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(72) DONDERO, RICHARD S., US
(72) GALTON, BRUCE C., US
(72) CASEY, LESLIE S., US
(71) CISTRON BIOTECHNOLOGY, INC., US

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(54) **IMMUNOMODULATEURS ENCAPSULES UTILISES COMME ADJUVANTS DE VACCINS**

(54) **ENCAPSULATED IMMUNOMODULATORS USEFUL AS VACCINE ADJUVANTS**

(57) La présente invention concerne des compositions comprenant un immunomodulateur encapsulé, tel que des cytokines et des lymphokines, qui est utilisé comme adjuvant pour stimuler une réponse immunitaire lorsqu'il est administré à un être humain ou à un animal. Par exemple, une lymphokine telle que l'IL-1α ou l'IL-1β. peut être utilisée comme immunomodulateur encapsulé dans une matrice de la présente invention. La composition encapsulée peut comprendre un antigène de vaccin, tel qu'un virus entier inactivé ou atténué, des peptides recombinés ou synthétiques et d'autres matériaux antigéniques. La matrice d'encapsulation peut être naturelle ou synthétique. La présente invention concerne également l'utilisation, chez un être humain ou un animal, d'un immunomodulateur encapsulé comme adjuvant dans le but de stimuler les réponses immunitaires à un antigène ou à un autre matériau envers lequel on désire provoquer une réponse immunitaire.

(57) The present invention concerns compositions comprising an encapsulated immunomodulator, such as cytokines and lymphokines, that is useful as an adjuvant for stimulating an immune response when administered to a human or animal. For example, a lymphokine such as IL-1α or IL-1β can be used as an immunomodulator encapsulated in a matrix according to the invention. The encapsulated composition can include a vaccine antigen, such as whole inactivated or attenuated virus, recombinant or synthetic peptides, and other antigenic materials. The encapsulation matrix can be natural or synthetic. The present invention also pertains to the use of an encapsulated immunomodulator in a human or animal as an adjuvant to increase immune responses to an antigen or other material to which an immune response is desired.

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(71) Applicant: CISTRON BIOTECHNOLOGY, INC. [US/US]; Box 2004, 10 Bloomfield Avenue, Pine Brook, NJ 07058 (US).

(72) Inventors: DONDERO, Richard, S.; 37 Hillside Avenue, Riverdale, NJ 07457 (US). GALTON, Bruce, C.; 8 Holden Lane, Madison, NJ 07940 (US). CASEY, Leslie, S.; Apartment 3B, 119 W. 88th Street, New York, NY 10024 (US).

(74) Agents: SALIWANCHIK, David, R. et al.; Saliwanchik, Lloyd & Saliwanchik, Suite A–1, 2421 N.W. 41st Street, Gainesville, FL 32606–6669 (US).

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(54) Title: ENCAPSULATED IMMUNOMODULATORS USEFUL AS VACCINE ADJUVANTS

(57) Abstract

The present invention concerns compositions comprising an encapsulated immunomodulator, such as cytokines and lymphokines, that is useful as an adjuvant for stimulating an immune response when administered to a human or animal. For example, a lymphokine such as IL–1α or IL–1β can be used as an immunomodulator encapsulated in a matrix according to the invention. The encapsulated composition can include a vaccine antigen, such as whole inactivated or attenuated virus, recombinant or synthetic peptides, and other antigenic materials. The encapsulation matrix can be natural or synthetic. The present invention also pertains to the use of an encapsulated immunomodulator in a human or animal as an adjuvant to increase immune responses to an antigen or other material to which an immune response is desired.

