suitable for use in making synthetic nanocarriers in accordance with the present invention. Such amphiphilic entities include, but are not limited to, phosphoglycerides; phosphatidylcholines; dipalmitoyl phosphatidylcholine (DPPC); dioleylphosphatidyl ethanolamine (DOPE); dioleyloxypropyltriethylammonium (DOTMA); dioleylphosphatidylethanolamine; cholesterol; cholesterol ester; diacetylchsterol; diacetylglycerol-succinate; diphospatidyl glycerol (DPPG); hexanedicarboxylic acid; fatty acids such as polyethylene glycol (PEG); polyethylene glycol-9-lauryl ether; a surface active fatty acid, such as palmitic acid or oleic acid; fatty acids; fatty acid monoglycerides; fatty acid diglycerides; fatty acid amides; sorbitan trioleate (Span®85) glycolcholate; sorbitan monolaurate (Span®20); polysorbate 20 (Tween®20); polysorbate 60 (Tween®60); polysorbate 65 (Tween®65); polysorbate 80 (Tween®80); polysorbate 85 (Tween®85); poloxamer; poloxamer 188; surfactin; a poloxomer; a sorbitan fatty acid ester such as sorbitan trioleate; lecithin; lyssolecithin; phosphatidylserine; phosphatidylcholine; phosphatidylethanolamine; phosphatidylylycerol; stearylamine; distearylamine; hexadecylamine; acetyl palmitate; glycerol ricinoleate; hexadecyl stearte; isopropyl myristate; tyloxapol; poly(ethylene oxide) glycol; poly(ethylene glycol)1000-phosphatidylethanolamine; poly(ethylene glycol)400-monostearate; phospholipids; synthetic and/or natural detergents having high surfactant properties; deoxycholates; cycloexetrins; chaotropic salts; ion pairing agents; and combinations thereof. An amphiphilic entity component may be a mixture of different amphiphilic entities. Those skilled in the art will recognize that this is an exemplary, not comprehensive, list of substances with surfactant activity. Any amphiphilic entity may be used in the production of synthetic nanocarriers to be used in accordance with the present invention.

In some embodiments, synthetic nanocarriers may optionally comprise one or more carbohydrates. Carbohydrates may be immobilized at the surface of the synthetic nanocarriers and/or contained within (encapsulated) the synthetic nanocarriers. In some embodiments, a carbohydrate is a polysaccharide, including but not limited to pullulan, cellulose, microcrystalline cellulose, hydroxypropyl methylcellulose (HPMC), hydroxyethyl cellulose (HEC), methylcellulose (MC), dextran, cycloexetrin, glycerol, hydroxyethyl starch, carrageenan, glycerol, amyllose, chitosan, N,O-carboxymethyl cellulose, algin and alginate acid, starch, chitin, inulin, konjac, glucomannan, pectin, heparin, hyaluronic acid, curdlan, and xanthan. In some embodiments, the inventive synthetic nanocarriers do not comprise (or specifically exclude) carbohydrates, such as a polysaccharide. In some embodiments, the carbohydrate may comprise a carbohydrate derivative such as a sugar alcohol, including but not limited to mannitol, sorbitol, xylitol, erythritol, maltitol, and lactitol.

In some embodiments, synthetic nanocarriers can comprise one or more polymers. In some embodiments, the synthetic nanocarriers comprise one or more polymers that is a nonmethoxy-terminated, pluronic polymer. In some embodiments, at least 1%, 2%, 3%, 4%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% (weight/weight) of the polymers that make up the synthetic nanocarriers are nonmethoxy-terminated, pluronic polymers. In some embodiments, all of the polymers that make up the synthetic nanocarriers are nonmethoxy-terminated, pluronic polymers. In some embodiments, the synthetic nanocarriers can comprise one or more polymers that is a nonmethoxy-terminated polymer. In some embodiments, at least 1%, 2%, 3%, 4%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, or 99% (weight/weight) of the polymers that make up the synthetic nanocarriers are nonmethoxy-terminated polymers. In some embodiments, all of the polymers that make up the synthetic nanocarriers are nonmethoxy-terminated polymers. In some embodiments, the synthetic nanocarriers comprise one or more polymers that do not comprise pluronic polymer. In some embodiments, at least 1%, 2%, 3%, 4%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, or 99% (weight/weight) of the polymers that make up the synthetic nanocarriers do not comprise pluronic polymer. In some embodiments, all of the polymers that make up the synthetic nanocarriers do not comprise pluronic polymer. In some embodiments, such a polymer can be surrounded by a coating layer (e.g., liposome, lipid monolayer, micelle, etc.). In some embodiments, various elements of the synthetic nanocarriers can be coupled with the polymer.

The immunosuppressants and/or antigens can be coupled to the synthetic nanocarriers by any of a number of methods. Generally, the coupling can be a result of bonding between the immunosuppressants and/or antigens and the synthetic nanocarriers. This bonding can result in the immunosuppressants and/or antigens being attached to the surface of the synthetic nanocarriers and/or contained within (encapsulated) the synthetic nanocarriers. In some embodiments, the immunosuppressants and/or antigens may be optionally comprised one or more lipids. In some embodiments, a synthetic nanocarrier may comprise a lipid bilayer. In some embodiments, a synthetic nanocarrier may comprise a lipid monolayer. In some embodiments, a synthetic nanocarrier may comprise a micelle. In some embodiments, a synthetic nanocarrier may comprise a non-polymeric core (e.g., metal particle, quantum dot, ceramic particle, bone particle, viral particle, proteins, nucleic acids, carbohydrates, etc.) surrounded by a lipid layer (e.g., lipid bilayer, lipid monolayer, etc.).
ments, however, the immunosuppressants and/or antigens are encapsulated by the synthetic nanocarriers as a result of the structure of the synthetic nanocarriers rather than bonding to the synthetic nanocarriers. In preferable embodiments, the synthetic nanocarriers comprise a polymer as provided herein, and the immunosuppressants and/or antigens are coupled to the polymer.

[0138] When coupling occurs as a result of bonding between the immunosuppressants and/or antigens and synthetic nanocarriers, the coupling may occur via a coupling moiety. A coupling moiety can be any moiety through which an immunosuppressant and/or antigen is bonded to a synthetic nanocarrier. Such moieties include covalent bonds, such as an amide bond or ester bond, as well as separate molecules that bond (covalently or non-covalently) the immunosuppressant and/or antigen to the synthetic nanocarrier. Such molecules include linkers or polymers or a unit thereof. For example, the coupling moiety can comprise a charged polymer to which an immunosuppressant and/or antigen electrostatically binds. As another example, the coupling moiety can comprise a polymer or unit thereof to which it is covalently bonded.

[0139] In preferred embodiments, the synthetic nanocarriers comprise a polymer as provided herein. These synthetic nanocarriers can be completely polymeric or they can be a mix of polymers and other materials.

[0140] In some embodiments, the polymers of a synthetic nanocarrier associate to form a polymeric matrix. In some of these embodiments, a component, such as an immunosuppressant or antigen, can be covalently associated with one or more polymers of the polymeric matrix. In some embodiments, covalent association is mediated by a linker. In some embodiments, a component can be noncovalently associated with one or more polymers of a polymeric matrix. For example, in some embodiments a component can be encapsulated within, surrounded by, and/or dispersed throughout a polymeric matrix. Alternatively or additionally, a component can be associated with one or more polymers of a polymeric matrix by hydrophobic interactions, charge interactions, van der Waals forces, etc. A wide variety of polymers and methods for forming polymeric matrices therefrom are known conventionally.

[0141] Polymers may be natural or unnatural (synthetic) polymers. Polymers may be homopolymers or copolymers comprising two or more monomers. In terms of sequence, copolymers may be random, block, or comprise a combination of random and block sequences. Typically, polymers in accordance with the present invention are organic polymers.

[0142] In some embodiments, the polymer comprises a polyester, polycarbonate, polyamide, or polyether, or unit thereof. In other embodiments, the polymer comprises poly (ethylene glycol) (PEG), polypeolpropylene glycol, poly(lactic acid), poly(glycolic acid), poly(lactic-co-glycolic acid), or a polycaprolactone, or unit thereof. In some embodiments, it is preferred that the polymer is biodegradable. Therefore, in these embodiments, it is preferred that if the polymer comprises a polyester, such as poly(ethylene glycol) or polypropylene glycol or unit thereof, the polymer comprises a block-co-polymer of a polyester and a biodegradable polymer such that the polymer is biodegradable. In other embodiments, the polymer does not solely comprise a polyester or unit thereof, such as poly(ethylene glycol) or polypeolpropylene glycol or unit thereof.

[0143] Other examples of polymers suitable for use in the present invention include, but are not limited to polyethylene, polycarbonates (e.g. poly(L-3-dioxan-2-one)), polyhydrides (e.g. poly(sebacic anhydride)), polypropylene, polylactides (e.g. polylactide-co-glycolide), polycaprolactone, polyhydroxycid (e.g. poly(β- hydroxalkanoate)), poly(ethers), polycyanacrylates, polyvinyl alcohols, polyleurethanes, polyphosphazenes, polycrylates, polyacrylates, polyurethanes, polyethylene, polyethylene-PEG copolymers, and poly(ethyleneimine), poly(ethylene imine)-PEG copolymers.

[0144] In some embodiments, polymers in accordance with the present invention include polymers which have been approved for use in humans by the U.S. Food and Drug Administration (FDA) under 21 C.F.R. §177.2000, including but not limited to polyesters (e.g., polylactic acid, poly(lactic-co-glycolic acid), polycaprolactone, polyvalerolactone, poly(l-3-dioxan-2-one)); polyhydrides (e.g., poly(sebacic anhydride)); polyethers (e.g., polyethylene glycol); polyurethanes; polyacrylates; and polycyanoacrylates.

[0145] In some embodiments, polymers can be hydrophilic. For example, polymers may comprise anionic groups (e.g., phosphate group, sulphate group, carboxylate group); cationic groups (e.g., quaternary amine group); or polar groups (e.g., hydroxyl group, thiol group, amine group). In some embodiments, a synthetic nanocarrier comprising a hydrophilic polymeric matrix generates a hydrophilic environment within the synthetic nanocarrier. In some embodiments, polymers can be hydrophobic. In some embodiments, a synthetic nanocarrier comprising a hydrophobic polymeric matrix generates a hydrophobic environment within the synthetic nanocarrier. Selection of the hydrophilicity or hydrophobicity of the polymer may have an impact on the nature of materials that are incorporated (e.g. coupled) within the synthetic nanocarrier.

[0146] In some embodiments, polymers may be modified with one or more moieties and/or functional groups. A variety of moieties or functional groups can be used in accordance with the present invention. In some embodiments, polymers may be modified with polyethylene glycol (PEG), with a carbohydrate, and/or with acyclic polycetals derived from polysaccharides (Papiosov, 2001, ACS Symposium Series, 786:301). Certain embodiments may be made using the general teachings of U.S. Pat. No. 5,543,158 to Gref et al., or WO publication WO2009/051837 by Von Andrian et al.

[0147] In some embodiments, polymers may be modified with a lipid or fatty acid group. In some embodiments, a fatty acid group may be one or more of butyric, caproic, caprylic, capric, lauric, myristic, palmitic, stearic, arachidic, behenic, or lignoceric acid. In some embodiments, a fatty acid group may be one or more of palmitoleic, oleic, vaccenic, linoleic, alpha-linoleic, gamma-linoleic, arachidonic, gadoleic, arachidonic, eicosapentaenoic, docosahexaenoic, or erucic acid.

[0148] In some embodiments, polymers may be polysters, including copolymers comprising lactic acid and glycolic acid units, such as poly(lactic acid-co-glycolic acid) and poly(lactide-co-glycolide), collectively referred to herein as “PLGA”; and homopolymers comprising glycolic acid units, referred to herein as “PGA,” and lactic acid units, such as poly-L-lactic acid, poly-D-lactic acid, poly-DL-lactic acid,
poly-L-lactide, poly-D-lactide, and poly-D,L-lactide, collectively referred to herein as “PLA.” In some embodiments, exemplary polyesters include, for example, poly(etheroxyacids; PEG copolymers and copolymers of lactide and glycolide (e.g., PLA-PEG copolymers, PGA-PEG copolymers, PLGA-PEG copolymers, and derivatives thereof. In some embodiments, polyesters include, for example, poly(caprolactone), poly(caprolactone)-PEG copolymers, poly(l-lactide-co-L-lysine), poly(serine ester), poly(4-hydroxy-L-proline ester), poly[(4-aminobutyl)-1,3-glycolic acid], and derivatives thereof.

[0149] In some embodiments, a polymer may be PLGA. PLGA is a biocompatible and biodegradable co-polymer of lactic acid and glycolic acid, and various forms of PLGA are characterized by the ratio of lactic acid:glycolic acid. Lactic acid can be L-lactic acid, D-lactic acid, or D,L-lactic acid. The degradation rate of PLGA can be adjusted by altering the lactic acid:glycolic acid ratio. In some embodiments, PLGA to be used in accordance with the present invention is characterized by a lactic acid:glycolic acid ratio of approximately 85:15, approximately 75:25, approximately 60:40, approximately 50:50, approximately 40:60, approximately 25:75, or approximately 15:85.

[0150] In some embodiments, polymers may be one or more acrylic polymers. In certain embodiments, acrylic polymers include, for example, acrylic acid and methacrylic acid copolymers, methyl methacrylate copolymers, ethoxyethyl methacrylates, cyanoethyl methacrylate, aminomethyl methacrylate copolymers, poly(acrylic acid), poly(methacrylic acid), methacrylic acid alkylamide copolymer, poly(methyl methacrylate), poly(methacrylic acid anhydride), methyl methacrylate, polymethacrylate, poly(methyl methacrylate) copolymers, polyacrylamide, aminomethyl methacrylate copolymer, glycidyl methacrylate copolymer, polycyanocrylates, and combinations comprising one or more of the foregoing polymers. The acrylic polymer may comprise fully-polymerized copolymers of acrylic and methacrylic acid esters with a low content of quaternary ammonium groups.

[0151] In some embodiments, polymers can be cationic polymers. In general, cationic polymers are able to condense and/or protect negatively charged strands of nucleic acids (e.g., DNA, or derivatives thereof). Amine-containing polymers such as polylysine (Zauner et al., 1998, Adv. Drug Del. Rev., 30:97; and Kabanov et al., 1995, Bioconjugate Chem., 6:7), poly(ethylene imine) (PEI; Bousif et al., 1995, Proc. Natl. Acad. Sci., USA, 1995, 92:7297), and polyamidoamine) dendrimers (Kukowska-Latallo et al., 1996, Proc. Natl. Acad. Sci., USA, 93:4897; Tang et al., 1996, Bioconjugate Chem., 7:703; and Haensler et al., 1993, Bioconjugate Chem., 4:372) are positively-charged at physiological pH, form ion pairs with nucleic acids, and mediate transfection in a variety of cell lines. In embodiments, the inventive synthetic nanocarriers may not comprise (or may exclude) cationic polymers.


[0153] In some embodiments, polymers can be linear or branched polymers. In some embodiments, polymers can be dendrimers. In some embodiments, polymers can be substantially cross-linked to one another. In some embodiments, polymers can be substantially free of cross-links. In some embodiments, polymers can be used in accordance with the present invention without undergoing a cross-linking step. It is further to be understood that inventive synthetic nanocarriers may comprise block copolymers, graft copolymers, blends, mixtures, and/or adducts of any of the foregoing and other polymers. Those skilled in the art will recognize that the polymers listed herein represent an exemplary, not comprehensive, list of polymers that can be of use in accordance with the present invention.

[0154] Compositions according to the invention comprise synthetic nanocarriers in combination with pharmaceutically acceptable excipients, such as preservatives, buffers, saline, or phosphate buffered saline. The compositions may be made using conventional pharmaceutical manufacturing and compounding techniques to arrive at useful dosage forms. In an embodiment, inventive synthetic nanocarriers are suspended in sterile saline solution for injection together with a preservative.

[0155] In embodiments, when preparing synthetic nanocarriers as carriers, methods for coupling components to the synthetic nanocarriers may be useful. If the component is a small molecule it may be of advantage to attach the component to a polymer prior to the assembly of the synthetic nanocarriers. In embodiments, it may also be an advantage to prepare the synthetic nanocarriers with surface groups that are used to couple the component to the synthetic nanocarrier through the use of these surface groups rather than attaching the component to a polymer and then using this polymer conjugate in the construction of synthetic nanocarriers.

[0156] In certain embodiments, the coupling can be a covalent linker. In embodiments, peptides according to the invention can be covalently coupled to the external surface via a 1,2,3-triazole linker formed by the 1,3-dipolar cycloaddition reaction of azido groups on the surface of the nanocarrier with an alkyne group or by the 1,3-dipolar cycloaddition reaction of alkynes on the
surface of the nanocarrier with components containing an azido group. Such cycloaddition reactions are preferably performed in the presence of a Cu(I) catalyst along with a suitable Cu(I)-ligand and a reducing agent to reduce Cu(I) compound to catalytic active Cu(I) compound. This Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC) can also be referred as the click reaction.

Additionally, the covalent coupling may comprise a covalent linker that comprises an amide linker, a disulfide linker, a thioether linker, a hydrazide linker, an imine or oxime linker, an urea or thiourea linker, an amidine linker, an amine linker, and a sulfonamide linker.

An amide linker is formed via an amide bond between an amine on one component with the carboxylic acid group of a second component such as the nanocarrier. The amide bond in the linker can be made using any of the conventional amide bond forming reactions with suitably protected amino acids or components and activated carboxylic acid such N-hydroxysuccinimide-activated ester.

A disulfide linker is made via the formation of a disulfide (S-S) bond between two sulfur atoms of the form, for instance, of R1-S-S-R2. A disulfide bond can be formed by thiol exchange of a thiol containing thiolsmercaptop group (—SH) with another activated thiol group on a polymer or nanocarrier or a nanocarrier containing thiolsmercaptop groups with a component containing activated thiol group.

A triazole linker, specifically a 1,2,3-triazole of the form

\[
\text{R}_1 \text{N} = \text{N} - \text{N} = \text{N} \text{R}_2
\]

wherein R1 and R2 may be any chemical entities, is made by the 1,3-dipolar cycloaddition reaction of an azide attached to a first component such as the nanocarrier with a terminal alkynyl attached to a second component such as the immunosuppressant or antigen. The 1,3-dipolar cycloaddition reaction is performed with or without a catalyst, preferably with Cu(I)-catalyst, which links the two components through a 1,2,3-triazole function. This chemistry is described in detail by Sharpless et al., Angew. Chem. Int. Ed. 41(14), 2596, (2002) and Meldal, et al. Chem. Rev., 2008, 108(8), 2952-3015 and is often referred to a “click” reaction or CuAAC.

In embodiments, a polymer containing an azide or alkynyl group, terminal to the polymer chain is prepared. This polymer is then used to prepare a synthetic nanocarrier in such a manner that a plurality of the alkynyl or azide groups are positioned on the surface of that nanocarrier. Alternatively, the synthetic nanocarrier can be prepared by another route, and subsequently functionalized with alkynyl or azide groups. The component is prepared with the presence of either an alkynyl (if the polymer contains an azide) or an azide (if the polymer contains an alkynyl) group. The component is then allowed to react with the nanocarrier via the 1,3-dipolar cycloaddition reaction with or without a catalyst which covalently couples the component to the particle through the 1,4-disubstituted 1,2,3-triazole linker.

A thioether linker is made by the formation of a sulfur-carbon (thioether) bond in the form, for instance, of R1-S-S-R2. Thioether can be made by either alkylation of a thiol/m mercaptan (—SH) group on one component such as the component with an alkylating group such as halide or epoxide on a second component such as the nanocarrier. Thioether linkers can also be formed by Michael addition of a thiol/m mercaptan group on one component to an electron-deficient alkene group on a second component such as a polymer containing a maleimide group or vinyl sulfone group as the Michael acceptor. In another way, thioether linkers can be prepared by the radical thiol-ene reaction of a thiol/m mercaptan group on one component with an alkene group on a second component such as a polymer or nanocarrier.

A hydrazide linker is made by the reaction of a hydrazide group on one component with an aldehyde/ketone group on the second component such as the nanocarrier.

A hydrazide linker is formed by the reaction of a hydrazide group on one component with a carboxylic acid group on the second component such as the nanocarrier. Such reaction is generally performed using chemistry similar to the formation of amide bond where the carboxylic acid is activated with an activating reagent.

A thiol-oxygen linker is formed by the reaction of an amine or N-alkoxymine (or amindoxy) group on one component with an aldehyde or ketone group on the second component such as the nanocarrier.

A urea or thiourea linker is prepared by the reaction of an amine group on one component with an isocyanate or thiolisocyanate group on the second component such as the nanocarrier.

An amidine linker is prepared by the reaction of an amine group on one component with an imidoester group on the second component such as the nanocarrier.

An amine linker is made by the alkylation reaction of an amine group on one component with an alkylating group such as halide, epoxide, or sulfonate ester group on the second component such as the nanocarrier. Alternatively, an amine linker can also be made by reductive amination of an amine group on one component with an aldehyde or ketone group on the second component such as the nanocarrier with a suitable reducing reagent such as sodium cyanoborohydrate or sodium triacetoxyborohydrate.

A sulfonamide linker is made by the reaction of an amine group on one component with a sulfanyl halide (such as sulfonyl chloride) group on the second component such as the nanocarrier.

A sulfone linker is made by Michael addition of a nucleophile to a vinyl sulfone. Either the vinyl sulfone or the nucleophile may be on the surface of the nanocarrier or attached to a component.

The component can also be conjugated to the nanocarrier via non-covalent conjugation methods. For example, a negative charged antigen or immunosuppressant can be conjugated to a positive charged nanocarrier through electrostatic adsorption. A component containing a metal ligand can also be conjugated to a nanocarrier containing a metal complex via a metal-ligand complex.

In embodiments, the component can be attached to a polymer, for example polyactic acid-block-polyethylene glycol, prior to the assembly of the synthetic nanocarrier or the synthetic nanocarrier can be formed with reactive or activatable groups on its surface. In the latter case, the component may be prepared with a group which is compatible with the
attachment chemistry that is presented by the synthetic nanocarriers’ surface. In other embodiments, a peptide can be attached to VLPs or liposomes using a suitable linker. A linker is a compound or reagent that capable of coupling two molecules together. In an embodiment, the linker can be a homobifunctional or heterobifunctional reagent as described in Hermanson 2008. For example, an VLP or liposome synthetic nanocarrier containing a carboxylic group on the surface can be treated with a homobifunctional linker, adipic dihydrazide (ADH), in the presence of EDC to form the corresponding synthetic nanocarrier with the ADH linker. The resulting ADH linked synthetic nanocarrier is then conjugated with a peptide containing an acid group via the other end of the ADH linker on NC to produce the corresponding VLP or liposome peptide conjugate.

[0173] For detailed descriptions of available conjugation methods, see Hermanson G T “Bioconjugate Techniques”, 2nd Edition Published by Academic Press, Inc., 2008. In addition to covalent attachment the component can be coupled by adsorption to a pre-formed synthetic nanocarrier or it can be coupled by encapsulation during the formation of the synthetic nanocarrier.

[0174] Any immunosuppressant as provided herein can be coupled to the synthetic nanocarrier. Immunosuppressants include, but are not limited to, statins; mTOR inhibitors, such as rapamycin or a rapamycin analog; TGF-β signaling agents; TGF-β receptor agonists; histone deacetylase (HDAC) inhibitors; corticosteroids; inhibitors of mitochondrial function, such as rotenone; P38 inhibitors; NF-κB inhibitors; adenosine receptor agonists; prostaglandin E2 agonists; phosphodiesterase inhibitors, such as phosphodiesterase 4 inhibitor; proteasome inhibitors; kinase inhibitors; G-protein coupled receptor agonists; G-protein coupled receptor antagonists; glucocorticoids; retinoids; cytokine inhibitors; cytokine receptor inhibitors; cytokine receptor activators; peryoxisome proliferator-activated receptor antagonists; peroxisome proliferator-activated receptor agonists; histone deacetylase inhibitors; calcineurin inhibitors; phosphatase inhibitors and oxidized ATPs. Immunosuppressants also include [D0, vitamin D3, cyclosporin A, aryl hydrocarbon receptor inhibitors, resveratrol, azathioprine, 6-mercaptopurine, aspirin, niflumic acid, estriol, triiodide, interleukins (e.g., II-1, II-8, cyclosporin A), siRNAs targeting cytokines or cytokine receptors and the like.

[0175] Examples of statins include atorvastatin (LIPI- TOR®), torvastatin (LESCOL®, LESCOL® XL), lovastatin (MEVACOR®, ALTITOCOR®, ALTIVORE®, mevastatin (COMPACTIN®), pitavastatin (LIVALO®), pravastatin (PRAVACHOL®, SELEKTIN®, LIPOSTAT®), rosuvastatin (CRESTOR®), and simvastatin (ZOCOR®, LIPEX®).

[0176] Examples of mTOR inhibitors include rapamycin and analogs thereof (e.g., CCL-779, RAD001, AP23573, C20-methylyrapamycin (C20-Marap), C16-(S)-butylsilfonamidorapamycin (C16-BSrap), C16-(S)-3-methylindol-3-ylmethylrapamycin (C16-Irap) (Bayle et al. Chemistry & Biology 2006. 13:99-107), AZD8055, BEZ235 (NVP-BEZ235), chrysophanic acid (chrysin), deforolimus (MK-8699), everolimus (RAD001), KU-60609, PI-103, PP224, temsirolimus, and WYE-354 (available from Selleck, Houston, Tex., USA).

[0177] Examples of TGF-β signaling agents include TGF-β ligands (e.g., activin A, GDF1, GDF11, bone morphogenetic proteins, nodal, TGF-βs) and their receptors (e.g., ACVR1B, ACVR1C, ACVR2A, ACVR2B, BMP1R, BMP1R1A, BMP1R1B, TGFBR1, TGFBR1I, R-SMADs/co-SMADs (e.g., SMAD1, SMAD2, SMAD3, SMAD4, SMAD5, SMAD8), and ligand inhibitors (e.g., follistatin, noggin, chordin, DUN, lefty, LTBP1, TIBBS1, Decorin).

[0178] Examples of inhibitors of mitochondrial function include atractyloside (dipotassium salt), bongkrekic acid (triammonium salt), carbonyl cyanide m-chlorophenylhydrazone, carboxyatractylloside (e.g., from Atractylis gummifera), Cgph-57157 (−)-Deguelin (e.g., from Manduca sexta), F6, hexokinase II/VII-DAC binding domain peptide, oligomycin, rotenone, Ru360, SFO1, and valinomycin (e.g., from Streptomyces fulvissimus) (EMD Biosciences, USA).

[0179] Examples of P38 inhibitors include SB-203580 (4-(4-(4-Fluorophenyl)-2-(4-methylsulfonylphenyl)-5-(4-pyridyl)- 1H-imidazole), SB-239063 (trans-1-(4-hydroxyethyl)-4-(4-fluorophenyl)-5-(2-methoxy-pyrimidin-4-yl) imidazole), SB-220025 (5-(2-amino-4-pyrimidinyl)-4-(4-fluorophenyl)-1-(1-piperidinyl)imidazole), and ARRY-797.

[0180] Examples of NF (e.g., N-kappaB) inhibitors include I/KB,1.2 (1,8-naphthyridin-2-yl)-phenol, 5-aminoacetylsac acid, BAY 11-7082, BAY 11-7085, CAPE (Caffeic Acid Phenethylster), diethylmaleate, IKK-2 Inhibitor IV, IMD 0534, lactacystin, MG-132 [Z-Leu-Leu-Leu-CHO], NFκB Activation Inhibitor III, NF-κB Activation Inhibitor II, JSH-23, purhenenide, Phenylarsine Oxide (PAO), PIM-16, pyrrolidinedithioacetic acid ammonium salt, QNZ, RO 106- 9920, rogalamide, rogalamide AL, rogalamide C, rogalamide I, rogalamide J, rogalaoal, (R)-MG-132, sodium sulcylate, triptolide (PG490), wderolalectin.

[0181] Examples of adenosine receptor agonists include CGS-21680 and ATL-146e.

[0182] Examples of prostaglandin E2 agonists include E-Prostanoid 2 and E-Prostanoid 4.

[0183] Examples of phosphodiesterase inhibitors (non-selective and selective inhibitors) include caffeine, aminophylline, IBMX (3-isobutyl-1-methylxanthine), paraxanthine, pentoxifylline, theobromine, theophylline, methylated xanthines, vinpocetine, eDNA (erythro-9-(2-hydroxy-3-nonenyl) adenosine), enaregline, enoximone (PERFANT™), milrinone, levosimendan, mesembrine, ibidilast, piclamilast, luteolin, drotaverine, rolflumilast (DAXASTM, DALIRESTM), sildenafil (REVATION®, VIAGRA®), tadalafil (AD- CIRCAX®, CIALIS®), vardenafil (LEVITRA®, StaXyn®, udenafil, avanafil, tadalafil, 4-methylpiperazine, and pyrazolyl pyrimidin-7-1.

[0184] Examples of proteasome inhibitors include bortezomib, disulfiram, epigallocatechin-3-gallate, and salinoproramide A.

[0185] Examples of kinase inhibitors include bevacizumab, BIBW 2992, cetuximab (ERBITUX®), imatinib (GLEEVEC®), trastuzumab (HERCEPTIN®), gefitinib (IRESSA®), ramituzumab (LUCENTIS®), pegaptanib, sorafenib, dasatinib, sunitinib, erlotinib, nilotinib, lapatinib, panitumunab, vandetanib, E7080, pazopanib, mubritinib.

[0186] Examples of glucocorticoids include hydrocortisone (cortisol), cortisone acetate, prednisone, prednisolone, methylprednisolone, dexamethasone, betamethasone, triamcinolone, beclometasone, fludrocortisone acetate, deoxycorticosterone acetate (DOCA), and aldosterone.

[0187] Examples of retinoids include retinol, retinal, tretinoin (retinoic acid, RETIN-A®), isotretinoin (ACCUTANE®), AMNESTEM®, CLARAVIS®, SOTRET®, alitretinoin (PANRETIN®), etretinate (TEGISONTM) and its
metabolite acitretin (SORIATAN®), tazarotene (TAZORAC®, AVAGE®, ZORAC®), bexarotene (TARGRETIN®), and adapalene (DIFFERENT®).

[0188] Examples of cytokine inhibitors include IL-1α, IL-1 receptor antagonist, IFNβ, TGF-β, uromodulin, Alpha-2-Macroglobulin, Cyclosporin A, Pentamidine, and Pentoxifylline (PENTOPAK®, PENTOXIL®, TRENAL®).

[0189] Examples of peroxisome proliferator-activated receptor agonists include pioglitazone, clobi-brate, GW1929, GW7647, L-165,041, LY 171883, PPARY activator, Fmoc-Leu, troglitazone, and WY-14643 (EMD4 Biosciences, USA).

[0190] Examples of peroxisome proliferator-activated receptor agonists include pioglitazone, clobiate, brate, GW1929, GW7647, L-165,041, LY 171883, PPARY activator, Fmoc-Leu, troglitazone, and WY-14643 (EMD4 Biosciences, USA).

[0191] Examples of histone deacetylase inhibitors include hydroxamic acids (or hydroxamates) such as trichostatin A, cyclic tetrapeptides (such as traxipin B) and depsipeptides, benzamides, electrophilic ketones, alfipacic acid compounds such as phenylbutyrate and valproic acid, hydroxamic acids such as vorinostat (SAHA), belinostat (PXD101), LAQ824, and panobinostat (LBHS89), benzamides such as entinostat (MS-275), C9194, and mocetinostat (MGCD0010), nicotinamide, derivatives of NAD, dihydrocoumarin, naphthyropyranone, and 2-hydroxynaphthaldehydes.

[0192] Examples of calcineurin inhibitors include cyclosporine, pimecrolimus, voclosporin, and tacrolimus.

[0193] Examples of phosphatase inhibitors include DN82002 hydrochloride, CP-91149, calcyulin A, calcitriol acid, cantharidin, cypermethrin, ethyl-3,4-diphenylphenol, for- triecin sodium salt, MAZ51, methyl-3,4-diphenol, nicotine, 95397, rotenarin, okadaic acid ammonium salt from prorocentrum concavum, okadaic acid, okadaic acid potassium salt, okadaic acid sodium salt, phenylarsine oxide, various phosphatase inhibitor cocktails, protein phosphatase 1C, protein phosphatase 2A inhibitor protein, protein phosphatase 2A1, protein phosphatase 2A2, sodium orthovanadate.

[0194] In some embodiments, antigens as described herein are also coupled to synthetic nanocarriers. In some embodiments, the antigens are coupled to the same or different synthetic nanocarriers as to which the immunosuppressants are coupled. In other embodiments, the antigens are not coupled to any synthetic nanocarriers. Antigens include any of the antigens provided herein, or fragments or derivatives thereof, such as antigens associated with inflammatory, autoimmune diseases, allergy, organ or tissue rejection, graft versus host disease, transplant antigens and therapeutic protein antigens. The epitopes, or proteins, polypeptides or peptides that comprise the epitopes can be obtained or derived from any of the antigens provided or otherwise known in the art.

[0195] Therapeutic proteins include, but are not limited to, infusable therapeutic proteins, enzymes, enzyme cofactors, hormones, blood clotting factors, cytokines and interleukins, growth factors, monoclonal antibodies, and polyclonal antibodies (e.g., that are administered to a subject as a replacement therapy), and proteins associated with Pompe’s disease (e.g., α-glucosidase alpha, rhGAA (e.g., Myozyme and Lumizyme (Genzyme))). Therapeutic proteins also include proteins involved in the blood coagulation cascade. Therapeutic proteins include, but are not limited to, Factor V, Factor VIII, Factor IX, Factor IX, von Willebrand Factor, von Heldebrand Factor, tissue plasminogen activator, insulin, growth hormone, erythropoietin alpha, VEGF, thrombopoietin, lysozyme, antithrombin and the like. Therapeutic proteins also include adipokines, such as leptin and adiponectin. Other examples of therapeutic proteins are as described below and elsewhere herein. Also included are fragments or derivatives of any of the therapeutic proteins provided as the antigen.

[0196] Examples of therapeutic proteins used in enzyme replacement therapy of subjects having a lysosomal storage disorder include, but are not limited to, imiglucerase for the treatment of Gaucher’s disease (e.g., CEREZYME™, α-galactosidase A (α-gal A) for the treatment of Fabry disease (e.g., agalactosidase beta, FABRYZYME™), α-glucosidase (GAA) for the treatment of Pompe disease (e.g., α-glucosidase alpha, LUMIZYME™, MOYOSYME™), aryl sulfatase B for the treatment of Mucopolysaccharidoses (e.g., laronidase, ALDURAZYME™, idursulfase, ELAPRASE™, aryl sulfatase B, NAGLYZyme™).

[0197] Examples of enzymes include oxidoreductases, transferases, hydrolases, isomerases, and ligases.

