Xavier RJ, Podolsky DK (2007) "Unravelling the pathogenesis of inflammatory bowel disease" *Nature* 448 (7152): 427–34; J. H. Cho (2008) "The genetics and immunopathogenesis of inflammatory bowel disease" *Nature Reviews Immunology* 8, 458-466).

[0018] Anti-inflammatory drugs and immune system suppressants may be used in the treatment of IBD, such as sulfasalazine (Azulfidine™), mesalamine (Asacol™, Rowasa™), corticosteroids (e.g. prednisone), azathioprine (Imuran™), mercaptopurine (Purinethol™), infliximab (Remicade™), adalimumab (Humira™), certolizumab pegol (Cimzia™), methotrexate (Rheumatrex™), cyclosporine (Gengraf™, Neoral™, Sandimmune™) or natalizumab (Tysabri™).

[0019] Alternative treatments for IBD have been suggested, including the use of various biological agents, or treatments that purportedly adjust natural intestinal flora, sometimes called probiotic treatments (US 2007/0258953; US 2008/0003207; WO 2007/076534; WO 2007/136719; WO 2010/099824). It has for example been reported that IBD may be treated with a deliberate infestation of parasitic worms, for example by consumption of the live ova of the Trichuris suis helminth (Summers et al. (2003) "Trichuris suis seems to be safe and possibly effective in the treatment of inflammatory bowel disease". Am. J. Gastroenterol. 98 (9): 2034–41; Büning et al., (2008) "Helminths as governors of inflammatory bowel disease" Gut 57:1182-1183; Weinstock and Elliott (2009) "Helminths and the IBD hygiene hypothesis" Inflamm Bowel Dis. 2009 Jan;15(1):128-33).

SUMMARY OF THE DISCLOSURE

[0019a] In one aspect, provided herein is a use of antigenic determinants from at least one microbial pathogen that is pathogenic in the bone for the manufacture of an anti-inflammatory composition for treating an inflammatory disease of the bone, wherein the microbial pathogen is selected from the group consisting of *Staphylococcus aureus, coagulase-negative staphylococci, Streptococcus pyogenes, Streptococcus pneumoniae, Streptococcus agalactiae, other streptococci spp., Escherichia coli, Pseudomonas spp., Enterobacter spp., Proteus spp. and Serratia spp.*, wherein the anti-inflammatory composition comprises whole killed

bacterial cells, and wherein the anti-inflammatory composition is formulated for administration by a route that is not enteric.

[0019b] In another aspect, provided herein is a use of antigenic determinants from at least one microbial pathogen that is pathogenic in the bone for the manufacture of an anti-inflammatory composition for treating an inflammatory disease of the bone, wherein the microbial pathogen is selected from the group consisting of *Staphylococcus aureus, coagulase-negative staphylococci, Streptococcus pyogenes, Streptococcus pneumoniae, Streptococcus agalactiae, other streptococci spp., Escherichia coli, Pseudomonas spp., Enterobacter spp., Proteus spp. and Serratia spp.*, wherein the anti-inflammatory composition comprises whole killed bacterial cells, and wherein the anti-inflammatory composition is for administration with an effective amount of an anti-inflammatory or immune suppressant medicament.

[0019c] In one aspect, provided herein is a use of antigenic determinants from at least one microbial pathogen that is pathogenic in the bone for the manufacture of an anti-inflammatory composition for treating an inflammatory disease of the bone, wherein the microbial pathogen is *Staphylococcus aureus*, wherein the antiinflammatory composition comprises whole killed bacterial cells, and wherein the inflammatory disease is an arthritis.

[0020] In one example a method of formulating an anti-inflammatory composition for treating a condition characterized by inflammation in a specific organ or tissue is provided. The method involves selecting at least one pathogen that is pathogenic in the specific organ or tissue; producing an antigenic composition comprising antigenic determinants that together are specific for the pathogen; and formulating the antigenic

be formulated for administration by a route that is not enteric. Optionally, the pathogen detailed herein is a bacteria, a virus, a protozoa, a fungus or a helminth. Further, the method may involve killing the pathogen to formulate the antigenic composition as a whole killed pathogen composition. Further, the pathogen may be a member of a species that is endogenous flora of the specific organ or tissue. Further, the pathogen may be an exogenous species.