DESCRIPTION

ENCAPSULATED IMMUNOMODULATORS USEFUL AS VACCINE ADJUVANTS

Background of the Invention

The immune system is regulated in part by a complex network of chemical signals. These signals include the interleukins such as IL-1α and IL-1β. IL-1β is a polypeptide hormone synthesized and secreted by stimulated monocytes. The initial translation product of IL-1β is a 31 kDa precursor polypeptide having relatively low biological activity. After synthesis, the 31 kDa precursor for IL-1β is enzymatically cleaved to its highly active mature form which has a size of about 17.5 kDa. The N-terminus of mature IL-1β derived from human activated monocytes has been characterized by an N-terminal amino acid sequence beginning with Ala-Pro. The N-terminal Ala residue of human mature IL-1β is in the 117 position and an Asp residue is in the 116 position counting from the N-terminus of human precursor IL-1β polypeptide. Mature IL-1β consists of the C-terminal 153 residues of the precursor polypeptide.

Many physiological actions and biological activities of IL-1β have been identified. IL-1β biological activity is often determined by assaying for stimulation of thymocyte proliferation. IL-1β activities include stimulation of B-lymphocyte maturation, lymphocyte proliferation, stimulation of fibroblast growth and induction of acute-phase protein synthesis by hepatocytes.

Other biological activities have been attributed to IL-1β polypeptides. These include control of differentiation and activation of lymphocytes, stimulation of lymphokine and prostaglandin production, promotion of inflammation, induction of acute phase proteins, stimulation of bone resorption, and alteration of the level of iron and zinc in blood. Moreover, it has been found that IL-1β can stimulate the hypothalamus-pituitary-adrenal axis, suggesting that IL-1β is integrated in the complex neuroendocrine network that controls homeostasis.

Maturation and release of mature IL-1β from macrophages does not proceed by conventional means normally associated with most secretory proteins because the

precursor IL-1β polypeptide lacks a hydrophobic signal sequence. Further, IL-1β is not associated with a membrane-bound compartment in monocytes. Most secretory proteins are characterized by the presence of a hydrophobic stretch of amino acids called a signal sequence. The signal sequence directs the translocation of the protein across the membrane of the endoplasmic reticulum during protein synthesis. The protein is subsequently ushered out of the cell via exocytosis. Most secreted proteins have a signal sequence at the amino terminal that is removed upon translocation. Other proteins, such as ovalbumin, have an internal signal sequence that is not removed upon translocation. The precursor form of IL-1β lacks any region (either amino terminal or internal) with sufficient hydrophobicity and length to qualify as a signal sequence.

Microencapsulation is the process of enveloping certain drugs, enzymes, toxins, or other substances in polymeric matrices. It can be used in controlled release or delayed release of drugs. The many applications for encapsulation, the available matrices, and techniques for making and using encapsulation matrices are extensively covered elsewhere (see, for example, Chang, T.M.S. [1977] *Biomedical applications of immobilized enzymes and proteins*, Vols. 1-2, New York, Plenum Press; Deasy, P.B. (ed.) [1984] "Microencapsulation and related drug processes," In J. Swarbrick (ed.), *Drugs and the pharmaceutical sciences: Vol. 20. Microencapsulation and related drug processes*, New York: Marcel Dekker, Inc.; McGinity, J.W. [1989] "Aqueous polymeric coatings for pharmaceutical dosage forms," *Drugs and the Pharmaceutical Sciences 36*; Nixon, J.R. (ed.) [1976] "Microencapsulation," In J. Swarbrick (ed.) *Drugs and the pharmaceutical sciences: Vol. 3*, New York, Marcel Dekker, Inc.). U.S. Patent No. 4,832,686 discloses the microencapsulation of IL-2 in a biocompatible polymer formulation.

Liposomes are closed structures that have a lipid bilayer membrane that can be used to encapsulate substances. The liposomes can be prepared using standard materials and methods well known in the art. For example, U.S. Patent No. 5,059,421 discloses methods for preparing targeted liposomes of a defined size distribution.

It is known that in many cases that both cellular and/or humoral immune responses to an antigen administered to an animal can be enhanced or increased by immunizing the animal with the antigen in conjunction with some type of adjuvant. An

adjuvant, in broad terms, may be thought of as a compound or composition which can enhance or amplify an animal's immune response (*e.g.*, an increase in antibody titer) to an antigen or immunogen. Various adjuvants are known in the art, including Freund's (complete and incomplete), muramyl dipeptide (MDP), and alum.