[0198] Examples of hormones include Melatonin (N-acetyl-5-methoxytryptamine), Serotonin, Thyroxine (or tetraiodothyronine) (a thyroid hormone), Triiodothyronine (a thyroid hormone), Epinephrine (or adrenaline), Norepinephrine (or noradrenaline), Dopamine (or prolactin inhibiting hormone), Anti-mullerian hormone (or mullerian inhibiting factor or hormone), Adiponectin, Adrenocorticotropin hormone (or corticotropin), Angiotensinogen and angiotensin, Antidiuretic hormone (or vasopressin, arginine vasopressin), Atrial-natriuretic peptide (or atriopeptin), Calcitonin, Cholecystokinin, Corticotropin-releasing hormone, Erythropoietin, Follicle-stimulating hormone, GnRH, GH, Glucagon, Glucagon-like peptide (GLP-1), GIP, Gonadotropin-releasing hormone, Growth hormone-releasing hormone, Human chorionic gonadotropin, Human placental lactogen, Growth hormone, Insulin, Insulin-like growth factor (or somatomedin), Leptin, Luteinizing hormone, Melanocyte stimulating hormone, Oxytocin, Parathyroid hormone, Prolactin, Relaxin, Secretin, Somatostatin, Thrombopoietin, Thyroid-stimulating hormone (or thyrotropin), Thyrotropin-releasing hormone, Cortisol, Aldosterone, Testosterone, Dehydroepiandrosterone, Androstenedione, Dihydrotestosterone, Estradiol, Estrone, Estradiol, Progesterone, Calcitriol (1,25-dihydroxyvitamin D3), Calcidiol (25-hydroxyvitamin D3), Prostaglandins, Leukotrienes, Prostacyc- lin, Thromboxane, Prolactin releasing hormone, Lipotropin, Brain natriuretic peptide, Neuropeptide Y, Histamine, Endothelin, Pancreatic polypeptide, Renin, and Enkephalin.

[0199] Examples of blood and blood coagulation factors include Factor I (fibrinogen), Factor II (prothrombin), tissue factor, Factor V (proaccelerin, labile factor), Factor VII (stable factor, proconvertin), Factor VIII (antihemophilic globulin), Factor IX (Christmas factor or plasma thrombo- plastin component), Factor X (Stuart-Prower factor), Factor Xa, Factor XI, Factor XII (Hageman factor), Factor XIII (fibrin-stabilizing factor), von Willebrand factor, prekallikrein (Fletcher factor), high-molecular weight kininogen (HMWK) (Fitzgerald factor), fibrinectin, fibrin, thrombin, antithrombin III, heparin cofactor II, protein C, protein S, protein Z, protein Z-related protease inhibitor (ZPI), plasmi- nogen, alpha 2-antiplasmin, tissue plasminogen activator (tPA), urokinase, plasminogen activator inhibitor-1 (PAI1), plasminogen activator inhibitor-2 (PAI2), cancer procoagulant, and epoetin alpha (Eprex, Procrit).
Examples of cytokines include lymphokines, interleukins, and chemokines, type 1 cytokinins, such as IFN-γ, TGF-β, and type 2 cytokines, such as IL-4, IL-10, and IL-13. Examples of growth factors include Adrenomedullin (AM), Angiopoietin (Ang), Autocrine motility factor, Bone morphogenetic proteins (BMPs), Brain-derived neurotrophic factor (BDNF), Epidermal growth factor (EGF), Erythropoietin (EPO), Fibroblast growth factor (FGF), Glial cell line-derived neurotrophic factor (GDNF), Granulocyte colony-stimulating factor (G-CSF), Granulocyte macrophage colony-stimulating factor (GM-CSF), Growth differentiation factor-9 (GDF9), Hepatocyte growth factor (HGF), Hepatoma-derived growth factor (HDFG), Insulin-like growth factor (IGF), Migration-stimulating factor, Myostatin (GDF-8), Nerve growth factor (NGF) and other neurotrophins, Platelet-derived growth factor (PDGF), Thrombopoietin (TPO), Transforming growth factor alpha (TGF-α), Transforming growth factor beta (TGF-β), Tumour necrosis factor-alpha (TNF-α), Vascular endothelial growth factor (VEGF), Wnt Signaling Pathway, placental growth factor (PIGF), ([Foetal Bovine Somatotrophin]) (FBS), IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, and IL-7.


Examples of infusion therapy or injectable therapeutic proteins include, for example, Tolcilizumab (Roche/Actemra®), alpha-1 antitrypsin (Kamada/AAT), Hematide® (Alfamyn and Takeda, synthetic peptide), abinterferon alfa-2b (Novartis/Zalbin™), Rhucin® (Pharming Group, C1 inhibitor replacement therapy), tesaromelittin (THERNotechnologies/Egrifta, synthetic growth hormone-releasing factor), ocrelizumab (Genentech, Roche and Biogen), belimumab (GlaxoSmithKline/Benlysta®), pegloticase (Savient Pharmaceuticals/Kryxstemx™), taliglucerase alfa (Protalix/Uplyso), agalsidase alfa (Shire/Replagal®), valganciclovir alfa (Shire).

Additional therapeutic proteins useful in accordance to aspects of this invention will be apparent to those of skill in the art, and the invention is not limited in this respect. In some embodiments, a component, such as an antigen or immunosuppressant, may be isolated. Isolated refers to the element being separated from its native environment and present in sufficient quantities to permit its identification or use. This means, for example, the element may be (i) selectively produced by expression cloning or (ii) purified as by chromatography or electrophoresis. Isolated elements may be, but need not be, substantially pure. Because an isolated element may be admixed with a pharmaceutically acceptable excipient in a pharmaceutical preparation, the element may comprise only a small percentage by weight of the preparation. The element is nonetheless isolated in that it is separated from the substances with which it may be associated in living systems, i.e., isolated from other lipids or proteins. Any of the elements provided herein can be included in the compositions in isolated form.

D. METHODS OF MAKING AND USING THE INVENTIVE COMPOSITIONS AND RELATED METHODS

Synthetic nanocarriers may be prepared using a wide variety of methods known in the art. For example, synthetic nanocarriers can be formed by methods as nanoparticles, size focusing using fluidic channels, spray drying, single and double emulsion solvent extraction, solvent extraction, phase separation, milling, microemulsion procedures, microfabrication, nanofabrication, sacrificial layers, simple and complex coacervation, and other methods well known to those of ordinary skill in the art. Alternatively or additionally, aqueous and organic solvent syntheses for monodisperse semiconductor, conductive, magnetic, organic, and other nanomaterials have been described (Pellegrino et al., 2005, Small, 1:48; Murray et al., 2000, Ann Rev. Mat. Sci., 30:545; and Trindade et al., 2001, Chem. Mat., 13:3843). Additional methods have been described in the literature (see,


[0208] In certain embodiments, synthetic nanocarriers are prepared by a nanoprecipitation process or spray drying. Conditions used in preparing synthetic nanocarriers may be altered to yield particles of a desired size or property (e.g., hydrophobicity, hydrophilicity, external morphology, “stickiness,” shape, etc.). The method of preparing the synthetic nanocarriers and the conditions (e.g., solvent, temperature, concentration, air flow rate, etc.) used may depend on the materials to be coupled to the synthetic nanocarriers and/or the composition of the polymer matrix.

[0209] If particles prepared by any of the above methods have a size range outside of the desired range, particles can be sized, for example, using a sieve.

[0210] Elements (i.e., components) of the inventive synthetic nanocarriers (such as moieties of which an immunofac- ture surface is comprised, targeting moieties, polymeric matrices, antigens, immunosuppressants and the like) may be coupled to the overall synthetic nanocarrier, e.g., by one or more covalent bonds, or may be coupled by means of one or more linkers. Additional methods of functionalizing synthetic nanocarriers may be adapted from Published US Patent Application 2006/0002852 to Saltzman et al., Published US Patent Application 2009/0028910 to DeSimone et al., or Published International Patent Application WO2008/127532 A1 to Murthy et al.

[0211] Alternatively or additionally, synthetic nanocarriers can be coupled to components directly or indirectly via non-covalent interactions. In non-covalent embodiments, the non-covalent coupling is mediated by non-covalent interactions including but not limited to charge interactions, affinity interac- tions, metal coordination, physical adsorption, host-guest interactions, hydrophobic interactions, TT stacking interac- tions, hydrogen bonding interactions, van der Waals interac- tions, magnetic interactions, electrostatic interactions, dipole-dipole interactions, and/or combinations thereof. Such couplings may be arranged to be on an external surface or an internal surface of an inventive synthetic nanocarrier. In embodiments, encapsulation and/or absorption is a form of coupling. In embodiments, the inventive synthetic nanocarriers can be combined with antigen by admixing in the same vehicle or delivery vehicle system.

[0212] Populations of synthetic nanocarriers may be combined to form pharmaceutical dosage forms according to the present invention using traditional pharmaceutical mixing methods. These include liquid-liquid mixing in which two or more suspensions, each containing one or more subsets of nanocarriers, are directly combined or are brought together via one or more vessels containing diluents. As synthetic nanocarriers may also be produced or stored in a powder form, dry powder-powder mixing could be performed as could the resuspension of two or more powders in a common medium. Depending on the properties of the nanocarriers and their interaction potentials, there may be advantages conferred to one or another route of mixing.

[0213] Typical inventive compositions that comprise synthetic nanocarriers may comprise inorganic or organic buffers (e.g., sodium or potassium salts of phosphate, carbonate, acetate, or citrate) and pH adjustment agents (e.g., hydrochloric acid, sodium or potassium hydroxide, salts of citrate or acetate, amino acids and their salts) antioxidants (e.g., ascorbic acid, alpha-tocopherol), surfactants (e.g., polysorbate 20, polysorbate 80, polyoxyethylene9-10 nonyl phenol, sodium deoxycholate), solution and/or cryo/lyo stabilizers (e.g., sucrose, lactose, mannitol, trehalose), osmotic adjustment agents (e.g., salts or sugars), antibacterial agents (e.g., benzic acid, phenol, gentamicin), anti-fogging agents (e.g., polydimethylsiloxane), preservatives (e.g., thimerosal, 2-phenoxyethanol, EDTA), polymeric stabilizers and viscosity-adjustment agents (e.g., polyvinylpyrrolidone, poloxamer 408, carboxymethylcellulose) and co-solvents (e.g., glycerol, polyethylene glycol, ethanol).

[0214] Compositions according to the invention comprise inventive synthetic nanocarriers in combination with pharmaceutically acceptable excipients. The compositions may be made using conventional pharmaceutical manufacturing and compounding techniques to arrive at useful dosage forms. Techniques suitable for use in practicing the present invention may be found in Handbook of Industrial Mixing: Science and Practice, Edited by Edward L. Paul, Victor A. Ariemo-Obeng, and Suzanne M. Kresta, 2004 John Wiley & Sons, Inc.; and Pharmaceutics: The Science of Dosage Form Design, 2nd Ed. Edited by M. E. Auten, 2001, Churchill Livingstone. In an embodiment, inventive synthetic nanocarriers are suspended in sterile saline solution for injection together with a preservative.

[0215] It is to be understood that the compositions of the invention can be made in any suitable manner, and the invention is in no way limited to compositions that can be produced using the methods described herein. Selection of an appropriate method may require attention to the properties of the particular moieties being associated.

[0216] In some embodiments, inventive synthetic nanocarriers are manufactured under sterile conditions or are termi- nally sterilized. This can ensure that resulting compositions are sterile and non-infectious, thus improving safety when compared to non-sterile compositions. This provides a valuable safety measure, especially when subjects receiving synthetic nanocarriers have immune defects, are suffering from infection, and/or are susceptible to infection. In some embodiments, inventive synthetic nanocarriers may be lyo-
philized and stored in suspension or as lyophilized powder depending on the formulation strategy for extended periods without losing activity.

[0217] The compositions of the invention can be administered by a variety of routes, including but not limited to subcutaneous, intranasal, oral, intravenous, intraperitoneal, intramuscular, transmucoosal, transmucosal, sublingual, rectal, ophthalmic, pulmonary, intradermal, transdermal, transcutaneous or intradermal or by a combination of these routes. Routes of administration also include administration by inhalation or pulmonary aerosol. Techniques for preparing aerosol delivery systems are well known to those of skill in the art (see, for example, Sciarr and Cutie, “Aerosols,” in Remington’s Pharmaceutical Sciences, 18th edition, 1990, pp. 1694-1712; incorporated by reference).

[0218] The transplantable grafts or therapeutic proteins provided as a cell-based therapy of the invention may be administered by parenteral, intraarterial, intranasal or intravenous administration or by injection to lymph nodes or anterior chamber of the eye or by local administration to an organ or tissue of interest. The administration may be by subcutaneous, intrathecal, intraventricular, intramuscular, intraperitoneal, intracoronary, intrapancreatic, intrahepatic or bronchial injection.

[0219] The compositions of the invention can be administered in effective amounts, such as the effective amounts described elsewhere herein. Doses of dosage forms contain varying amounts of populations of synthetic nanocarriers and/or varying amounts of immunosuppressants and/or antigens, according to the invention. The amount of synthetic nanocarriers and/or immunosuppressants and/or antigens present in the inventive dosage forms can be varied according to the nature of the antigens, the therapeutic benefit to be accomplished, and other such parameters. In embodiments, dose ranging studies can be conducted to establish optimal therapeutic amount of the population of synthetic nanocarriers and the amount of immunosuppressants and/or antigens to be present in the dosage form. In embodiments, the synthetic nanocarriers and/or the immunosuppressants and/or antigens are present in the dosage form in an amount effective to generate a tolerogenic immune response using conventional dose ranging studies and techniques in subjects. Inventive dosage forms may be administered at a variety of frequencies. In a preferred embodiment, at least one administration of the dosage form is sufficient to generate a pharmacologically relevant response. In more preferred embodiments, at least two administrations, at least three administrations, or at least four administrations, of the dosage form are utilized to ensure a pharmacologically relevant response.

[0220] Prophylactic administration of the inventive compositions can be initiated prior to the onset of disease, disorder or condition or therapeutic administration can be initiated after a disorder, disorder or condition is established.

[0221] In some embodiments, administration of synthetic nanocarriers is undertaken e.g., prior to administration of a therapeutic protein or transplantable graft or exposure to an allergen. In exemplary embodiments, synthetic nanocarriers are administered at one or more times including, but not limited to, 30, 25, 20, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0 days prior to administration of a therapeutic protein or transplantable graft or exposure to an allergen. In addition or alternatively, synthetic nanocarriers can be administered to a subject following administration of a therapeutic protein or transplantable graft or exposure to an allergen. In exemplary embodiments, synthetic nanocarriers are administered at one or more times including, but not limited to, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, 30, etc. days following administration of a therapeutic protein or transplantable graft or exposure to an allergen.

[0222] In some embodiments, a maintenance dose (e.g., of a synthetic nanocarrier composition provided herein) is administered to a subject after an initial administration has resulted in a tolerogenic response in the subject, for example to maintain the tolerogenic effect achieved after the initial dose, to prevent an undesired immune reaction in the subject, or to prevent the subject becoming a subject at risk of experiencing an undesired immune response or an undesired level of an immune response. In some embodiments, the maintenance dose is the same dose as the initial dose the subject received. In some embodiments, the maintenance dose is a lower dose than the initial dose. For example, in some embodiments, the maintenance dose is about \( \frac{1}{8} \), about \( \frac{1}{8} \), about \( \frac{1}{8} \), about \( \frac{1}{8} \), about \( \frac{1}{8} \), about \( \frac{1}{8} \), about \( \frac{1}{8} \), about \( \frac{1}{8} \), about \( \frac{1}{8} \), about \( \frac{1}{8} \), about \( \frac{1}{8} \), about \( \frac{1}{8} \), about \( \frac{1}{8} \), or about \( \frac{1}{8} \), \( \frac{1}{8} \), or about \( \frac{1}{8} \), \( \frac{1}{8} \), \( \frac{1}{8} \), (weight/weight) of the initial dose.

[0223] The compositions and methods described herein can be used to induce or enhance a tolerogenic immune response amounts to suppress, modulate, direct or redirect an undesired immune response for the purpose of immune suppression. The compositions and methods described herein can be used in the diagnosis, prophylaxis and/or treatment of diseases, disorders or conditions in which immune suppression (e.g., tolerogenic immune response) would confer a treatment benefit. Such diseases, disorders or conditions include inflammatory diseases, autoimmune diseases, allergies, organ or tissue rejection and graft versus host disease. The compositions and methods described herein can also be used in subjects who have undergone or will undergo transplantation. The compositions and methods described herein can also be used in subjects who have received, are receiving or will receive a therapeutic protein against which they have generated or are expected to generate an undesired immune response.

[0224] Autoimmune diseases include, but are not limited to, rheumatoid arthritis, multiple sclerosis, immune-mediated or Type I diabetes mellitus, inflammatory bowel disease (e.g., Crohn’s disease or ulcerative colitis), systemic lupus erythematosus, psoriasis, scleroderma, autoimmune thyroid disease, alopecia areata, Grave’s disease, Guillain-Barré syndrome, celiac disease, Sjogren’s syndrome, rheumatic fever, gastritis, autoimmune atrophic gastritis, autoimmune hepatitis, insulinitis, oophoritis, orchitis, uveitis, phacogenic uveitis, myasthenia gravis, primary myxoedema, pernicious anemia, autoimmune haemolytic anemia, Addison’s disease, scleroderma, Goodpasture’s syndrome, nephritis, for example, glomerulonephritis, psoriasis, pneumonia, splenic granulomas, pemphigoid, sympathetic ophthalmia, idiopathic thromboelypoplastic purpura, idiopathic leucopenia, Wegener’s granulomatosis and poly/dermatomyositis.

[0225] Some additional exemplary autoimmune diseases, associated autoantigens, and autoantibodies, which are contemplated for use in the invention, are described in Table 1 below:
<table>
<thead>
<tr>
<th>Autoantibody Type</th>
<th>Autoantibody</th>
<th>Autoantigen</th>
<th>Autoimmune disease or disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-SSA/Ro autoantibodies</td>
<td>Anti-SSA/Ro</td>
<td>ribonucleoproteins</td>
<td>Systemic lupus erythematosus, neonatal heart block, primary Sjögren’s syndrome</td>
</tr>
<tr>
<td>Anti-SS-B autoantibodies</td>
<td>Anti-SS-B</td>
<td>ribonucleoproteins</td>
<td>Primary Sjögren’s syndrome</td>
</tr>
<tr>
<td>Anti-centromere antibodies</td>
<td>Anti-centromere</td>
<td>centromere</td>
<td>CREST syndrome</td>
</tr>
<tr>
<td>Anti-neutrophil nuclear antibody-2</td>
<td>Anti-neu-2</td>
<td>Rij[dissambiguation needed] DNA</td>
<td>Opsoclonus</td>
</tr>
<tr>
<td>Anti-dsDNA</td>
<td>Anti-dsDNA</td>
<td>double-stranded DNA</td>
<td>SLE</td>
</tr>
<tr>
<td>Anti-Jo1</td>
<td>Anti-Jo1</td>
<td>histidine-RNA ligase</td>
<td>Inflammatory myopathy</td>
</tr>
<tr>
<td>Anti-Smith</td>
<td>Anti-Smith</td>
<td>snRNP core proteins</td>
<td>SLE</td>
</tr>
<tr>
<td>Anti-topoisomerase antibodies</td>
<td>Anti-topo1</td>
<td>Type I topoisomerase</td>
<td>Systemic sclerosis (anti-Scl-70 antibodies)</td>
</tr>
<tr>
<td>Anti-histone antibodies</td>
<td>Anti-histone</td>
<td>histones</td>
<td>SLE and Drug-induced LE[2]</td>
</tr>
<tr>
<td>Anti-sp100 antibodies[4]</td>
<td>Anti-sp100</td>
<td>Sp100 nuclear antigen</td>
<td>Coeliac disease</td>
</tr>
<tr>
<td>Anti-transglutaminase antibodies</td>
<td>Anti-TG</td>
<td>ganglioside GQ1B</td>
<td>Miller-Fisher Syndrome</td>
</tr>
<tr>
<td>Anti-ganglioside antibodies</td>
<td>Anti-TG</td>
<td>ganglioside GD3</td>
<td>Acute motor axonal neuropathy (AMAN)</td>
</tr>
<tr>
<td>Anti-actin antibodies</td>
<td>Anti-actin</td>
<td>actin</td>
<td>Multifocal motor neuropathy with conduction block (MMN)</td>
</tr>
<tr>
<td>Liver kidney microsomal type 1 antibody</td>
<td>Anti-TG</td>
<td>IgG</td>
<td>Microscopic polyangiitis, Chung-Strauss syndrome, systemic vasculitides (non-specific)</td>
</tr>
<tr>
<td>Lupus anticoagulant antibodies</td>
<td>Anti-thrombin</td>
<td>thrombin</td>
<td>Systemic lupus erythematosus</td>
</tr>
<tr>
<td>Anti-neutrophil cytoplasmic antibody</td>
<td>Anti-neu-1</td>
<td>phospholipid proteins in neutrophil cytoplasm</td>
<td>Antiphospholipid syndrome</td>
</tr>
<tr>
<td>p-ANCA</td>
<td>c-ANCA</td>
<td>neutrophil perinuclear</td>
<td>Wegener’s granulomatosis</td>
</tr>
<tr>
<td>Rheumatoid factor</td>
<td>Anti-smooth muscle antibody</td>
<td>IgG smooth muscle</td>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td>Anti-mitochondrial antibody</td>
<td>Anti-SRPN</td>
<td>mitochondria</td>
<td>Chronic autoimmune hepatitis</td>
</tr>
<tr>
<td>Anti-SRP</td>
<td></td>
<td>signal recognition particle</td>
<td>Polymyositis[10]</td>
</tr>
<tr>
<td>Anti-VGCC</td>
<td></td>
<td>nicotinic acetylcholine receptor</td>
<td>Scleroderma</td>
</tr>
<tr>
<td>Anti-VGCC</td>
<td></td>
<td>muscle-specific kinase (MUSK)</td>
<td>Myasthenia gravis</td>
</tr>
<tr>
<td>Anti-VGCC</td>
<td></td>
<td>voltage-gated calcium channel (P/Q-type)</td>
<td>Lambert-Eaton myasthenic syndrome</td>
</tr>
<tr>
<td>Anti-VGCC</td>
<td></td>
<td>thyroid peroxidase (microsomal)</td>
<td>Hashimoto’s thyroiditis</td>
</tr>
<tr>
<td>Anti-VGCC</td>
<td></td>
<td>TSH receptor</td>
<td>Graves’ disease</td>
</tr>
<tr>
<td>Anti-VGCC</td>
<td></td>
<td>Hu</td>
<td>Paraneoplastic cerebellar syndrome</td>
</tr>
<tr>
<td>Anti-VGCC</td>
<td></td>
<td>Yo (cerebellar Purkinje Cells) amphiplasia</td>
<td>Paraneoplastic cerebellar syndrome</td>
</tr>
<tr>
<td>Anti-VGCC</td>
<td></td>
<td>voltage-gated potassium channel (VGKC)</td>
<td>Stiff person syndrome, paraneoplastic cerebellar syndrome</td>
</tr>
<tr>
<td>Anti-VGCC</td>
<td></td>
<td></td>
<td>Limbic encephalitis, Isaac’s Syndrome (autoimmune neuromyotonia)</td>
</tr>
</tbody>
</table>
Inflammatory diseases include, but are not limited to, Alzheimer’s, arthritis, asthma, atherosclerosis, Crohn’s disease, colitis, cystic fibrosis, dermatitis, diverticulitis, hepatitis, irritable bowel syndrome (IBS), lupus erythematosus, muscular dystrophy, nephritis, Parkinson’s, shingles and ulcerative colitis. Infectious diseases also include, for example, cardiovascular disease, chronic obstructive pulmonary disease (COPD), bronchiectasis, chronic cholecystitis, tuberculosis, Hashimoto’s thyroiditis, sepsis, sarcoidosis, silicosis and other pneumoconioses, and an implanted foreign body in a wound, but are not so limited. As used herein, the term “sepsis” refers to a well-recognized clinical syndrome associated with a host’s systemic inflammatory response to microbial invasion. The term “sepsis” as used herein refers to a condition that is typically signaled by fever or hypothermia, tachycardia, and tachypnea, and in severe instances can progress to hypotension, organ dysfunction, and even death.

In some embodiments, the inflammatory disease is non-autoimmune inflammatory bowel disease, post-surgical adhesions, coronary artery disease, hepatic fibrosis, acute respiratory distress syndrome, acute inflammatory pancreatitis, endoscopic retrograde cholangiopancreatography-induced pancreatitis, burns, atherogenesis of coronary, cerebral and peripheral arteries, appendicitis, cholecystitis, diverticulitis, visceral fibrotic disorders, wound healing, skin scarring disorders (keloids, hradinmad suppurativa), granulomatous disorders (sarcoioidosis, primary biliary cirrhosis), asthma, pyoderma gangreosum, Sweet’s syndrome, Behcet’s disease, primary sclerosing cholangitis or an abscess. In some preferred embodiments the inflammatory disease is inflammatory bowel disease (e.g., Crohn’s disease or ulcerative colitis).

In other embodiments, the inflammatory disease is an autoimmune disease. The autoimmune disease in some embodiments is rheumatoid arthritis, rheumatic fever, ulcerative colitis, Crohn’s disease, autoimmune inflammatory bowel disease, insulin-dependent diabetes mellitus, diabetes mellitus, juvenile diabetes, spontaneous autoimmune diabetes, gastritis, autoimmune gastritis, autoimmune hepatitis, thyroiditis, Hashimoto’s thyroiditis, insulitis, oophoritis, orchitis, uveitis, phacogenic uveitis, multiple sclerosis, myasthenia gravis, primary myxoedema, thyrotoxicosis, pernicious anemia, autoimmune haemolytic anemia, Addison’s disease, Ankylosing spondylitis, sarcoidosis, scleroderma, Goodpasture’s syndrome, Guillain-Barre syndrome, Graves’ disease, glomerulonephritis, psoriasis, pemphigus vulgaris, pemphigoid, exema, bullous pemphigous, sympathetic ophthalmia, idiopathic thrombocytopenic purpura, idiopathic fevropenia, Sjogren’s syndrome, systemic sclerosis, Wegener’s granulomatosis, poly/dermatomyositis, primary biliary cirrhosis, primary sclerosing cholangitis, lupus or systemic lupus erythematosus.

Graft versus host disease (GVHD) is a complication that can occur after a pluripotent cell (e.g., stem cell) bone marrow transplant in which the newly transplanted material results in an attack on the transplant recipient’s body. In some instances, GVHD takes place after a blood transfusion. Graft-versus-host-disease can be divided into acute and chronic forms. The acute or fulminant form of the disease (aGVHD) is normally observed within the first 100 days post-transplant, and is a major challenge to transplants owing to associated morbidity and mortality. The chronic form of graft-versus-host-disease (cGVHD) normally occurs after 100 days. The appearance of moderate to severe cases of cGVHD adversely influences long-term survival.

EXAMPLES

Example 1

Immune Response of Synthetic Nanocarriers with Coupled Rapamycin with and without Ovalbumin Peptide (323-339)

Materials

Ovalbumin peptide 323-339, a 17 amino acid peptide known to be a T and B cell epitope of Ovalbumin protein, was purchased from Biochem Americas Inc. (3132 Kashiwa Street, Torrance Calif. 90505; Part #4065609). Rapamycin was purchased from TSK CHEM (185 Wilson Street, Framingham, Mass. 01702; Product Catalogue | R1017). PLGA with a lactide/glycolide ratio of 3:1 and an inherent viscosity of 0.75 dl/g was purchased from SurModics Pharmaceuticals (756 Torn Martin Drive, Birmingham, Ala. 35211; Product Code 7525 DLG 7A). Polyvinyl alcohol (85-89% hydrolyzed) was purchased from EMD Chemicals (Product Number 1.41350.1001).

Solution 1: Ovalbumin peptide 323-339 @20 mg/mL in dilute hydrochloric acid aqueous solution. The solution was prepared by dissolving ovalbumin peptide in 0.13 M hydrochloric acid solution at room temperature.

Solution 2: Rapamycin @50 mg/mL in methylene chloride. The solution was prepared by dissolving rapamycin in pure methylene chloride.

Solution 3: PLGA @100 mg/mL in methylene chloride. The solution was prepared by dissolving PLGA in pure methylene chloride.
Solution 4: Polyvinyl alcohol (a 50 mg/mL in 100 mM pH 8 phosphate buffer.

Method for Preparing Synthetic Nanocarrier Containing Rapamycin and Ovalbumin (323-339)

A primary water-in-oil emulsion was prepared first. W/O1 was prepared by combining solution 1 (0.2 mL), solution 2 (0.2 mL), and solution 3 (1.0 mL) in a small pressure tube and sonicating at 50% amplitude for 40 seconds using a Branson Digital Sonifier 250. A secondary emulsion (W/O1/W2) was then prepared by combining solution 4 (3.0 mL) with the primary W/O1 emulsion, vortexing for 10 s, and sonicating at 30% amplitude for 60 seconds using the Branson Digital Sonifier 250.

The W/O1/W2 emulsion was added to a beaker containing 70 mM pH 8 phosphate buffer solution (30 mL) and stirred at room temperature for 2 hours to allow the methylene chloride to evaporate and for the synthetic nanocarriers to form. A portion of the synthetic nanocarriers were washed by transferring the synthetic nanocarrier suspension to a centrifuge tube and centrifuging at 21,000g and 4°C for one hour, removing the supernatant, and re-suspending the pellet in phosphate buffered saline. The washing procedure was repeated, and the pellet was re-suspended in phosphate buffered saline for a final synthetic nanocarrier dispersion of about 10 mg/mL.

The amounts of peptide and rapamycin in the synthetic nanocarriers were determined by HPLC analysis. The total dry-synthetic nanocarrier mass per mL of suspension was determined by a gravimetric method.

Method for Synthetic Nanocarrier Containing Rapamycin

A primary water-in-oil emulsion was prepared first. W/O1 was prepared by combining 0.13 M hydrochloric acid solution (0.2 mL), solution 2 (0.2 mL), and solution 3 (1.0 mL) in a small pressure tube and sonicating at 50% amplitude for 40 seconds using a Branson Digital Sonifier 250. A secondary emulsion (W/O1/W2) was then prepared by combining solution 4 (3.0 mL) with the primary W/O1 emulsion, vortexing for 10 s, and sonicating at 30% amplitude for 60 seconds using the Branson Digital Sonifier 250.

The W/O1/W2 emulsion was added to a beaker containing 70 mM pH 8 phosphate buffer solution (30 mL) and stirred at room temperature for 2 hours to allow the methylene chloride to evaporate and for the synthetic nanocarriers to form. A portion of the synthetic nanocarriers were washed by transferring the synthetic nanocarrier suspension to a centrifuge tube and centrifuging at 21,000g and 4°C for one hour, removing the supernatant, and re-suspending the pellet in phosphate buffered saline. The washing procedure was repeated, and the pellet was re-suspended in phosphate buffered saline for a final synthetic nanocarrier dispersion of about 10 mg/mL.

The amount of rapamycin in the synthetic nanocarrier was determined by HPLC analysis. The total dry-synthetic nanocarrier mass per mL of suspension was determined by a gravimetric method.

Method for Measuring Rapamycin Load

Approximately 3 mg of synthetic nanocarriers were collected and centrifuged to separate supernatant from synthetic nanocarrier pellet. Acetonitrile was added to the pellet, and the sample was sonicated and centrifuged to remove any insoluble material. The supernatant and pellet were injected on RP-HPLC and absorbance was read at 278 nm. The µg found in the pellet were used to calculate % entrapped (load), µg in supernatant and pellet were used to calculate total µg recovered.

Method for Measuring Ovalbumin (323-339) Load

Approximately 3 mg of synthetic nanocarriers were collected and centrifuged to separate supernatant from synthetic nanocarrier pellet. Trifluoroethanol was added to the pellet and the sample was sonicated to dissolve the polymer, 0.2% trifluoroacetic acid was added and sample was sonicated and then centrifuged to remove any insoluble material. The supernatant and pellet were injected on RP-HPLC and absorbance was read at 215 nm. The µg found in the pellet were used to calculate % entrapped (load), µg in supernatant and pellet were used to calculate total µg recovered.

Antigen-specific Tolerogenic Dendritic Cells (Tdc) Activity on Treg Cell Development

The assay included the use of OTII mice which have a transgenic T-cell receptor specific for an immune-dominant ovalbumin (323-339). In order to create antigen-specific tDCs, CD11c+ splenocytes were isolated, and the ovalbumin (323-339) peptide added in vitro at 1 µg/ml or no antigen. Soluble or nanocarrier-encapsulated rapamycin was then added to the DCs for 2 hours which were then washed extensively to remove free rapamycin from the culture. Purified responder CD4+CD25- cells were isolated from OTII mice and added to TDC at a 10:1 T to DC ratio. The mixture of TDC and OTII T-cells were then cultured for 4-5 days, and the frequency of T cells (CD4+CD25highFoxp3+) were analyzed by flow cytometry as shown in FIG. 1. Regions were selected based on isotype controls.

Example 2

Mesoporous Silica Nanoparticles with Coupled Ibuprofen (Prophetic)

Mesoporous SiO2 nanoparticle cores are created through a sol-gel process. Hexadecytrimethyl-ammonium bromide (CTAB) (0.5 g) is dissolved in deionized water (500 mL), and then 2 M aqueous NaOH solution (3.5 mL) is added to the CTAB solution. The solution is stirred for 30 min, and then Tetraethoxysilane (TEOS) (2.5 mL) is added to the solution. The resulting gel is stirred for 3 h at a temperature of 80°C. The white precipitate which forms is captured by filtration, followed by washing with deionized water and drying at room temperature. The remaining surfactant is then extracted from the particles by suspension in an ethanol solution of HCl overnight. The particles are washed with ethanol, centrifuged, and redispersed under ultrasonication. This wash procedure is repeated two additional times.

The SiO2 nanoparticles are then functionalized with amino groups using (3-aminopropyl)-triethoxysilane (APMTS). To do this, the particles are suspended in ethanol (30 mL), and APMTS (50 µL) is added to the suspension. The suspension is allowed to stand at room temperature for 2 h and then is boiled for 4 h, keeping the volume constant by periodically adding ethanol. Remaining reactants are removed by five cycles of washing by centrifugation and redispersing in pure ethanol.
[0246] In a separate reaction, 1-4 nm diameter gold seeds are created. All water used in this reaction is first deionized and then distilled from glass. Water (45.5 mL) is added to a 100 mL round-bottom flask. While stirring, 0.2 M aqueous NaOH (1.5 mL) is added, followed by a 1% aqueous solution of tetraethyl(dimethyl)phosphate chloride (THPC) (1.0 mL). Two minutes after the addition of THPC solution, a 10 mg/mL aqueous solution of chloroauric acid (2 mL), which has been aged at least 15 min, is added. The gold seeds are purified through dialysis against water.

[0247] To form the core-shell nanocarriers, the amine-functionalized SiO2 nanoparticles formed above are first mixed with the gold seeds for 2 h at room temperature. The gold-decorated SiO2 particles are collected through centrifugation and mixed with an aqueous solution of chloroauric acid and potassium bicarbonate to form the gold shell. The particles are then washed by centrifugation and redispersed in water. Ibuprofen is loaded by suspending the particles in a solution of sodium ibuprofen (1 mg/L) for 72 h. Free ibuprofen is then washed from the particles by centrifugation and redispersing in water.

Example 3
Liposomes Containing Cyclosporine A (Prophetic)

[0248] The liposomes are formed using thin film hydration. 1,2-Dipalmitoyl-sn-glycero-3-phosphocholine (DPPC) (32 μmol), cholesterol (32 μmol), and cyclosporin A (6.4 μmol) are dissolved in pure chloroform (3 mL). This lipid solution is added to a 50 mL round-bottom flask, and the solvent is evaporated on a rotary evaporator at a temperature of 60°C. The flask is then flushed with nitrogen gas to remove remaining solvent. Phosphate buffered saline (2 mL) and five glass beads are added to the flask, and the lipid film is hydrated by shaking at 60°C for 1 h to form a suspension. The suspension is transferred to a small pressure tube and sonicated at 60°C for four cycles of 30s pulses with a 30 s delay between each pulse. The suspension is then left undisturbed at room temperature for 2 h to allow for complete hydration. The liposomes are washed by centrifugation followed by resuspension in fresh phosphate buffered saline.