[0025] In another example, a method of treating an individual for a condition characterized by inflammation in a specific organ or tissue is provided. The method involves administering to the individual an anti-inflammatory composition comprising antigenic determinants. The antigenic determinants are selected or formulated so that together they are specific for at least one pathogen that is pathogenic in the specific organ or tissue. Optionally, the anti-inflammatory composition may be administered at an administration site in successive doses given at a dosage interval of between one hour and one month, over a dosage duration of at least two weeks.

[0026] In another example, use of an anti-inflammatory composition for treating an individual for a condition characterized by inflammation in a specific organ or tissue is disclosed. The anti-inflammatory composition contains antigenic determinants selected or formulated so that together they are specific for at least one microbial pathogen that is pathogenic in the specific organ or tissue.

[0027] In another example, use of an anti-inflammatory composition to formulate a medicament for treating an individual for a condition characterized by inflammation in a specific organ or tissue is disclosed. The anti-inflammatory composition contains antigenic determinants selected or formulated so that together they are specific for at least one microbial pathogen that is pathogenic in the specific organ or tissue.

[0028] Optionally, the uses disclosed herein include those in which the individual has a cancer situated in the organ or tissue. Further, and optionally, the anti-

inflammatory composition may be administered at an administration site in successive doses given at a dosage interval of between one hour and one month, over a duration of at least two weeks.

[0029] In one example, a method of comparing immune responses is provided. The method involves administering to an animal having an organ or tissue a medicament having an antigenic composition having antigenic determinants selected or formulated so that together the antigenic determinants are specific for at least one microbial pathogen that is pathogenic in the organ or tissue, extracting a quantifiable immune sample from the organ or tissue, measuring a characteristic of the immune response in the organ or tissue in the quantifiable immune sample following the administration of the medicament, and, comparing the characteristic of the immune response in the quantifiable immune sample to a corresponding characteristic of the immune response in a reference immune sample obtained from a corresponding organ or tissue. Optionally, the reference immune sample may be obtained from the corresponding organ or tissue in the animal prior to the step of administering the medicament. Optionally, the reference immune sample may be obtained from the corresponding organ or tissue in a second animal. Optionally, the animal may have a cancer situated in the organ or tissue.

[0030] Comparing the characteristic of the immune response may involve comparing, in the quantifiable and reference immune samples, an indication of the numbers of any one or more of the following cells: inflammatory monocytes, macrophages, CD11b+ Gr-1+ cells, dendritic cells, CD11c+ MHC class II+ cells, CD4+ T cells, CD8+ T cells, or NK cells. Optionally, the macrophages may include any one or more of the following: M1-like macrophages or M2-like macrophages. Further, comparing the characteristic of the immune response may involve comparing a shift in an activation state of macrophages. Optionally, the macrophages may shift from being M2-like macrophages to being M1-like macrophages. Further and optionally, the macrophages may shift from being M1-like macrophages to being M2-like macrophages.

[0034] Optionally, the medicament may be administered at an administration site in successive doses given at a dosage interval of between one hour and one month, over a dosage duration of at least one week. Optionally, the medicament may be administered intradermally or subcutaneously. Optionally, the medicament may be administered in a dose so that each dose is effective to cause a visible localized inflammatory immune response at the administration site. Optionally, the medicament may be administered so that visible localized inflammation at the administration site occurs within 1 to 48 hours. Further and optionally, the animal may be a mammal. Optionally, the animal may be a human or a mouse.

[0035] In another example, a method of selecting a therapeutic preparation suitable for treating an individual for a cancer in a specific organ or tissue is provided. The method involves providing an animal having a cancer situated in a specific organ or tissue, providing a test preparation having one or more antigenic determinants of a microbial pathogen which is pathogenic in the corresponding specific organ or tissue in a healthy individual, measuring a characterisic of the immune response in a reference immune sample obtained from the organ or tissue of the animal, administering the test preparation to the animal, measuring a characteristic of the immune response in a quantifiable immune sample obtained from a corresponding organ or tissue of the animal, comparing the characteristic of the immune response in the in the reference and quabtifiable immune samples, and treating an enhanced characterisic of the immune response in the quantifiable immune sample compared to the reference immune sample as an indication of the suitability of the test preparation as a therapeutic preparation. Optionally, the animal is sacrificed before the quantifiable immune sample has been obtained.