More recently, polypeptides and small peptides have been used as adjuvants. U.S. Patent No. 5,503,841 discloses the use of interleukin-2 (IL-2) as an adjuvant with vaccines. U.S. Patent No. 5,206,014 discloses the use of a peptide fragment of human IL-1β as an adjuvant with antigens having low immunogenicity. However, systemic administration of immunomodulators, such as IL-2, as adjuvants can result in an overstimulation or dysfunctional activation of the immune system of the animal. Systemic *in vivo* administration of IL-1β has been associated with unwanted side effects, including fever and nausea. Thus, there remains a need in the art for adjuvants that stimulate or activate appropriate cells of the immune system with minimal systemic exposure.

Brief Summary of the Invention

The present invention pertains to novel compositions and methods useful as vaccine adjuvants. The compositions of the subject invention are immunomodulators encapsulated within a matrix. The immunomodulators may be, for example, cytokines or lymphokines. In a preferred embodiment, interleukin compounds such as IL-1α and/or IL-1β are utilized according to the subject invention. In a specific embodiment the subject invention provides adjuvant compositions comprising encapsulated IL-1β. The encapsulated IL-1β composition can optionally include a vaccine antigen, such as whole inactivated or attenuated virus, recombinant or synthetic peptides, and other antigenic materials. Use of encapsulated IL-1β permits presentation of IL-1β to antigen presenting cells with minimal systemic exposure.

The present invention also pertains to the use of encapsulated immunomodulators for use as a means to increase immune responses in a patient. In an exemplified embodiment of the present invention encapsulated IL-1α or IL-1β can be used as the immunomodulator for increasing immune responses. Typically, encapsulated IL-1β is

used as an adjuvant to stimulate or increase an immune response to an immunogen or antigen, such as those used in vaccine preparations.

The encapsulated immunomodulator of the subject invention can be administered in the presence or absence of a vaccine antigen. The antigen can be encapsulated with the immunomodulator or it can be administered in a composition external to the encapsulated immunomodulator. The encapsulated immunomodulator of the subject invention can be administered either prior to or subsequent to vaccine antigen administration.

Brief Description of the Drawings

Figure 1 shows anti-influenza A IgG antibody titer obtained after immunization of rats with the one of the following: influenza A/Beijing H_3N_3 vaccine mixed with mature IL-1β (no encapsulation), influenza A/Beijing H_3N_3 vaccine alone (no encapsulation), or influenza A/Beijing H_3N_3 vaccine and mature IL-1β encapsulated together in liposomes.

Brief Description of the Sequences

SEQ ID NO. 1 is an amino acid sequence of human mature IL-1β.

Detailed Disclosure of the Invention

The subject invention pertains to novel compositions comprising an encapsulated immunomodulator for the use as an adjuvant. Specifically exemplified herein is the use of an interleukin compound such as IL-1α or IL-1β as the encapsulated immunomodulator. In a preferred embodiment, the immunomodulator is IL-1β. The encapsulated IL-1β compositions can be used as an adjuvant.

Encapsulated immunomodulator compositions of the present invention can optionally include or be used in conjunction with a vaccines, such as whole inactivated or attenuated virus, recombinant or synthetic polypeptides or peptides, haptens, and other antigenic or immunogenic materials. Using the methods and materials of the present invention provides for presentation of IL-1β, either in the presence or absence of a

vaccine, to antigen presenting cells of the immune system but with minimal systemic exposure of the patient to IL-1β.