Example 4
Polymeric Nanocarrier Containing Polymer-Rapamycin Conjugate (Prophetic)

[0249] Preparation of PLGA-rapamycin conjugate:
[0250] PLGA polymer with acid end group (7525 DLGLA, acid number 0.46 mmol/g, Lakeshore Biomaterials, 5 g, 2.3 mmol, 1 eq) is dissolved in 30 mL of dichloromethane (DCM). N,N-Dicyclohexylcarbodiimide (1.2 eq, 2.8 mmol, 0.57 g) is added followed by rapamycin (1 eq, 2.3 mmol, 2.1 g) and 4-dimethylaminoopyridine (DMAP) (2.0 eq, 4.6 mmol, 0.56 g). The mixture is stirred at rt for 2 days. The mixture is then filtered to remove insoluble dicyclohexylurea. The filtrate is concentrated to ca. 10 mL in volume and added to 100 mL of isopropyl alcohol (IPA) to precipitate out the PLGA-rapamycin conjugate. The IPA layer is removed and the polymer is then washed with 50 mL of IPA and 50 mL of methyl t-butyl ether (MTBE). The polymer is then dried under vacuum at 35°C for 2 days to give PLGA-rapamycin as a white solid (ca. 6.5 g).

[0251] Preparation of nanocarrier containing PLGA-rapamycin conjugate and ovalbumin peptide (323-339):
[0252] Nanocarrier containing PLGA-rapamycin is prepared according to the procedure described in Example 1 as follows:

[0253] Solutions for nanocarrier formation are prepared as follows:
[0254] Solution 1: Ovalbumin peptide 323-339 @20 mg/mL in dilute hydrochloric acid aqueous solution. The solution is prepared by dissolving ovalbumin peptide in 0.15 M hydrochloric acid solution at room temperature. Solution 2: PLGA-rapamycin @100 mg/mL in methylene chloride. The solution is prepared by dissolving PLGA-rapamycin in pure methylene chloride. Solution 3: PLA-PEG @100 mg/mL in methylene chloride. The solution is prepared by dissolving PLA-PEG in pure methylene chloride. Solution 4: Polyvinyl alcohol @ 50 mg/mL in 100 mM pH 8 phosphate buffer.

[0255] A primary water-in-oil emulsion is prepared first. W1/O1 is prepared by combining solution 1 (0.2 mL), solution 2 (0.75 mL), and solution 3 (0.25 mL) in a small pressure tube and sonicated at 50% amplitude for 40 seconds using a Branson Digital Sonifier 250. A secondary emulsion (W1/O1/W2) is then prepared by combining solution 4 (3.0 mL) with the primary W1/O1 emulsion, vortexing for 10 s, and sonicated at 50% amplitude for 60 seconds using the Branson Digital Sonifier 250. The W1/O1/W2 emulsion is added to a beaker containing 70 mL pH 8 phosphate buffer solution (30 mL) and stirred at room temperature for 2 hours to allow the methylene chloride to evaporate and for the nanocarriers to form. A portion of the nanocarriers is washed by transferring the nanocarrier suspension to a centrifuge tube and centrifuging at 75,600 g and 4°C for 35 min, removing the supernatant, and re-suspending the pellet in phosphate buffered saline. The washing procedure is repeated, and the pellet is re-suspended in phosphate buffered saline for a final nanocarrier dispersion of about 10 mg/mL.

Example 5
Preparation of Gold Nanocarriers (AuNCs) Containing Rapamycin (Prophetic)

[0256] Preparation of HS-PEG-rapamycin:
[0257] A solution of PEG acid disulfide (1.0 eq), rapamycin (2.0-2.5 eq), DCC (2.5 eq) and DMAP (3.0 eq) in dry DMF is stirred at rt overnight. The insoluble dicyclohexylurea is removed by filtration and the filtrate is added to isopropyl alcohol (IPA) to precipitate out the PEG-disulfide-ds-rapamycin ester and washed with IPA and dried. The polymer is then treated with tris(2-carboxyethyl)phosphine hydrochloride in DMF to reduce the PEG disulfide to thiol PEG rapamycin ester (HS-PEG-rapamycin). The resulting polymer is recovered by precipitation from IPA and dried as previously described and analyzed by NMR and GPC.

[0258] Formation of Gold NCs (AuNCs):
[0259] An aq. solution of 500 mL of 1 mM HAuC14 is heated to reflux for 10 mM with vigorous stirring in a 1 L round-bottom flask equipped with a condenser. A solution of 50 mL of 40 mM of trisodium citrate is then rapidly added to the stirring solution. The resulting deep wine red solution is kept at reflux for 25-30 min and the heat is withdrawn and the solution is cooled to room temperature. The solution is then filtered through a 0.8 μm membrane filter to give the AuNCs solution. The AuNCs are characterized using visible spectro-
copy and transmission electron microscopy. The AuNCs are ca. 20 nm diameter capped by citrate with peak absorption at 520 nm.

**[0260]** AuNCs conjugate with HS-PEG-rapamycin:

**[0261]** A solution of 150 μL of HS-PEG-rapamycin (10 μM in 10 mM pH 9.0 carbonate buffer) is added to 1 mL of 20 nm diameter citrate-capped gold nanocarriers (1.16 mM) to produce a molar ratio of thiol to gold of 2500:1. The mixture is stirred at room temperature under argon for 1 hour to allow complete exchange of thiol with citrate on the gold nanocarriers. The AuNCs with PEG-rapamycin on the surface is then purified by centrifuge at 12,000 g for 30 minutes. The supernatant is decanted and the pellet containing AuNC—S-PEG-rapamycin is then pellet washed with 1× PBS buffer. The purified Gold-PEG-rapamycin nanocarriers are then resuspended in suitable buffer for further analysis and bioassays.

**Example 6**

**Mesoporous Silica-Told Core-Shell Nanocarriers Containing Ovalbumin (Prophetic)**

**[0262]** Mesoporous SiO2 nanoparticle cores are created through a sol-gel process. Hexadecyltrimethyl-ammonium bromide (CTAB) (0.5 g) is dissolved in deionized water (500 mL), and then 2 M aqueous NaOH solution (3.5 mL) is added to the CTAB solution. The solution is stirred for 30 mM, and then Tetraethoxysilane (TEOS) (2.5 mL) is added to the solution. The resulting gel is stirred for 3 h at a temperature of 80°C. The white precipitate which forms is captured by filtration, followed by washing with deionized water and drying at room temperature. The remaining surfactant is then extracted from the particles by suspension in an ethanolic solution of HCl overnight.

The particles are washed with ethanol, centrifuged, and redispersed under ultrasonication. This wash procedure is repeated two additional times.

**[0263]** The SiO2 nanoparticles are then functionalized with amino groups using (3-aminopropyl)-triethoxysilane (APM). To do this, the particles are suspended in ethanol (30 mL), and APM (50 μL) is added to the suspension. The suspension is allowed to stand at room temperature for 2 h and then is boiled for 4 h, keeping the volume constant by periodically adding ethanol. Remaining reactants are removed by five cycles of washing by centrifugation and redispersing in pure ethanol.

**[0264]** In a separate reaction, 1-4 nm diameter gold seeds are created. All water used in this reaction is first deionized and then distilled from glass. Water (45.5 mL) is added to 100 mL round-bottom flask. While stirring, 0.2 M aqueous NaOH (1.5 mL) is added, followed by 1% aqueous solution of tetraakis(hydroxymethyl)phosphonium chloride (THPC) (1.0 mL). Two minutes after the addition of THPC solution, a 10 mg/mL aqueous solution of chloroauric acid (2 mL), which has been aged at least 15 mM, is added. The gold seeds are purified through dialysis against water.

**[0265]** To form the core-shell nanocarriers, the amino-functionalized SiO2 nanoparticles formed above are first mixed with the gold seeds for 2 h at room temperature. The gold-decorated SiO2 particles are collected through centrifugation and mixed with an aqueous solution of chloroauric acid and potassium bicarbonate to form the gold shell. The particles are then washed by centrifugation and redispersed in water. Thiocarboxylated Ovalbumin [made by treating Ovalbumin with 2-iminothiolane hydrochloride] is loaded by suspending the particles in a solution of thiocarboxylated Ovalbumin (1 mg/L) for 72 h. The particles are then pellet washed with 1× PBS (pH 7.4) to remove free protein. The resulting silica-gold core-shell nanocarriers containing Ovalbumin are then re-suspended in 1× PBS for further analysis and assays.

**Example 7**

**Liposomes Containing Rapamycin and Ovalbumin (Prophetic)**

**[0266]** The liposomes are formed by thin film hydration. L-2-Dipalmitoyl-sn-glycero-3-phosphocholine (DPPC) (32 μmol), cholesterol (32 μmol), and rapamycin (6.4 μmol) are dissolved in pure chloroform (3 mL). This lipid solution is added to a 10 mL glass tube and the solvent is removed under nitrogen gas stream and desiccated for 6 h. under vacuum. Multilamellar vesicles are obtained by hydration of the film with 2.0 mL of 25 mM MOPS buffer pH 8.5, containing excess amount of Ovalbumin. The tube is vortexed until the lipid film is peeled off from the tube surface. To break the multilamellar vesicles into monolamellar, ten cycles of freezing (liquid nitrogen) and thawing (30°C water bath) are applied. The sample is then diluted to 1 mL in 25 mM MOPS buffer pH 8.5. Size of the resulting liposome is homogenized by extrusion by passing the sample 10 fold through a 200 nm pore poly-carbonate filters. The resulting liposomes are then used for further analysis and bioassays.

**Example 8**

**Polymeric Nanocarriers Composed of Modified Polyamino Acid with Surface Conjugated Ovalbumin (Prophetic)**

**[0267]** Step-1. Preparation of Poly(γ-glutamic acid) (γ-PGA) modified with L-phenylalanine ethyl ester (L-PAE): 4.7 unit mmol of γ-PGA (Mn ~ 300 kD) is dissolved in 0.3 N NaHCO3 aqueous solution (50 mL). L-PAE (4.7 mmol) and EDC.HCl (4.7 mmol) are added to the solution and stirred for 30 min at 4°C. The solution is then maintained at room temperature with stirring for 24 h. Low-molecular-weight chemicals are removed by dialysis using dialysis membrane with MWCO 50.0 kD. The resulting γ-PGA-graft-L-PAE is obtained by freeze-drying.

**[0268]** Step-2. Preparation of nanoparticles from γ-PGA-graft-L-PAE polymer: Nanoparticles composed of γ-PGA-graft-L-PAE are prepared by a precipitation and dialysis method. γ-PGA-graft-L-PAE (20 mg) was dissolved in 2 mL of DMSO followed by addition of 2 mL of water to form a translucent solution. The solution is then dialyzed against distilled water using cellulose membrane tubing (50,000 MWCO) to form the nanoparticles and to remove the organic solvents for 72 h at room temperature. The distilled water is exchanged at intervals of 12 h. The resulting nanoparticle solution (10 mg/mL in water) is then used for antigen conjugation.

**[0269]** Step-3. Ovalbumin conjugation to γ-PGA nanoparticles: Surface carboxylic acid groups of the γ-PGA nanoparticles (10 mg/mL) are first activated by EDC and NHS (10 mg/mL each in phosphate buffer, pH 5.8) for 2 h at ambient temperature. After pellet washing to remove excess EDC/ NHS, the activated nanoparticles are mixed with 1 mL of Ovalbumin (10 mg/mL) in phosphate-buffered saline (PBS, pH 7.4) and the mixture is incubated at 4-8°C for 24 h. The resulting Ovalbumin conjugated γ-PGA nanoparticles are
washed twice with PBS and resuspended at 5 mg/mL in PBS for further analysis and bioassays.

**Example 9**

Erythropoietin (EPO)-encapsulated γ-PGA Nanoparticles (Prophetic)

To prepare the EPO-encapsulated γ-PGA nanoparticles, 0.25-4 mg of EPO is dissolved in 1 mL of PBS (pH 7.4) and 1 mL of the γ-PGA-graft-L-PAE (10 mg/mL in DMSO) is added to the EPO solution. The resulting solution is centrifuged at 14,000g for 15 min and repeatedly rinsed with PBS. The resulting EPO-encapsulated γ-PGA nanoparticles are then resuspended in PBS (5 mg/mL) for further analysis and bioassay.

**Example 10**

Preparation of Gold Nanocarriers (AuNCs) Containing Ovalbumin (Prophetic)

Step-1. Formation of Gold NCs (AuNCs): An aq. solution of 500 mL of 1 mM AuCl4 is heated to reflux for 10 mM with vigorous stirring in a 1 L round-bottom flask equipped with a condenser. A solution of 50 mL of 40 mM of trisodium citrate is then rapidly added to the stirring solution. The resulting deep wine red solution is kept at reflux for 25-30 mM and the heat is withdrawn and the solution is cooled to room temperature. The solution is then filtered through a 0.8 μm membrane filter to give the AuNCs solution. The AuNCs are characterized using visible spectroscopy and transmission electron microscopy. The AuNCs are ca. 20 nm diameter capped by citrate with peak absorption at 520 nm.

Step-2. Conjugation of Ovalbumin to AuNCs: A solution of 150 μl of thiolated Ovalbumin (10 μM in 10 mM pH 9.0 carbonate buffer) is added to 1 mL of 20 nm diameter citrate-capped gold nanocarriers (1.16 nM) to produce a molar ratio of thiol to gold of 2500:1. The mixture is stirred at room temperature under argon for 1 hour to allow complete exchange of thiol with citrate on the gold nanocarriers. The AuNCs with Ovalbumin on the surface is then purified by centrifugation at 12,000 g for 30 minutes. The supernatant is decanted and the pellet containing AuNC-Ovalbumin is then pellet washed with 1× PBS buffer. The purified Gold-Ovalbumin nanocarriers are then resuspended in suitable buffer for further analysis and bioassays.

**Example 11**

Evaluating Tolerogenic Immune Response to Antigen In Vivo (Prophetic)

Balb/c mice are immunized with an antigen in incomplete Freund's adjuvant to induce innate immune cell proliferation (e.g., macrophage proliferation). Subsequently, a composition of the invention comprising the antigen and an immunosuppressant is administered subcutaneously in a dose-dependent manner. The same mice are then again exposed to the antigen, and the level of macrophage proliferation is again assessed. Changes in the macrophage population are then monitored with a reduction upon subsequent challenge with the antigen indicating a tolerogenic immune response.

**Example 12**

Evaluating In Vitro Reduction of Innate Immune Cells (Prophetic)

A cell population comprising innate immune cells and antibodies is contacted in vitro with a composition provided herein. After a time sufficient for the composition to interact with the antibodies, a decrease in the number of innate immune cells, or cytokines produced by the cells, is expected. A time sufficient for the decrease in the population of cells is, in some embodiments, a period of about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 1 week, about 2 weeks, about 3 weeks, or about 4 weeks. In some embodiments, the number of innate immune cells is decreased after that time, for example, to at least about 5 times, at least about 10 times, at least about 20 times, at least about 50 times, at least about 100 times, at least about 1,000 times, at least about 10,000 times, or at least about 1,000,000 times less as compared to the original total or relative number of innate immune cells in the population. In some embodiments, the number of innate immune cells is decreased after that time, for example, to about 1%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 40%, about 50%, about 75%, about 90%, or about 95% of the original total or relative number of innate immune cells in the population. In some embodiments, the total and/or relative number of innate immune cells in the population is determined before the population of cells is contacted with a composition provided herein to establish a baseline number of innate immune cells in the population. In some embodiments, the population of cells is contacted once with a composition provided herein. In some embodiments, the population of cells is contacted repeatedly with a composition provided herein. The number and/or presence of innate immune cells in the population of cells is also determined after the contacting. In some embodiments, the number and/or presence of innate immune cells is monitored over a period of time, for example, by performing a plurality of subsequent innate immune cell detection assays. In some embodiments, the number and/or presence of innate immune cells in the population of cells is determined by taking a sample from the cell population that is representative of the cell population, staining cells contained in that sample with antibodies or staining agents that specifically detect innate immune cell markers, and detecting cells that express innate immune cell markers in the sample, for example, by FACS or by immunohistochemistry. In some embodiments, the innate immune cells are quantified. In some embodiments, the population of innate immune cells determined after the contacting is compared to the quantity of innate immune cells before the contacting, for example, to the baseline number of innate immune cells, wherein, if the number of innate immune cells in the population of cells is lower after the contacting than the baseline number, then it is determined that a tolerogenic response to the composition has occurred.

**Example 13**

Evaluating In Vivo Reduction of Innate Immune Cells (Prophetic)

A cell population comprising innate immune cells is contacted in vivo with a composition provided herein by
The document discusses the administration of a composition to a subject, subcutaneous administration to a subject. After a time sufficient for the composition to interact with antibodies in the subject, a decrease in the number of innate immune cells, or cytokines produced by the cells, is expected. A time sufficient for the decrease in the number of innate immune cells in the population is, in some embodiments, a period of about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 1 week, about 2 weeks, about 3 weeks, or about 4 weeks. In some embodiments, the period of time sufficient to effect a decrease in the number of innate immune cells is longer than 4 weeks. In some embodiments, the number of innate immune cells is decreased after that time to at least about 5 times, at least about 10 times, at least about 20 times, at least about 50 times, at least about 100 times, at least about 1,000 times, at least about 10,000 times, or at least about 1,000,000 times less as compared to the original total or relative number of innate immune cells in the subject. In some embodiments, the number of innate immune cells is decreased after that time, for example, to about 1%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 40%, about 50%, about 75%, about 90%, or about 95% of the original total or relative innate immune cells in the subject. In some embodiments, innate immune cells are present in the subject before the administration, but are absent or near absent after the administration.

In some embodiments, the total and/or relative number of innate immune cells in the subject is determined before the subject is administered a composition provided herein to establish a baseline number of innate immune cells in the subject. In some embodiments, the composition provided herein is administered to a subject once. In some embodiments, a composition provided herein is administered to a subject multiple times, for example, until a desired decrease of innate immune cells is observed in the subject. The number and/or presence of innate immune cells in the subject is determined after the administration. In some embodiments, the number and/or presence of innate immune cells is monitored over a period of time, for example, by performing a plurality of subsequent innate immune cell detection assays. In some embodiments, the number and/or presence of innate immune cells in the subject is determined by taking a sample from the subject, for example, a peripheral blood sample, or a lymph sample, that is representative of a lymphocyte population in the subject, staining cells contained in that sample with antibodies or staining agents that specifically detect innate immune cell markers, and detecting cells that express innate immune cell markers in the sample, for example, by FACS or by immunochemistry. In some embodiments, the innate immune cells are quantified. In some embodiments, the quantity of innate immune cells determined after administration is compared to the quantity of innate immune cells before administration, for example, to the baseline number of innate immune cells, wherein, if the number of innate immune cells in the subject is lower after the administration than the baseline number, then it is determined that a tolerogenic response to the composition has occurred.

Example 14
Assessing the Effects of Nanocarriers with Antigens and Immunosuppressants

Nanocarrier 1

Ovalbumin peptide 323-339, a 17 amino acid peptide known to be a T and B cell epitope of Ovalbumin protein, was purchased from Bochem Americas Inc. (3132 Kashiwa Street, Torrance Calif. 90505; Part #4065609). PLGA with a lactide:glycolide ratio of 3:1 and an inherent viscosity of 0.75 dL/g was purchased from SurModics Pharmaceuticals (75 Tom Martin Drive, Birmingham, Ala. 35211; Product Code 7525 DLG 7A). PLA-PEG block co-polymer with a PEG block of approximately 5,000 Da and PLA block of approximately 20,000 Da was synthesized. Polyvinyl alcohol (85-89% hydrolyzed) was purchased from EMD Chemicals (Product Number 1.41350.1001).

Solutions were prepared as follows: Solution 1: Ovalbumin peptide 323-339 @20 mg/mL in dilute hydrochloric acid aqueous solution. The solution was prepared by dissolving ovalbumin peptide in 0.13 M hydrochloric acid solution at room temperature. Solution 2: PLGA @100 mg/mL in methylene chloride. The solution was prepared by dissolving PLGA in pure methylene chloride. Solution 3: PLA-PEG @100 mg/mL in methylene chloride. The solution was prepared by dissolving PLA-PEG in pure methylene chloride. Solution 4: Polyvinyl alcohol @50 mg/mL in 100 mM pH 8 phosphate buffer. A primary water-in-oil emulsion was prepared first. W1/O1 was prepared by combining solution 1 (0.2 mL), solution 2 (0.75 mL), and solution 3 (0.25 mL) in a small pressure tube and sonicating at 50% amplitude for 40 seconds using a Branson Digital Sonifier 250. A secondary emulsion (W1/O1/W2) was then prepared by combining solution 4 (3.0 mL) with the primary W1/O1 emulsion, vortexing for 10 s, and sonicating at 30% amplitude for 60 seconds using the Branson Digital Sonifier 250.

The W1/O1/W2 emulsion was added to a beaker containing 70 mM pH 8 phosphate buffer solution (30 mL) and stirred at room temperature for 2 hours to allow the methylene chloride to evaporate and for the nanocarriers to form. A portion of the nanocarriers were washed by transferring the nanocarrier suspension to a centrifuge tube and centrifuging at 75,600 x g and 4°C for 35 min, removing the supernatant, and re-suspending the pellet in phosphate buffered saline. The washing procedure was repeated, and the pellet was re-suspended in phosphate buffered saline for a final nanocarrier dispersion of about 10 mg/mL.

Nanocarrier size was determined by dynamic light scattering. The amount of peptide in the nanocarrier was determined by HPLC analysis. The total dry-nanocarrier mass per mL of suspension was determined by a gravimetric method.

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Infusion therapy products were prepared as follows: Solution 1: Ovalbumin peptide 323-339 @20 mg/mL in dilute hydrochloric acid aqueous solution. The solution was prepared by dissolving ovalbumin peptide in 0.13 M hydrochloric acid solution at room temperature. Solution 2: Rapamycin @50 mg/mL in methylene chloride. The solution was prepared by dissolving rapamycin in pure methylene chloride. Solution 3: PLGA @100 mg/mL in methylene chloride. The solution was prepared by dissolving PLGA in pure methylene chloride. Solution 4: PLGA-PEG @100 mg/mL in methylene chloride. The solution was prepared by dissolving PLGA-PEG in pure methylene chloride. Solution 5: Polyvinyl alcohol @50 mg/mL in 100 mM pH 8 phosphate buffer.

The W1/O1/W2 emulsion was added to a beaker containing 70 mM pH 8 phosphate buffer solution (30 mL) and stirred at room temperature for 2 hours to allow the methylene chloride to evaporate and for the nanocarriers to form. A portion of the nanocarriers were washed by transferring the nanocarrier suspension to a centrifuge tube and centrifuging at 21,000 x g and 4°C for 45 min, removing the supernatant, and resuspending the pellet in phosphate buffered saline. The washing procedure was repeated, and the pellet was re-suspended in phosphate buffered saline for a final nanocarrier dispersion of about 10 mg/mL.

The effective diameters of the nanocarriers were determined by dynamic light scattering (DLS). A suspension of the nanocarriers was diluted with purified water to achieve a final synthetic nanocarrier suspension concentration of approximately 0.01 to 0.1 mg/mL. The diluted suspension was prepared directly inside a suitable cuvette for DLS analysis. The cuvette was then placed in a Brookhaven Instruments Corp. ZetaPALS, allowed to equilibrate to 25°C, and then scanned for sufficient time to acquire a stable and reproducible distribution based on appropriate inputs for viscosity of the medium and refractive indices of the sample. The effective diameter, or mean of the distribution, was then reported.

**Immunization**

The nanocarriers were thawed and equilibrated. Initial dilutions constituted a 10x stock solution, and were further diluted to a concentration of 100 µg/mL in OVA323-339 or a 1x solution. This 1x solution was used for injections of 200 µl per i.v. injection. Animals were immunized with OVA protein (OVA) and treated with OVA323-339 Peptide Immunization routes were as follows: 10µg of OVA44 mg Alum i.p. in 400 µl per each Balb/C immunologically naive female mouse. Experimental groups consisted of 5 animals each. Spleen cells were restimulated with antigen using CFSE or CTO to determine the amount of Ag-specific proliferation.

**Levels of Specific Types of Immune Cells**

FCS files were analyzed using FlowJo software. 7AAD positive cells (a nuclear dye that label dead cells) positive cells were excluded and cell morphologies dependent on expression of CD4, CD8, Gr-1, F4/80, B220, TCRb and CD11b were quantified. Gating strategy for Eosinophils→7AAD-F4/80- Gr-1+ TCRb- CD11b+Gr-1+

**Results**

**FIG. 2** demonstrate the effectiveness of the nanocarriers in an animal model. Specifically, FIG. 2 demonstrates a reduction in the number of eosinophils in lavage samples from animal subjects treated with synthetic nanocarriers comprising OVA323-339 and immunosuppressant.
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<210> SEQ ID NO 17
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens arrestin epitope

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Leu Leu Ala Asn
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<210> SEQ ID NO 18
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens arrestin epitope

<400> SEQUENCE: 18
Leu Leu Lys Lys Leu Gly Ser Asn Thr Tyr Pro Phe Leu Leu Thr Phe
1  5  10  15
Pro Asp Tyr Leu
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<210> SEQ ID NO 19
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens arrestin epitope

<400> SEQUENCE: 19
Leu Thr Phe Arg Arg Asp Leu Tyr Phe Ser Arg Val Gln Val Tyr Pro
1  5 10  15
Pro Val Gly Ala
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<210> SEQ ID NO 20
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens arrestin epitope

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Phe Lys Lys Ile

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Asp Thr Asn Leu

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Gln Pro Ala Pro

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Ala Thr Asp Ser

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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Homo sapiens arrestin epitope

<400> SEQUENCE: 21

Asn Arg Glu Arg Arg Gly Ile Ala Lieu. Asp Gly Lys Ile Llys His Glu

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<210> SEQ ID NO 22
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<223> OTHER INFORMATION: Homo sapiens arrestin epitope

<400> SEQUENCE: 22

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<223> OTHER INFORMATION: Homo sapiens arrestin epitope

<400> SEQUENCE: 23

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<223> OTHER INFORMATION: Homo sapiens arrestin epitope

<400> SEQUENCE: 24

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<212> TYPE: PRT
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**OTHER INFORMATION:** Homo sapiens arrestin epitope

**SEQUENCE:**

Gln Val Glu Leu Val Asp Gly Val Asp Leu Val Leu Val

Lys Gly Lys Lys

**SEQ ID NO 26**

**LENGTH:** 20

**TYPE:** PRT

**ORGANISM:** Artificial Sequence

**FEATURE:**

**OTHER INFORMATION:** Homo sapiens arrestin epitope

**SEQUENCE:**

Arg Val Glu Tyr Pro Val Gly Ala Ala Ser Thr Pro Thr Lys

Leu Glu Glu Ser

**SEQ ID NO 27**

**LENGTH:** 20

**TYPE:** PRT

**ORGANISM:** Artificial Sequence

**FEATURE:**

**OTHER INFORMATION:** Homo sapiens arrestin epitope

**SEQUENCE:**

Ser Arg Asp Lys Ser Val Thr Ile Tyr Leu Gly Asn Arg Asp Tyr Ile

Asp His Val Ser

**SEQ ID NO 28**

**LENGTH:** 20

**TYPE:** PRT

**ORGANISM:** Artificial Sequence

**FEATURE:**

**OTHER INFORMATION:** Homo sapiens arrestin epitope

**SEQUENCE:**

Thr Leu Thr Leu Pro Leu Ala Asn Arg Glu Arg Arg

Asp Ile Ala Leu Asp

**SEQ ID NO 29**

**LENGTH:** 20

**TYPE:** PRT

**ORGANISM:** Artificial Sequence

**FEATURE:**

**OTHER INFORMATION:** Homo sapiens arrestin epitope

**SEQUENCE:**

Val Ala Thr Glu Val Pro Phe Arg Leu Met His Pro Glu Pro Glu Asp

Pro Ala Lys Glu

**SEQ ID NO 30**
Val Asp Pro Asp Leu Val Lys Lys Lys Val Tyr Val Thr Leu Thr  
1   5   10  15  
Cys Ala Phe Arg  
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Val Val Leu Tyr Ser Ser Asp Tyr Tyr Val Lys Pro Val Ala Met Glu  
1   5   10  15  
Glu Ala Gln Glu  
20

Tyr Gln Ile Lys Val Lys Leu Thr Val Ser Gly Phe Leu Gly Glu Leu  
1   5   10  15  
Thr Ser Ser Glu  
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Ala Leu Tyr Leu Val Cys Gly Glu Arg  
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Ser His Leu Val Glu Ala Leu Tyr Leu Val  
1   5   10

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TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Homo sapiens chaperonin (HSP60) epitope

SEQUENCE: 35
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1      5

SEQ ID NO 36
LENGTH: 9
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Homo sapiens Collagen alpha-3(IV) chain epitope

SEQUENCE: 36
Gly Ser Pro Ala Thr Trp Thr Thr Arg
1      5

SEQ ID NO 37
LENGTH: 9
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Homo sapiens collagen, type II, alpha 1 isoform 1 precursor epitope

SEQUENCE: 37
Ala Arg Gly Gln Pro Gly Val Met Gly
1      5

SEQ ID NO 38
LENGTH: 9
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Homo sapiens DNA topoisomerase 1 epitope

SEQUENCE: 38
Lys Met Leu Asp His Glu Tyr Thr Thr
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SEQ ID NO 39
LENGTH: 9
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Homo sapiens ezrin epitope

SEQUENCE: 39
Glu Tyr Thr Ala Lys Ile Ala Leu Leu
1      5

SEQ ID NO 40
LENGTH: 10
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Homo sapiens ezrin epitope

SEQUENCE: 40
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<211> LENGTH: 9
<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens glial fibrillary acidic protein isoform 2 epitope

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<210> SEQ ID NO 42
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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens glial fibrillary acidic protein isoform 2 epitope

<400> SEQUENCE: 42
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<210> SEQ ID NO 43
<211> LENGTH: 9
<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens glucagon receptor epitope

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1  5

<210> SEQ ID NO 44
<211> LENGTH: 9
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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens glucose-6-phosphatase, catalytic, related epitope

<400> SEQUENCE: 44
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1  5

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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Glutamate decarboxylase 1 epitope

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1  5  10  15

<210> SEQ ID NO 46
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<223> OTHER INFORMATION: Homo sapiens Glutamate decarboxylase 2 epitope
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1      5      10

Phe Leu Gln Asp Val Met Asn Ile Leu
1      5

Leu Leu Gln Glu Tyr Asn Trp Glu Leu
1      5

Arg Met Glu Tyr Gly Thr Thr Met Val
1      5      10

Val Met Asn Ile Leu Leu Gln Tyr Val Val
1      5      10
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Glutamate decarboxylase 2 epitope

<400> SEQUENCE: 52

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1 5 10

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<220> FEATURE:
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<220> FEATURE:
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<400> SEQUENCE: 55

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<210> SEQ ID NO 56
<211> LENGTH: 15
<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Glutamate decarboxylase 2 epitope

<400> SEQUENCE: 56

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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Glutamate decarboxylase 2 epitope

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<210> SEQ ID NO 58
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Leu Arg Arg Tyr Leu Glu Asn Gly Lys
1      5

Val Met Ala Pro Arg Thr Val Leu Leu
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Ala Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr
1     5       10

Ala Leu Asn Glu Asp Leu Ser Ser Trp Thr Ala Ala Asp Thr
1     5       10

Ala Leu Asn Glu Asp Leu Ser Ser Trp Thr Ala Ala Asp Thr
1     5       10

Ala Leu Asn Glu Asp Leu Ser Ser Trp Thr Ala Ala Asp Thr
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Ala Leu Asn Glu Asp Leu Ser Ser Trp Thr Ala Ala Asp Thr
1     5       10
Leu Leu Arg Gly Tyr His Gln Asp Ala Tyr
1 5 10

<210> SEQ ID NO 70
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<223> OTHER INFORMATION: Homo sapiens HLA-B27 epitope

<400> SEQUENCE: 70
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1 5 10 15

<210> SEQ ID NO 71
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<212> TYPE: PRT
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<223> OTHER INFORMATION: Homo sapiens HLA-B27 epitope

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1 5 10

<210> SEQ ID NO 72
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<212> TYPE: PRT
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1 5 10

<210> SEQ ID NO 73
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Arg Leu Leu Pro Leu Leu Ala Leu Leu Ala Leu
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Ser Leu Gln Lys Arg Gly Ile Val Glu Gln
1 5 10

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<223> OTHER INFORMATION: Homo sapiens Insulin precursor epitope

<400> SEQUENCE: 78
Ser Leu Gln Pro Leu Ala Leu Glu Gly
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<210> SEQ ID NO 79
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<223> OTHER INFORMATION: Homo sapiens Insulin precursor epitope

<400> SEQUENCE: 79
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<210> SEQ ID NO 80
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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Insulin precursor epitope

<400> SEQUENCE: 80
Val Cys Gly Glu Arg Gly Phe Phe Tyr Thr
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<210> SEQ ID NO 81
<211> LENGTH: 8
<212> TYPE: PRT
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FEATURE: OTHER INFORMATION: Homo sapiens Insulin precursor epitope

SEQUENCE: 81
Trp Gly Pro Asp Pro Ala Ala Ala
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SEQ ID NO 82
LENGTH: 9
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Homo sapiens Insulin precursor epitope

SEQUENCE: 82
Phe Tyr Thr Pro Lys Thr Arg Arg Glu
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SEQ ID NO 83
LENGTH: 8
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Homo sapiens Insulin precursor epitope

SEQUENCE: 83
Gly Glu Arg Gly Phe Phe Tyr Thr
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SEQ ID NO 84
LENGTH: 9
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Homo sapiens Insulin precursor epitope

SEQUENCE: 84
Glu Arg Gly Phe Phe Tyr Thr Pro Lys
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SEQ ID NO 85
LENGTH: 10
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Homo sapiens Insulin precursor epitope

SEQUENCE: 85
Leu Cys Gly Ser His Leu Val Glu Ala Leu
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SEQ ID NO 86
LENGTH: 10
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Homo sapiens Insulin precursor epitope

SEQUENCE: 86
Leu Val Cys Gly Glu Arg Gly Phe Phe Tyr
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SEQ ID NO 87
LENGTH: 10
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Phe Leu Ile Val Leu Ser Val Ala Leu
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Lys Leu Gln Val Phe Leu Ile Val Leu
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Phe Leu Trp Ser Val Phe Met Leu Ile
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<210> SEQ ID NO 95
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<223> OTHER INFORMATION: Homo sapiens islet-specific glucose-6-phosphatase-related protein isoform 1 epitope
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Tyr Leu Leu Arg Val Leu Asn Ile
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<210> SEQ ID NO 96
<211> LENGTH: 9
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<223> OTHER INFORMATION: Homo sapiens keratin 6C epitope
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Ala Leu Gln Lys Ala Lys Gln Asp Leu
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<210> SEQ ID NO 97
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens keratin 6C epitope
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<210> SEQ ID NO 98
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FEATURE: OTHER INFORMATION: Homo sapiens Keratin, type I cytoskeletal 17
(Cytokeratin 17) (K17) (CK 17) (Version 2) epitope