[0036] Optionally, comparing the characteristic of the immune response may involve comparing, in the quantifiable and reference immune samples, an indication of the numbers of any one or more of the following cells: inflammatory monocytes, macrophages, CD11b+ Gr-1+ cells, dendritic cells, CD11c+ MHC class II+ cells, CD4+

cells, CD4+ T cells, CD8+ T cells, or NK cells. Optionally, the macrophages may include any one or more of the following: M1-like macrophages or M2-like macrophages. Optionally, the differential gene expression may be produced as a result of a shift in an activation state of the macrophages. Optionally, the macrophages may shift from being M2-like macrophages to being M1-like macrophages. Further and optionally, the macrophages may shift from being M1-like macrophages to being M2-like macrophages.

[0040] In another example, a method of selectively targeting an immune response to a cancerous tissue or an organ in a human subject is provided. The method involves administering to the subject a medicament having an effective amount of a microbial pathogen antigenic composition, wherein the microbial pathogen may be pathogenic in the specific cancerous organ or tissue of the subject and the antigenic composition comprises antigenic determinants that together are specific for the microbial pathogen. Optionally, the antigenic composition may include a whole killed bacterial cell composition. Optionally, the medicament may be administered to the subject in an amount and for a time that is effective to up-regulate an immune response in the cancerous organ or tissue of the subject. Optionally, the method may further involve measuring a characteristic of the immune response. The method also includes treatment of pre-cancerous lesions including, but not limited to, actinic keratosis, cervical dysplasia, and colonic adenomas.

[0041] In another example, a method for treating a human subject for a cancer situated in a tissue or an organ is provided. The method involves administering to the subject a medicament having an effective amount of a microbial pathogen antigenic composition comprising a whole killed bacterial cell composition, wherein the microbial pathogen is pathogenic in the specific organ or tissue of the subject within which the cancer is situated. The medicament may be administered to the subject in an amount and for a time that is effective to modulate an immune response. Optionally, the modulation of the immune response may involve a shift in the activation state of macrophages.

activation state of the macrophages. The macrophages may shift from being M2-like macrophages to being M1-like macrophages. Optionally, the macrophages may shift from being M1-like macrophages to being M2-like macrophages.

[0044] Further and optionally, comparing the characteristic of the immune response may involve identifying, in the quantifiable and reference immune samples, differential gene expression produced by any one or more of the following cells: inflammatory monocytes, macrophages, CD11b+ Gr-1+ cells, dendritic cells, CD11c+ MHC class II+ cells, CD4+ T cells, CD8+ T cells, or NK cells. The macrophages may include any one or more of the following: M1-like macrophages or M2-like macrophages. Optionally, the differential gene expression may be produced as a result of a shift in an activation state of the macrophages. Further and optionally, the macrophages may shift from being M2-like macrophages to being M1-like macrophages. The macrophages may shift from being M1-like macrophages to being M2-like macrophages.

[0045] In another example, a method of monitoring efficacy of a treatment regime in an individual being treated for a cancer in a specific organ or tissue is provided. The method involves measuring a characteristic of an immune response in a post-treatment immune sample obtained from the specific organ or tissue after the individual has been subject to the treatment regime for a period of time, wherein the presence of a characteristic of the immune response which is greater in magnitude than would be expected had the individual not been subject to the treatment regime, is indicative of the efficacy of the treatment regime; and the treatment regime involves administering a preparation comprising one or more antigenic determinants of a microbial pathogen which is pathogenic in the corresponding specific organ or tissue in a healthy subject.