In a preferred embodiment, IL-1β is used as the immunomodulator. More preferably, the IL-1β used with the present invention is human IL-1β. The IL-1β can be either in precursor form or mature form. The IL-1β can be human mature IL-1β, or a biologically active fragment or variant thereof, when the encapsulated IL-1β is to be administered to a human. Preferably, the IL-1β used with the present invention has the amino acid sequence shown in SEQ ID NO. 1. IL-1β from other animal species can be also be used when the present invention is administered to non-human species. The IL-1β can be isolated from animal cells, synthesized, or produced by recombinant gene expression means.

In one embodiment, additional molecules and/or immunomodulators, such as cytokines, interleukins and biologically active peptides are also encapsulated with an immunomodulator of the present invention or are administered in conjunction with the present invention. Preferably, IL-1α and/or IL-1β is a first immunomodulator which is encapsulated along with a second, different immunomodulator. For example, IL-2, IL-4, IL-12, and others, can be encapsulated along with IL-1α and/or IL-1β. Other suitable molecules are known in the art which the skilled artisan would understand as being useful in the subject invention.

Immunomodulators can be incorporated into an encapsulation matrix using methods known in the art. The encapsulation matrix can be natural or synthetic. For example, an immunomodulator such as IL-1β can be incorporated in a biocompatible polymer material such as lactic acid, glycolide and glutamic acid. In preferred embodiment, the encapsulation matrix is a liposome. The liposomes may be produced by any of the standard liposome preparation techniques which are well known and readily carried out by those skilled in the art. Such liposome preparation techniques are described in, for example, U.S. Patent No. 5,252,348.

Immunomodulators can be encapsulated in the matrix in a suitable buffer or carrier solution. The encapsulation matrix can also include molecules that target the encapsulated materials to specific tissues or cell types, *e.g.*, antigen presenting cells. For example, liposomes can have receptor molecules in the lipid bilayer for targeting to

specific desired cells. In one embodiment, liposomes can have the Fc portion of immunoglobulin incorporated in the lipid bilayer for targeting to cells which express Fc receptors on their surface. In another embodiment, the encapsulation matrix may contain antibodies that are immunoreactive with a molecule expressed on the surface of a target cell (*e.g.*, antibodies to MHC class II molecules can be used to target antigen presenting cells). Antigen presenting cells can include mononuclear phagocytes, B lymphocytes, dendritic cells, Langerhans cells and endothelial cells.

The immunomodulator can also be incorporated in an encapsulation matrix that provides for controlled and/or continuous release of the immunomodulator once administered to a patient. The IL-1β, or IL-1α, or other immunomodulator may be encapsulated in a matrix which provides for continuous release over time. Alternatively, the matrix may be specifically adapted to release the immunomodulator upon some event such as a change in pH which results from a local infection. See, for example, U.S. Patent No. 5,554,147 for a description of pH sensitive biopolymers.

The subject invention also concerns methods for enhancing immune responses in an animal or human by administering an effective amount of encapsulated of an encapsulated immunomodulator to the person or animal in need of such treatment. In a preferred embodiment, encapsulated IL-1β can be used as an adjuvant to increase immune responses to an immunogen or antigen, such as those used in vaccine compositions. Preferably, the vaccine composition can comprise whole inactivated or attenuated virus, subunits of viral components, recombinant or synthetic polypeptides or peptides, haptens, and other antigenic or immunogenic materials. The encapsulated IL-1β can be administered in the presence or absence of a vaccine composition. Preferably, the encapsulated IL-1β is administered in a pharmaceutically acceptable carrier. The vaccine composition can be encapsulated together with IL-1β or it can be administered in a composition external to the encapsulated IL-1β. The encapsulated IL-1β of the subject invention can also be administered either prior to or subsequent to vaccine administration.

The amount of IL-1β or other immunomodulator to be administered according to the subject methods of the invention can be readily determined by a person skilled in the art having the benefit of the instant disclosure.

The encapsulated compositions of the present invention can be administered to an animal or human parenterally, for example, by intramuscular or subcutaneous injection.

The methods and compositions of the present invention can be used with vaccines directed to treating or immunizing animals and/or humans against bacteria, viruses, tumor cells, fungus, and parasites.