SEQUENCE: 104

Leu Arg Arg Val Leu Asp Glu Leu Thr Leu Ala Arg Thr Asp Leu Glu
1 5 10 15
Met Gln Ile Glu
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SEQ ID NO 105
LENGTH: 9
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE: OTHER INFORMATION: Homo sapiens Keratin, type I cytoskeletal 17
(Cytokeratin 17) (K17) (CK 17) (Version 2) epitope

SEQUENCE: 105

Ala Leu Glu Glu Ala Asn Ala Asp Leu
1 5

SEQ ID NO 106
LENGTH: 9
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE: OTHER INFORMATION: Homo sapiens Keratin, type I cytoskeletal 17
(Cytokeratin 17) (K17) (CK 17) (Version 2) epitope

SEQUENCE: 106

Ala Asn Ala Asp Leu Glu Val Lys Ile
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SEQ ID NO 107
LENGTH: 9
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE: OTHER INFORMATION: Homo sapiens Keratin, type I cytoskeletal 17
(Cytokeratin 17) (K17) (CK 17) (Version 2) epitope

SEQUENCE: 107

Ala Arg Thr Asp Leu Glu Met Gln Ile
1 5

SEQ ID NO 108
LENGTH: 9
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE: OTHER INFORMATION: Homo sapiens Keratin, type I cytoskeletal 17
(Cytokeratin 17) (K17) (CK 17) (Version 2) epitope

SEQUENCE: 108

Ala Ser Tyr Leu Asp Lys Val Arg Ala
1 5

SEQ ID NO 109
LENGTH: 9
TYPE: PRT
ORGANISM: Artificial Sequence
SEQUENCE: 109
Asp Val Asn Gly Leu Arg Arg Val Leu
1 5

SEQUENCE: 110
Gly Leu Arg Arg Val Leu Asp Glu Leu
1 5

SEQUENCE: 111
Ile Ser Ser Val Leu Ala Gly Ala Ser Cys Pro Ala
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SEQUENCE: 112
Leu Asp Lys Val Arg Ala Leu Glu Glu
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SEQUENCE: 113
Gln Ile Glu Gly Leu Lys Glu Glu Leu
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SEQUENCE: 114
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<210> SEQ ID NO 115
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<222> FEATURE:
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Arg Leu Ala Ser Tyr Leu Asp Lys Val
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<210> SEQ ID NO 116
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<400> SEQUENCE: 116

Ser Tyr Leu Asp Lys Val Arg Ala
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<400> SEQUENCE: 117

Ser Tyr Leu Asp Lys Val Arg Ala Leu Glu Glu Ala Asn Ala Asp Leu
1 5 10 15

Glu Val Lys Ile
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<210> SEQ ID NO 118
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   OTHER INFORMATION: Homo sapiens maspin epitope

<400> SEQUENCE: 118

Gly Leu Glu Lys Ile Glu Lys Gin Leu
1 5

<210> SEQ ID NO 119
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<222> FEATURE:
   OTHER INFORMATION: Homo sapiens maspin epitope

<400> SEQUENCE: 119

Met Gly Asn Ile Asp Ser Ile Asn Cys Lys
1 5 10

<210> SEQ ID NO 120
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens maspin epitope

<400> SEQ ID NO 120
Tyr Ser Leu Lys Leu Ile Lys Arg Leu
1 5

<210> SEQ ID NO 121
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens MBP protein epitope

<400> SEQ ID NO 121
Ala Ser Gln Lye Arg Pro Ser Gln Arg His Gly Ser Lye Tyr Leu Ala
1 5 10 15
Thr Ala Ser Thr
20

<210> SEQ ID NO 122
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens MBP protein epitope

<400> SEQ ID NO 122
Glu Asn Pro Val Val His Fhe Phe Lye Ann Ile Val Thr Pro Arg
1 5 10 15

<210> SEQ ID NO 123
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens MBP protein epitope

<400> SEQ ID NO 123
Val Val His Phe Phe Lye Ann Ile Val
1 5

<210> SEQ ID NO 124
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens MBP protein epitope

<400> SEQ ID NO 124
Asp Glu Ann Pro Val Val His Phe Phe Lye Ann Ile Val Thr Pro Arg
1 5 10 15
Thr Pro Pro

<210> SEQ ID NO 125
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens MBP protein epitope
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<400> SEQUENCE: 125

His His Pro Ala Arg Thr Ala His Tyr Gly Ser Leu Pro Gln Lys Ser
1     5      10      15

His Gly Arg Thr
20

<400> SEQUENCE: 126

Val Val His Phe Phe Lys Asn Ile Val Thr Pro Arg Thr Pro Pro Pro
1     5      10      15

Ser Gln Gly Lys
20

<400> SEQUENCE: 127

Ala Ser Gln Lys Arg Pro Ser Gln Arg His Gly Ser Tyr Leu Ala
1     5      10      15

Thr Ala Ser Thr Met
20

<400> SEQUENCE: 128

Phe Lys Gly Val Asp Ala Gln Gly Thr Leu Ser Lys Ile Phe Lys Leu
1     5      10      15

Gly Gly Arg Asp
20

<400> SEQUENCE: 129

Arg Pro Gly Phe Gly Tyr Gly Gly Thr Leu Ser Lys Ser Ala
1     5      10      15

His Lys Gly

<400> SEQUENCE: 130

Arg Pro Gly Phe Gly Tyr Gly Gly Thr Leu Ser Lys Ser Ala
1     5      10      15
<220> FEATURE: Homo sapiens MBP protein epitope

<400> SEQUENCE: 130

Ala Ser Gln Lys Arg Pro Ser Gln Arg His Gly Ser Lys Tyr Leu Ala
1   5   10   15

Thr Ala Ser Thr Met Asp His Ala Arg His Gly Phe Leu Pro Arg His
20  25  30

Arg Asp Thr Gly Ile Leu
35

<210> SEQ ID NO 131
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

Lys Tyr Leu Ala Thr Ala Ser Thr Met
1   5

<210> SEQ ID NO 132
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

Gly Leu Ser Leu Ser Arg Phe Ser Trp Gly Ala Glu Gly Gln Arg Pro
1   5   10   15

Gly Phe Gly Tyr
20

<210> SEQ ID NO 133
<211> LENGTH: 43
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

Phe Gly Gly Asp Arg Gly Ala Pro Lys Arg Gly Ser Gly Lys Asp Ser
1   5   10   15

His His Pro Ala Arg Thr Ala His Tyr Gly Ser Leu Pro Gln Lys Ser
20  25  30

His Gly Arg Thr Gln Asp Glu Asn Pro Val Val
35  40

<210> SEQ ID NO 134
<211> LENGTH: 40
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

Gly Leu Ser Leu Ser Arg Phe Ser Trp Gly Ala Glu Gly Gln Arg Pro
1   5   10   15

Gly Phe Gly Tyr Gly Gly Arg Ala Ser Asp Tyr Lys Ser Ala His Lys
Gly Phe Lys Gly Val Asp Ala Gln

<210> SEQ ID NO 135
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens MHC class I related protein A epitope
<400> SEQUENCE: 135

Ala Ala Ala Ala Ile Phe Val Ile

<210> SEQ ID NO 136
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Myelin basic protein epitope
<400> SEQUENCE: 136

Ser Leu Ser Arg Phe Ser Trp Gly Ala

<210> SEQ ID NO 137
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Myelin basic protein epitope
<400> SEQUENCE: 137

Asp Tyr Lys Ser Ala His Lys Gly Phe

<210> SEQ ID NO 138
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens myelin basic protein epitope
<400> SEQUENCE: 138

Ser Lys Ile Phe Lys Leu Gly Gly Arg Asp Ser Arg Ser Gly Ser Pro

<210> SEQ ID NO 139
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens myelin basic protein epitope
<400> SEQUENCE: 139

Met Ala Arg

<210> SEQ ID NO 140
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens myelin proteolipid protein epitope

<400> SEQUENCE: 140

Phe Leu Tyr Gly Ala Leu Leu Leu Ala
1  5

<210> SEQ ID NO 141
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens myelin proteolipid protein epitope

<400> SEQUENCE: 141

Lys Leu Ile Glu Thr Tyr Phe Ser Lys
1  5

<210> SEQ ID NO 142
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Myelin-associated glycoprotein precursor epitope

<400> SEQUENCE: 142

Leu Met Trp Ala Lys Ile Gly Pro Val
1  5

<210> SEQ ID NO 143
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Myelin-associated glycoprotein precursor epitope

<400> SEQUENCE: 143

Ser Leu Leu Leu Glu Leu Glu Glu Val
1  5

<210> SEQ ID NO 144
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Myelin-associated glycoprotein precursor epitope

<400> SEQUENCE: 144

Val Leu Phe Ser Ser Asp Phe Arg Ile
1  5

<210> SEQ ID NO 145
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Myosin heavy chain, skeletal muscle, adult 2 (Myosin heavy chain IIa) (MYHC-IIa) epitope

<400> SEQUENCE: 145
Glu Phe Glu Lys Met Arg Arg Asp Leu
1 5

SEQ ID NO 146
LENGTH: 9
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Homo sapiens Myosin heavy chain, skeletal muscle, adult 2 (Myosin heavy chain IIa) (MyHC-IIa) epitope

Ly6 Met Arg Arg Asp Leu Glu Glu Ala
1 5

SEQ ID NO 147
LENGTH: 12
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Homo sapiens peroxiredoxin-2 isoform a epitope

Glu Val Lys Leu Ser Asp Tyr Lys Gly Lys Tyr Val
1 5 10

SEQ ID NO 148
LENGTH: 10
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Homo sapiens proinsulin precursor epitope

His Leu Cys Gly Ser His Leu Val Glu Ala
1 5 10

SEQ ID NO 149
LENGTH: 10
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Homo sapiens proinsulin precursor epitope

Ala Leu Trp Gly Pro Asp Pro Ala Ala Ala
1 5 10

SEQ ID NO 150
LENGTH: 9
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Homo sapiens proinsulin precursor epitope

Arg Leu Leu Pro Leu Leu Ala Leu Leu
1 5
<400> SEQUENCE: 151
Ala Leu Trp Met Arg Leu Leu Pro Leu Leu
1      5      10

<210> SEQ ID NO 152
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens proinsulin precursor epitope

<400> SEQUENCE: 152
Trp Met Arg Leu Leu Pro Leu Leu Ala Leu
1      5      10

<210> SEQ ID NO 153
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Homo sapiens proinsulin precursor epitope

<400> SEQUENCE: 153
Pro Leu Ala Leu Glu Gly Ser Leu Gln Lys
1      5      10

<210> SEQ ID NO 154
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens proinsulin precursor epitope

<400> SEQUENCE: 154
Pro Leu Leu Ala Leu Leu Ala Leu Trp Gly
1      5      10

<210> SEQ ID NO 155
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Receptor-type tyrosine-protein phosphatase-like N precursor epitope

<400> SEQUENCE: 155
Leu Leu Pro Pro Leu Leu Glu His Leu
1      5

<210> SEQ ID NO 156
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Receptor-type tyrosine-protein phosphatase-like N precursor epitope

<400> SEQUENCE: 156
Ser Leu Ala Ala Gly Val Lys Leu Leu
1      5

<210> SEQ ID NO 157
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURES:
<223> OTHER INFORMATION: Homo sapiens Receptor-type tyrosine-protein phosphatase-like N precursor epitope

<400> SEQUENCE: 157
Ser Leu Ser Pro Leu Gln Ala Glu Leu

<210> SEQ ID NO 158
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURES:
<223> OTHER INFORMATION: Homo sapiens Receptor-type tyrosine-protein phosphatase-like N precursor epitope

<400> SEQUENCE: 158
Ala Leu Thr Ala Val Ala Glu Glu Val

<210> SEQ ID NO 159
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURES:
<223> OTHER INFORMATION: Homo sapiens Receptor-type tyrosine-protein phosphatase-like N precursor epitope

<400> SEQUENCE: 159
Ser Leu Tyr His Val Tyr Glu Val Asn Leu

<210> SEQ ID NO 160
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURES:
<223> OTHER INFORMATION: Homo sapiens Receptor-type tyrosine-protein phosphatase-like N precursor epitope

<400> SEQUENCE: 160
Thr Ile Ala Asp Phe Trp Gln Met Val

<210> SEQ ID NO 161
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURES:
<223> OTHER INFORMATION: Homo sapiens Receptor-type tyrosine-protein phosphatase-like N precursor epitope

<400> SEQUENCE: 161
Val Ile Val Met Leu Thr Pro Leu Val

<210> SEQ ID NO 162
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURES:
<223> OTHER INFORMATION: Homo sapiens Receptor-type tyrosine-protein phosphatase-like N precursor epitope
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<400> SEQUENCE: 162

Met Val Trp Glu Ser Gly Cys Thr Val
  1  5

<210> SEQ ID NO 163
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens S-arrestin epitope

<400> SEQUENCE: 163

Phe Leu Gly Glu Leu Thr Ser Ser Glu Val Ala Thr Glu Val
  1  5  10

<210> SEQ ID NO 164
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens S-arrestin epitope

<400> SEQUENCE: 164

Ile Tyr Phe His
  5  10

<210> SEQ ID NO 165
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens S-arrestin epitope

<400> SEQUENCE: 165

Gly Glu Ala Glu Glu Gly Lys Arg Asp Lys Asn Asp Wall Asp Glu
  1  5  10  15

<210> SEQ ID NO 166
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens S-arrestin epitope

<400> SEQUENCE: 166

Thr Val Lys Lys
  5  10

<210> SEQ ID NO 167
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens S-arrestin epitope

<400> SEQUENCE: 167

His Pro Glu Pro Ala Lys Glu Ser Tyr Gln Asp Ala Ann
  1  5  10  15
Leu Val Phe Glu
20

<210> SEQ ID NO 168
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens S-arrestin epitope
<400> SEQUENCE: 168

Ile Lys Ala Phe Val Glu Gln Val Ala Asn Val Val Leu Tyr Ser Ser
1 5 10 15

Asp Tyr Tyr Val
20

<210> SEQ ID NO 169
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens S-arrestin epitope
<400> SEQUENCE: 169

Lys Ser Ser Val Arg Leu Leu Ile Arg Lys Val Gln His Ala Pro Leu
1 5 10 15

Glu Met Gly Pro
20

<210> SEQ ID NO 170
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens S-arrestin epitope
<400> SEQUENCE: 170

Gln Pro Arg Ala Glu Ala Ala Trp Gln Phe Phe Met Ser Asp Lys Pro
1 5 10 15

Leu His Leu Ala
20

<210> SEQ ID NO 171
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens S-arrestin epitope
<400> SEQUENCE: 171

Ser Tyr Gln Asp Ala Asn Leu Val Phe Glu Glu Phe Ala Arg His Asn
1 5 10 15

Leu Lys Asp Ala
20

<210> SEQ ID NO 172
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens S-arrestin epitope
<400> SEQUENCE: 172
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FEATURE: Homo sapiens S-arrestin epitope

**<220>** FEATURES:

**<223>** OTHER INFORMATION: Homo sapiens SS protein SS-56 epitope

**<400>** SEQUENCE: 177

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Tyr Gly Gln Glu Asp Ile Asp Val Ile Gly Leu Thr Phe Arg Arg Asp
1 5 10 15
Leu Tyr Phe Ser
20
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**<210>** SEQ ID NO 179

**<211>** LENGTH: 10

**<212>** TYPE: PRT

**<213>** ORGANISM: Artificial Sequence

**<220>** FEATURE:

**<223>** OTHER INFORMATION: Homo sapiens Steroid 21-hydroxylase epitope

**<400>** SEQUENCE: 178

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Tyr Thr Cys Pro Leu Cys Arg Ala Pro Val
1 5 10
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**<210>** SEQ ID NO 179

**<211>** LENGTH: 8

**<212>** TYPE: PRT

**<213>** ORGANISM: Artificial Sequence

**<220>** FEATURE:

**<223>** OTHER INFORMATION: Homo sapiens Steroid 21-hydroxylase epitope

**<400>** SEQUENCE: 179

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Glu Pro Leu Ala Arg Leu Glu Leu
1 5
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**<210>** SEQ ID NO 180

**<211>** LENGTH: 20

**<212>** TYPE: PRT

**<213>** ORGANISM: Artificial Sequence

**<220>** FEATURE:

**<223>** OTHER INFORMATION: Homo sapiens Steroid 21-hydroxylase epitope

**<400>** SEQUENCE: 180

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Glu Pro Leu Ala Arg Leu Glu Leu Phe Val Val Leu Thr Arg Leu Leu
1 5 10 15
Gln Ala Phe Thr
20
```

**<210>** SEQ ID NO 181

**<211>** LENGTH: 20

**<212>** TYPE: PRT

**<213>** ORGANISM: Artificial Sequence

**<220>** FEATURE:

**<223>** OTHER INFORMATION: Homo sapiens Steroid 21-hydroxylase epitope

**<400>** SEQUENCE: 181

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Ile Lys Asp Asp Asn Leu Met Pro Ala Tyr Tyr Lys Cys Ile Gln Glu
1 5 10 15
Val Leu Lys Thr
20
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**<210>** SEQ ID NO 182

**<211>** LENGTH: 20

**<212>** TYPE: PRT

**<213>** ORGANISM: Artificial Sequence

**<220>** FEATURE:

**<223>** OTHER INFORMATION: Homo sapiens Steroid 21-hydroxylase epitope
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<400> SEQUENCE: 182
Ile Arg Asp Ser Met Glu Pro Val Val Glu Gin Thr Gin Glu Phe
  1  5  10  15
Cys Glu Arg Met
  20

<210> SEQ ID NO 183
<211> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens T-cell receptor V beta chain 13.1 epitope
<400> SEQUENCE: 182
Leu Gly Arg Ala Gly Leu Thr Tyr
  1  5

<210> SEQ ID NO 184
<211> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens transaldolase 1 epitope
<400> SEQUENCE: 183
Leu Leu Phe Ser Phe Ala Gin Ala Val
  1  5

<210> SEQ ID NO 185
<211> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Vasoactive intestinal polypeptide receptor 1 precursor epitope
<400> SEQUENCE: 185
Arg Arg Lys Trp Arg Arg Trp His Leu
  1  5

<210> SEQ ID NO 186
<211> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Vasoactive intestinal polypeptide receptor 1 precursor epitope
<400> SEQUENCE: 186
Arg Arg Lys Trp Arg Arg Trp His Leu
  1  5

<210> SEQ ID NO 187
<211> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Arachis hypogaea 2S protein 1 epitope
<400> SEQUENCE: 187
Ala His Ala Ser Ala Gin Gin Trp Glu Leu Gin Gly Asp Arg Arg
  1  5  10  15
Cys Gln Ser Gln
20

<210> SEQ ID NO 188
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Arachis hypogaea 2S protein 1 epitope
<400> SEQUENCE: 188

Ala Lys Leu Thr Ile Leu Val Ala Leu Ala Leu Phe Leu Leu Ala Ala
1 5 10 15
His Ala Ser Ala
20

<210> SEQ ID NO 189
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Arachis hypogaea 2S protein 1 epitope
<400> SEQUENCE: 189

Ala Leu Gln Gln Ile Met Glu Asn Gln Ser Asp Arg Leu Gln Gly Arg
1 5 10 15
Gln Gln Glu

<210> SEQ ID NO 190
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Arachis hypogaea 2S protein 1 epitope
<400> SEQUENCE: 190

Ala Asn Leu Arg Pro Cys Glu Gln His Leu Met Gln Lys Ile Gln Arg
1 5 10 15
Asp Glu Asp Ser
20

<210> SEQ ID NO 191
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Arachis hypogaea 2S protein 1 epitope
<400> SEQUENCE: 191

Cys Asn Glu Leu Asn Glu Phe Glu Asn Asn Gln Arg Cys Met Cys Glu
1 5 10 15
Ala Leu Gln Gln
20

<210> SEQ ID NO 192
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens 5-hydroxytryptamine receptor 2C
(5-HT-2C) (Serotonin receptor 2C) (5-HT2C) (5-HTR2C) (5HT-1C)
epitope
<400> SEQUENCE: 192
Pro Arg Gly Thr Met Gln Ala Ile Asn Asn Glu Arg Lys Ala Ser Lys
1  5  10  15

<210> SEQ ID NO 193
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Allergen Bos d 2 precursor epitope

<400> SEQUENCE: 193
Asp Gln Gly Thr Cys Leu Leu Leu Thr Glu Val Ala
1  5  10

<210> SEQ ID NO 194
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Allergen Bos d 2 precursor epitope

<400> SEQUENCE: 194
Glu Leu Glu Lys Tyr Gln Gln Leu Asn Ser Glu Arg Gly Val
1  5  10

<210> SEQ ID NO 195
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Allergen Bos d 2 precursor epitope

<400> SEQUENCE: 195
Gly Glu Arg Ile Thr Lys Met Thr Gly Leu Ala Lys
1  5  10

<210> SEQ ID NO 196
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Allergen Bos d 2 precursor epitope

<400> SEQUENCE: 196
Pro Gly Glu Trp Arg Ile Ile Tyr Ala Ala Asp Asn Lys
1  5  10

<210> SEQ ID NO 197
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Allergen Bos d 2 precursor epitope

<400> SEQUENCE: 197
Arg Ile Glu Cys Ile Asn Asp Cys
1  5

<210> SEQ ID NO 198
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURES:
<223> OTHER INFORMATION: Bos taurus Allergen Bos d 2 precursor epitope

<400> SEQUENCE: 198
Val Ala Lys Arg Glu Gly Tyr Val Tyr Val Leu
1 5 10

<210> SEQ ID NO 199
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURES:
<223> OTHER INFORMATION: Bos taurus Allergen Bos d 2 precursor epitope

<400> SEQUENCE: 199
Val Ser Glu Asn Met Leu Val Thr Tyr Val
1 5 10

<210> SEQ ID NO 200
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURES:
<223> OTHER INFORMATION: Bos taurus Allergen Bos d 2 precursor epitope

<400> SEQUENCE: 200
Asp Glu Gly Thr Cys Leu Leu Leu Thr Glu Val Ala
1 5 10

<210> SEQ ID NO 201
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURES:
<223> OTHER INFORMATION: Bos taurus Allergen Bos d 2 precursor epitope

<400> SEQUENCE: 201
Glu Leu Glu Lys Tyr Gln Gln Leu Asn Ser Glu Arg Gly Val
1 5 10

<210> SEQ ID NO 202
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURES:
<223> OTHER INFORMATION: Bos taurus Allergen Bos d 2 precursor epitope

<400> SEQUENCE: 202
Glu Leu Glu Lys Tyr Gln Gln Leu Asn Ser Glu Arg Gly Val Pro Asn
1 5 10 15

<210> SEQ ID NO 203
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURES:
<223> OTHER INFORMATION: Bos taurus Allergen Bos d 2 precursor epitope

<400> SEQUENCE: 203
Gly Glu Arg Ile Thr Lys Met Thr Glu Gly Leu Ala Lys
1 5 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Allergen Bos d 2 precursor epitope
<400> SEQUENCE: 204

Pro Gly Glu Trp Arg Ile Ile Tyr Ala Ala Asp Asn Lys
1  5  10

<210> SEQ ID NO 205
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Allergen Bos d 2 precursor epitope
<400> SEQUENCE: 205

Arg Ile Glu Cys Ile Asn Asp Cys
1  5

<210> SEQ ID NO 206
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Allergen Bos d 2 precursor epitope
<400> SEQUENCE: 206

Val Ala Lys Arg Glu Gly Tyr Val Tyr Val Leu
1  5  10

<210> SEQ ID NO 207
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Allergen Bos d 2 precursor epitope
<400> SEQUENCE: 207

Val Ser Glu Asn Met Leu Val Thr Tyr Val
1  5  10

<210> SEQ ID NO 208
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cryptomeria japonica Allergen Cry j 2 epitope
<400> SEQUENCE: 208

Asp Ile Phe Ala Ser Lys Asn Phe His Leu Gln Lys Asn
1  5  10

<210> SEQ ID NO 209
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cryptomeria japonica Allergen Cry j 2 epitope
<400> SEQUENCE: 209

Gly Ile Ile Ala Ala Tyr Gln Asn Pro Ala Ser Trp Lys
1  5  10
Continued

**Sequence 210**

Lys Leu Thr Ser Gly Lys Ile Ala Ser Cys Leu Asn
1      5      10

**Sequence 211**

Gln Phe Ala Lys Leu Thr Gly Phe Thr Leu Met Gly
1      5      10

**Sequence 212**

Ile Asn Gln Gln Leu Asn Pro Lys
1

**Sequence 213**

Ile Asn Gln Gln Leu Asn Pro Lys Thr Asn Lys Tsp Glu Asp Lys
1      5      10      15

**Sequence 214**

Leu Asn Pro Lys Thr Asn Lys Tsp Glu Asp Lys
1      5      10

**Sequence 215**

Aspergillus fumigatus allergen I/a; Asp f I/a epitope

**Sequence 216**

Cryptomeria japonica Allergen Cry j 2 epitope

**Sequence 217**

Cryptomeria japonica Allergen Cry j 2 epitope
<400> SEQUENCE: 215

Ile Asn Gln Gln Leu Asn Pro Lys
1 5

<210> SEQ ID NO 216
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aspergillus fumigatus allergen I/a; Asp f I/a epitope

<400> SEQUENCE: 216

Ile Asn Gln Gln Leu Asn Pro Lys Thr Asn Lys Trp Glu Asp Lys
1 5 10 15

<210> SEQ ID NO 217
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aspergillus fumigatus allergen I/a; Asp f I/a epitope

<400> SEQUENCE: 217

Leu Asn Pro Lys Thr Asn Lys Trp Glu Asp Lys
1 5 10

<210> SEQ ID NO 218
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aspergillus fumigatus allergen I/a; Asp f I/a epitope

<400> SEQUENCE: 218

Thr Asn Lys Trp Glu Asp Lys
1 5

<210> SEQ ID NO 219
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aspergillus fumigatus allergen I/a; Asp f I/a epitope

<400> SEQUENCE: 219

Leu Asn Pro Lys Thr Asn Lys Trp Glu Asp Lys Arg
1 5 10

<210> SEQ ID NO 220
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides farinae Allergen Mag epitope

<400> SEQUENCE: 220

Pro Arg Leu Ser Trp His Gln Tyr Thr Lys Arg Asp Ser Arg Glu
1 5 10 15

<210> SEQ ID NO 221
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides farinae Allergen Mag epitope

<400> SEQUENCE: 221

Thr Val Asp Leu Ile Ser Pro Val Thr Lys Arg Ala Ser Leu Lys
1  5 10 15

<210> SEQ ID NO 222
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Alpha-S1-casein precursor epitope

<400> SEQUENCE: 222

Ala Trp Tyr Tyr Val Leu Gly Thr Glu Tyr Thr Asp Ala Pro Ser
1  5 10 15

Phe Ser

<210> SEQ ID NO 223
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Alpha-S1-casein precursor epitope

<400> SEQUENCE: 223

Asp Ala Tyr Pro Ser Gly Ala Trp Tyr Val Pro Leu Gly Thr Glu
1  5 10 15

Tyr Thr

<210> SEQ ID NO 224
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Alpha-S1-casein precursor epitope

<400> SEQUENCE: 224

Asp Ile Gly Ser Glu Ser Thr Glu Asp Gln Ala Met Glu Asp Ile Lys
1  5 10 15

Gln Met

<210> SEQ ID NO 225
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Alpha-S1-casein precursor epitope

<400> SEQUENCE: 225

Glu Asp Ile Lys Gln Met
1  5

<210> SEQ ID NO 226
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Alpha-S1-casein precursor epitope
<400> SEQUENCE: 226

Glu Pro Met Ile Gly Val Asn Gln Glu Leu Ala Tyr
1 5 10

<210> SEQ ID NO 227
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Alpha-S1-casein precursor epitope

<400> SEQUENCE: 227

Glu Pro Met Ile Gly Val Asn Gln Glu Leu Ala Tyr Phe Tyr Pro Glu Leu Phe
1 5 10 15

<210> SEQ ID NO 228
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Arachis hypogaea Ara h 2.01 allergen epitope

<400> SEQUENCE: 228

Glu Leu Asn Glu Phe Glu Asn Gln Arg Cys Met Cys Glu Ala Leu Gln
1 5 10 15

<210> SEQ ID NO 229
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Arachis hypogaea Ara h 2.01 allergen epitope

<400> SEQUENCE: 229

Ser Gln Leu Glu Arg Ala Asn Leu Arg Pro Cys Glu Gln His Leu Met Ser Gln Leu Glu Arg Ala Asn Leu Arg Pro Cys Glu Gln His Leu Met
1 5 10 15

<210> SEQ ID NO 230
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cryptomeria japonica Cry J 1 precursor epitope

<400> SEQUENCE: 230

Gly Ala Thr Arg Asp Arg Pro Leu Trp Ile Ile Phe Ser Gly Asn Gly Ala Thr Arg Asp Arg Pro Leu Trp Ile Ile Phe Ser Gly Asn
1 5 10 15

<210> SEQ ID NO 231
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cryptomeria japonica Cry J 1 precursor epitope

<400> SEQUENCE: 231

Ile Phe Ser Gly Asn Met Asn Ile Lys Leu Lys Met Pro Met Tyr Ile Ile Phe Ser Gly Asn Met Asn Ile Lys Leu Lys Met Pro Met Tyr Ile
1 5 10 15

Ala Gly Tyr Lys
<210> SEQ ID NO 232  
<211> LENGTH: 20  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Cryptomeria japonica Cry j 1 precursor epitope  
<400> SEQUENCE: 232

Lys Met Pro Met Tyr Ile Ala Gly Tyr Lys Thr Phe Asp Gly Arg Gly  
Ala Gln Val Tyr  

<210> SEQ ID NO 233  
<211> LENGTH: 20  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Cryptomeria japonica Cry j 1 precursor epitope  
<400> SEQUENCE: 233

Leu Gly His Asp Asp Ala Tyr Ser Asp Asp Lys Ser Met Lys Val Thr  
Val Ala Phe Asn  

<210> SEQ ID NO 234  
<211> LENGTH: 19  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Cryptomeria japonica Cry j 1 precursor epitope  
<400> SEQUENCE: 234

Ser Gly Lys Tyr Glu Gly Gly Asn Ile Tyr Thr Lys Gly Ala Phe  
Asn Val Glu  

<210> SEQ ID NO 235  
<211> LENGTH: 11  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Cochliobolus lunatus Cytochrome c epitope  
<400> SEQUENCE: 235

Glu Asn Pro Lys Lys Tyr Ile Pro Gly Thr Lys  

<210> SEQ ID NO 236  
<211> LENGTH: 11  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Cochliobolus lunatus Cytochrome c epitope  
<400> SEQUENCE: 236

Gly Leu Phe Gly Arg Lys Thr Gly Ser Val Ala
<210> SEQ ID NO 237
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cochliobolus lunatus Cytochrome c epitope
<400> SEQUENCE: 237
Lys Ile Gly Pro Glu Leu His Gly Leu 1 5

<210> SEQ ID NO 238
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cochliobolus lunatus Cytochrome c epitope
<400> SEQUENCE: 238
Leu Lys Ala Gly Glu Gly Asn Lys Ile Gly Pro Glu 1 5 10

<210> SEQ ID NO 239
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cochliobolus lunatus Cytochrome c epitope
<400> SEQUENCE: 239
Leu Lys Lys Pro Lys Arg Asn Asp Leu Ile 1 5 10

<210> SEQ ID NO 240
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides farinae Der f 2 allergen epitope
<400> SEQUENCE: 240
Gly Leu Glu Ile Asp Val Pro Gly Ile Asp Thr Asn Ala Cys His Phe Val 1 5 10 15
Val Lys

<210> SEQ ID NO 241
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides farinae Der f 2 allergen epitope
<400> SEQUENCE: 241
Pro Gly Ile Asp Thr Asn Ala Cys His Phe Val Lys Cys Pro Leu Val 1 5 10 15
Lys Gly Glu Gln Gln 20

<210> SEQ ID NO 242
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> OTHER INFORMATION: Dermatophagoides pteronyssinus Der p 1 allergen epitope
<400> SEQUENCE: 242

Arg Phe Gly Ile Ser Tyr Cys Glu Ile Tyr Pro Pro Asn Ala 15
Lys Ile Arg

<210> SEQ ID NO 243
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides pteronyssinus Der p 1 allergen epitope
<400> SEQUENCE: 243

Ala Val Asn Ile Val Gly Tyr Ser Asn Ala Glu Gly Val Asp Tyr
Thr His Ala 15

<210> SEQ ID NO 244
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Chironomus thummi globin Ctt 3-1 epitope
<400> SEQUENCE: 244

Phe Ala Gly Lys Asp Leu Glu Ser Ile Lys Gly Thr Ala Pro Phe 15
Glu Thr His Ala

<210> SEQ ID NO 245
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Chironomus thummi globin Ctt 3-1 epitope
<400> SEQUENCE: 245

Gly Thr Ala Pro Phe Glu Thr His Ala Asn Arg

<210> SEQ ID NO 246
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Chironomus thummi globin Ctt 3-1 epitope
<400> SEQUENCE: 246

Lys Gly Thr Ala Pro Phe Glu Thr His Ala Asn Arg Ile Val Gly Phe
Phe Ser Lys Ile Ile

<210> SEQ ID NO 247
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
OTHER INFORMATION: Chironomus thummi thummi Globin CTT-III epitope

SEQ ID NO 247
LENGTH: 20
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Chironomus thummi thummi Globin CTT-III epitope

 Ala His Thr Asp Phe Ala Gly Ala Glu Ala Ala Trp Gly Ala Thr Leu
1 5 10 15
Amp Thr Phe Phe Gly
20

SEQ ID NO 248
LENGTH: 21
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Chironomus thummi thummi Globin CTT-III epitope

 Phe Ala Gly Lys Asp Leu Glu Ser Ile Lys Gly Thr Ala Pro Phe Glu
1 5 10 15
Ile His Ala Asn
20

SEQ ID NO 249
LENGTH: 21
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Chironomus thummi thummi Globin CTT-III epitope

 Val Asn Thr Phe Val Ala Ser His Ile Lys Pro Arg Gly Val Thr His Asp
1 5 10 15
Gln Leu Asn Asn Phe
20

SEQ ID NO 250
LENGTH: 8
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Chironomus thummi thummi Globin CTT-III precursor epitope

 Ala Asp Pro Ser Ile Met Ala Lys
1 5

SEQ ID NO 251
LENGTH: 21
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Chironomus thummi thummi Globin CTT-III precursor epitope

 Ala Asp Pro Ser Ile Met Ala Lys Phe Thr Gln Phe Ala Gly Lys Asp
1 5 10 15
Leu Glu Ser Ile Lys
20

SEQ ID NO 252
LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Chironomus thummi thummi Globin CTT-III precursor epitope

<400> SEQUENCE: 252
Ala Glu Ala Ala Trp
1  5

<210> SEQ ID NO 253
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Chironomus thummi thummi Globin CTT-III precursor epitope

<400> SEQUENCE: 253
Ala Glu Ala Ala Trp Gly Ala Thr Leu Asp Thr Phe Phe Gly Met Ile
1  5  10  15  20
Phe Ser Lys Met

<210> SEQ ID NO 254
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Chironomus thummi thummi Globin CTT-III precursor epitope

<400> SEQUENCE: 254
Ala Gly Phe Val Ser Tyr Met Lys
1  5

<210> SEQ ID NO 255
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phaseolus vulgaris Glycine-rich cell wall structural protein 1.8 precursor epitope

<400> SEQUENCE: 255
Gly Gly Tyr Gly Asp Gly Gly Ala His Gly Gly Tyr Gly Gly
1  5  10  15

<210> SEQ ID NO 256
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Group V allergen Phl p 5 epitope

<400> SEQUENCE: 256
Ala Thr Pro Glu Ala Lys Tyr Asp Ala Tyr Val Ala Thr Leu Ser
1  5  10  15

<210> SEQ ID NO 257
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Group V allergen Phil p 5 epitope

<400> SEQUENCE: 257

Phe Thr Val Phe Glu Ala Ala Phe Asn Ala Ile Lys Ala Gly
1   5    10    15

<210> SEQ ID NO 258
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Group V allergen Phil p 5 epitope

<400> SEQUENCE: 258

Lys Tyr Asp Ala Tyr Val Ala Thr Leu Ser Glu Ala Leu Arg Ile
1   5    10    15

<210> SEQ ID NO 259
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Group V allergen Phil p 5 epitope

<400> SEQUENCE: 259

Pro Ala Asn Asp Lys Phe Thr Val Phe Glu Ala Ala Phe Asn
1   5    10    15

<210> SEQ ID NO 260
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Group V allergen Phil p 5 epitope

<400> SEQUENCE: 260

Pro Lys Gly Gly Ala Glu Ser Ser Lys Ala Ala Leu Thr Ser
1   5    10    15

<210> SEQ ID NO 261
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens KIAA1224 protein epitope

<400> SEQUENCE: 261

Asp Leu Glu Ser Tyr Leu Glu Leu Asn Cys Glu Arg Gly Thr Trp Arg
1   5    10    15

<210> SEQ ID NO 262
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Lepidoglyphus destructor Lep D 2 precursor epitope

<400> SEQUENCE: 262

Lys Gly Glu Ala Leu Asp Phe Asn Tyr Gly Met Thr Ile Pro Ala
1   5    10    15
<210> SEQ ID NO 263
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Corylus avellana lipid transfer protein precursor epitope

<400> SEQUENCE: 263
Ala Gly Leu Pro Gly Lys Cys Gly Val Asn Ile Pro
1    5

<210> SEQ ID NO 264
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Corylus avellana lipid transfer protein precursor epitope

<400> SEQUENCE: 264
Ala Lys Gly Ile Ala Gly Leu Asn Pro Asn Ile Ala
1    5

<210> SEQ ID NO 265
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Corylus avellana lipid transfer protein precursor epitope

<400> SEQUENCE: 265
Cys Gly Val Asn Ile Pro Tyr Ile Ser Pro Ser
1    5

<210> SEQ ID NO 266
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Corylus avellana lipid transfer protein precursor epitope

<400> SEQUENCE: 266
Cys Lys Gly Val Arg Ala Val Asn Asp Ala Ser Arg
1    5

<210> SEQ ID NO 267
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Corylus avellana lipid transfer protein precursor epitope

<400> SEQUENCE: 267
Cys Val Leu Tyr Leu Lys Asn Gly Gly Val Leu Pro
1    5

<210> SEQ ID NO 268
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
Homo sapiens Lipocalin 1 (tear prealbumin) epitope

SEQ ID NO 268 LENGTH: 15 TYPE PRT ORGANISM: Artificial Sequence FEATURE:

Lys Pro Val Arg Gly Val Lys Val Gly Arg Asp Pro Lys Asn Ann
1     5     10    15

Dermatophagoides farinae Mag3 epitope

SEQ ID NO 269 LENGTH: 15 TYPE PRT ORGANISM: Artificial Sequence FEATURE:

Glu Phe Asn Thr Glu Phe Thr Ile His Ala Asp Lys Ann Ann Leu
1     5     10    15

Dermatophagoides farinae Mag3 epitope

SEQ ID NO 270 LENGTH: 15 TYPE PRT ORGANISM: Artificial Sequence FEATURE:
Phe Thr Ile His Ala Asp Lys Ann Ann Leu Lys Met His Met Asp
1     5     10    15

Dermatophagoides farinae Mag3 epitope

SEQ ID NO 271 LENGTH: 15 TYPE PRT ORGANISM: Artificial Sequence FEATURE:

Lys Met His Met Asp Phe Pro Asn Val Phe Gln Ala Asp Leu Thr
1     5     10    15

Apium graveolens Major allergen Api g 1 epitope

SEQ ID NO 272 LENGTH: 13 TYPE PRT ORGANISM: Artificial Sequence FEATURE:

Ala Leu Phe Lys Ala Leu Glu Ala Tyr Leu Ile Ala Ann
1     5

Apium graveolens Major allergen Api g 1 epitope

SEQ ID NO 273 LENGTH: 12 TYPE PRT ORGANISM: Artificial Sequence FEATURE:

Asp Ala Val Val Pro Glu Glu Asn Ile Lys Tyr Ala
1     5
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Apium graveolens Major allergen Api g 1 epitope

<400> SEQUENCE: 274

Asp Ile Leu Leu Gly Phe Ile Glu Ser Ile Glu Asn
1  5  10

<210> SEQ ID NO 275
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Apium graveolens Major allergen Api g 1 epitope

<400> SEQUENCE: 275

Gly Gly Ser Ile Cys Lys Tyr Thr Ala Ile Phe His
1  5  10

<210> SEQ ID NO 276
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Apium graveolens Major allergen Api g 1 epitope

<400> SEQUENCE: 276

Gly Val Glu Thr His Val Leu Glu Leu Thr Ser Ser
1  5  10

<210> SEQ ID NO 277
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aspergillus fumigatus Major allergen Asp f 2 precursor epitope

<400> SEQUENCE: 277

Phe Gly Asn Arg Pro Thr Met Glu Ala Val Gly Ala Tyr Asp Val
1  5  10  15

<210> SEQ ID NO 278
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aspergillus fumigatus Major allergen Asp f 2 precursor epitope

<400> SEQUENCE: 278

Met Glu Ala Val Gly Ala Tyr Asp Val Ile Val Asn Gly Asp Lys
1  5  10  15

<210> SEQ ID NO 279
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Canis lupus familiaris Major allergen Can f 1 precursor epitope

<400> SEQUENCE: 279
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Ala Leu Glu Asp Phe Arg Glu Phe Ser Arg Ala Lys Gly Leu Asn Gln
  1     5     10    15

<210> SEQ ID NO 280
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Canis lupus familiaris Major allergen Can f 1 precursor epitope
<400> SEQUENCE: 280

Asp Gln Glu Val Pro Glu Lys Pro Ser Val Thr Pro Met Ile Leu
  1     5     10    15

<210> SEQ ID NO 281
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Corylus avellana major allergen Cor a 1.0401 epitope
<400> SEQUENCE: 281

Ala Gly Lys Glu Lys Ala Ala Gly Leu Phe Lys Ala
  1     5     10

<210> SEQ ID NO 282
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Corylus avellana major allergen Cor a 1.0401 epitope
<400> SEQUENCE: 282

Ala Gly Leu Phe Lys Ala Val Glu Ala Tyr Leu Leu
  1     5     10

<210> SEQ ID NO 283
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Corylus avellana major allergen Cor a 1.0401 epitope
<400> SEQUENCE: 283

Ala Pro Gln His Phe Thr Ser Ala Glu Asn Leu Glu
  1     5     10

<210> SEQ ID NO 284
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Corylus avellana major allergen Cor a 1.0401 epitope
<400> SEQUENCE: 284

Ala Arg Leu Phe Lys Ser Phe Val Leu Asp Ala Asp
  1     5     10

<210> SEQ ID NO 285
<211> LENGTH: 12
```
Glule Asp His Ala Asn Phe Lys Tyr Cys Tyr Ser
1 5 10