[0046] The method detailed herein may further involve measuring the characteristic of the immune response in a pre-treatment reference sample, wherein the pre-treatment reference sample was obtained from the specific organ or tissue before, at the same time as or after commencement of the treatment regime, but prior to obtaining the post-

[0049] Further and optionally, comparing the characteristic of the immune response may involve identifying, in the reference and immune samples, cytokines produced by any one or more of the following cells: inflammatory monocytes, macrophages, CD11b+ Gr-1+ cells, dendritic cells, CD11c+ MHC class II+ cells, CD4+ T cells, CD8+ T cells, or NK cells. The macrophages may include any one or more of the following: M1-like macrophages or M2-like macrophages. Optionally, the cytokines may be produced as a result of a shift in an activation state of the macrophages. The macrophages may shift from being M2-like macrophages to being M1-like macrophages. Further and optionally, the macrophages may shift from being M1-like macrophages to being M2-like macrophages.

[0050] Optionally, comparing the characteristic of the immune response may involve identifying, in the reference and immune samples, differential gene expression produced by any one or more of the following cells: inflammatory monocytes, macrophages, CD11b+ Gr-1+ cells, dendritic cells, CD11c+ MHC class II+ cells, CD4+ T cells, CD8+ T cells, or NK cells. The macrophages may include any one or more of the following: M1-like macrophages or M2-like macrophages. The differential gene expression may be produced as a result of a shift in an activation state of the macrophages. The macrophages may shift from being M2-like macrophages to being M1-like macrophages. Optionally, the macrophages may shift from being M1-like macrophages to being M2-like macrophages.

[0051] As detailed herein in another example, the disclosure provides methods for formulating an immunogenic composition for treating a cancer situated in a specific organ or tissue in a mammal, such as human patient. The method may include selecting at least one microbial pathogen that is naturally pathogenic in the organ or tissue of the mammal within which the cancer is situated. An antigenic composition may be produced that includes antigenic determinants that together are specific for or characteristic of the microbial pathogen.

[0052] A diagnostic step may be used to identify the specific organ or tissue within which the cancer is situated, prior to producing the antigenic composition targeted to the site of the cancer. The site of the cancer may be a primary site, or a secondary site of metastasis. The antigenic composition may be sufficiently specific that it would be capable of eliciting an immune response in the mammal specific to the microbial pathogen. The antigenic composition may be a bacterial composition, for example derived from a bacterial species or species that are endogenous to the flora of the patient or from an exogenous species or species. In alternative examples, the antigenic composition may be derived from a virus or viruses. Accordingly, the microbial pathogen from which the antigenic composition is derived may be a virus. The microbial pathogen may be killed. In alternative examples, the microbial pathogen may be live or attenuated. Immunogenic compositions of the disclosure may also be formulated or administered with anti-inflammatory modalities, such as an NSAID. The site of administration may be at a site distant from the site of the cancer, for example in an organ or tissue that is not the organ or tissue within which the cancer is situated, for example the skin or subcutaneous tissue.

[0053] The antigenic composition may for example be formulated for subcutaneous injection, intradermal injection or oral administration. In examples for subcutaneous or intradermal injection, the dosing or formulation of the antigenic composition may be adjusted in order to produce a localized immune reaction visible in the skin at the site of administration, for example an area of inflammation from 2mm to 100mm in diameter appearing, for example, 2 - 48 hours after administration and lasting, for example, 2 - 72 hours or longer. The antigenic composition may be formulated for repeated subcutaneous or intradermal administration, for example at alternating successive sites.

[0054] In some examples, the disclosure involves methods of treating a mammal for a cancer situated in a tissue or an organ. In alternative examples, the treatment may anticipate the development of the cancer in the tissue, for example if the site of a

primary tumour suggests the likelihood of metastasis to a particular tissue or organ, then the patient may be prophylactically treated to prevent or ameliorate metastasis to that tissue or organ. The method may include administering to the subject an effective amount of an antigenic composition comprising antigenic determinants that together are specific for at least one microbial pathogen. An example of the disclosure involves the use of a microbial pathogen that is pathogenic in the specific organ or tissue of the mammal within which the cancer is situated. The antigenic composition may be administered, for example by subcutaneous or intradermal injection at an administration site, in successive doses given at a dosage interval, for example of between one hour and one month, over a dosage duration, for example of at least 1 week, 2 weeks, 2 months, 6 months, 1, 2, 3, 4, or 5 years or longer. Each injection dose may for example be metered so that it is effective to cause visible localized inflammation at the administration site, appearing, for example, 1 – 48 hours after injection.