All references cited herein are incorporated by reference.

Following are examples which illustrate procedures for practicing the invention. These examples should not be construed as limiting. All percentages are by weight and all solvent mixture proportions are by volume unless otherwise noted.

Example 1 – Encapsulation of IL-1β and Vaccine Experiment.

This investigation employed four groups of female Sprague-Dawley rats. The investigation was for 58 days and the purpose was to evaluate the use of IL-1β as an adjuvant. The vaccine used for these experiments was influenza A/Beijing H_3N_3 (Parke Davis). Each animal's weight was recorded prior to dosing on Day 0, and then animals were administered 100 microliters of a sample comprising liposome encapsulated IL-1β intramuscularly. Thereafter, the animals were reweighed and their weight recorded every seven days prior to their blood being drawn for the duration of the study. On day 30, animals were administered a booster dose of the test sample. Blood was collected on days 0, 7, 14, 28, 37, and 58 for determining serum IgG ELISA titers. Animals were observed daily for sickness or mortality. On day 58, the rats were weighed and euthanized.

Groups:

I. Influenza A/Beijing H_3N_3 vaccine mixed with mature IL-1β (no encapsulation)

II. Influenza A/Beijing H_3N_3 vaccine alone (no encapsulation)

III. Influenza A/Beijing H_3N_3 vaccine and mature IL-1β encapsulated together in liposomes

As shown in Figure 1, animals receiving the liposome encapsulated IL-1β mixed with Influenza A/Beijing H_3N_3 vaccine showed a significant increase in anti-influenza A antibody titer over those animals receiving vaccine alone or non-encapsulated vaccine/IL-1β.

Example 2 – Vaccine Compositions

The encapsulated immunomodulator compositions described herein can be advantageously used in conjunction with an antigenic or immunogenic composition for the preparation of a vaccine. Such a composition, when administered to a person or animal, increases immune responses to the administered vaccine antigen as compared to vaccine antigen when administered alone.

Vaccines can be prepared by procedures well known in the art. For example, such vaccines can be prepared as injectables, *e.g.*, liquid solutions or suspensions. Solid forms for solution in, or suspension in, a liquid prior to injection also can be prepared. Optionally, the preparation also can be emulsified. The encapsulated immunomodulator compositions and active antigenic ingredient or ingredients can be mixed with excipients which are pharmaceutically acceptable and compatible with the active ingredient. Examples of suitable excipients are water, saline, dextrose, glycerol, ethanol, or the like, and combinations thereof. In addition, if desired, the vaccine can contain minor amounts of auxiliary substances such as wetting or emulsifying agents, pH buffering agents, or adjuvants such as aluminum hydroxide or muramyl dipeptide or variations thereof. Also, cholera toxin subunit B or other agents which stimulate antibody production at mucosal sites can be used. In the case of peptides, coupling to larger molecules such as KLH or tetanus toxoid sometimes enhances immunogenicity. Vaccines are conventionally administered parenterally, by injection, for example, either subcutaneously or intramuscularly. Additional formulations which are suitable for other modes of administration include suppositories and, in some cases, oral formulations. For suppositories, traditional binders and carriers include, for example, polyalkalene glycols or triglycerides. Suppositories can be formed from mixtures containing the active ingredient in the range of about 0.5% to about 10%, preferably about 1 to about 2%. Oral

formulations can include such normally employed excipients as, for example, pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, and the like. These compositions can take the form of solutions, suspensions, tablets, pills, capsules, sustained release formulations or powders and contain from about 10% to about 95% of active ingredient, preferably from about 25% to about 70%.

The compounds can be formulated into the vaccine as neutral or salt forms. Pharmaceutically acceptable salts include the acid addition salts (formed with the free amino groups of the peptide) and which are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids as acetic, oxalic, tartaric, mandelic, and the like. Salts formed with the free carboxyl groups can also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, 2-ethylamino ethanol, histidine, procaine, and the like.