Glu Leu Phe Lys Ala Ile Glu Ala Tyr Leu Ile Ala Asn
1 5 10

Asp Gly Tyr Aen Val Phe Arg Ile Ser Glu Phe Glu Asn Asp Glu His
1 5 10 15

Asp Lys Asp Arg Pro Phe Gln Leu Phe Glu Phe Tyr Ala Arg Glu Pro
1 5 10 15

Asp Leu Thr Lys Ile Asp Arg Cys Phe Gln Leu Arg Gly Asn Gly Val
1 5 10 15


-continued

Amp Arg Pro Phe Gln Leu Phe Glu Phe Tyr Ala Arg Glu Pro Asp Val

1 5 10 15

<210> SEQ ID NO 291
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Equus caballus Major allergen Equ c 1 precursor epitope

<400> SEQUENCE: 291

Asp Val Ser Pro Glu Ile Lys Glu Phe Val Lys Ile Val Gln Lys

1 5 10 15

<210> SEQ ID NO 292
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Felis catus major allergen I epitope

<400> SEQUENCE: 292

Glu Asn Ala Arg Ile Leu Lys Asn Cys Val Asp Ala Lys Met Thr Glu

1 5 10 15

Glu

<210> SEQ ID NO 293
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Felis catus major allergen I epitope

<400> SEQUENCE: 293

Arg Asp Val Asp Leu Phe Leu Thr Gly Thr Pro Asp Glu Tyr Val Glu

1 5 10 15

Gln

<210> SEQ ID NO 294
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Felis catus major allergen I epitope

<400> SEQUENCE: 294

Thr Gly Thr Pro Asp Glu Tyr Val Glu Gln Val Ala Gln Tyr Lys Ala

1 5 10 15

Leu

<210> SEQ ID NO 295
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Felis catus Major allergen I polypeptide chain 1 precursor epitope

<400> SEQUENCE: 295

Asp Val Asp Leu Phe Leu Thr Gly Thr Pro Asp Glu Tyr Val Glu Gln

1 5 10 15
-continued-

Lys Glu Asn Ala Leu Ser Leu Leu Asp Lys Ile Tyr Thr Ser Pro Leu
1 5 10 15

<210> SEQ ID NO 301
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Felis catus major allergen I, polypeptide chain 1 epitope

<400> SEQUENCE: 301

Lys Met Thr Glu Glu Asp Lys Glu Asn Ala Leu Ser Leu Leu Asp Lys
1 5 10 15

<210> SEQ ID NO 302
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Malus x domestica Major allergen Mal d 1 epitope

<400> SEQUENCE: 302

Gly Leu Phe Lys Leu Ile Glu Ser Tyr Leu Lys Asp His Pro Asp
1 5 10 15

<210> SEQ ID NO 303
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Prunus avium Major allergen Pru av 1 epitope

<400> SEQUENCE: 303

Asn Leu Phe Lys Leu Ile Glu Thr Tyr Leu Lys Gly His Pro Asp
1 5 10 15

<210> SEQ ID NO 304
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Hevea brasiliensis Major latex allergen Hev b 5 epitope

<400> SEQUENCE: 304

Ala Ala Pro Ala Glu Gly Glu Lys Pro Ala Glu Glu Lys Pro Ile
1 5 10 15

Thr Glu Ala Ala
20

<210> SEQ ID NO 305
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Hevea brasiliensis Major latex allergen Hev b 5 epitope

<400> SEQUENCE: 305

Ala Glu Glu Lys Pro Ile Thr Glu Ala Ala Glu Thr Ala Thr Thr
1 5 10 15

Glu Val Pro Val
<210> SEQ ID NO 306
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Hevea brasiliensis Major latex allergen Hev b 5 epitope

<400> SEQUENCE: 306

Ala Pro Ala Glu Pro Ala Pro Glu Thr Glu Lys Ala Glu
1  5
10 15

Glu Val Glu Lys
20

<210> SEQ ID NO 307
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Hevea brasiliensis Major latex allergen Hev b 5 epitope

<400> SEQUENCE: 307

Ala Pro Glu Ala Asp Gln Thr Pro Glu Glu Lys Pro Ala Glu Pro
1  5
10 15

Glu Pro Val Ala
20

<210> SEQ ID NO 308
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides pteronyssinus Major mite fecal allergen Der p 1 epitope

<400> SEQUENCE: 308

Ala Ser Glu Gln Glu Thr Ala Asp Ala Thr Pro Glu Lys Glu Glu Pro
1  5
10 15

Thr Ala Ala Pro
20

<210> SEQ ID NO 309
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides pteronyssinus Major mite fecal allergen Der p 1 epitope

<400> SEQUENCE: 309

Tyr Ala Tyr Val Ala Arg Glu Gln Ser Cys Arg
1  5
10

<210> SEQ ID NO 310
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides pteronyssinus Major mite fecal allergen Der p 1 epitope
<400> SEQUENCE: 310

Ala Leu Ala Gln Thr His Thr Ala Ile Ala Val Ile Ile Gly Ile Lys
1      5      10      15
Asp Leu Asp

<210> SEQ ID NO 311
<211> LENGTH: 35
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Olea europaea Major pollen allergen epitope

<400> SEQUENCE: 311

Glu Asp Ile Pro Gln Pro Pro Val Ser Gln Phe His Ile Gln Gly Gln
1      5      10      15
Val Tyr Cys Asp Thr Cys Arg Ala Gly Phe Ile Thr Glu Leu Ser Glu
20     25     30
Phe Ile Pro
35

<210> SEQ ID NO 312
<211> LENGTH: 34
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Olea europaea Major pollen allergen epitope

<400> SEQUENCE: 312

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

<210> SEQ ID NO 313
<211> LENGTH: 34
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Olea europaea Major pollen allergen epitope

<400> SEQUENCE: 313

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

<210> SEQ ID NO 314
<211> LENGTH: 53
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Olea europaea Major pollen allergen epitope

<400> SEQUENCE: 314

Leu Val Glu Arg Asp His Lys Asn Glu Phe Cys Glu Ile Thr Leu Ile
1      5      10      15
Ser Ser Gly Arg Lys Asp Cys Asn glu Ile Pro Thr Glu Gly Trp Ala
20     25     30
Lys Pro Ser Leu Lys Phe Lys Leu Asn Thr Val Asn Gly Thr Thr Arg Thr Val Asn Pro Leu

SEQ ID NO 315
LENGTH: 33
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Olea europaea Major pollen allergen epitope

Met Leu Val Glu Arg Asp His Lys Asn Glu Phe Cys Glu Ile Thr Leu Ile Ser Ser Gly Arg Lys Asp Cys Asn Glu Ile Pro Thr Glu Gly Trp

SEQ ID NO 316
LENGTH: 12
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Artemisia vulgaris Major pollen allergen Art v 1 precursor epitope

Ala Gly Gly Ser Pro Ser Pro Pro Ala Asp Gly Gly

SEQ ID NO 317
LENGTH: 12
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Artemisia vulgaris Major pollen allergen Art v 1 precursor epitope

Ala Gly Ser Lys Leu Cys Glu Thr Ser Lys Thr

SEQ ID NO 318
LENGTH: 12
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Artemisia vulgaris Major pollen allergen Art v 1 precursor epitope

Cys Asp Lys Lys Cys Ile Glu Trp Glu Lys Ala Gln

SEQ ID NO 319
LENGTH: 12
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Artemisia vulgaris Major pollen allergen Art v 1 precursor epitope
Amp Gly Gly Ser Pro Pro Pro Pro Ala Asp Gly Gly
1      5      10

<210> SEQ ID NO 320
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artemisia vulgaris Major pollen allergen Art v 1 precursor epitope

<400> SEQUENCE: 320
Glu Lys Thr Ser Lys Thr Tyr Ser Gly Lys Cys Asp
1      5      10

<210> SEQ ID NO 321
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Betula pendula Major pollen allergen Bet v 1-A epitope

<400> SEQUENCE: 321
 Ala Ala Arg Leu Phe Lys Ala Phe Ile Leu Asp Gly
1      5      10

<210> SEQ ID NO 322
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Betula pendula Major pollen allergen Bet v 1-A epitope

<400> SEQUENCE: 322
 Ala Ala Arg Leu Phe Lys Ala Phe Ile Leu Asp Gly Asp Asn Leu
1      5      10  15

<210> SEQ ID NO 323
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Betula pendula Major pollen allergen Bet v 1-A epitope

<400> SEQUENCE: 323
 Ala Glu Gln Val Lys Ala Ser Lys Glu Met Gly Glu
1      5      10

<210> SEQ ID NO 324
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Betula pendula Major pollen allergen Bet v 1-A epitope

<400> SEQUENCE: 324
 Ala Phe Ile Leu Asp Gly Asp Asn Leu Phe Pro Lys Val Ala Pro Gln
1      5      10  15

Ala Ile Ser Ser Val
20
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<td>OTHER INFORMATION: Betula pendula Major pollen allergen Bet v 1-A epitope</td>
<td>Ala Ile Ser Ser Val Glu Asn Ile Glu Asn Gly</td>
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<td>OTHER INFORMATION: Betula pendula Major pollen allergen Bet v 1-A epitope</td>
<td>Glu Thr Leu Leu Arg Ala Val Glu Ser Tyr Leu Ala His Ser</td>
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<td>PRT</td>
<td>Artificial Sequence</td>
<td>OTHER INFORMATION: Chamaecyparis obtusa Major pollen allergen Cha o 1 precursor epitope</td>
<td>Gly Glu Thr Leu Leu Arg Ala Val Glu Ser Tyr Leu Ala His Ser</td>
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<td>Ala Asn Asn Tyr Asp Pro Trp Ser Ile Tyr Ala Ile Gly Gly Ser Ser Asn Pro Thr</td>
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<td>Ala Ser Thr Gly Val Thr Ile Ser Asn Asn His Phe Phe Asn His</td>
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<td>Lys Val Met Leu</td>
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Chamaecyparis obtusa Major pollen allergen Cha o 1 precursor epitope

<400> SEQUENCE: 330

Cys Ala Asn Trp Val Trp Arg Ser Thr Gln Asp Ser Phe Asn Asn Gly
1 5 10 15
Ala Tyr Phe Val
20

<210> SEQ ID NO 331
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Chamaecyparis obtusa Major pollen allergen Cha o 1 precursor epitope

<400> SEQUENCE: 331

Asp Ala Ile Thr Met Arg Asn Val Thr Asp Val Trp Ile Asp His Asn
1 5 10 15
Ser Leu Ser Asp
20

<210> SEQ ID NO 332
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Chamaecyparis obtusa Major pollen allergen Cha o 1 precursor epitope

<400> SEQUENCE: 332

Asp Ala Asn Trp Asp Gln Asn Arg Met Lys Leu Ala Asp Cys Ala Val
1 5 10 15
Gly Phe Gly Ser
20

<210> SEQ ID NO 333
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cynodon dactylon Major pollen allergen Cyn d 1 epitope

<400> SEQUENCE: 333

Ala Ile Gly Asp Lys Pro Gly Pro Asn Ile Thr Ala Thr Tyr Gly Asn
1 5 10 15
Lys Trp Leu Glu
20

<210> SEQ ID NO 334
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cynodon dactylon Major pollen allergen Cyn d 1
epitope

<400> SEQUENCE: 334
Cys Tyr Glu Ile Lys Cys Lys Glu Pro Val Glu Cys Ser Gly Glu Pro
1    5     10    15
Val Leu Val Lys
20

<410> SEQ ID NO 335
<411> LENGTH: 20
<412> TYPE: PRT
<413> ORGANISM: Artificial Sequence
<414> FEATURE:
<415> OTHER INFORMATION: Cynodon dactylon Major pollen allergen Cyn d 1 epitope
<400> SEQUENCE: 335
Asp His Gly Ala Cys Gly Tyr Lys Asp Val Asp Lys Pro Pro Phe
1    5     10    15
Asp Gly Met Thr
20

<410> SEQ ID NO 336
<411> LENGTH: 20
<412> TYPE: PRT
<413> ORGANISM: Artificial Sequence
<414> FEATURE:
<415> OTHER INFORMATION: Cynodon dactylon Major pollen allergen Cyn d 1 epitope
<400> SEQUENCE: 336
Glu Gly Gly Ala His Leu Val Gln Asp Asp Val Ile Pro Ala Asn Trp
1    5     10    15
Lys Pro Asp Thr
20

<410> SEQ ID NO 337
<411> LENGTH: 20
<412> TYPE: PRT
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<414> FEATURE:
<415> OTHER INFORMATION: Cynodon dactylon Major pollen allergen Cyn d 1 epitope
<400> SEQUENCE: 337
Phe Lys Asp Gly Leu Gly Cys Gly Ala Cys Tyr Glu Ile Lys Cys Lys
1    5     10    15
Glu Pro Val Glu
20

<410> SEQ ID NO 338
<411> LENGTH: 15
<412> TYPE: PRT
<413> ORGANISM: Artificial Sequence
<414> FEATURE:
<415> OTHER INFORMATION: Phleum pratense Major pollen allergen Phl p 4 precursor epitope
<400> SEQUENCE: 338
Phe Ala Glu Tyr Lys Ser Asp Tyr Val Tyr Gin Pro Phe Pro Lys
1    5     10    15
<210> SEQ ID NO 339
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Major pollen allergen Phl p 4 precursor epitope

<400> SEQUENCE: 339

Met Leu Leu Arg Lys Tyr Gly Ile Ala Glu Asn Val Ile Asp
1 5 10 15

<210> SEQ ID NO 340
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Major pollen allergen Phl p 4 precursor epitope

<400> SEQUENCE: 340

Asn Ser Phe Lys Pro Phe Ala Glu Tyr Lys Ser Asp Tyr Val Tyr
1 5 10 15

<210> SEQ ID NO 341
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Rattus norvegicus Major urinary protein precursor epitope

<400> SEQUENCE: 341

Ala Ser Asn Lys Arg Glu Lys Ile Glu Glu Asn Gly Ser Met Arg Val
1 5 10 15
Phe Met Gln His
20

<210> SEQ ID NO 342
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Rattus norvegicus Major urinary protein precursor epitope

<400> SEQUENCE: 342

Asp Ile Lys Glu Lys Phe Ala Lys Leu Cys Glu Ala His Gly Ile Thr
1 5 10 15
Arg Asp Asn Ile
20

<210> SEQ ID NO 343
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Rattus norvegicus Major urinary protein precursor epitope

<400> SEQUENCE: 343

Glu Glu Ala Ser Ser Thr Arg Gly Asn Leu Asp Val Ala Lys Leu Asn
1 5 10 15
Gly Asp Trp Phe
<210> SEQ ID NO 344
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Rattus norvegicus Major urinary protein precursor epitope

<400> SEQUENCE: 344

Glu Glu Asn Gly Ser Met Val Phe Met Glu His Ile Asp Val Leu
1  5  10  15

Glu Asn Ser Leu
20

<210> SEQ ID NO 345
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Rattus norvegicus Major urinary protein precursor epitope

<400> SEQUENCE: 345

Glu Asn Ser Leu Gly Phe Lys Arg Ile Leu Gly Asn Gly Glu Cys
1  5  10  15

Arg Glu Leu Tyr
20

<210> SEQ ID NO 346
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides farinae Mite group 2 allergen Der f 2 precursor epitope

<400> SEQUENCE: 346

Asp Ile Lys Tyr Thr Trp Asn Val Lys Ile Ala Pro Lys Ser Glu
1  5  10  15

Asn Val Val Val Thr
20

<210> SEQ ID NO 347
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides farinae Mite group 2 allergen Der f 2 precursor epitope

<400> SEQUENCE: 347

Asp Asn Gly Val Leu Ala Cys Ala Ile Ala Thr His Gly Lys Ile Arg
1  5  10  15

Asp
Der f 2 precursor epitope

SEQUENCE: 348

Glu Ala Leu Phe Asp Ala Asn Gln Thr Lys Thr Ala Lys Ile Glu
1       5       10      15
Ile Lys Ala Ser Leu
20

SEQ ID NO 349
LENGTH: 45
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE: OTHER INFORMATION: Dermatophagoides farinae Mite group 2 allergen
Der f 2 precursor epitope

SEQUENCE: 349

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

SEQ ID NO 350
LENGTH: 19
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE: OTHER INFORMATION: Dermatophagoides farinae Mite group 2 allergen
Der f 2 precursor epitope

SEQUENCE: 350

Thr Lys Thr Ala Lys Ile Glu Lys Ala Ser Leu Asp Gly Leu Glu
1       5       10      15
Ile Asp Val

SEQ ID NO 351
LENGTH: 14
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE: OTHER INFORMATION: Dermatophagoides pteronyssinus Mite group 2 allergen Der p 2 epitope

SEQUENCE: 351

Ala Ser Ile Asp Gly Leu Gly Val Asp Val Pro Gly Ile Asp
1       5       10

SEQ ID NO 352
LENGTH: 15
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE: OTHER INFORMATION: Dermatophagoides pteronyssinus Mite group 2 allergen Der p 2 epitope

SEQUENCE: 352

Phe Glu Ala Val Gln Asn Thr Lys Thr Ala Lys Ile Glu Ile Lys
1       5       10      15

SEQ ID NO 353
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides pteronyssinus Mite group 2 allergen Der p 2 epitope

<400> SEQUENCE: 353

Arg Gly Lys Pro Pro Gln Leu Glu Ala Val Phe Glu Ala Val Gln Asn
1  5  10  15

Thr

<210> SEQ ID NO 354
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides pteronyssinus Mite group 2 allergen Der p 2 precursor epitope

<400> SEQUENCE: 354

Cys His Gly Ser Glu Pro Cys Ile His Arg Gly Lys Pro Phe
1  5  10  15

<210> SEQ ID NO 355
<211> LENGTH: 27
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides pteronyssinus Mite group 2 allergen Der p 2 precursor epitope

<400> SEQUENCE: 355

Cys Pro Leu Val Lys Gly Gln Gln Tyr Asp Ile Lys Tyr Thr Trp Asn
1  5  10  15

Val Pro Lys Ile Ala Pro Lys Ser Glu Asn Val
20  25

<210> SEQ ID NO 356
<211> LENGTH: 26
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides pteronyssinus Mite group 2 allergen Der p 2 precursor epitope

<400> SEQUENCE: 356

Asp Ile Lys Tyr Thr Trp Asn Val Pro Lys Ile Ala Pro Lys Ser Glu
1  5  10  15

Asn Val Val Val Thr Val Lys Val Met Gly
20  25

<210> SEQ ID NO 357
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides pteronyssinus Mite group 2 allergen Der p 2 precursor epitope

<400> SEQUENCE: 357

Asp Gln Val Asp Val Lys Asp Cys Ala Asn His Glu Ile Lys Lys
1  5  10  15
<210> SEQ ID NO 358
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides pteronyssinus Mite group 2 allergen Der p 2 precursor epitope

<400> SEQUENCE: 359

Amp Gln Val Asp Val Lys Asp Cys Ala Asn His Glu Ile Lys Lys Val
1   5  10  15
Leu Val Pro Gly
20

<210> SEQ ID NO 359
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides pteronyssinus Mite group 2 allergen Der p 2 precursor epitope

<400> SEQUENCE: 359

Cys His Gly Ser Glu Pro Cys Ile Ile His Arg Gly Lys Pro Phe
1   5  10  15

<210> SEQ ID NO 360
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Lepidoglyphus destructor Mite group 2 allergen Lep d 2 precursor epitope

<400> SEQUENCE: 360

Amp His Gly Val Met Ala Cys Gly Thr Val His Gly Gln Val Glu
1   5  10  15

<210> SEQ ID NO 361
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Lepidoglyphus destructor Mite group 2 allergen Lep d 2 precursor epitope

<400> SEQUENCE: 361

Gly Cys Lys Phe Ile Lys Cys Pro Val Lys Lys Gly Glu Ala Leu
1   5  10  15

<210> SEQ ID NO 362
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Lepidoglyphus destructor Mite group 2 allergen Lep d 2 precursor epitope

<400> SEQUENCE: 362

Gly Glu Lys Met Thr Leu Glu Ala Lys Phe Ala Ala Asn Gln Asp
1   5  10  15

<210> SEQ ID NO 363
<211> LENGTH: 15
-continued

<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Lepidoglyphus destructor Mite group 2 allergen
  Lep d 2 precursor epitope

<400> SEQUENCE: 363

Gly Glu Val Thr Glu Leu Asp Ile Thr Gly Cys Ser Gly Asp Thr
  1   5   10  15

<210> SEQ ID NO 364
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Lepidoglyphus destructor Mite group 2 allergen
  Lep d 2 precursor epitope

<400> SEQUENCE: 364

Gly Lys Met Thr Phe Lys Asp Cys Gly His Gly Glu Val Thr Glu
  1   5   10  15

<210> SEQ ID NO 365
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Neurofilament heavy polypeptide
  (NP-H) (Neurofilament triplet H protein) (200 kDa neurofilament
  protein) epitope

<400> SEQUENCE: 365

Tyr Gln Glu Ala Ile Gln Gln Leu Asp Ala Glu Leu Arg Asn Thr Lys
  1   5   10  15

<210> SEQ ID NO 366
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Prunus persica Non-specific lipid-transfer
  protein 1 epitope

<400> SEQUENCE: 366

Ala Ala Ala Leu Pro Gly Lys Cys Gly Val
  1   5   10

<210> SEQ ID NO 367
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Prunus persica Non-specific lipid-transfer
  protein 1 epitope

<400> SEQUENCE: 367

Ala Cys Cys Asn Gly Ile Arg Asn Val Asn
  1   5   10

<210> SEQ ID NO 368
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Prunus persica Non-specific lipid-transfer
  protein 1 epitope
<400> SEQUENCE: 368
Ala Pro Cys Ile Pro Tyr Val Arg Gly Gly
1 5 10

<210> SEQ ID NO 369
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Prunus persica Non-specific lipid-transfer protein 1 epitope

<400> SEQUENCE: 369
Ile Arg Asn Val Asn Asn Leu Ala Arg Thr
1 5 10

<210> SEQ ID NO 370
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Prunus persica Non-specific lipid-transfer protein 1 epitope

<400> SEQUENCE: 370
Ile Ser Ala Ser Thr Asn Cys Ala Thr Val Lys
1 5 10

<210> SEQ ID NO 371
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Prunus persica Non-specific lipid-transfer protein 1 epitope

<400> SEQUENCE: 371
Asn Leu Ala Arg Thr Thr Pro Asp Arg Gln
1 5 10

<210> SEQ ID NO 372
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Gallus gallus Ovalbumin epitope

<400> SEQUENCE: 372
Cys Phe Asp Val Phe Lys Glu Leu Lys Val
1 5 10

<210> SEQ ID NO 373
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Gallus gallus Ovalbumin epitope

<400> SEQUENCE: 373
Gly Ser Ile Gly Ala Ala Ser Met Glu Phe
1 5 10

<210> SEQ ID NO 374
Ile Gly Leu Phe Arg Val Ala Ser Met Ala Ser Glu Lys Met Lys Ile
1 5 10 15
Leu Glu

Ile Lys His Ile Ala Thr Asn Ala Val Leu Phe Phe Gly Arg Cys Val
1 5 10 15
Ser Pro

Ile Met Ser Ala Leu Ala Met Val Tyr Leu Gly Ala Lys
1 5 10

Ala Glu Val Asp Cys Ser Arg Phe Pro Asn Ala Thr Asp Lys
1 5 10

Ala Thr Asp Lys Glu Gly Lys Asp Val Leu Val Cys Asn Lys
1 5 10
| Ala Val Val Glu Ser Asn Gly Thr Leu Thr Leu Ser His Phe Gly Lys |
|-----------------|---|---|---|---|
| 1               | 5 | 10| 15|

Cys

<210> SEQ ID NO 380
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Gallus gallus Ovomucoid precursor epitope

<400> SEQUENCE: 380

Cys Leu Leu Cys Ala Tyr Ser Ile Glu Phe Gly Thr Asn Ile Ser Lys

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<210> SEQ ID NO 381
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Gallus gallus Ovomucoid precursor epitope

<400> SEQUENCE: 381

Asp Asn Glu Cys Leu Leu Cys Ala His Lys Val Glu Gln Gly Ala Ser

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Val Asp Lys Arg

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<210> SEQ ID NO 382
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Musa acuminata pectate lyase epitope

<400> SEQUENCE: 382

Gly His Ser Asp Glu Leu Thr Ser Asp Lys Ser Met Gln Val Thr Ile

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<210> SEQ ID NO 383
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Zinnia violacea Pectate lyase precursor epitope

<400> SEQUENCE: 383

Gly His Ser Asp Ser Tyr Thr Gln Asp Lys Asn Met Gln Val Thr Ile

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<210> SEQ ID NO 384
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides farinae Peptidase 1 precursor (Major mite fecal allergen Der f 1) (Allergen Der f 1) epitope

<400> SEQUENCE: 384

Asp Gly Arg Thr Ile Ile Gln His Asp Asn Gly Tyr Gln Pro Asn Tyr

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His Ala Val Asn Ile
<210> SEQ ID NO 385
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides farinae Peptidase 1 precursor (Major mite fecal allergen Der f 1) (Allergen Der f 1) epitope

<400> SEQUENCE: 385

Amp Leu Arg Ser Leu Arg Thr Val Thr Pro Ile Arg Met Gln Gly Gly Cys Gly Ser
1  5  10  15

Ala Tyr Leu

<210> SEQ ID NO 386
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides farinae Peptidase 1 precursor (Major mite fecal allergen Der f 1) (Allergen Der f 1) epitope

<400> SEQUENCE: 386

Gly Cys Gly Ser Cys Trp Ala Phe Ser Gly Val Ala Ala Thr Glu Ser
1  5  10  15

Ala Tyr Leu

<210> SEQ ID NO 387
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides farinae Peptidase 1 precursor (Major mite fecal allergen Der f 1) (Allergen Der f 1) epitope

<400> SEQUENCE: 387

Ile Arg Glu Ala Leu Thr Gln Thr His Thr Ala Ile Ala Val Ile Ile
1  5  10  15

Gly Ile Lys Amp Leu

<210> SEQ ID NO 388
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides farinae Peptidase 1 precursor (Major mite fecal allergen Der f 1) (Allergen Der f 1) epitope

<400> SEQUENCE: 388

Ile Arg Met Gln Gly Gly Cys Gly Ser Cys Trp Ala Phe Ser Gly Val
1  5  10  15

Ala Ala Thr

<210> SEQ ID NO 389
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Euroglyphus maynei Peptidase 1 precursor (Mite group 1 allergen Eur m 1) (Allergen Eur m 1) epitope
Phenylalanine Arg His Tyr Asp Gly Arg Thr Ile Met Gln His Asp Asn Gly Tyr
1      5      10      15

Gln Pro Asn

<210> SEQ ID NO 390
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Euroglyphus maynei Peptidase 1 precursor (Mite group 1 allergen Eur m 1) (Allergen Eur m 1) epitope

<400> SEQUENCE: 390

Gly Arg Thr Ile Met Gln His Asp Asn Gly Tyr Gln Pro Asn Tyr His
1      5      10      15

Ala Val Asn

<210> SEQ ID NO 391
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Euroglyphus maynei Peptidase 1 precursor (Mite group 1 allergen Eur m 1) (Allergen Eur m 1) epitope

<400> SEQUENCE: 391

His Ala Val Asn Ile Val Gly Tyr Gly Asn Thr Gln Gly Val Asp Tyr
1      5      10      15

Trp Ile Val

<210> SEQ ID NO 392
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Euroglyphus maynei Peptidase 1 precursor (Mite group 1 allergen Eur m 1) (Allergen Eur m 1) epitope

<400> SEQUENCE: 392

Asn Tyr Ile Arg Gln Ala Leu Thr Gln Thr His Thr Ala Val Ala Val
1      5      10      15