[0055] In another example, methods are provided for treating cancers of a specific organ or tissue in a subject by administering one or more antigens of one or more microbial pathogens, such as bacterial or viral species that are pathogenic in the specific organ or tissue.

[0056] In alternative examples, the pathogenic microbial species may be capable of causing infection naturally, (*i.e.,* without human intervention) in the specific organ or tissue in a healthy subject, or may have caused an infection in the specific organ or tissue in a healthy subject. In alternative examples, the antigen may be administered by administering a whole microbial species. In alternative examples, the method may, for example, include administering at least two or more microbial species, or administering at least three or more microbial species, and the microbes may be bacteria or viruses. In alternative examples, the method may further include administering a supplement or an adjuvant. An example of the disclosure involves

administering antigenic compositions so as to elicit an immune response in said subject.

[0057] In alternative examples, the microbial pathogen in the antigenic composition may be killed, and thus rendered non-infectious. In some examples, the antigenic composition is administered at a site distant from the cancer site, and in selected examples of this kind, methods of the disclosure may be carried out so that they do not produce infection at the cancer site.

[0058] As detailed herein, various examples of the disclosure involve treating cancers. In this context, treatment may be carried out so as to provide a variety of outcomes. For example, treatment may: provoke an immune reaction that is effective to inhibit or ameliorate the growth or proliferation of a cancer; inhibit the growth or proliferation of cancer cells or tumors; cause remission of a cancer; improve quality of life; reduce the risk of recurrence of a cancer; inhibit metastasis of a cancer; or, improve patient survival rates in a patient population. In this context, extending the life expectancy of a patient, or patient population, means to increase the number of patients who survive for a given period of time following a particular diagnosis. In some examples, treatment may be of patients who have not responded to other treatments, such as patients for whom a chemotherapy or surgery has not been an effective treatment. Treatment in alternative examples may for example be before or after onset of cancer. For example prophylactic treatment may be undertaken, for example of patients diagnosed as being at risk of a particular cancer. For example a patient having a genetic or lifestyle predisposition to cancer of a certain tissue or organ may be treated with an immunogenic composition comprising antigenic determinants of a pathogen that is pathogenic in that organ or tissue. Similarly, the prophylactic treatment of metastasis may be undertaken, so that patients having a primary cancer with a propensity to metastasize to a particular tissue or organ may be treated with an immunogenic composition comprising antigenic determinants of a pathogen that is pathogenic in that organ or tissue.

[0059] In another example, a method of treating a cancer situated in a lung in a subject is provided. The method involves administering to the subject an effective amount of an antigen of one or more microbial species that is pathogenic in the lung and administering to the subject an effective amount of a platinum-containing chemotherapeutic agent. The microbial species may be a viral pathogen or a bacterial pathogen or a fungal pathogen.

[0060] The viral pathogen may be, without limitation: influenza, adenovirus, respiratory syncytial virus, or parainfluenza. The bacterial pathogen may be, without limitation: *Streptococcus pneumoniae, Moraxella catarrhalis, Mycoplasma pneumoniae, Klebsiella pneumoniae, Haemophilus influenza, Staphylococcus aureus, Chlamydia pneumoniae*, or *Legionella pneumophila*. The fungal pathogen may be, without limitation: *Aspergillus fumigatus*, *Blastomyces sp., Coccidiodes immitis, Coccidiodes posadasii, Cryptococcus neoformans, Cryptococcus gattii, Fusarium sp., Histoplasma capsulatum, Paecilomyces sp., Paracoccidiodes brasiliensis, Penicillium marneffei, Pneumocystis jiroveci, Pseudallescheria boydii, Scedosporium apiospermum, Rhizopus sp., Mucor sp., Absidia sp., Cunninghamella sp., Scedosporium prolificans, Stachybotrys chartarum, Trichoderma longibrachiatium,* or *Trichosporon sp.* Further, the platinum-containing chemotherapeutic agent may be, without limitation: Cisplatin, carboplatin or oxaliplatin.