A vaccine of the subject invention can be administered in a manner compatible with the dosage formulation, and in such amount as will be therapeutically effective and immunogenic. The quantity to be administered can depend on the subject to be treated and the degree of protection desired. Advantageously, methods known to promote mucosal immunity can be combined with systemic immunity promoters to maximize immune responses. Suitable regimes for initial administration and booster shots are also variable, but are typified by an initial administration followed in one or two week intervals by a subsequent injection or other administration.

It should be understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this application and the scope of the appended claims.

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT INFORMATION:

Applicant Name(s): CISTRON BIOTECHNOLOGY, INC.
Street address: Box 2004, 10 Bloomfield Avenue
City: Pine Brook
State/Province: New Jersey
Country: US
Postal code/Zip: 07058
Phone number: (973) 575-1700
Fax number: (973) 575-4854

(ii) TITLE OF INVENTION: IL-1 Muteins: Their Preparation and Method of Use to Inhibit IL-1 Activity

(iii) NUMBER OF SEQUENCES: 1

(iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: Saliwanchik, Lloyd & Saliwanchik
(B) STREET: 2421 N.W. 41st Street, Suite A-1
(C) CITY: Gainesville
(D) STATE: FL
(E) COUNTRY: USA
(F) ZIP: 32606

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(viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: Saliwanchik, David R.
(B) REGISTRATION NUMBER: 31,794
(C) REFERENCE/DOCKET NUMBER: C-201

(ix) TELECOMMUNICATION INFORMATION:
(A) TELEPHONE: 352-375-8100
(B) TELEFAX: 352-372-5800

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 269 amino acids
(B) TYPE: amino acid

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

Met Ala Glu Val Pro Lys Leu Ala Ser Glu Met Met Ala Tyr Tyr Ser
1 5 10 15

Gly Asn Glu Asp Asp Leu Phe Phe Glu Ala Asp Gly Pro Lys Gln Met
20 25 30

Lys Cys Ser Phe Gln Asp Leu Asp Leu Cys Pro Leu Asp Gly Gly Ile
35 40 45

Gln Leu Arg Ile Ser Asp His His Tyr Ser Lys Gly Phe Arg Gln Ala
50 55 60

Ala Ser Val Val Val Ala Met Asp Lys Leu Arg Lys Met Leu Val Pro
65 70 75 80

Cys Pro Gln Thr Phe Gln Glu Asn Asp Leu Ser Thr Phe Phe Pro Phe
85 90 95

Ile Phe Glu Glu Glu Pro Ile Phe Phe Asp Thr Trp Asp Asn Glu Ala
100 105 110

Tyr Val His Asp Ala Pro Val Arg Ser Leu Asn Cys Thr Leu Arg Asp
115 120 125

Ser Gln Gln Lys Ser Leu Val Met Ser Gly Pro Tyr Glu Leu Lys Ala
130 135 140

Leu His Leu Gln Gly Gln Asp Met Glu Gln Gln Val Val Phe Ser Met
145 150 155 160

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

Gly Leu Lys Glu Lys Asn Leu Tyr Leu Ser Cys Val Leu Lys Asp Asp
180 185 190

Lys Pro Thr Leu Gln Leu Glu Ser Val Asp Pro Lys Asn Tyr Pro Lys
195 200 205

Lys Lys Met Glu Lys Arg Phe Val Phe Asn Lys Ile Glu Ile Asn Asn
210 215 220

Lys Leu Glu Phe Glu Ser Ala Gln Phe Pro Asn Trp Tyr Ile Ser Thr
225 230 235 240

Ser Gln Ala Glu Asn Met Pro Val Phe Leu Gly Gly Thr Lys Gly Gly
245 250 255

Gln Asp Ile Thr Asp Phe Thr Met Gln Phe Val Ser Ser
260 265

Claims

1. A composition for modulating an immune response in an animal or human, said composition comprising an immunomodulator encapsulated in a matrix.