Ile Ile Gly

<210> SEQ ID NO 393
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Euroglyphus maynei Peptidase 1 precursor (Mite group 1 allergen Eur m 1) (Allergen Eur m 1) epitope

<400> SEQUENCE: 393

Pro Tyr Val Ala Arg Gln Ser Cys His Arg Pro Asn Ala Gln Arg
1      5      10      15

Tyr Gly Leu

<210> SEQ ID NO 394
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
FEATURE:

OTHER INFORMATION: Phleum pratense Phl p 3 allergen epitope

SEQUENCE: 394

 Ala Val Gln Val Thr Phe Thr Val Gln Lys Gly Ser Asp Pro Lys
  1  5  10  15

SEQ ID NO 395
LENGTH: 15
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Phleum pratense Phl p 3 allergen epitope

SEQUENCE: 395

 Glu Glu Trp Glu Pro Leu Thr Lys Gly Asn Val Trp Glu Val
  1  5  10  15

SEQ ID NO 396
LENGTH: 15
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Phleum pratense Phl p 3 allergen epitope

SEQUENCE: 396

 Phe Thr Val Gln Lys Gly Ser Asp Pro Lys Lys Leu Val Leu Asp
  1  5  10  15

SEQ ID NO 397
LENGTH: 15
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Phleum pratense Phl p 3 allergen epitope

SEQUENCE: 397

 Phe Thr Val Gln Lys Gly Ser Asp Pro Lys Lys Leu Val Leu Asn
  1  5  10  15

SEQ ID NO 398
LENGTH: 15
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Phleum pratense Phl p 3 allergen epitope

SEQUENCE: 398

 Gly Ser Asp Pro Lys Lys Leu Val Leu Asp Ile Lys Tyr Thr Arg
  1  5  10  15

SEQ ID NO 399
LENGTH: 15
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Apis mellifera Phospholipase A2 precursor epitope

SEQUENCE: 399

 Cys Asp Cys Asp Asp Lys Phe Tyr Asp Cys Leu Lys Asn Ser Ala
  1  5  10  15

SEQ ID NO 400
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Apis mellifera Phospholipase A2 precursor epitope

<400> SEQUENCE: 400

Cys Leu His Tyr Thr Val Asp Lys Ser Lys Pro Lys
1  5  10

<210> SEQ ID NO 401
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Apis mellifera Phospholipase A2 precursor epitope

<400> SEQUENCE: 401

Cys Arg Thr His Asp Met Cys Pro Asp Val Met Ser Ala Gly Glu
1  5  10  15

<210> SEQ ID NO 402
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Apis mellifera Phospholipase A2 precursor epitope

<400> SEQUENCE: 402

Asp Thr Ile Ser Ser Tyr Phe Val Gly Lys Met Tyr Phe Asn Leu Ile
1  5  10  15

Amp Thr

<210> SEQ ID NO 403
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Apis mellifera Phospholipase A2 precursor epitope

<400> SEQUENCE: 403

Glu Arg Thr Glu Gly Arg Cys Leu His Tyr Thr Val Asp Lys Ser Lys
1  5  10  15

Pro Lys

<210> SEQ ID NO 404
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Spiroplasma citri plectroivirus spv1-r8a2b orf 14 transmembrane protein epitope

<400> SEQUENCE: 404

His Val Ile Glu Val Gln Gln Ile Asn Ser Glu Arg Ser Trp Phe Phe
1  5  10  15

<210> SEQ ID NO 405
<211> LENGTH: 20
<212> TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Lolium perenne pollen allergen epitope

<400> SEQUENCE: 405

Cys Gly Tyr Lys Asp Val Asp Lys Ala Pro Phe Asn Gly Met Thr Gly
1 5 10 15
Cys Gly Asn Thr
20

<210> SEQ ID NO 406
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Lolium perenne pollen allergen epitope

<400> SEQUENCE: 406

Gly Ala Gly Pro Lys Asp Asn Gly Gly Ala Cys Gly Tyr Lys Asp Val
1 5 10 15
Asp Lys Ala Pro
20

<210> SEQ ID NO 407
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Lolium perenne pollen allergen epitope

<400> SEQUENCE: 407

Ser Glu Val Glu Asp Val Ile Pro Glu Gly Trp Lys Ala Asp Thr Ser
1 5 10 15
Tyr Ser Ala Lys
20

<210> SEQ ID NO 408
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Lolium perenne pollen allergen epitope

<400> SEQUENCE: 408

Val Glu Lys Gly Ser Asn Pro Asn Tyr Leu Ala Ile Leu Val Lys Tyr
1 5 10 15
Val Asp Gly Asp
20

<210> SEQ ID NO 409
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Lolium perenne pollen allergen epitope

<400> SEQUENCE: 409

Tyr Pro Asp Asp Thr Lys Pro Thr Phe His Val Glu Lys Gly Ser Asn
1 5 10 15
Pro Asn Tyr Leu
20
<210> SEQ ID NO 410
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Ambrosia artemisiifolia Pollen allergen Amb a 1.1 precursor epitope

<400> SEQUENCE: 410
Gly Ala Gly Asp Glu Asn Ile Glu Asp Arg Gly Met Leu Ala Thr Val
1 5 10 15

<210> SEQ ID NO 411
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Ambrosia artemisiifolia Pollen allergen Amb a 1.1 precursor epitope

<400> SEQUENCE: 411
Gly Ala Gly Asp Glu Asn Ile Glu Asp Arg Gly Met Leu Ala Thr Val
1 5 10 15

<210> SEQ ID NO 412
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Ambrosia artemisiifolia Pollen allergen Amb a 2 precursor epitope

<400> SEQUENCE: 412
Gly Ala Ser Asp Thr His Phe Gin Asp Leu Lys Met His Val Thr Leu
1 5 10 15

<210> SEQ ID NO 413
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Ambrosia artemisiifolia Pollen allergen Amb a 2 precursor epitope

<400> SEQUENCE: 413
Gly Ala Ser Asp Thr His Phe Gin Asp Leu Lys Met His Val Thr Leu
1 5 10 15

<210> SEQ ID NO 414
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Ambrosia artemisiifolia var. elatior Pollen allergen Amb a 3 epitope

<400> SEQUENCE: 414
Glu Glu Ala Tyr His Ala Cys Asp Ile Lys Asp
1 5 10

<210> SEQ ID NO 415
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
OTHER INFORMATION: Ambrosia artemisiifolia var. elatior Pollen allergen Amb a 3 epitope

SEQUENCE: 415

Gly Lys Val Tyr Leu Val Gly Gly Pro Gly Leu Gly Gly Trp Lys
1 5 10 15

SEQ ID NO 416
LENGTH: 15
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Ambrosia artemisiifolia var. elatior Pollen allergen Amb a 3 epitope

SEQUENCE: 416

Leu Gly Gly Trp Lys Leu Gln Ser Asp Pro Arg Ala Tyr Ala Leu
1 5 10 15

SEQ ID NO 417
LENGTH: 15
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Ambrosia artemisiifolia var. elatior Pollen allergen Amb a 3 epitope

SEQUENCE: 417

Pro Gly Gly Pro Asp Arg Phe Thr Leu Leu Thr Pro Gly Ser His
1 5 10 15

SEQ ID NO 418
LENGTH: 15
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Ambrosia artemisiifolia var. elatior Pollen allergen Amb a 5 epitope

SEQUENCE: 418

Ala Tyr Cys Cys Ser Asp Pro Gly Arg Tyr Cys Pro Trp Gln Val
1 5 10 15

SEQ ID NO 419
LENGTH: 20
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Ambrosia artemisiifolia var. elatior Pollen allergen Amb a 5 epitope

SEQUENCE: 419

Cys Gly Glu Lys Arg Ala Tyr Cys Cys Ser Asp Pro Gly Arg Tyr Cys
1 5 10 15

Pro Trp Gln Val
20
Asp Pro Gly Arg Tyr Cys Pro Trp Gln Val Val Cys Tyr Glu Ser Ser
1  5  10  15
Glu

<210> SEQ ID NO 421
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Ambrosia artemisiifolia var. elatior Pollen allergen Amb a 5 epitope

<400> SEQUENCE: 421
Aasp Pro Gly Arg Tyr Cys Pro Trp Gln Val Val Cys Tyr Glu Ser Ser
1  5  10  15
Glu Ile Cys Ser
20

<210> SEQ ID NO 422
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Ambrosia artemisiifolia var. elatior Pollen allergen Amb a 5 epitope

<400> SEQUENCE: 422
Gly Asn Val Cys Gly Glu Lys Arg Ala Tyr Cys Cys Ser Asp Pro
1  5  10  15

<210> SEQ ID NO 423
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Ambrosia artemisiifolia var. elatior Pollen allergen Amb a 5 epitope

<400> SEQUENCE: 423
Leu Val Pro Cys Ala Trp Ala Gly Asn Val Cys Gly Glu Lys Arg
1  5  10  15

<210> SEQ ID NO 424
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Ambrosia artemisiifolia var. elatior Pollen allergen Amb a 5 epitope

<400> SEQUENCE: 424
Leu Val Pro Cys Ala Trp Ala Gly Asn Val Cys Gly Glu Lys Arg Ala
1  5  10  15
Tyr Cys Cys Ser
20

<210> SEQ ID NO 425
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Ambrosia artemisiifolia var. elatior Pollen
allergen Amb a 5 epitope

Val Cys Tyr Glu Ser Ser Glu Ile Cys Ser Lys Lys Cys Gly Lys
1  5  10  15

SEQ ID NO 426
LENGTH: 20
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Ambrosia trifida Pollen allergen Amb a 5 precursor epitope

Cys Gly Lys Val Gly Lys Tyr Cys Ser Pro Ile Gly Lys Tyr Cys
1  5  10  15
Val Cys Tyr Asp
20

SEQ ID NO 427
LENGTH: 20
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Ambrosia trifida Pollen allergen Amb a 5 precursor epitope

Asp Asp Gly Leu Cys Tyr Glu Thr Arg Cys Gly Lys Val Gly Lys
1  5  10  15
Tyr Cys Cys Ser
20

SEQ ID NO 428
LENGTH: 12
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Ambrosia trifida Pollen allergen Amb a 5 precursor epitope

Gly Lys Tyr Cys Val Cys Tyr Asp Ser Lys Ala Ile
1  5  10

SEQ ID NO 429
LENGTH: 14
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Ambrosia trifida Pollen allergen Amb a 5 precursor epitope

Pro Ile Gly Lys Tyr Cys Val Cys Tyr Asp Ser Lys Ala Ile
1  5  10

SEQ ID NO 430
LENGTH: 20
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Ambrosia trifida Pollen allergen Amb a 5
<400> SEQUENCE: 430
Pro Ile Gly Lys Tyr Cys Val Cys Tyr Asp Ser Lys Ala Ile Cys Asn
1  5  10  15
Lys Asn Cys Thr
20

<210> SEQ ID NO 431
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Ambrosia trifida Pollen allergen Amb t 5 precursor epitope

<400> SEQUENCE: 431
Val Cys Tyr Asp Ser Lys Ala Ile Cys Asn Lys Asn Cys Thr
1  5  10

<210> SEQ ID NO 432
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Betula pendula pollen allergen Bet v 1 epitope

<400> SEQUENCE: 432
His Glu Val Lys Ala Glu Gln Val Lys Ala Thr Lys Glu Met Gly
1  5  10  15

<210> SEQ ID NO 433
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Poa pratensis Pollen allergen KBG 60 precursor epitope

<400> SEQUENCE: 433
Ala Ala Asn Lys Tyr Lys Thr Phe Val Ala Thr Phe Gly Ala Ala Ser
1  5  10  15
Asn Lys Ala Phe
20

<210> SEQ ID NO 434
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Poa pratensis Pollen allergen KBG 60 precursor epitope

<400> SEQUENCE: 434
Ala Ala Pro Ala Asp Lys Phe Thr Val Phe Glu Ala Ala Ala Phe
1  5  10  15
Asp Ala Ile Lys
20

<210> SEQ ID NO 435
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Poa pratensis Pollen allergen KBG 60 precursor epitope

SEQUENCE: 435
Ala Ala Val Asp Ser Ser Lys Ala Ala Leu Thr Ser Lys Leu Asp Ala
1 5 10 15
Ala Tyr Lys Leu
20

SEQ ID NO 436
LENGTH: 20
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Poa pratensis Pollen allergen KBG 60 precursor epitope

SEQUENCE: 436
Ala Glu Glu Val Lys Ala Thr Pro Ala Gly Glu Leu Gln Val Ile Asp
1 5 10 15
Lys Val Asp Ala
20

SEQ ID NO 437
LENGTH: 20
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Poa pratensis Pollen allergen KBG 60 precursor epitope

SEQUENCE: 437
Ala Phe Lys Val Ala Ala Thr Ala Ala Asn Ala Ala Pro Ala Asn Asp
1 5 10 15
Lys Phe Thr Val
20

SEQ ID NO 438
LENGTH: 20
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Lolium perenne Pollen allergen Lol p 1 precursor epitope

SEQUENCE: 438
Ala Phe Gly Ser Met Ala Lys Gly Glu Glu Gln Asn Val Arg Ser
1 5 10 15
Ala Gly Glu Leu
20

SEQ ID NO 439
LENGTH: 20
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Lolium perenne Pollen allergen Lol p 1 precursor epitope

SEQUENCE: 439
Ala Gly Glu Leu Glu Leu Gln Phe Arg Arg Val Lys Cys Lys Tyr Pro
1 5 10 15
Amp Asp Thr Lys
20

 Ala Lys Ser Thr Trp Tyr Gly Lys Pro Thr Gly Ala Gly Pro Lys Asp
1    5    10    15
Aan Gly Gly Ala
20

 Ala Pro Tyr His Phe Asp Leu Ser Gly His Ala Phe Gly Ser Met Ala
1    5    10    15
Lys Lys Gly Glu
20

 Ile Ala Pro Tyr His Phe Asp Leu Ser Gly His Ala
1    5    10

 Ala Ala Leu Thr Lys Ala Ile Thr Ala Met Thr Gln Ala Gln Lys Ala
1    5    10    15
Gly Lys Pro Ala
20
precursor epitope

-Ala Ala Asn Ala Ala Pro Thr Asn Asp Lys Phe Thr Val Phe Glu Ser
1 5 10 15

-Ala Phe Asn Lys
20

-Ala Asp Lys Phe Lys Ile Phe Glu Ala Ala Phe Ser Glu Ser Ser Lys
1 5 10 15

-Gly Leu Leu Ala
20

-Ala Phe Ser Glu Ser Ser Lys Gly Leu Leu Ala Thr Ser Ala Ala Lys
1 5 10 15

-Ala Pro Gly Leu
20

-Ala Tyr Ala Ala Thr Val Ala Ala Ala Pro Glu Val Lys Tyr Ala Val
1 5 10 15

-Phe Glu Ala Ala
20

-Ala Cys Ser Gly Glu Pro Val Val Val His Ile Thr
1 5 10

-Ala Cys Ser Gly Glu Pro Val Val Val His Ile Thr
Ala Glu Asp Val Ile Pro Glu Gly Trp Lys Ala Asp
1    5
10

Ala Gly Glu Leu Glu Leu Gln Phe Arg Arg Val Lys
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Asp Lys Trp Ile Glu Leu Lys Glu Ser Trp Gly Ala
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Asp Lys Trp Leu Asp Ala Lys Ser Thr Trp Tyr Gly
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<223> OTHER INFORMATION: Phleum pratense Pollen allergen Phl p 2 epitope

<400> SEQUENCE: 460

Glu His Gly Ser Asp Glu Trp Val Ala Met Thr Lys Gly Gly Gly
1  5  10  15

<210> SEQ ID NO 461
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Pollen allergen Phl p 2 epitope

<400> SEQUENCE: 461

Glu Trp Val Ala Met Thr Lys Gly Gly Gly Val Trp Thr Phe
1  5  10  15

<210> SEQ ID NO 462
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Pollen allergen Phl p 2 epitope

<400> SEQUENCE: 462

Gly Val Trp Thr Phe Asp Ser Glu Glu Pro Leu Gln Gly Pro Phe
1  5  10  15

<210> SEQ ID NO 463
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Pollen allergen Phl p 2 epitope

<400> SEQUENCE: 463

Lys Asn Val Phe Asp Asp Val Val Pro Glu Lys Tyr Ile Gly
1  5  10  15

<210> SEQ ID NO 464
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Pollen allergen Phl p 2 epitope

<400> SEQUENCE: 464

Leu Gln Gly Pro Phe Asn Phe Arg Phe Leu Thr Glu Lys Gly Met
1  5  10  15

<210> SEQ ID NO 465
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Pollen allergen Phl p 4 epitope

<400> SEQUENCE: 465

Phe Lys Pro Phe Ala Glu Tyr Lys Ser Asp Tyr Val Tyr Glu Pro
1  5  10  15

<210> SEQ ID NO 466
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Pollen allergen Phl p 4 epitope

<400> SEQUENCE: 466

Phe Pro Lys Glu Val Trp Glu Gln Ile Phe Ser Thr Trp Leu Leu
1  5  10  15

<211> SEQ ID NO 467
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Pollen allergen Phl p 4 epitope

<400> SEQUENCE: 467

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1  5  10  15

<211> SEQ ID NO 468
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<400> SEQUENCE: 468

Gly Ile Val Val Ala Trp Lys Val Arg Leu Leu Pro Val Pro Pro
1  5  10  15

<211> SEQ ID NO 469
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Pollen allergen Phl p 4 epitope

<400> SEQUENCE: 469

Asn Arg Asn Asn Thr Phe Lys Pro Phe Ala Glu Tyr Lys Ser Asp
1  5  10  15

<211> SEQ ID NO 470
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Pollen allergen Phl p 5a epitope

<400> SEQUENCE: 470

Glu Val Lys Tyr Thr Val Phe Glu Thr Ala Leu Lys
1  5  10

<211> SEQ ID NO 471
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Phleum pratense Pollen allergen Phl p 5a epitope

<400> SEQUENCE: 471

Asn Ala Gly Phe Lys Ala Ala Leu Ala Gly Ala Gly Val Glu Pro Ala
Asp Lys Tyr

 Ala Ala Gly Lys Ala Thr Thr Glu Glu Gin Lys Leu Ile Glu Asp Ile
 1  5    10  15
  Ann Val Gly Phe Lys Ala Ala Val Ala Ala Ala Ala
 20 25

 Ala

 Ala Ala Val Ala Ala Ala Ala Ala Ser Val Pro Ala Ala Asp Lys Phe Lys
 1  5    10  15
 Thr Phe Glu

 Ala Lys Phe Asp Ser Phe Val Ala Ser Leu Thr Glu Ala Leu Arg Val
 1  5    10  15
 Ile Ala Gly Ala Leu Glu Val His Ala Val Lys
 20 25
 Ala Met Ser Glu Val Gin Lys Val Gin Pro Ala Thr Gly Ala Ala
  1   5   10   15

Thr Val Ala

 Ala Arg Trp Lys Asn Ser Lys Ile Trp Leu Gin Phe Ala Gin Leu Thr
  1   5   10   15

Asp Phe Asn Leu
  20

 Ala Val Leu Leu Val Pro Ala Asn Lys Lys Phe Phe Val Asn Asn Leu
  1   5   10   15

Val Phe Arg Gly
  20

 Ala Gly Thr Ile Val Ala Gln Pro Pro Ala Arg Trp Lys Asn Ser
  1   5   10   15

Lys Ile Trp Leu
  20

 Ala Gly Thr Ile Val Ala Gln Pro Pro Ala Arg Trp Lys Asn Ser
  1   5   10   15

Lys Ile Trp Leu
  20

 Ala Gly Thr Ile Val Ala Gln Pro Pro Ala Arg Trp Lys Asn Ser
  1   5   10   15

Lys Ile Trp Leu
  20

 Ala Gly Thr Ile Val Ala Gln Pro Pro Ala Arg Trp Lys Asn Ser
  1   5   10   15

Lys Ile Trp Leu
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 Ala Gly Thr Ile Val Ala Gln Pro Pro Ala Arg Trp Lys Asn Ser
  1   5   10   15

Lys Ile Trp Leu
  20

 Ala Gly Thr Ile Val Ala Gln Pro Pro Ala Arg Trp Lys Asn Ser
  1   5   10   15

Lys Ile Trp Leu
  20

 Ala Gly Thr Ile Val Ala Gln Pro Pro Ala Arg Trp Lys Asn Ser
  1   5   10   15

Lys Ile Trp Leu
  20

 Ala Gly Thr Ile Val Ala Gln Pro Pro Ala Arg Trp Lys Asn Ser
  1   5   10   15

Lys Ile Trp Leu
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<210> SEQ ID NO 481
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Chamaecyparis obtusa Polygalacturonase epitope

<400> SEQUENCE: 481
Phe Gly Glu Cys Glu Gly Val Lys Ile Gin Gly Leu Lys Ile Lys Ala
1  5     10  15
Pro Arg Asp Ser
20

<210> SEQ ID NO 482
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cryptomeria japonica Polygalacturonase precursor epitope

<400> SEQUENCE: 482
Ala Ala Tyr Gin Asn Ala Ser Trp Lys Asn Asn Arg Ile Trp
1  5  10  15

<210> SEQ ID NO 483
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cryptomeria japonica Polygalacturonase precursor epitope

<400> SEQUENCE: 483
Ala Cys Lys Lys Pro Ser Ala Met Leu Leu Val Pro Gin Asn Lys
1  5  10  15

<210> SEQ ID NO 484
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cryptomeria japonica Polygalacturonase precursor epitope

<400> SEQUENCE: 484
Ala Ile Lys Phe Asp Phe Ser Thr Gly Leu Ile Gin Gly Leu
1  5  10  15

<210> SEQ ID NO 485
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cryptomeria japonica Polygalacturonase precursor epitope

<400> SEQUENCE: 485
Ala Ile Asn Ile Phe Asn Val Glu Lys Tyr Gin Ala Val Gly Asp
1  5  10  15

<210> SEQ ID NO 486
<211> LENGTH: 15
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cryptomeria japonica Polygalacturonase precursor epitope

<400> SEQUENCE: 486

Ala Asn Gly Tyr Phe Ser Gly His Val Ile Pro Ala Cys Lys Asn
1    5
10   15

<210> SEQ ID NO 487
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Arabidopsis thaliana Probable pectate lyase 10 precursor epitope

<400> SEQUENCE: 487

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

<210> SEQ ID NO 488
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Profilin-2/4 epitope

<400> SEQUENCE: 488

Leu Gly His Asp Gly Thr Val Trp Ala Gln Ser Ala Asp Phe Pro
1    5
10   15

<210> SEQ ID NO 489
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Hevea brasiliensis Pro-hevein precursor epitope

<400> SEQUENCE: 489

Asp Glu Tyr Cys Ser Pro Asp His Asn Cys Gln Ser Asn Cys Lys Asp
1    5
10   15

Ser Gly Glu Gly
20

<210> SEQ ID NO 490
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Hevea brasiliensis Pro-hevein precursor epitope

<400> SEQUENCE: 490

Glu Gln Cys Gly Arg Gln Ala Gly Gly Lys Leu Cys Pro Asn Asn Leu
1    5
10   15

Cys Cys Ser Gln
20

<210> SEQ ID NO 491
<211> LENGTH: 43
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
OTHER INFORMATION: Hevea brasiliensis Pro-hevein precursor epitope

SEQUENCE: 491

Glu Glu Cys Gly Arg Gln Ala Gly Gly Lys Leu Cys Pro Asn Asn Leu
1  5  10  15
Cys Cys Ser Gln Trp Gly Trp Cys Gly Ser Thr Asp Glu Tyr Cys Ser
20  25  30
Pro Asp His Asn Cys Gln Ser Asn Cys Lys Asp
35  40

SEQ ID NO 492
LENGTH: 20
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Hevea brasiliensis Pro-hevein precursor epitope

SEQUENCE: 492

Lys Leu Cys Pro Asn Asn Leu Cys Ser Gln Trp Gly Trp Cys Gly
1  5  10  15
Ser Thr Asp Glu
20

SEQ ID NO 493
LENGTH: 20
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Hevea brasiliensis Pro-hevein precursor epitope

SEQUENCE: 493

Asn Gly Gly Leu Asp Leu Asp Val Asn Val Phe Arg Gln Leu Asp Thr
1  5  10  15
Asp Gly Lys Gly
20

SEQ ID NO 494
LENGTH: 10
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Prunus persica pru p 1 epitope

SEQUENCE: 494

Gly Lys Cys Gly Val Ser Ile Pro Tyr Lys
1  5  10

SEQ ID NO 495
LENGTH: 10
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Prunus persica pru p 1 epitope

SEQUENCE: 495

Ile Thr Cys Gly Gln Val Ser Ser Ser Leu
1  5  10

SEQ ID NO 496
LENGTH: 10
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Prunus persica pru p 1 epitope

SEQUENCE: 496
Ser Ile Pro Tyr Lys Ile Ser Ala Ser Thr
1 5 10

SEQ ID NO 497
LENGTH: 15
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Prunus persica pru p 1 epitope

SEQUENCE: 497
Asp Arg Gln Ala Ala Cys Asn Cys Leu Lys Gln Leu Ser Ala Ser
1 5 10 15

SEQ ID NO 498
LENGTH: 15
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Prunus persica pru p 1 epitope

SEQUENCE: 498
Val Asn Pro Asn Ala Ala Ala Leu Pro Gly Cys Gly Val
1 5 10 15

SEQ ID NO 499
LENGTH: 16
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Arabidopsis thaliana Putative pectate lyase 17 precursor epitope

SEQUENCE: 499
Gly His Asn Asp Asp Phe Val Lys Asp Val Lys Met Lys Val Thr Val
1 5 10 15

SEQ ID NO 500
LENGTH: 16
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Homo sapiens RAD51-like 1 isoform 1 epitope

SEQUENCE: 500
Thr Arg Leu Ile Leu Gln Tyr Leu Asp Ser Glu Arg Arg Gln Ile Leu
1 5 10 15

SEQ ID NO 501
LENGTH: 16
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Aspergillus fumigatus Ribonuclease mitogillin precursor epitope

SEQUENCE: 501
Asp Pro Gly Pro Ala Arg Val Ile Tyr Thr Tyr Pro Asn Lys Val Phe
1 5 10 15
 Ala Thr Trp Thr Cys Ile Asn Gln Gln Leu Asn Pro Lys Thr Asn Lys
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  Trp Glu Asp Lys
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 His Tyr Leu Leu Glu Phe Pro Thr Phe Pro Asp Gly His Asp Tyr Lys
 1  5    10    15
  Phe Asp Ser Lys
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 Lys Phe Asp Ser Lys Lys Pro Lys Glu Asp Pro Gly Pro Ala Arg Val
 1  5    10    15
  Ile Tyr Thr Tyr
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Ser Tyr Pro His Trp Phe Thr Asn Gly Tyr Asp Gly Asn Gly Lys Leu
1 5 10 15
Ile Lys Gly Arg
20

<210> SEQ ID NO 507
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Hevea brasiliensis Rubber elongation factor protein epitope

<400> SEQUENCE: 507
Ala Glu Asp Glu Asp Asn Gln Gln Gly Gln Gly Glu Gly Leu Lys Tyr
1 5 10 15
Leu Gly Phe

<210> SEQ ID NO 508
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Hevea brasiliensis Rubber elongation factor protein epitope

<400> SEQUENCE: 508
Phe Ser Asn Val Tyr Leu Phe Ala Lys Asp Lys Ser Gly Pro Leu Gln
1 5 10 15
Pro Gly Val

<210> SEQ ID NO 509
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Hevea brasiliensis Rubber elongation factor protein epitope

<400> SEQUENCE: 509
Lys Phe Val Asp Ser Thr Val Val Ala Ser Val Thr Ile Ile Asp Arg
1 5 10 15
Ser Leu Pro

<210> SEQ ID NO 510
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Hevea brasiliensis Rubber elongation factor protein epitope

<400> SEQUENCE: 510
Gln Pro Gly Val Asp Ile Ile Glu Gly Pro Val Lys Asn Val Ala Val
1 5 10 15
Pro Leu Tyr

<210> SEQ ID NO 511
<211> LENGTH: 19
<212> TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Hevea brasiliensis Rubber elongation factor protein epitope

SEQUENCE: 511
Arg Ser Leu Pro Pro Ile Val Lys Asp Ala Ser Ile Glu Val Val Ser
1  5  10  15
Ala Ile Arg

SEQ ID NO 512
LENGTH: 17
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Bos taurus Serum albumin precursor epitope

SEQUENCE: 512
Asp Asp Ser Pro Asp Leu Pro Lys Leu Lys Pro Asp Pro Asn Thr Leu
1  5  10  15
Cys

SEQ ID NO 513
LENGTH: 20
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Bos taurus Serum albumin precursor epitope

SEQUENCE: 513
Glu Lys Asp Ala Ile Pro Glu Asn Leu Pro Pro Leu Thr Ala Asp Phe
1  5  10  15
Ala Glu Asp Lys

SEQ ID NO 514
LENGTH: 9
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Bos taurus Serum albumin precursor epitope

SEQUENCE: 514
Glu Ser His Ala Gly Cys Glu Lys Ser
1  5

SEQ ID NO 515
LENGTH: 10
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Bos taurus Serum albumin precursor epitope

SEQUENCE: 515
His Pro Glu Tyr Ala Val Ser Val Leu Leu
1  5  10
Leu Ser Leu Ile Leu Asn Arg Leu Cys
1 5

Amp Phe Val Arg Ala Ala Gly Val Tyr Ala Val Asp
1 5 10

Lys Tyr Leu Amp Phe Val Arg Ala Ala Gly Val Tyr
1 5 10

Asn Val Val Lys Thr Val Val Thr Pro Val Tyr Tyr
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Ala Val Ala Ala
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1  5  10

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1  5  10

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<223> OTHER INFORMATION: Carya illinoinsensis 11S legumin protein epitope

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Leu Pro

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1  5
   10

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<212> TYPE: PRT
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<223> OTHER INFORMATION: Sesamum indicum 2S seed storage protein 1 epitope

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1  5
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<223> OTHER INFORMATION: Bertholletia excelsa 2S sulfur-rich seed storage protein precursor (Allergen Ber e 1) epitope

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1  5
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1  5
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   15
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20  25
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Leu Asp Arg Arg Cys His Ser Ser
35  40
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<211> LENGTH: 10
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<400> SEQUENCE: 548

Gln Glu Lys Leu Gln Val Ala Leu Gly Glu
1  5  10

<210> SEQ ID NO 549
<211> LENGTH: 21
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<223> OTHER INFORMATION: Homo sapiens 5-hydroxytryptamine (serotonin) receptor 4 epitope

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Ser Thr Tyr Cys Val
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<210> SEQ ID NO 550
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Lys Lys Glu Arg Asp Glu Lys Val Lys Gly Glu Arg Arg Asn Thr Asp
35 40      46

Thr Arg
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Glu Asp Cys

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<400> SEQUENCE: 556

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<210> SEQ ID NO 557
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<223> OTHER INFORMATION: Ceratophyllum demersum acidic Cym d 1 isoallergen isoform 1 precursor epitope

<400> SEQUENCE: 557

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Arg Cys Ile Pro Leu Asp Ser Leu Thr Pro Ala Asn
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<400> SEQUENCE: 558

Glu Glu Ala Phe Leu Ser Ser Asp Glu Ser Glu Ser Asp Ser Phe
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Leu Leu Asp Asn Leu Asp Leu Thr Leu Asp
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Arg Cys Ile Pro Leu Asp Ser Leu Thr Pro Ala Asn
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Thr Arg
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Leu Leu Asp Asn Leu Asp Leu Thr Leu Asp
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Thr Arg
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Leu Leu Asp Asn Leu Asp Leu Thr Leu Asp
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Arg Cys Ile Pro Leu Asp Ser Leu Thr Pro Ala Asn
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Thr Arg
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Glu Asp Cys
Gln Asp Asp Val Ile Pro Glu Asp Trp Lys Pro Asp Thr Val Tyr Lys
1 5 10 15
Ser Lys Ile Glu Gly Phe
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<210> SEQ ID NO 558
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<223> OTHER INFORMATION: Cynodon dactylon acidic Cyn d 1 isocallergen isoform 3 precursor epitope

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Arg Val Lys Cys Glu Tyr Pro Ser Asp Thr Lys Ile Thr Phe His Val
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35 40 45
 Ala Gly
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Ala Ala Ala Ala Ala Ala Lys
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<210> SEQ ID NO 560
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Glu Ser Glu Glu Ser Asp Asp Asp Met Gly Phe Gly Leu Phe Asp
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<210> SEQ ID NO 561
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<223> OTHER INFORMATION: Homo sapiens acidic ribosomal phosphoprotein (P2) epitope

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Ala Pro Ala Ala Gly Ser Ala Pro Ala Ala Ala Glu Glu Lys Lys
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  35

Asp Asp Gln Cys Gln Arg Gln Leu Gln Arg
  1   5  10

Glu Glu Ser Glu Asp Glu Lys Arg Arg Trp Gly Gln Arg Asp Asn
  1   5  10  15

Ala Lys Ser Ser Pro Tyr Gln Lys Lys Thr
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<210> SEQ ID NO 574
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<220> FEATURE:
<223> OTHER INFORMATION: Aspergillus fumigatus allergen I/a; Asp f I/a epitope

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<223> OTHER INFORMATION: Dermatophagoides farinae Allergen Mag epitope

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1 5 10

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Gln Gly Pro His Val Ile Ser Arg Ile Tyr Gln Thr Ala Thr 400 5 10

Lys Thr Asn Tyr Ser Ser Ser Ile Ile Leu Glu Tyr 680 1 5 10

Asp Ile Ser Thr Glu Glu Ala Tyr Lys Leu Lys Asn Gly Arg Gln Glu 860 1 5 10 15
Val Glu Val Phe Arg Pro Phe Gin Ser Arg Tyr Glu Lys Glu Glu Glu 1040 20 25 30

Glu Glu Arg Glu Arg 1220

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1  5  10  15
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20 25 30

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<223> OTHER INFORMATION: Triticum aestivum Alpha/beta-gliadin A-II precursor epitope

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1  5  10

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1  5  10

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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens alpha1A-voltage-dependent calcium channel epitope

<400> SEQUENCE: 587
Glu Asp Ser Asp Glu Asp Glu Phe Gln Ile Thr Glu
1  5  10

<210> SEQ ID NO 588
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens alpha-2 type XI collagen epitope

<400> SEQUENCE: 588
Gly Ser Leu Asp Ser Leu Arg Arg Glu Ile Glu Gln Met Arg Arg
1  5  10  15

<210> SEQ ID NO 589
<211> LENGTH: 20
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus alpha2(I) collagen epitope
<400>_SEQUENCE: 589

Leu Pro Gly Leu Lys Gly His Asn Gly Leu Gln Gly Leu Pro Gly Leu
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Ala Gly His His
20

<210> SEQ ID NO 590
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<223> OTHER INFORMATION: Triticum aestivum Alpha-amylase inhibitor 0.28
 precursor (CIII) (GMAL-1) epitope
<400>_SEQUENCE: 590

Ala Tyr Pro Amp Val
1    5

<210> SEQ ID NO 591
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Alpha-enolase epitope
<400>_SEQUENCE: 591

Lys Ile His Ala Arg Glu Ile Phe Asp Ser Arg Gly Asn Pro Thr Val
1    5    10    15

Glu

<210> SEQ ID NO 592
<211> LENGTH: 15
<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens alpha-fibrinogen precursor epitope
<400>_SEQUENCE: 592

