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 ~~INVENTION~~DISCLOSURE

[0020] In one aspect 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

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.

[0028a] In an aspect, there is provided the use of an anti-inflammatory composition to formulate a medicament for treating an individual for an inflammatory bowel disease (IBD) characterized by inflammation in a region of the gastrointestinal tract (GIT), wherein the anti-inflammatory composition comprises antigenic determinants selected or formulated so that together they are specific for at least one microbial pathogen that is pathogenic in the region of the GIT, and wherein:

the region is a small bowel region, and the pathogen is selected from the group consisting of *Escherichia coli*, *Clostridium difficile*, *Bacteroides fragilis*, *Bacteroides vulgatus*, *Bacteroides thetaiotaomicron*, *Clostridium perfringens*, *Salmonella enteriditis*, *Yersinia enterocolitica*, *Shigella flexneri*, adenoviruses, astroviruses, caliciviruses, noroviruses, rotaviruses, and cytomegalovirus; or,

the region is a colon or rectum region, and the pathogen is selected from the group consisting of *Escherichia coli*, *Clostridium difficile*, *Bacteroides fragilis*, *Bacteroides vulgatus*, *Bacteroides thetaiotaomicron*, *Clostridium perfringens*, *Salmonella enteriditis*, *Yersinia enterocolitica*, *Shigella flexneri*, adenoviruses, astroviruses, caliciviruses, noroviruses, rotaviruses, and cytomegalovirus; or,

the region is an anus region, and the pathogen is selected from the group consisting of E. *coli*, *Streptococcus pyogenes*, *Bacteroides* spp., *Fusobacterium* spp., anaerobic streptococci, *Clostridium* spp., *Enterobacter* spp., *Pseudomonas aeruginosa*, *Treponema pallidum*, and herpes simplex virus; or,

the region is an oral region, and the pathogen is selected from the group consisting of *Prevotella melaninogenicus*, anaerobic streptococci, viridans streptococci, *Actinomyces* spp., *Peptostreptococcus* spp., *Bacteroides* spp., herpes simplex virus, coxsackieviruses, and Epstein-Barr virus; or,

the region is a stomach region, and the pathogen is selected from the group consisting of *Streptococcus pyogenes*, *Helicobacter pylori*, cytomegalovirus, herpes simplex virus, Epstein-Barr virus, rotaviruses, noroviruses, and adenoviruses.

[0029] In one aspect, 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.

[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 aspect, the ~~invention~~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 embodiments, 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 embodiments, the microbial pathogen may be live or attenuated. Immunogenic compositions of the ~~invention~~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 embodiments 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 embodiments, the ~~invention~~disclosure involves methods of treating a mammal for a cancer situated in a tissue or an organ. In alternative embodiments, 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 aspect of the ~~invention~~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 aspect, 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 embodiments, 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 embodiments, the antigen may be administered by administering a whole microbial species. In alternative embodiments, 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 embodiments, the method may further include administering a supplement or an adjuvant. An aspect of the ~~invention~~disclosure involves

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

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

[0058] As detailed herein, various aspects of the ~~invention~~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 embodiments, 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 embodiments 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.

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 aspect, 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 aspects, the ~~invention~~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