[0061] In another example, use of an effective amount of an antigen of one or more microbial species that is pathogenic in the lung is provided to formulate a medicament for use with a platinum-containing chemotherapeutic agent for treating lung cancer in a subject. In another example, use of an effective amount of an antigen of one or more microbial species that is pathogenic in the lung is provided for use with a platinum-containing chemotherapeutic agent for treating lung cancer in a subject. The microbial species may be a viral pathogen or a bacterial pathogen or a fungal pathogen.

[0062] The viral pathogen may be, without limitation: influenza, adenovirus, respiratory syncytial virus, or parainfluenza. The bacterial pathogen may be, without limitation: *Streptococcus pneumoniae, Moraxella catarrhalis, Mycoplasma pneumoniae, Klebsiella pneumoniae, Haemophilus influenza, Staphylococcus aureus, Chlamydia pneumoniae*, or *Legionella pneumophila*. The fungal pathogen may be, without limitation: *Aspergillus fumigatus*, *Blastomyces sp., Coccidiodes immitis, Coccidiodes posadasii, Cryptococcus neoformans, Cryptococcus gattii, Fusarium sp., Histoplasma capsulatum, Paecilomyces sp., Paracoccidiodes brasiliensis, Penicillium marneffei, Pneumocystis jiroveci, Pseudallescheria boydii, Scedosporium apiospermum, Rhizopus sp., Mucor sp., Absidia sp., Cunninghamella sp., Scedosporium prolificans, Stachybotrys chartarum, Trichoderma longibrachiatium,* or *Trichosporon sp.* Further, the platinum-containing chemotherapeutic agent may be, without limitation: Cisplatin, carboplatin or oxaliplatin.

[0063] In another example, an effective amount of an antigen of one or more microbial species that is pathogenic in the lung is provided to formulate a medicament for use with a platinum-containing chemotherapeutic agent for treating lung cancer in a subject. In another example, an effective amount of an antigen of one or more microbial species that is pathogenic in the lung is provided for use with a platinum-containing chemotherapeutic agent for treating lung cancer in a subject. The microbial species may be a viral pathogen or a bacterial pathogen or a fungal pathogen.

[0064] The viral pathogen may be, without limitation: influenza, adenovirus, respiratory syncytial virus, or parainfluenza. The bacterial pathogen may be, without limitation: *Streptococcus pneumoniae, Moraxella catarrhalis, Mycoplasma pneumoniae, Klebsiella pneumoniae, Haemophilus influenza, Staphylococcus aureus, Chlamydia pneumoniae*, or *Legionella pneumophila*. The fungal pathogen may be, without limitation: *Aspergillus fumigatus*, *Blastomyces sp., Coccidiodes immitis, Coccidiodes posadasii, Cryptococcus neoformans, Cryptococcus gattii, Fusarium sp., Histoplasma capsulatum, Paecilomyces sp., Paracoccidiodes brasiliensis, Penicillium marneffei, Pneumocystis*

jiroveci, Pseudallescheria boydii, Scedosporium apiospermum, Rhizopus sp., Mucor sp., Absidia sp., Cunninghamella sp., Scedosporium prolificans, Stachybotrys chartarum, Trichoderma longibrachiatium, or *Trichosporon sp.* Further, the platinum-containing chemotherapeutic agent may be, without limitation: Cisplatin, carboplatin or oxaliplatin.

[0065] In another example, a kit is provided. The kit includes an antigen of one or more microbial species that is pathogenic in the lung, a platinum-containing chemotherapeutic agent; and instructions for providing the antigen and the platinum-containing chemotherapeutic agent to a subject in need thereof. The microbial species may be a viral pathogen or a bacterial pathogen or a fungal pathogen.

[0066] The viral pathogen may be, without limiting the foregoing: influenza, adenovirus, respiratory syncytial virus, or parainfluenza. The bacterial pathogen may be, without limitation: *Streptococcus pneumoniae, Moraxella catarrhalis, Mycoplasma pneumoniae, Klebsiella pneumoniae, Haemophilus influenza, Staphylococcus aureus, Chlamydia pneumoniae*, or *Legionella pneumophila*. The fungal pathogen may be, without limitation: *Aspergillus fumigatus*, *Blastomyces sp., Coccidiodes immitis, Coccidiodes posadasii, Cryptococcus neoformans, Cryptococcus gattii, Fusarium sp., Histoplasma capsulatum, Paecilomyces sp., Paracoccidiodes brasiliensis, Penicillium marneffei, Pneumocystis jiroveci, Pseudallescheria boydii, Scedosporium apiospermum, Rhizopus sp., Mucor sp., Absidia sp., Cunninghamella sp., Scedosporium prolificans, Stachybotrys chartarum, Trichoderma longibrachiatium,* or *Trichosporon sp.* Further, the platinum-containing chemotherapeutic agent may be, without limitation: Cisplatin, carboplatin or oxaliplatin.