Gly Pro Arg Val Val Glu Arg His Gln Ser Ala Cys Lys Asp Ser
1    5    10    15

<210> SEQ ID NO 593
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Triticum aestivum Alpha-gliadin epitope
<400>_SEQUENCE: 593

Leu Gly Gln Gly Ser Phe Arg Pro Ser Gln Gln Asn
1    5    10

<210> SEQ ID NO 594
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Alpha-lactalbumin epitope
<400> SEQUENCE: 594
Lys Asp Leu Lys Gy Gly Gly Val Ser
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<210> SEQ ID NO 595
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Alpha-lactalbumin precursor epitope

<400> SEQUENCE: 595
Lys Cys Glu Val Phe Arg Glu Leu Asp Leu Lys Gly Tyr
  1   5       10

<210> SEQ ID NO 596
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus alpha-S1-casein epitope

<400> SEQUENCE: 596
Leu Asn Glu Asn Leu Leu Arg Phe Phe Val Ala Pro Phe Pro Gln Val
  1   5      10   15
Phe Gly Lys Glu
      20

<210> SEQ ID NO 597
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Alpha-S1-casein precursor epitope

<400> SEQUENCE: 597
Ala Met Glu Asp Ile Lys Gln Met Glu Ala
  1   5       10

<210> SEQ ID NO 598
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus Alpha-S2-casein precursor epitope

<400> SEQUENCE: 598
Glu Asn Leu Cys Ser Thr Phe Cys Lys Glu
  1   5       10

<210> SEQ ID NO 599
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens anti-beta-amyloid peptide immunoglobulin heavy chain variable region epitope

<400> SEQUENCE: 599
Ala His Ile Trp Trp Asn Asp
  1   5
-continued

<210> SEQ ID NO 600
<211> LENGTH: 24
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Aquaporin-4 epitope

<400> SEQUENCE: 600

Phe Cys Pro Asp Val Glu Phe Lys Arg Arg Phe Lys Ala Phe Ser
1   5   10  15
Lys Ala Ala Gln Gln Thr Lys Gly
20

<210> SEQ ID NO 601
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Araeis hypogaeas Ara h 2.01 allergen epitope

<400> SEQUENCE: 601

Cys Cys Asn Glu Leu Asn Glu Phe Glu Asn Asn Gln Arg Cys Met
1   5   10  15

<210> SEQ ID NO 602
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens ATP-dependent DNA helicase 2 subunit 2 epitope

<400> SEQUENCE: 602

Glu Glu Ala Ser Gly Ser Ser Val Thr Ala Glu Glu Ala Lys Lys Phe
1   5   10  15
Leu Ala Pro Lys
20

<210> SEQ ID NO 603
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens autoantigen epitope

<400> SEQUENCE: 603

Glu Ile Arg Val Arg Leu Gln Ser Ala Ser Pro Ser Thr Arg Trp Thr
1   5   10
Glu Leu Asp Asp Val Lys Arg Leu Leu Lys Gly Ser
20  25

<210> SEQ ID NO 604
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Band 3 anion transport protein epitope

<400> SEQUENCE: 604

Leu Phe Lys Pro Pro Lys Tyr His Pro Asp Val Pro Tyr Val Lys Arg
1   5   10  15
<210> SEQ ID NO 605
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Glycine max Bd 36K (34 kDa maturing seed protein) epitope

<400> SEQUENCE: 605

Glu Asp Trp Gly Glu Asp Gly Tyr Ile Trp Ile Gln Arg Asn Thr
1  5  10  15

<210> SEQ ID NO 606
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Bence Jones protein HAG epitope

<400> SEQUENCE: 606

Ala Trp His Gln Gln Gln Pro
1  5

<210> SEQ ID NO 607
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Betula pendula Bet v 4 epitope

<400> SEQUENCE: 607

Phe Ala Arg Ala Asn Arg Gly Leu
1  5

<210> SEQ ID NO 608
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Musa acuminata beta-1, 3-glucanase epitope

<400> SEQUENCE: 608

Gly Leu Phe Tyr Pro Asn Lys Gln Pro
1  5

<210> SEQ ID NO 609
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Hevea brasiliensis beta-1,3-glucanase epitope

<400> SEQUENCE: 609

Gly Leu Phe Phe Pro Asp Lys Pro Lys Tyr Asn Leu Asn Phe
1  5  10  15

<210> SEQ ID NO 610
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Olea europaea beta-1,3-glucanase-like protein epitope

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Ala Ala Ser Asp Ile Ser Leu Leu Asp Ala Gin Ser Ala Pro Leu Arg
1  5  10  15

<210> SEQ ID NO 617
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<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Botulinum neurotoxin type B epitope

<400> SEQUENCE: 617

Trp Lys Ala Pro Ser Ser Pro
1  5

<210> SEQ ID NO 618
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens bullous pemphigoid antigen epitope

<400> SEQUENCE: 618

Lys Ser Thr Ala Lys Asp Cys Thr Phe Lys Pro Asp Phe Glu Met Thr
1  5  10  15

Val Lys Glu

<210> SEQ ID NO 619
<211> LENGTH: 20
<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Bullous pemphigoid antigen 1, isoforms 1/2/3/4/5/6 epitope

<400> SEQUENCE: 619

Leu Thr Asp Thr Lys Thr Gly Leu His Phe Asn Ile Asn Glu Ala Ile
1  5  10  15

Glu Gin Gly Thr
20

<210> SEQ ID NO 620
<211> LENGTH: 8
<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Paspopyrum esculentum BW 16kDa allergen epitope

<400> SEQUENCE: 620

Glu Gly Val Arg Asp Leu Lys Glu
1  5

<210> SEQ ID NO 621
<211> LENGTH: 17
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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens calcium channel, alpha 1A subunit isoform 3 epitope

<400> SEQUENCE: 621
Gly Asn Ile Gly Ile Asp Val Glu Asp Glu Asp Ser Asp Glu Asp Glu
1 5 10 15

Phe

 Ala Val Cys Arg Thr Ser Met Cys Ser Ile Gln Ser Ala Pro Pro
1 5 10 15

Lys Glu Gln Phe Leu Asp Gly Asp Gly Trp Thr Ser Arg Trp Ile Glu
1 5 10 15

Ser Lys

Phe Val Ala Gln Asn Ile Asp Ser Leu Asn Leu Asp
1 5 10

Asp Arg Asn Gly Thr His Leu Asp Ala
1 5

Gly Pro Ser Arg Arg Gly Pro Ser Leu Gly Ala Ser Ser His
1 5 10

Gly Pro Ser Arg Arg Gly Pro Ser Leu Gly Ala Ser Ser His
1 5 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens centromere protein B, 80kDa epitope

<400> SEQUENCE: 627

Met Glu Pro Lys Arg Arg Gin Leu Thr Phe
1   5   10

<210> SEQ ID NO 629
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens centromere protein-A epitope

<400> SEQUENCE: 628

Glu Ala Pro Arg Arg Ser Pro Ser Pro
1   5   10

<210> SEQ ID NO 629
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Betula pendula Chain A, Birch Pollen Profilin epitope

<400> SEQUENCE: 629

Ala Gin Ser Ser Ser Phe Pro Gin Phe Lys Pro Gin Glu Ile Thr Gly
1   5   10   15

Ile

<210> SEQ ID NO 630
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Chain A, Crystal Structure Of The Glycosylated Five-Domain Human Beta2-Glycoprotein I Purified From Blood Plasma epitope

<400> SEQUENCE: 630

Arg Gly Gly Met Arg
1   5

<210> SEQ ID NO 631
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Chain H, Three-Dimensional Structure Of A Human Immunoglobulin With A Hinge Deletion epitope

<400> SEQUENCE: 631

Ala Leu Pro Ala Pro Ile Glu
1   5

<210> SEQ ID NO 632
<211> LENGTH: 27
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens cholesterol side-chain cleavage
enzyme P450scc (EC 1.14.15.67) epitope

<400> SEQUENCE: 632

Phe Asp Pro Glu Arg Phe Asp Pro Thr Arg Trp Leu Ser Lys Asp Lys
1   5   10   15
Ann Ile Thr Tyr Phe Arg Ann Leu Gly Phe Gly
20  25

<210> SEQ ID NO 633
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens citrate synthase epitope

<400> SEQUENCE: 633

Ala Leu Lys His Leu Pro Ann Asp Pro Met
1   5   10

<210> SEQ ID NO 634
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens claudin 11 epitope

<400> SEQUENCE: 634

Ala His Arg Glu Thr
1   5

<210> SEQ ID NO 635
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Coagulation factor VIII precursor epitope

<400> SEQUENCE: 635

Ala Pro Asp Arg Ser Tyr Lys Ser Gln Tyr
1   5   10

<210> SEQ ID NO 636
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Oncorhynchus mykiss collagen a2(I) epitope

<400> SEQUENCE: 636

Met Lys Gly Leu Arg Gly His Gly Gly Leu Gln Gly Met Pro Gly Pro
1   5   10   15
Ann Gly Pro Ser
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<210> SEQ ID NO 637
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Collagen alpha-1(II) chain epitope

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**TYPE:** PRT  
**ORGANISM:** Artificial Sequence  
**FEATURE:**  
**OTHER INFORMATION:** Homo sapiens collagen alpha-1(VII) chain precursor epitope

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**ORGANISM:** Artificial Sequence  
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**OTHER INFORMATION:** Homo sapiens Collagen alpha-1(VII) chain epitope

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**FEATURE:**  
**OTHER INFORMATION:** Homo sapiens Collagen alpha-3(IV) chain epitope

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**OTHER INFORMATION:** Homo sapiens collagen VII epitope

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**ORGANISM:** Artificial Sequence  
**FEATURE:**  
**OTHER INFORMATION:** Bos taurus collagen, type I, alpha 2 epitope

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  36  40  45

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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens collagen, type II, alpha 1 epitope

<400> SEQUENCE: 643
Pro Pro Gly Pro Thr Gly Ala Ser Gly
  1   5

<210> SEQ ID NO 644
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens collagen, type II, alpha 1 isoform
  1 precursor epitope

<400> SEQUENCE: 644
Ala Arg Gly Leu Thr Gly Arg Pro Gly Asp Ala
  1   6   10

<210> SEQ ID NO 645
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens collagen, type II, alpha 1 isoform
  2 precursor epitope

<400> SEQUENCE: 645
Leu Val Gly Pro Arg Gly Glu Arg Gly Phe Pro
  1   5   10

<210> SEQ ID NO 646
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Complement C1q subcomponent
  subunit A epitope

<400> SEQUENCE: 646
Lys Gly Glu Gln Gly Gly Pro Gly Ala
  1   5

<210> SEQ ID NO 647
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Condensin-2 complex subunit D3
  epitope

<400> SEQUENCE: 647
Pro Thr Pro Glu Thr Gly Pro Leu Gln Arg
  1   5   10

<210> SEQ ID NO 648
<211> LENGTH: 15
<212> TYPE: PRT
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<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Arachis hypogaea Conglutin-7 precursor epitope

<400> SEQUENCE: 648

Ala Ala His Ala Ser Ala Arg Gln Gln Trp Glu Leu Gln Gly Aep
1  5  10  15

<210> SEQ ID NO 649  
<211> LENGTH: 8  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Periplaneta americana Cr-PII allergen epitope

<400> SEQUENCE: 649

Ile Arg Ser Trp Phe Gly Leu Pro
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<210> SEQ ID NO 650  
<211> LENGTH: 11  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Cochliobolus lunatus Cytochrome c epitope

<400> SEQUENCE: 650

Glu Asn Pro Lys Lys Tyr Ile Pro Gly Thr Lys
1  5  10

<210> SEQ ID NO 651  
<211> LENGTH: 10  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Rattus norvegicus Cytochrome P450 3A1 epitope

<400> SEQUENCE: 651

Asp Met Val Leu Asn Glu Thr Leu Arg Leu
1  5  10

<210> SEQ ID NO 652  
<211> LENGTH: 15  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Homo sapiens cytoskeleton-associated protein 5 isoform b epitope

<400> SEQUENCE: 652

Cys Gln Ala Leu Val Arg Met Leu Ala Lys Lys Pro Gly Trp Lys
1  5  10  15

<210> SEQ ID NO 653  
<211> LENGTH: 9  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Dermatophagoides farinae Der f 2 epitope

<400> SEQUENCE: 653

Ile Ala Thr His Ala Lys Ile Arg Aep
1  5
His Ile Gly Gly Leu Ser Ile Leu Asp Pro Ile Phe Gly Val Leu
1  5  10  15

<210> SEQ ID NO 655
<211> LENGTH: 43
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides pteronyssinus Der p 1 allergen epitope

<400> SEQUENCE: 655

Ala Arg Glu Gln Ser Cys Arg Arg Pro Asn Ala Gln Arg Phe Gly Ile
1  5 10  15
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Ala Leu Ala Gln Thr His Ser Ala Ile Ala Val
35 40

<210> SEQ ID NO 656
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides pteronyssinus Der p 7 allergen polypeptide epitope

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1  5 10  15

<210> SEQ ID NO 657
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Desmoglein-1 epitope

<400> SEQUENCE: 657

Arg Glu Trp Ile Lys Phe Ala Ala Ala Cys Arg Glu
1  5 10

<210> SEQ ID NO 658
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Desmoglein-3 precursor epitope

<400> SEQUENCE: 658

Arg Glu Trp Val Lys Phe Ala Lys Pro Cys Arg Glu
1  5 10

<210> SEQ ID NO 659
<211> LENGTH: 30
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens desmoglein-3 preproprotein epitope

<400> SEQUENCE: 659

Ser Gln Glu Pro Ala Gly Thr Pro Met Phe Leu Leu Ser Arg Asn Thr
1  5  10  15
Gly Glu Val Arg Thr Leu Thr Asn Ser Leu Asp Arg Glu Gln
20  25  30

<210> SEQ ID NO 660
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens desmoplakin epitope

<400> SEQUENCE: 660

Gly Asn Ser Ser Tyr Ser Tyr Ser Tyr Ser Phe Ser
1  5  10

<210> SEQ ID NO 661
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens desmoplakin isoform II epitope

<400> SEQUENCE: 661

Leu Val Asp Arg Lys Thr Gly Ser Glu Tyr Asp Ile Gln Asp Ala Ile
1  5  10  15
Asp Lys Gly Leu
20

<210> SEQ ID NO 662
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens dihydrolipoamide S-acetyltransferase (E2 component of pyruvate dehydrogenase complex), isoform CRA.a epitope

<400> SEQUENCE: 662

Ala Glu Ile Glu Thr Asp Lys Ala Thr Ile Gly Phe Glu Val Gln Glu
1  5  10  15
Glu Gly

<210> SEQ ID NO 663
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens DNA topoisomerase 1 epitope

<400> SEQUENCE: 663

Gly Val Pro Ile Glu Lys Ile Tyr Asn Lys Thr Gln Arg Glu Lys Phe
1  5  10  15
Ala

<210> SEQ ID NO 664
His Arg Ser Gly Glu Thr Glu Asp Thr Phe Ile Ala Asp Leu Ser Val
Gly Leu Arg Ser Gly Gln Ile

<210> SEQ ID NO 669
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens enolase 1 variant epitope

<400> SEQUENCE: 669

Lys Ile His Ala Arg Glu Ile Phe Asp Ser Arg Gly Aen Pro Thr Val

<210> SEQ ID NO 670
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Hevea brasiliensis ENSP-like protein epitope

<400> SEQUENCE: 670

Phe Pro Leu Ile Thr Cys Cys Gly Tyr Gly Gly Lys Tyr Asn Phe Ser Val Thr Ala Pro Cys

<210> SEQ ID NO 671
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens envoplakin epitope

<400> SEQUENCE: 671

Ala Gly Glu Thr Lys Pro Ser Ser Ser Leu Ser Ser Ile Gly Ser Ile Ile Ser Lys Ser Pro

<210> SEQ ID NO 672
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Fagopyrum esculentum Pag e 1 epitope

<400> SEQUENCE: 672

 Ala Val Val Leu Lys Ala Gly Aen Glu Gly Leu Glu

<210> SEQ ID NO 673
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Pas AMA epitope

<400> SEQUENCE: 673
Cys Val Pro

1

<210> SEQ ID NO 674
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<222> OTHER INFORMATION: Homo sapiens PGA protein epitope

<400> SEQUENCE: 674

Ser Arg Ala Leu Ala Arg Glu Val Asp Leu Lys Asp Tyr Glu Asp Gln
1  5 10   15
Gln Lys

<210> SEQ ID NO 675
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<222> OTHER INFORMATION: Homo sapiens PGB protein epitope

<400> SEQUENCE: 675

Ala Arg Gly His Arg Pro Leu Asp Lys Arg Glu Glu Ala Pro Ser
1  5 10   15
Leu Arg Pro Ala
20

<210> SEQ ID NO 676
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<222> OTHER INFORMATION: Homo sapiens fibrin beta epitope

<400> SEQUENCE: 676

Ala Asn Lys Tyr Gln Ile Ser Val Asn Lys Tyr Arg Gly Thr Ala Gly
1  5 10   15
Asn Ala Leu

<210> SEQ ID NO 677
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<222> OTHER INFORMATION: Homo sapiens fibrinogen alpha chain isoform
alpha preproprotein epitope

<400> SEQUENCE: 677

Asp Ser Pro Gly Ser Gly Asn Ala Arg Pro Asn Asn Pro Asp Trp
1  5 10   15

<210> SEQ ID NO 678
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<222> OTHER INFORMATION: Homo sapiens Fibrinogen alpha chain precursor
epitope

<400> SEQUENCE: 678

Phe Leu Ala Glu Gly Gly Val Arg Gly Pro Arg Val Val Glu Arg
1  5 10   15
His

<210> SEQ ID NO 679
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens fibrinogen alpha chain preproprotein, isoform alpha epitope

<400> SEQUENCE: 679

Asp His Glu Gly Thr His Ser Thr Lys Arg Gly His Ala Lys Ser Arg
1      5     10    15
Pro Val Arg Gly
20

<210> SEQ ID NO 680
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens fibrinogen beta chain epitope

<400> SEQUENCE: 680

Pro Arg Lys Gln Cys Ser Lys Glu Asp Gly Gly Gly Trp Trp Tyr
1      5     10    15

<210> SEQ ID NO 681
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens fibrinogen beta chain, isoform CHA_d epitope

<400> SEQUENCE: 681

Asn Glu Glu Gly Phe Phe Ser Ala Arg Gly His Arg Pro Leu Asp Lys
1      5     10    15

Lys

<210> SEQ ID NO 682
<211> LENGTH: 24
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens fibrinogen beta chain, isoform CHA_l epitope

<400> SEQUENCE: 682

Glu Glu Ala Pro Ser Leu Arg Pro Ala Pro Pro Pro Ile Ser Gly Gly
1      5     10    15
Gly Tyr Arg Ala Arg Pro Ala Lys
20

<210> SEQ ID NO 683
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Fibronectin precursor epitope

<400> SEQUENCE: 683
Leu Thr Ser Arg Pro Ala
1  5

<210> SEQ ID NO 684
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens filaggrin epitope

<400> SEQUENCE: 684

Asp Ser Gly His Arg Gly Tyr Ser Gly Ser Gln Ala Ser Asp Asn Glu
1  5  10  15

Gly His

<210> SEQ ID NO 685
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Pollistatin-related protein 1 epitope

<400> SEQUENCE: 685

Leu Lys Phe Val Glu Gln Asn Glu
1  5

<210> SEQ ID NO 686
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Forkhead box protein E3 epitope

<400> SEQUENCE: 686

Pro Thr Pro Ala Pro Gly Pro Gly Arg Arg
1  5  10

<210> SEQ ID NO 687
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens QAD65 autoantigen glutamic acid decarboxylase epitope

<400> SEQUENCE: 687

Ala Pro Ala Met Ile Pro Pro
1  5

<210> SEQ ID NO 688
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Triticum aestivum Gamma-gliadin precursor epitope

<400> SEQUENCE: 688

Leu Gln Pro Gln Gln Pro Phe Pro Gln Gln
1  5  10

<210> SEQ ID NO 689
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Chironomus thummi thummi Globin CTP-III epitope

<400> SEQUENCE: 689

Ala His Thr Asp Phe Ala Gly Ala Glu Ala Ala Trp Gly Ala Thr Leu
1      5      10    15
Asp Thr Phe Phe Gly
20

<210> SEQ ID NO 690
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Chironomus thummi thummi Globin CTP-III precursor epitope

<400> SEQUENCE: 690

Gly Val Thr His Asp Gln Leu Asn Asn Phe Arg
1     5     10

<210> SEQ ID NO 691
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Chironomus thummi thummi Globin CTP-IV precursor epitope

<400> SEQUENCE: 691

Lys Ala His Thr Asp Phe Ala Gly Ala Glu Ala Ala Trp Gly Ala Thr
1     5     10    15
Leu Asp Ala Phe Phe Gly Met
20

<210> SEQ ID NO 692
<211> LENGTH: 36
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Chironomus thummi thummi Globin CTP-VI precursor epitope

<400> SEQUENCE: 692

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

<210> SEQ ID NO 693
<211> LENGTH: 35
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Chironomus thummi thummi Globin CTP-VIII epitope

<400> SEQUENCE: 693

Ile Val Gly Phe Phe Ser Glu Val Ile Gly Leu Ile Gly Asn Pro Glu
-continued

Aaa Arg Pro Ala Leu Lys Thr Leu Ile Asp Gly Leu Ala Ser Ser His  
20 25 30

Lys Ala Arg  
35

<210> SEQ ID NO 694  
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<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Hevea brasiliensis Glucan endo-1,3-beta-glucosidase, basic vacuolar isoform epitope

<400> SEQUENCE: 694

Ala Trp Leu Ala Gln Phe Val Leu Pro  
1  5

<210> SEQ ID NO 695  
<211> LENGTH: 20  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Homo sapiens glutamate decarboxylase epitope

<400> SEQUENCE: 695

Phe Arg Glu Arg Gln Ser Ser Lys Leu Leu Ser Cys Glu Asn Ser  
1  5 10 15

Amp Arg Asp Ala  
20

<210> SEQ ID NO 696  
<211> LENGTH: 20  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Homo sapiens Glutamate decarboxylase 1 epitope

<400> SEQUENCE: 696

Met Ala Ser Ser Thr Pro Ser Ser Ala Thr Ser Asn Ala Gly  
1  5 10 15

Ala Asp Pro Asn  
20

<210> SEQ ID NO 697  
<211> LENGTH: 19  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Homo sapiens Glutamate decarboxylase 2 epitope

<400> SEQUENCE: 697

Pro Gly Ser Gly Phe Trp Ser Phe Gly Ser Glu Asp Gly Ser Gly Asp  
1  5 10 15

Ser Glu Asn

<210> SEQ ID NO 698  
<211> LENGTH: 15  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Homo sapiens glutamate receptor, ionotropic,
-continued

**H-methyl D-aspartate 3A epitope**

<400> **SEQUENCE:** 698

Ser Val Ser Tyr Asp Asp Trp Asp Tyr Ser Leu Glu Ala Arg Val  
1      5      10     15

<210> **SEQ ID NO:** 699  
<211> **LENGTH:** 14  
<212> **TYPE:** PRT  
<213> **ORGANISM:** Artificial Sequence  
<220> **FEATURE:**  
<223> **OTHER INFORMATION:** Homo sapiens glutathione peroxidase-GI epitope

<400> **SEQUENCE:** 699

Asn Glu His Pro Val Phe Ala Tyr Leu Lys Asp Lys Leu Pro  
1      5      10

<210> **SEQ ID NO:** 700  
<211> **LENGTH:** 14  
<212> **TYPE:** PRT  
<213> **ORGANISM:** Artificial Sequence  
<220> **FEATURE:**  
<223> **OTHER INFORMATION:** Triticum aestivum Glutenin, high molecular weight subunit DXS epitope

<400> **SEQUENCE:** 700

Ala Gln Gly Gln Gln Pro Gly Gln Gln Gly Gln Gln Gln Gln  
1      5      10

<210> **SEQ ID NO:** 701  
<211> **LENGTH:** 5  
<212> **TYPE:** PRT  
<213> **ORGANISM:** Artificial Sequence  
<220> **FEATURE:**  
<223> **OTHER INFORMATION:** Triticum aestivum Glutenin, high molecular weight subunit DXS precursor epitope

<400> **SEQUENCE:** 701

Gln Gln Pro Gly Gln  
1      5

<210> **SEQ ID NO:** 702  
<211> **LENGTH:** 5  
<212> **TYPE:** PRT  
<213> **ORGANISM:** Artificial Sequence  
<220> **FEATURE:**  
<223> **OTHER INFORMATION:** Triticum aestivum Glutenin, low molecular weight subunit precursor epitope

<400> **SEQUENCE:** 702

Gln Gln Gln Pro Pro  
1      5

<210> **SEQ ID NO:** 703  
<211> **LENGTH:** 15  
<212> **TYPE:** PRT  
<213> **ORGANISM:** Artificial Sequence  
<220> **FEATURE:**  
<223> **OTHER INFORMATION:** Phaseolus vulgaris Glycin-rich cell wall structural protein 1.0 precursor epitope

<400> **SEQUENCE:** 703

Gly Gly Tyr Gly Asp Gly Gly Ala His Gly Gly Tyr Gly Gly  
1      5      10     15
Ala Leu Ser Arg Leu Val Leu Arg Arg Asn Ala Leu Arg Arg Pro
1 5 10 15

Gly Ala Ile Val Thr Val Lys Gly Leu Ser Val Ile
1 5 10

Ala Leu Ser Arg Cys Thr Leu Asn Arg Asn Ala Leu Arg Arg Pro
1 5 10 15

Ala Asn Val Pro Pro Ala Asp Lys Tyr Lys Thr Phe Glu Ala Ala
1 5 10 15

Ile Asp Ala Pro Lys Pro Lys Lys Met Lys Lys Glu Lys Glu Met Asn
1 5 10 15

Gly Glu Thr Arg Glu Lys Ser Pro Lys Leu Lys Asn Gly Phe Pro His
20 25 30

Pro Glu Pro Asp Cys Asn
35
<220> FEATURES:
<223> OTHER INFORMATION: Homo sapiens H1 histone family, member 0 epitope

<400> SEQUENCE: 709

Lys Glu Ile Lys Lys Val Ala Thr Pro Lys Lys Ala Ser Lys Pro Lys
1   5  10    15

Lys

<210> SEQ ID NO 710
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens heat shock 60kDa protein 1 (chaperonin) epitope

<400> SEQUENCE: 710

Ala Tyr Ala Lys Asp Val Lys Phe Gly Ala Asp Ala
1   5  10

<210> SEQ ID NO 711
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Heat shock protein HSP 90-beta epitope

<400> SEQUENCE: 711

Gly Leu Glu Leu Pro Glu
1   5

<210> SEQ ID NO 712
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens high mobility group protein 17 epitope

<400> SEQUENCE: 712

Lys Lys Ala Pro Ala Lys Lys Gly Lys Val Pro Lys Gly Lys
1   5  10    15

<210> SEQ ID NO 713
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens High mobility group protein B1 epitope

<400> SEQUENCE: 713

Ala Lys Gly Lys Pro Asp Ala Ala Lys Lys Gly Val Val Lys Ala Glu
1   5  10    15

Lys Ser Lys Lys Lys

20

<210> SEQ ID NO 714
<211> LENGTH: 15
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<223> OTHER INFORMATION: Homo sapiens high-mobility group box 2 epitope

<400> SEQUENCE: 714

Phe Glu Asp Met Ala Lys Ser Asp Lys Ala Arg Tyr Asp Arg Glu
1 5 10 15

<210> SEQ ID NO: 715
<211> LENGTH: 43
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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens histidyl-tRNA synthetase, cytoplasmic epitope

<400> SEQUENCE: 715

Ala Glu Arg Ala Ala Leu Glu Leu Val Lys Leu Gln Gly Glu Arg
1 5 10 15

Val Arg Gly Leu Lys Gln Gln Lys Ala Ser Ala Glu Leu Ile Glu Glu
20 25 30

Glu Val Ala Lys Leu Leu Lys Leu Lys Ala Gln
35 40

<210> SEQ ID NO: 716
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Histone H1.4 epitope

<400> SEQUENCE: 716

Ser Glu Thr Ala Pro Ala Ala Pro Ala Ala Pro Ala Glu Lys
1 5 10 15

<210> SEQ ID NO: 717
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens histone H1b epitope

<400> SEQUENCE: 717

Lys Pro Lys Ala Ala Lys Pro Lys Ala Ala Ala Ala Lys Lys Lys
1 5 10 15

<210> SEQ ID NO: 718
<211> LENGTH: 20
<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Histone H2A.Z epitope

<400> SEQUENCE: 718

Gly Lys Ala Lys Thr Lys Ala Val Ser Arg Ser Gln Arg Ala Gly Leu
1 5 10 15

Gln Phe Pro Val
20

<210> SEQ ID NO: 719
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens histone H3 epitope
<400> SEQUENCE: 719

Leu Pro Phe Gln Arg Leu Val Arg Glu Ile Ala Gln Asp Phe Lys
  1  5  10  15

<210> SEQ ID NO 720
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Histone H3-like centromeric protein A epitope

<400> SEQUENCE: 720

Lys Pro Glu Ala Pro Arg Arg Ser Pro
  1  5  10

<210> SEQ ID NO 721
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens HLA class I histocompatibility antigen, B-27 alpha chain precursor epitope

<400> SEQUENCE: 721

Lys Ala Lys Ala Gln Thr Asp Arg
  1  5

<210> SEQ ID NO 722
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens HLA-B27 epitope

<400> SEQUENCE: 722

 Ala Lys Ala Gln Thr Asp Arg Glu Asp Leu Arg Thr Leu Leu Arg Tyr
  1  5  10  15

<210> SEQ ID NO 723
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens HLA-DR3 epitope

<400> SEQUENCE: 723

Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gin Lys Asp Leu Leu Glu Gin
  1  5  10  15

Lys Arg Gly Arg
  20

<210> SEQ ID NO 724
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens HMG-17 epitope

<400> SEQUENCE: 724

Asp Gly Lys Ala Lys Val Lys Gln Arg Gly Arg Ser Ala
  1  5  10  15
SEQ ID NO 725
LENGTH: 13
TYPE: PRT
ORGANISM: Artificial Sequence
OTHER INFORMATION: Homo sapiens HNF4A281 protein epitope

SEQUENCE: 725

Glu Thr Thr Glu Glu Ser Leu Arg Asn Tyr Tyr Glu Gln
1 5 10

SEQ ID NO 726
LENGTH: 35
TYPE: PRT
ORGANISM: Artificial Sequence
OTHER INFORMATION: Homo sapiens hypothetical protein epitope

SEQUENCE: 726

Ala Asn Glu Asp Ala Ala Gln Gly Ile Ala Asn Trp Asp Ala Val Gln
1 5 10 15
Asp Ile Ala Asn Glu Asp Gly Phe His Gly Ile Asp Ile Glu Asp Ala
20 25 30

Ala Gln Gly
35

SEQ ID NO 727
LENGTH: 12
TYPE: PRT
ORGANISM: Artificial Sequence
OTHER INFORMATION: Oryza sativa Japonica Group hypothetical protein epitope

SEQUENCE: 727

Ala Phe Asn His Phe Gly Ile Gln Leu Val Gln Arg
1 5 10

SEQ ID NO 728
LENGTH: 20
TYPE: PRT
ORGANISM: Artificial Sequence
OTHER INFORMATION: Homo sapiens Ig alpha-1 chain C region epitope

SEQUENCE: 729

Pro Val Pro Ser Thr Pro Pro Thr Pro Ser Pro Ser Thr Pro Pro Thr
1 5 10 15

Pro Ser Pro Ser
20

SEQ ID NO 729
LENGTH: 7
TYPE: PRT
ORGANISM: Artificial Sequence
OTHER INFORMATION: Homo sapiens Ig gamma-1 chain C region epitope

SEQUENCE: 729

Lys Phe Asn Trp Tyr Val Asp
1 5
Asp Gly Ser Phe Phe Leu Tyr
1  5

Cys Ser Val Met His Glu Gly
1  5

Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr
1  5  10  15

Ala Pro Ser Val Thr Leu Phe
1  5

Asp Lys Ser Arg Trp Gln Glu
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Asp Gly Ser Phe Phe Leu Tyr
1  5

Cys Ser Val Met His Glu Gly
1  5

Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr
1  5  10  15

Ala Pro Ser Val Thr Leu Phe
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Asp Lys Ser Arg Trp Gln Glu
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Asp Gly Ser Phe Phe Leu Tyr
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Cys Ser Val Met His Glu Gly
1  5

Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr
1  5  10  15

Ala Pro Ser Val Thr Leu Phe
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Asp Lys Ser Arg Trp Gln Glu
1  5

Asp Gly Ser Phe Phe Leu Tyr
1  5

Cys Ser Val Met His Glu Gly
1  5

Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr
1  5  10  15

Ala Pro Ser Val Thr Leu Phe
1  5

Asp Lys Ser Arg Trp Gln Glu
1  5

Asp Gly Ser Phe Phe Leu Tyr
1  5

Cys Ser Val Met His Glu Gly
1  5

Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr
1  5  10  15

Ala Pro Ser Val Thr Leu Phe
1  5

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<223> OTHER INFORMATION: Homo sapiens interferon beta precursor epitope

<400> SEQUENCE: 742

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 1  5  10

<210> SEQ ID NO 743
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<212> TYPE: PRT
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<220> FEATURES:
<223> OTHER INFORMATION: Homo sapiens interferon-alpha 2 epitope

<400> SEQUENCE: 743

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 1  5  10

<210> SEQ ID NO 744
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<212> TYPE: PRT
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<220> FEATURES:
<223> OTHER INFORMATION: Homo sapiens Inlet amyloid polypeptide precursor epitope

<400> SEQUENCE: 744

Met Gly Ile Leu Lys Leu Gln Val Phe Leu Ile Val Leu Ser Val Ala
 1  5  10  15

Leu Asn His Leu Lys Ala Thr Pro Ile Glu Ser His Gln Val Glu Lys
 20  25  30

Arg Lys Cys Asn Thr
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<220> FEATURES:
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<400> SEQUENCE: 745

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<223> OTHER INFORMATION: Homo sapiens m3 muscarinic cholinergic receptor epitope

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Phe Tyr Gly Arg
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<210> SEQ ID NO 753
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<223> OTHER INFORMATION: Anisakis simplex Major allergen Ani s 1 epitope

<400> SEQUENCE: 753

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1     5    10      15

<210> SEQ ID NO 754
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<223> OTHER INFORMATION: Aspergillus fumigatus Major allergen Asp f 1 epitope

<400> SEQUENCE: 754

Leu Asn Pro Lys Thr Asn Lys Trp Glu Asp Lys Arg Tyr
1     5    10

<210> SEQ ID NO 755
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<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Aspergillus fumigatus Major allergen Asp f 2 epitope

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Ala His Ile Leu Arg Trp Gly Asn Glu Ser
1     5    10

<210> SEQ ID NO 756
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<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Bos taurus major allergen beta-lactoglobulin epitope

<400> SEQUENCE: 756

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1     5    10      15

Glu Lys Thr Lys
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<212> TYPE: PRT
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<223> OTHER INFORMATION: Felis catus Major allergen I polypeptide chain 1 precursor epitope

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1   5   10

<210> SEQ ID NO 758
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<223> OTHER INFORMATION: Felis catus Major allergen I polypeptide chain 2 precursor epitope