2. The composition according to claim 1, wherein said immunomodulator comprises IL-1α or IL-1β polypeptide, or a fragment or variant thereof.

3. The composition according to claim 2, wherein said immunomodulator is an IL-1β polypeptide.

4. The composition according to claim 3, wherein said IL-1β polypeptide is human mature IL-1β.

5. The composition according to claim 4, wherein said IL-1β polypeptide has an amino acid sequence shown in SEQ ID NO. 1.

6. The composition according to claim 1, wherein said composition further comprises a second immunomodulator.

7. The composition according to claim 6, wherein said second immunomodulator is selected from the group consisting of IL-2, IL-4, IL-12, and biologically active fragments and variants thereof.

8. The composition according to claim 1, wherein said composition further comprises an antigenic composition.

9. The composition according to claim 8, wherein said vaccine composition is selected from the group consisting of whole inactivated virus, attenuated virus, recombinant or synthetic polypeptides, haptens, antigens, and immunogens.

10. The composition according to claim 1, wherein said encapsulation matrix is a liposome.

11. The composition according to claim 1, wherein said encapsulation matrix comprises a biocompatible polymer.

12. The composition according to claim 11, wherein said biocompatible polymer is selected from the group consisting of lactic acid, glycolide and glutamic acid.

13. The composition according to claim 1, wherein said matrix comprises a molecule for targeting said encapsulated composition to a target tissue or cell.

14. The composition according to claim 13, wherein said targeting molecule is an Fc portion of immunoglobulin.

15. The composition according to claim 13, wherein said targeting molecule is an antibody that is immunoreactive with a molecule expressed on the surface of said target tissue or cell.

16. The composition according to claim 15, wherein said antibody binds to MHC class II molecules.

17. A method for modulating an immune response of an animal to an antigen, immunogen, or vaccine, said method comprising administering to the animal a composition comprising an immunomodulator encapsulated in a matrix.

18. The method according to claim 17, wherein said immunomodulator comprises an IL-1β polypeptide, an IL-1α polypeptide, or a fragment or variant thereof.

19. The method according to claim 17, wherein said encapsulated immunomodulator is administered prior to administration of said antigen, immunogen, or vaccine.

20. The method according to claim 17, wherein said encapsulated immunomodulator is administered subsequent to administration of said antigen, immunogen, or vaccine.

21. The method according to claim 19, wherein said polypeptide is human mature IL-1β.

22. The method according to claim 17, wherein a second encapsulated immunomodulator is administered.

23. The method according to claim 22, wherein said second immunomodulator is selected from the group consisting of IL-2, IL-4, IL-12, and biologically active fragments and variants thereof.

24. The method according to claim 17, wherein said method further comprises administering a vaccine composition.

25. The method according to claim 24, wherein said vaccine composition is selected from the group consisting of whole inactivated virus, attenuated virus, recombinant or synthetic polypeptides, haptens, antigens, and immunogens.

26. The method according to claim 17, wherein said encapsulation matrix is a liposome.

27. The method according to claim 17, wherein said encapsulation matrix comprises a biocompatible polymer.

28. The method according to claim 27, wherein said biocompatible polymer is selected from the group consisting of lactic acid, glycolide and glutamic acid.

29. The method according to claim 17, wherein said matrix comprises a molecule for targeting said encapsulated composition to a target tissue or cell.

30. The method according to claim 29, wherein said targeting molecule is an Fc portion of immunoglobulin.

31. The method according to claim 29, wherein said targeting molecule is an antibody that is immunoreactive with a molecule expressed on the surface of said target tissue or cell.

32. The method according to claim 31, wherein said antibody binds to MHC class II molecules.

33. The method according to claim 17, wherein said encapsulated immunomodulator is administered parenterally.

34. The method according to claim 17, wherein said encapsulated immunomodulator is administered by intramuscular or subcutaneous injection.