[0067] In various examples, the disclosure provides methods for formulating and using an immunogenic composition for treating an IBD. The IBD may for example be an IBD that is symptomatic in one or more regions of the GIT of a human patient, such as Crohn's disease, ulcerative colitis, collagenous colitis, lymphocytic colitis, ischaemic

Claims

1. Use of antigenic determinants from at least one microbial pathogen that is pathogenic in the bone for the manufacture of an anti-inflammatory composition for treating an inflammatory disease of the bone, wherein the microbial pathogen is selected from the group consisting of *Staphylococcus aureus, coagulase-negative staphylococci, Streptococcus pyogenes, Streptococcus pneumoniae, Streptococcus agalactiae, other streptococci spp., Escherichia coli, Pseudomonas spp., Enterobacter spp., Proteus spp. and Serratia spp.*, wherein the anti-inflammatory composition comprises whole killed bacterial cells, and wherein the anti-inflammatory composition is formulated for administration by a route that is not enteric.

2. The use according to claim 1, wherein the anti-inflammatory composition is formulated for administration intradermally or subcutaneously.

3. The use according to claim 1 or 2, wherein the anti-inflammatory composition is for administration with an effective amount of an antiinflammatory or immune suppressant medicament.

4. The use according to claim 3, wherein the anti-inflammatory or immune suppressant medicament is sulfasalazine, mesalamine, a corticosteroid, azathioprine, mercaptopurine, infliximab, adalimumab, certolizumab pegol, methotrexate, cyclosporine or natalizumab.

5. Use of antigenic determinants from at least one microbial pathogen that is pathogenic in the bone for the manufacture of an anti-inflammatory composition for treating an inflammatory disease of the bone, wherein the microbial pathogen is selected from the group consisting of *Staphylococcus aureus, coagulase-negative staphylococci, Streptococcus pyogenes, Streptococcus pneumoniae, Streptococcus agalactiae, other streptococci spp., Escherichia coli, Pseudomonas spp., Enterobacter spp., Proteus spp. and Serratia spp.*, wherein the anti-inflammatory composition comprises whole killed bacterial cells, and wherein the anti-inflammatory composition is for administration with an effective amount of an anti-inflammatory or immune suppressant medicament.

6. The use according to claim 5, wherein the anti-inflammatory or immune suppressant medicament is sulfasalazine, mesalamine, a corticosteroid, azathioprine, mercaptopurine, infliximab, adalimumab, certolizumab pegol, methotrexate, cyclosporine or natalizumab.

7. The use according to any one of claims 1 to 6, wherein the inflammatory disease is selected from the group consisting of temporal arthritis (giant cell arthritis), juvenile arthritis, psoriatic arthritis, reactive arthritis (Reiter's syndrome), rheumatoid arthritis,

enthesitis-related arthritis, juvenile idiopathic arthritis, juvenile rheumatoid arthritis, osteoarthritis and Paget's disease of bone.

8. The use according to any one of claims 1 to 6, wherein the inflammatory disease is an arthritis, and the pathogen is *Staphylococcus aureus*.

9. Use of antigenic determinants from at least one microbial pathogen that is pathogenic in the bone for the manufacture of an anti-inflammatory composition for treating an inflammatory disease of the bone, wherein the microbial pathogen is *Staphylococcus aureus*, wherein the antiinflammatory composition comprises whole killed bacterial cells, and wherein the inflammatory disease is an arthritis.

10. The use according to any one of claims 1 to 9, wherein the antiinflammatory composition comprises antigenic determinants of two or more pathogens that are each pathogenic in the bone.