<400> SEQUENCE: 758

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<210> SEQ ID NO 759
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<212> TYPE: PRT
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<223> OTHER INFORMATION: Felis catus major allergen I, polypeptide chain 1 epitope

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<220> FEATURE:
<223> OTHER INFORMATION: Turbo cornutus major allergen Tur c1 - Turbo cornutus epitope

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Leu Glu Asp Glu Leu Leu Ala Glu Lys Tyr Lys Ala Ile Ser
1  5  10  15

Asp Glu Leu Asp Gln Thr Phe Ala Glu Leu Ala Gly Tyr
20  25

<210> SEQ ID NO 761
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<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides pteronyssinus major house dust allergen epitope

<400> SEQUENCE: 761

Leu Ala His Arg Asn Gln Ser Leu Asp Leu Ala Glu Gln Glu Leu Val
1   5   10  15

Asp Cys Ala Ser Gln His Gly Cys His
20  25
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<223> OTHER INFORMATION: Hevea brasiliensis Major latex allergen Hev b 5 epitope

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1 5

<210> SEQ ID NO 763
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<223> OTHER INFORMATION: Dermatophagoides pteronyssinus Major mite fecal allergen Der p 1 epitope

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Ala Arg Glu Gin Ser Cys Arg Arg Arg Asn Ala Gin Arg Phe Gly Ile
1 5 10 15

Ser Asn Tyr Cys Gin Ile Tyr Pro Pro Asn Ala Asn Lys Ile Arg Glu
20 25 30

Ala Leu Ala Gin Pro Gin Arg Tyr Cys Arg His
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<210> SEQ ID NO 764
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<223> OTHER INFORMATION: Olea europaea Major pollen allergen epitope

<400> SEQUENCE: 764

Phe Thr Glu Val Gly Tyr Thr Arg Ala Glu Gly Leu
1 5 10

<210> SEQ ID NO 765
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<220> FEATURE:
<223> OTHER INFORMATION: Betula pendula Major pollen allergen Bet v 1-A epitope

<400> SEQUENCE: 765

Amp Gly Asp Asn Leu Phe Pro Lys Val Ala
1 5 10

<210> SEQ ID NO 766
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<223> OTHER INFORMATION: Chamaecyparis obtusa Major pollen allergen Cha o 1 precursor epitope

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Trp Arg Ser Thr Gin Asp Ser Phe Asn Asn Gly
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<223> OTHER INFORMATION: Corylus avellana Major pollen allergen Cor a 1 epitope

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Leu

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<220> FEATURE:
<223> OTHER INFORMATION: Holcus lanatus Major pollen allergen Hol l 1 precursor epitope

<400> SEQUENCE: 768

Ala Lys Ser Thr Trp Tyr Gly lys Pro Thr Gly Ala Gly Pro Lys Asp
1    5    10    15

Asn Gly Gly Ala Cys Gly Tyr Lys Asp Val Asp
20    25

<210> SEQ ID NO 769
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<223> OTHER INFORMATION: Juniperus ashei Major pollen allergen Jun a 1 precursor epitope

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1    5    10

<210> SEQ ID NO 770
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<223> OTHER INFORMATION: Olea europaea Major pollen allergen Ole e 1 epitope

<400> SEQUENCE: 770

Ser Gly Arg Lys Asp Cys Asn Glu Ile Pro Thr Glu Gly Trp Val Lys
1    5    10    15

Pro Ser Leu Lys Phe Ile Leu Asn Thr Val Asn Gly Thr Thr Arg Thr
20    25    30

Val Asn

<210> SEQ ID NO 771
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<223> OTHER INFORMATION: Malus x domestica mal d 3 epitope

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<223> OTHER INFORMATION: Homo sapiens MBP protein epitope

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<210> SEQ ID NO 773
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<223> OTHER INFORMATION: Homo sapiens melanin-concentrating hormone receptor 1, isoform CRA_a epitope

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1  5 10  15
Asn Ser Gln Leu Leu Leu Ser Pro Gly Ser Pro Pro
20  25 30

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<223> OTHER INFORMATION: Homo sapiens Melanocyte protein Pmel 17 precursor epitope

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Gln Val Pro Thr Thr Glu Val Val Gly Thr Thr Pro Gly Gln Ala Pro
1  5 10  15

<210> SEQ ID NO 775
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<223> OTHER INFORMATION: Homo sapiens MHC classII HLA-DRB1 epitope

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Glu Gln Arg Arg Ala Ala
1  5

<210> SEQ ID NO 776
<211> LENGTH: 20
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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens MHC HLA-DR1-beta epitope

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Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp Leu Leu Glu Gln
1  5 10  15
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Glu Glu Ala Glu Thr Leu Ser Lys Ile Leu Leu Lys Asp Leu Lys Glu
1 5 10 15

Amp Pro Cys Ile Ile
1 5

Amp Gln Val Amp Val Lys Amp Ala Asn His Glu Ile Lys Lys
1 5 10 15

Ala Ala Asn Glu Asp Thr Ala Lys Val Thr Ile Lys Val Leu Ala Lys
1 5 10 15

Val Ala Gly Thr Thr Ile Glu Val Pro Gly Leu Glu Thr Asp Gly Cys
20 25 30

Lys

Ala Ala Ser Val Pro Glu
1 5

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<223> OTHER INFORMATION: Triticum aestivum monomeric alpha-amylase inhibitor epitope
<400> SEQUENCE: 781

Ala Ala Ser Val Pro Glu
1 5
<210> SEQ ID NO 783
<211> LENGTH: 17
<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Myelin basic protein epitope

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Asp Ser Tyr Thr Leu Thr Glu Leu Ala Tyr Ala Glu Ile Arg Val
1  5  10  15

Lys

<210> SEQ ID NO 784
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<212> TYPE: PRT
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<223> OTHER INFORMATION: Homo sapiens Myelin basic protein epitope

<400> SEQUENCE: 784

Ile Val Thr Pro Arg Thr Pro Pro Ser Gln Gly Lys
1  5  10

<210> SEQ ID NO 785
<211> LENGTH: 26
<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens myelin oligodendrocyte glycoprotein epitope

<400> SEQUENCE: 785

 Ala Leu Val Gly Asp Glu Val Glu Leu Pro Cys Arg Ile Ser Pro Gly
1  5  10  15

Lys Asn Ala Thr Gly Met Glu Leu Gly Trp
20  25

<210> SEQ ID NO 786
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<212> TYPE: PRT
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<223> OTHER INFORMATION: Homo sapiens myelin oligodendrocyte glycoprotein isoform alpha6 precursor epitope

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His Arg Thr Phe Glu
1  5

<210> SEQ ID NO 787
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<212> TYPE: PRT
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<223> OTHER INFORMATION: Homo sapiens myelin proteolipid protein epitope

<400> SEQUENCE: 787

Ala Asp Ala Arg Met
1  5

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<212> TYPE: PRT
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<223> OTHER INFORMATION: Homo sapiens Myelin-associated glycoprotein precursor epitope

<400> SEQUENCE: 788

Gly His Trp Gly Ala Trp Met Pro Ser Ser Ile Ser Ala Phe Glu Gly
1  5  10  15
Thr Cys Val Ser Ile
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<212> TYPE: PRT
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<223> OTHER INFORMATION: Homo sapiens Myelin-oligodendrocyte glycoprotein precursor epitope

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Gly Gln Phe Arg Val Ile Gly Pro Arg His Pro Ile Arg Ala Leu Val
1  5  10  15
Gly Asp Glu Val Glu Leu Pro Cys Arg Ile
20  25

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<223> OTHER INFORMATION: Homo sapiens Myeloblastin precursor epitope

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Ala His Arg Pro Pro Ser Pro Ala
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<210> SEQ ID NO 791
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<223> OTHER INFORMATION: Homo sapiens Myeloperoxidase epitope

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Gly Ser Ala Ser Pro Met Glu Leu Leu Ser
1  5  10

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<220> FEATURES:
<223> OTHER INFORMATION: Homo sapiens Myosin-11 epitope

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1  5     10     15
Gln Glu Leu Arg
20

<210> SEQ ID NO 793
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Homo sapiens Neurofilament heavy polypeptide (NF-H) (Neurofilament triplet H protein) (200 kDa neurofilament protein) epitope

<400> SEQUENCE: 793

Ala Lys Ser Pro Glu Lys Ala Lys
1  5

<210> SEQ ID NO 794
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<223> OTHER INFORMATION: Homo sapiens nicotinic acetylcholine receptor alpha subunit hR alpha subunit epitope

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<210> SEQ ID NO 795
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<223> OTHER INFORMATION: Homo sapiens Non-histone chromosomal protein HMG-17 epitope

<400> SEQUENCE: 795

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1  5     10

<210> SEQ ID NO 796
<211> LENGTH: 9
<212> TYPE: PRT
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<220> FEATURES:
<223> OTHER INFORMATION: Prunus armeniaca Non-specific lipid-transfer protein 1 epitope

<400> SEQUENCE: 796

Val Asn Pro Asn Asn Ala Ala Ala Leu
1  5

<210> SEQ ID NO 797
<211> LENGTH: 15
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<213> ORGANISM: Artificial Sequence
<220> FEATURES:
<223> OTHER INFORMATION: Prunus armeniaca Non-specific lipid-transfer protein 1 (LTP 1) (Major allergen Pru ar 3) epitope
Leu Ala Arg Thr Thr Pro Asp Arg Arg Thr Ala Cys Asn Cys Leu
1     5       10      15

Leu Ala Arg Thr Thr Ala Asp Arg Arg Ala Ala Cys Asn Cys Leu Lys
1     5       10      15
Gln Leu

Ala Asp Arg Gln Thr Ala Cys Asn Cys Leu Lys Asn Leu Ala Gly
1     5       10      15

Asp Trp Glu Tyr Ser Val Trp Leu Ser Asn
1     5       10

Glu Val Phe Ile Ser Ala Pro Arg
1     5

Glu Asp Val Pro Gln Pro Pro Val Ser Gln Phe His
1     5       10
<210> SEQ ID NO 803
<211> LENGTH: 25
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Olea europaea Ole e 1.0102 protein epitope

<400> SEQUENCE: 803

Glu Asp Val Pro Gln Pro Pro Val Ser Gln Pro His Ile Gln Gly Gln
1   5   10   15
Val Tyr Cys Asp Thr Cys Arg Ala Gly
20  25

<210> SEQ ID NO 804
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Triticum aestivum Omega gliadin storage protein epitope

<400> SEQUENCE: 804

Gln Gln Pro Gln Gln Ser Phe Pro Gln Gln
1   5   10

<210> SEQ ID NO 805
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<400> SEQUENCE: 805

Gln Gln Phe His Gln Gln Gln
1   5

<210> SEQ ID NO 806
<211> LENGTH: 35
<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Aspergillus fumigatus Oryzin precursor epitope

<400> SEQUENCE: 806

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

<210> SEQ ID NO 807
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Gallus gallus Ovalbumin epitope

<400> SEQUENCE: 807

Cys Phe Asp Val Phe Lys Glu Leu Lys
1   5
Cys Asn Phe Cys Asn Ala Val Val Glu Ser
1  5  10

Ala Glu Val Asp Cys Ser Arg Phe Pro Asn Ala Thr Asp Lys
1  5  10

Ala Ser Trp Asp Trp Arg Lys Lys Gly Val
1  5  10

Pro Gln Glu Phe Ser Lys Thr Tyr Gln
1  5  10

Glu Ala Leu Thr Lys His Phe Gln Asp
1  5

-continued
Lys Ala Ala Ser Gly Ser Thr Gly Asp Gln Lys Val Gln Ile Ser Tyr
1  5  10  15

Tyr Gly Pro Lys
20

<210> SEQ ID NO 814
<211> LENGTH: 9
<212> TYPE: PRT
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<223> OTHER INFORMATION: Parietaria judaica Par j epitope

<400> SEQUENCE: 814
Gly Thr Ser Ser Cys Arg Leu Val Pro
1  5

<210> SEQ ID NO 915
<211> LENGTH: 47
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Blomia tropicalis Paramycin epitope

<400> SEQUENCE: 915
Glu Lys Leu Arg Asp Gln Lys Glu Ala Leu Ala Arg Glu Asn Lys Lys
1  5  10  15
Leu Ala Asp Leu Ala Glu Ala Lys Ser Gln Leu Asn Asp Ala His
20  25
Arg Arg Ile His Glu Gln Glu Ile Glu Ile Lys Arg Leu Glu Asn
30  35  40  45

<210> SEQ ID NO 916
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Gadus morhua callarias Parvalbumin beta epitope

<400> SEQUENCE: 916
Ala Ala Glu Ala Ala Cys Phe Lys
1  5

<210> SEQ ID NO 917
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Salmo salar parvalbumin like l epitope

<400> SEQUENCE: 917
Ala Asp Ile Lys Thr Ala Leu Glu Ala Arg Lys Ala Ala Asp Thr
1  5  10  15

<210> SEQ ID NO 918
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Juniperus ashei Pathogenesis-related protein precursor epitope

<400> SEQUENCE: 918
Ala Asp Ile Asn Ala Val Cys Pro Ser Glu Leu Lys
<210> SEQ ID NO 819
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Nicotiana tabacum Pectate lyase epitope

<400> SEQUENCE: 819

Ala Tyr Asn Phe Gly Lys Arg Leu Asp Gln Arg
1 5 10

<210> SEQ ID NO 820
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Musa acuminate AAA Group pectate lyase 2 epitope

<400> SEQUENCE: 820

Ala Phe Asn Phe Gly Glu Gly Leu Ile Gln Arg
1 5 10

<210> SEQ ID NO 821
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Farfantepenaeus aztecus Pen a 1 allergen epitope

<400> SEQUENCE: 821

Ala Asn Ile Gln Leu Val Glu Lys Asp Lys Ala Leu Ser Asn Ala
1 5 10 15

<210> SEQ ID NO 822
<211> LENGTH: 43
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Dermatophagoides pteronyssinus Peptidase 1 precursor (Major mite fecal allergen Der p 1) (Allergen Der p 1) epitope

<400> SEQUENCE: 822

Ala Arg Glu Gln Ser Cys Arg Arg Pro Asn Ala Gln Arg Phe Gly Ile
1 5 10 15

Ser Asn Tyr Cys Gln Ile Tyr Pro Pro Asn Val Asn Lys Ile Arg Glu
20 25 30

Ala Leu Ala Gln Thr His Ser Ala Ile Ala Val
35 40

<210> SEQ ID NO 823
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Homo sapiens pericentriolar material 1 protein epitope

<400> SEQUENCE: 823

Lys Asp Cys
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Arg Ala Arg Ala Lys Trp
  1  5

<210> SEQ ID NO 829
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens plexin domain containing 1, isoform CRA_b epitope

<400> SEQUENCE: 829

Asn Cys Ser Trp Cys His Val Leu Gln Arg Cys Ser
  1  5 10

<210> SEQ ID NO 830
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens PM/Scl 100kD nucleolar protein epitope

<400> SEQUENCE: 830

Cys Ile Ala Ala Lys Lys Ile Lys Gln Ser Val Gly Arg Lys Ser
  1  5 10 15

<210> SEQ ID NO 831
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Betula pendula Polcalcin Bet v 4 epitope

<400> SEQUENCE: 831

Phe Gly Arg Ala Asn Arg Gly Leu
  1  5

<210> SEQ ID NO 832
<211> LENGTH: 36
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Polcalcin Phl p 7 (Calcium-binding pollen allergen Phl p 7) (B7) epitope

<400> SEQUENCE: 832

Ala Asp Asp Met Glu Arg Ile Phe Lys Arg Phe Asp Thr Asn Gly Asp
  1  5 10 15

Gly Lys Ile Ser Leu Ser Glu Leu Thr Asp Ala Leu Arg Thr Leu Gly
  20 25 30

Ser Thr Ser Ser
  35

<210> SEQ ID NO 833
<211> LENGTH: 26
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Lolium perenne pollen allergen epitope

<400> SEQUENCE: 833

Glu Gly Gly Thr Lys Ser Glu Val Glu Asp Val Ile Pro Glu Gly Trp
Lys Ala Asp Thr Ser Tyr Ser Ala Lys
20 25

SEQ ID NO 934
LENGTH: 12
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Ambrosia artemisiifolia Pollen allergen Amb a 1.4 epitope

SEQUENCE: 934

Ala Phe Asn Lys Phe Thr Asp Asn Val Asp Gln Arg
1 5 10

SEQ ID NO 935
LENGTH: 8
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Ambrosia artemisiifolia Pollen allergen Amb a 2 precursor epitope

SEQUENCE: 935

Met Pro Arg Cys Arg Phe Gly Phe
1 5

SEQ ID NO 936
LENGTH: 15
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Ambrosia artemisiifolia var. elatior Pollen allergen Amb a 3 epitope

SEQUENCE: 936

Cys Asp Ile Lys Asp Pro Ile Arg Leu Glu Pro Gly Gly Pro Asp
1 5 10 15

SEQ ID NO 937
LENGTH: 31
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Betula pendula pollen allergen Bet v 1 epitope

SEQUENCE: 937

Lys Ala Glu Gin Val Lys Ala Ser Lys Glu Met Gly Glu Thr Leu Leu
1 5 10 15

Arg Ala Val Glu Ser Tyr Leu Leu Ala His Ser Asp Ala Tyr Asn
20 25 30

SEQ ID NO 938
LENGTH: 20
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Poa pratensis Pollen allergen KGB 60 precursor epitope

SEQUENCE: 938

Ala Ala Asn Lys Tyr Lys Thr Phe Val Ala Thr Phe Gly Ala Ala Ser
1 5 10 15
Asn Lys Ala Phe

20

<210> SEQ ID NO 839
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Lolium perenne Pollen allergen Lol p 2-A (Lol p II-A) epitope

<400> SEQUENCE: 839

Glu Lys Gly Met Arg Asn Val Phe Asp Asp Val Val Pro Ala Asp Phe
1  5  10  15

Lys Val Gly Thr Thr Tyr Lys Pro Glu
20  25

<210> SEQ ID NO 840
<211> LENGTH: 27
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Lolium perenne Pollen allergen Lol p 3 (Lol p III) epitope

<400> SEQUENCE: 840

Lys Gly Gly Met Lys Asn Val Phe Asp Glu Val Ile Pro Thr Ala Phe
1  5  10  15

Thr Val Gly Lys Thr Tyr Thr Pro Glu Tyr Asn
20  25

<210> SEQ ID NO 841
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Lolium perenne Pollen allergen Lol p VA precursor epitope

<400> SEQUENCE: 841

Ala Ala Glu Gly Ala Thr Pro Glu Ala Lys Tyr Asp
1  5  10

<210> SEQ ID NO 842
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Phleum pratense Pollen allergen Phl p 1 precursor epitope

<400> SEQUENCE: 842

Ala Pro Tyr His Phe Asp Leu Ser Gly His Ala Phe Gly Ala Met
1  5  10  15

<210> SEQ ID NO 843
<211> LENGTH: 8
<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Zea mays pollen allergen Phl p 11 epitope

<400> SEQUENCE: 843
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 Gly Gly Gln Gly Ser Arg His Glu Gln Ala Arg

 Ala Phe Arg Leu Glu Glu Ile Ala Ala Ile

 Trp Ala Gln Ser Thr Asp Phe Pro Gin Phe Lys Pro Glu Glu Ile Thr

 Ala Ile Met Asn Asp Gin Pro Gly Ser Leu Ala Pro Thr Gly

 Leu Tyr Leu Gly Gln Gly Thr Tyr Met Val Ile Gln Gly Glu Pro Gly

 Ala Val Ile Arg Gly Lys Lys Gly
Glu Gln Cys Gly Arg Gln Ala Gly Gly Lys Leu Cys Pro Asn Asn Leu  
1 5 10 15

Cys Cys Ser Gln Trp Gly Trp Cys Gly Ser Thr Asp Glu Tyr Cys Ser  
20 25 30

Pro Asp His Asn Cys Gin Ser Asn Cys Lys Asp  
35 40

<210> SEQ ID NO 854  
<211> LENGTH: 15  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Homo sapiens Proliferating cell nuclear antigen epitope

<400> SEQUENCE: 854
Leu Lys Tyr Tyr Leu Ala Pro Lys Ile Glu Asp Glu Glu Gly Ser  
1 5 10 15

<210> SEQ ID NO 855  
<211> LENGTH: 9  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Homo sapiens Proline-rich transmembrane protein 2 epitope

<400> SEQUENCE: 855
His Ser Glu Ala Glu Thr Gly Pro Pro  
1 5

<210> SEQ ID NO 856  
<211> LENGTH: 15  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Homo sapiens proteasome (prosome, macropain) activator subunit 3 (PA28 gamma; K1), isoform CRA_a epitope

<400> SEQUENCE: 856
Leu Asp Gly Pro Thr Tyr Lys Arg Leu Asp Glu Cys Glu Glu  
1 5 10 15

<210> SEQ ID NO 857  
<211> LENGTH: 13  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Homo sapiens protein tyrosine phosphatase-like autoantigen epitope

<400> SEQUENCE: 857
Gly Ala His Gly Asp Thr Thr Pro Glu Tyr Gin Asp Leu  
1 5 10

<210> SEQ ID NO 858  
<211> LENGTH: 20  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Homo sapiens protein-arginine deiminase type-4 epitope

<400> SEQUENCE: 858
Ala Phe Phe Pro Asn Met Val Asn Met Leu Val Leu Gly Lys His Leu
1 5 10 15

Gly Ile Pro Lys
20

<210> SEQ ID NO 859
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<223> OTHER INFORMATION: Homo sapiens proteainase 3 epitope

<400> SEQUENCE: 859

Cys Ala Thr Arg Leu Phe Pro Asp Phe Phe Thr Arg Val Ala Leu
1 5 10 15

<210> SEQ ID NO 860
<211> LENGTH: 10
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Prunus persica pru p 1 epitope

<400> SEQUENCE: 860

Gly Lys Cys Gly Val Ser Ile Pro Tyr Lys
1 5 10

<210> SEQ ID NO 861
<211> LENGTH: 15
<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Prunus dulcis prumin 1 precursor epitope

<400> SEQUENCE: 861

Glu Glu Ser Gln Gln Gln Gln Ser Ser Gln Gln Gly Arg Gln Gln Gln Gln
1 5 10 15

<210> SEQ ID NO 862
<211> LENGTH: 15
<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Prunus dulcis prumin 2 precursor epitope

<400> SEQUENCE: 862

Asp Ser Gln Pro Gln Gln Phe Gln Gln Gln Gln Gln Gln Gln Gln
1 5 10 15

<210> SEQ ID NO 863
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Hesperocypris arizonica putative allergen Cup a 1 epitope

<400> SEQUENCE: 863

Trp Arg Phe Thr Arg Asp Ala Phe Thr Asn Gly
1 5 10

<210> SEQ ID NO 864
<211> LENGTH: 11
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Putative MTLV-1-related endogenous sequence (p25) epitope

<400> SEQUENCE: 864
Pro Thr Arg Ala Pro Ser Gly Pro Arg Pro Pro
1  5  10

<210> SEQ ID NO 965
<211> LENGTH: 8
<212> TYPE: PRO
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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Putative small nuclear ribonucleoprotein polypeptide B-like protein 1 epitope

<400> SEQUENCE: 865
Glu Ile His Ser Lys Thr Lys Ser
1  5

<210> SEQ ID NO 866
<211> LENGTH: 18
<212> TYPE: PRO
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Receptor tyrosine-protein kinase erbB-2 precursor epitope

<400> SEQUENCE: 866
Pro Glu Ser Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala Pro Leu Gln
1  5  10  15
Pro Glu

<210> SEQ ID NO 867
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<212> TYPE: PRO
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens Receptor-type tyrosine-protein phosphatase-like N precursor epitope

<400> SEQUENCE: 867
Lys Glu Arg Leu Ala Ala Leu Gly Pro Glu Gly Ala His
1  5  10

<210> SEQ ID NO 868
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<212> TYPE: PRO
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens recombinant IgG2 heavy chain epitope

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1  5  10

<210> SEQ ID NO 869
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<212> TYPE: PRO
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Homo sapiens Replication protein A 32 kDa
subunit epitope

Arg Ser Phe Gln Asn Lys Lys Ser Leu Val Ala Phe Lys Ile Met Pro
1  5  10  15
Leu Glu Asp Met
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<223> OTHER INFORMATION: Aspergillus fumigatus Ribonuclease mitogillin precursor epitope

<400> SEQUENCE: 870
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<223> OTHER INFORMATION: Homo sapiens ribosomal protein L7 epitope

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1  5  10  15
Arg Lys Ala Arg Arg Lys Leu
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<210> SEQ ID NO 873
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Mangifera indica ripening-related pectate lyase epitope

<400> SEQUENCE: 873
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<210> SEQ ID NO 874
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens RNA binding protein, autoantigentic (inRNP-associated with lethal yellow homolog (mouse); isoform CRA_c epitope
1   5       10     15
Gly Gly Gly Ser Ser
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<223> OTHER INFORMATION: Homo sapiens Ro ribonucleoprotein epitope

<400> SEQUENCE: 875
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1   5       10     15
Leu Cys Phe Gly Ser
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**FEATURE:**
*OTHER INFORMATION:* Homo sapiens steroid 17-alpha-hydroxylase/17,20 lyase epitope

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**SEQ ID NO 904**
**LENGTH:** 12
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**ORGANISM:** Artificial Sequence
**FEATURE:**
*OTHER INFORMATION:* Cryptomeria japonica Sugi basic protein precursor epitope

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**FEATURE:**
*OTHER INFORMATION:* Aspergillus fumigatus Superoxide dismutase epitope

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**SEQUENCE:** 905
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Tyr Thr Leu Pro Pro Leu Pro Tyr Pro Tyr Asp Ala Leu Gln Pro Tyr
1  5  10  15

Ile Ser Gln Gln Ile Met Glu Leu His His Lys Lye His His Gln Thr
20  25  30

Tyr Val Aan Gly Leu Aan Ala Ala Leu Glu Ala Gln Lye Ala Ala
35  40  45

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<400> SEQUENCE: 906

Arg Ser Leu Asp Phe Gln Ala Thr Thr Met Phe
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1  5  10  15

Glu Arg

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Glu Phe Lys Lys Arg Phe Ser Asp Ala Thr Ser Lys Ala His Gln
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Gln Pro Leu Lys Glu Gln Pro Ala Leu Aan Asp Ser Arg Tyr Cys Leu
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1 5 10 15

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1 5 10

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<223> OTHER INFORMATION: Homo sapiens TCR V-beta 6.1 epitope

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1 5 10 15

Ala Asp Asp Ser Gly
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Asp Pro Ile Ser Gly His Val Ser Leu Phe
1 5 10

<210> SEQ ID NO 915
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<223> OTHER INFORMATION: Homo sapiens Thyroglobulin epitope

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Leu Ile Gly Ser
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<223> OTHER INFORMATION: Homo sapiens Thyroid peroxidase epitope

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Gly Leu Pro Arg Leu Glu Thr Pro Ala Asp Leu Ser Thr Ala Ile Ala
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Ser Arg Ser

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<223> OTHER INFORMATION: Homo sapiens thyroid stimulating hormone receptor epitope

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Glu Ile Ile Gly Phe Gly Glu Lys Asn Pro Glu Glu Glu
1   5   10   15

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Glu Glu Glu Glu Asp Glu Ile Ile Gly Phe Gly Glu Lys Asn
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Gly Gln Glu Leu Lys Asn Pro Glu Glu Thr Leu Gln Ala Phe Asp
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Ser His Tyr Asp
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ORGANISM: Artificial Sequence

OTHER INFORMATION: Trichophyton rubrum Tri r 2 allergen epitope

SEQUENCE: 921

Asp Cys Aaa Gly His Gly Thr His Val Ala Gly Thr Val Gly Gly Thr
1     5     10    15
Lys Tyr Gly Leu
20

SEQ ID NO 922
LENGTH: 15
TYPE: PRT
ORGANISM: Artificial Sequence

OTHER INFORMATION: Homo sapiens trinucleotide repeat containing 6A, isoform CRA_b epitope

SEQUENCE: 922

Ala Phe Leu Ser Val Asp His Leu Gly Gly Gly Gly Glu Ser Met
1     5     10    15

SEQ ID NO 923
LENGTH: 15
TYPE: PRT
ORGANISM: Artificial Sequence

OTHER INFORMATION: Homo sapiens trinucleotide repeat containing 6A, isoform CRA_c epitope

SEQUENCE: 923

Trp Gly Ser Ser Ser Val Gly Pro Gln Ala Leu Ser Lys Ser Gly
1     5     10    15

SEQ ID NO 924
LENGTH: 36
TYPE: PRT
ORGANISM: Artificial Sequence

OTHER INFORMATION: Homo sapiens tripartite motif-containing 67 epitope

SEQUENCE: 924

Leu Gly Gly Ala Gly Gly Gly Gly Asp His Ala Asp Lys Leu Ser
1     5     10    15
Leu Tyr Ser Glu Thr Asp Ser Gly Tyr Gly Ser Tyr Thr Pro Ser Leu
20    25    30
Lys Ser Pro Asn
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SEQ ID NO 925
LENGTH: 10
TYPE: PRT
ORGANISM: Artificial Sequence

OTHER INFORMATION: Triticum aestivum Triticum aestivum proteins epitope

SEQUENCE: 925

Leu Pro Gln Gln Gln Ile Pro Gln Gln Pro
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SEQ ID NO 926
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Phe Leu Ala Glu Glu Ala Asp Arg Lys
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<210> SEQ ID NO 927
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1     5     10     15

Ile Pro Ser Leu
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<220> FEATURE:
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<220> FEATURE:
<223> OTHER INFORMATION: Homo sapiens tumor necrosis factor ligand superfamily member 6 epitope

<400> SEQUENCE: 929

Glu Trp Glu Asp Thr Tyr Gly Ile Val Leu
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<223> OTHER INFORMATION: Paralichthys olivaceus type 1 collagen alpha 2 epitope

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1     5     10     15

Ser Gly Pro Ser
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<220> FEATURES:
<223> OTHER INFORMATION: Triticum aestivum type 1 non-specific lipid transfer protein precursor epitope

<400> SEQUENCE: 931

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Asn Ala Met Lys Ile Ser Phe Ala Lys Lys
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Pro Ala Pro Gly Met Arg Pro Pro
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Met Cys Gln Cys Val Gln Lys Tyr Gly Thr Glu Phe Cys Lys Lys Arg
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Leu Ala

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<400> SEQUENCE: 938

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<400> SEQUENCE: 939

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<223> OTHER INFORMATION: Homo sapiens Vimentin epitope

<400> SEQUENCE: 940

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<223> OTHER INFORMATION: Homo sapiens von Willebrand factor epitope

<400> SEQUENCE: 941

 His  | Cys  | Gln  | Ile  | Cys  | His  | Cys  | Asp  | Val  | Val  | Arg  | Leu  | Thr  | Cys  | Glu  |
1. A method comprising:
administering to a subject a composition according to a
protocol that was previously shown to suppress antigen-
specific activation of innate immune cells in one or more
test subjects;
wherein the composition comprises:
(i) a first population of synthetic nanocarriers coupled to
immunosuppressants, and
(ii) a second population of synthetic nanocarriers coupled
to B cell and/or MHC Class II-restricted epitopes of an
antigen.
2. A method comprising:
suppressing antigen-specific activation of innate immune
cells in a subject by administering to the subject a com-
position that comprises:
(i) a first population of synthetic nanocarriers coupled to
immunosuppressants, and
(ii) a second population of synthetic nanocarriers coupled
to B cell and/or MHC Class II-restricted epitopes that
are cognate epitopes of an antigen.
3. A method comprising:
administering to a subject a composition that comprises:
(i) a first population of synthetic nanocarriers coupled to
immunosuppressants, and
(ii) a second population of synthetic nanocarriers coupled
to B cell and/or MHC Class II-restricted epitopes of an
antigen, wherein the composition is in an amount effec-
tive to suppress antigen-specific activation of innate
immune cells in the subject.
4. The method of claim 1, wherein the composition is in an
amount effective to suppress antigen-specific activation of
innate immune cells in the subject.
5. The method of claim 1, wherein the first population and
the second population are the same population.
6. The method of claim 1, wherein the B cell epitopes are
bound by antibodies and form complexes with the antibodies.
7. (canceled)
8. The method of claim 1, wherein the antigen is a therapeu-
tic protein, an autoantigen, an allergen, or is associated
with an inflammatory disease, an autoimmune disease, organ
or tissue rejection or graft versus host disease.
9. The method of claim 1, wherein the method further
comprises assessing antigen-specific activation of innate
immune cells in the subject prior to and/or after the admin-
istration of the composition.
10. The method of claim 1, wherein the subject has or is at
risk of having an inflammatory disease, an autoimmune
disease, an allergy, organ or tissue rejection or graft versus host
disease.
11. The method of claim 1, wherein the subject has undergone
or will undergo transplantation.
12. The method of claim 1, wherein the subject has or is at
risk of having an undesired innate immune response against a
therapeutic protein that is being administered or will be
administered to the subject.
13-15. (canceled)
16. The method of claim 1, wherein the immunosuppres-
sants comprise a statin, an mTOR inhibitor, a TGF-β signal-
ing agent, a corticosteroid, an inhibitor of mitochondrial
function, a P38 inhibitor, an NF-κB inhibitor, an adenosine
receptor agonist, a prostaglandin E2 agonist, a phosphodi-
esterase 4 inhibitor, an HDAC inhibitor or a proteasome
inhibitor.
17. (canceled)
18. The method of claim 1, wherein the load of the immunosuppressants and/or epitopes on average across the first and/or second population of synthetic nanocarriers is between 0.0001% and 50% (weight/weight).

19. (canceled)

20. The method of claim 1, wherein the synthetic nanocarriers of the first population and/or second population comprise lipid nanoparticles, polymeric nanoparticles, metallic nanoparticles, surfactant-based emulsions, dendrimers, buckyballs, nanowires, virus-like particles or peptide or protein particles.

21.30. (canceled)

31. The method of claim 1, wherein the mean of a particle size distribution obtained using dynamic light scattering of the synthetic nanocarriers of the first and/or second population is a diameter greater than 100 nm.

32.35. (canceled)

36. The method of claim 1, wherein the aspect ratio of the synthetic nanocarriers of the first population and second population is greater than 1:1, 1:1.2, 1:1.5, 1:2, 1:3, 1:5, 1:7 or 1:10.

37. A composition comprising:
(i) a first population of synthetic nanocarriers coupled to immunosuppressants;
(ii) a second population of synthetic nanocarriers coupled to B cell and/or MHC Class II-restricted epitopes of an antigen; and
(iii) a pharmaceutically acceptable excipient,

wherein the composition is in an amount effective to suppress antigen-specific activation of innate immune cells.

38. A composition comprising:
(i) a first population of synthetic nanocarriers coupled to immunosuppressants;
(ii) a second population of synthetic nanocarriers coupled to B cell and/or MHC Class II-restricted epitopes of an antigen; and
(iii) a transplantable graft or therapeutic protein; and optionally
(iv) a pharmaceutically acceptable excipient.

39-42. (canceled)

43. A method, comprising:
(a) preparing a composition comprising a first population of synthetic nanocarriers coupled to immunosuppressants, and a second population of synthetic nanocarriers coupled to B cell and/or MHC Class II-restricted epitopes or an antigen, and
(b) assessing the antigen-specific activation of innate immune cells of the composition.

44-45. (canceled)

46. A dosage form comprising the composition of claim 1.

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