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Application Details	
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TITLE OF INVENTION	A SYSTEM FOR PROVIDING AN INTERFACE FOR AN EFFECTIVE COMMUNICATION IN IMPROVING EMPLOYEE MORALE
FIELD OF INVENTION	COMPUTER SCIENCE
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(57) Abstract :
A method of evaluation of a reconstitutable dry suspension to improve the dissolution of poorly water-soluble celecoxib. A poorly aqueous soluble non-ionizable polymer; wherein said nanoparticles have an average size of less than 500 nm; and said nanoparticles comprise a solid core. A COX-2 inhibitor having a solubility in water of less than 1 mg/mL over the pH range of 6.5 to 7.5 at 25°C, wherein at least 90 wt% of said COX. Wet granulating celecoxib or a pharmaceutically acceptable salt thereof and one or more excipients to obtain a wet granulate, wherein said wet granulate does not include amlodipine. The water-soluble polymer carrier is a celecoxib solid dispersion, characterized in that the polyvinylpyrrolidone (PVP). Dissolving celecoxib, a water soluble polymer carrier, and a solubilizer in a solvent to form a solid dispersion solution. Mixing the adsorbent with the solid dispersion solution to form a mixed liquid. The excipient(s) are selected from the group consisting of pharmaceutically acceptable diluents, disintegrants, binding agents, wetting agents and lubricants.

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FORM 2

THE PATENTS ACT, 1970

(39 of 1970)

&

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COMPLETE SPECIFICATION

(See sections 10; rule 13)

TITLE OF THE INVENTION

AN ANALYSIS OF THE ADVANTAGES AND DRAWBACKS OF LIPOSOME-INDUCED INNATE IMMUNE RESPONSES

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AN ANALYSIS OF THE ADVANTAGES AND DRAWBACKS OF LIPOSOME-INDUCED INNATE IMMUNE RESPONSES

BACKGROUND

Technical Field

[0001] The embodiments herein generally relate to method of analyzing the advantages and drawbacks of liposome-induced innate immune responses.

Description of the Related Art

[0002] The immune system is a complex network of cellular and humoral components that act in concert to recognize foreign and potentially dangerous substances in the body and eliminate them in a highly targeted and controlled manner. It can be generally divided into innate and adaptive immune systems. The success of immunomodulatory approaches in the treatment or prevention of various infectious diseases is remarkable. Nevertheless, there may be more diseases that can be addressed using immunotherapeutic approaches.

[0003] New insights into the underlying mechanisms of immune evasion include vaccines, in combination with immune checkpoint inhibitors or other treatments, either directly or indirectly, to enhance the efficacy of therapeutic vaccination, along with combination therapy regimens. Or form the basis of the development of immunomodulatory components. These vaccines or immunomodulatory components consist of tumor-specific CD4 + and CD8 + T cells specific for the target malignancy, which prime or boost an effective adaptive immune response that provides antitumor response and clinical benefit. can do.

[0004] Stimulating an immune response depend largely on mixtures of compounds known to be individually immunomodulatory. Currently, the compounds used in the clinic are batch mixtures of immunostimulants, optionally in combination with antigens, which have been empirically determined to induce innate and adaptive immune responses, respectively. Despite the development of the last century, conventional approaches have resulted in only two FDA-approved immunostimulants: (1) alum, which is a combination of aluminum salts, and (2) monophosphorylate lipid a. While alum has, in particular, an impressive safety record and efficacy in infectious diseases, it is becoming increasingly clear that these agents are not sufficient to induce an effective immune response against more complex diseases.

SUMMARY

[0005] In view of the foregoing, an embodiment herein provides a primary cell that interact with systemically administered liposomes are those of the mononuclear phagocyte system (MPS) such as hepatic Kupffer cells, circulating monocytes, and tissue macrophages. While phagocytic clearance of liposomes is often viewed as unfavorable in terms of drug pharmacokinetics, it has also been successfully exploited as a strategy for delivering iron-based nanoparticles to lymph nodes for imaging of occult metastases in the sentinel (tumor-draining) lymph nodes of prostate cancer patients. This supports that nanoparticles may be useful for delivery of therapies to cells and organs of the MPS. Successful examples include liposomal delivery of clodronate for depletion of tumor associated macrophages.

[0006] In addition to the delivery of drugs, liposomes may also be used for many other purposes through the modification of their composition and cargo. In vaccinology, for

example, liposomes can be formulated with the inclusion of antigens (lipids, nucleic acids, proteins, and peptides), and/or with pathogen-associated molecular patterns (PAMPs), which confer adjuvant properties aimed at modulating the inflammatory microenvironment where T lymphocyte priming occurs (11, 12). At the moment, a number of liposome formulations are in clinical trials as adjuvant for prophylactic as well as therapeutic vaccines against malaria, influenza, tuberculosis (TB), human immunodeficiency virus (HIV), and dengue fever.

[0007] Results are expressed as the average percentage of pentamer positive cells in the population of CD8β positive / CD19 negative cell population, +/− standard deviation. Background staining detected in splenocytes isolated from naive cells was subtracted. Compared to group 3, * p = <0.025, ** p = <0.005. Hemagglutination inhibition (HAI) titer following a single vaccination against rHA as prescribed in the present invention.

[0008] Group 2 mice were treated with 0.5 μg rHA and 2.5 μg polyI: C (vaccine I, present invention) per 50 μl dose formulated as lyophilized liposomes / polyI: C (low) / hydrophobic carrier did. Indices of humoral (IgG1) and cellular (IgG2A) immune responses were measured by ELISA as described herein. For each treatment group, the log10 values of the endpoint antibody titer were averaged, and the standard deviation at each time point was calculated. It is a graph which shows the average tumor volume of the C57BL / 6 mouse | mouth which transplanted HPV16E7 expression C3 cell and was vaccinated as follows after 8 days.

[0009] These and other aspects of the embodiments herein will be better appreciated and understood when considered in conjunction with the following description and the accompanying drawings. It should be understood, however, that the following descriptions, while indicating preferred embodiments and numerous specific details thereof, are given by

way of illustration and not of limitation. Many changes and modifications may be made within the scope of the embodiments herein without departing from the spirit thereof, and the embodiments herein include all such modifications.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] The embodiments herein will be better understood from the following detailed description with reference to the drawings, in which:

[0011] Fig. 1 illustrates a method of analyzing the advantages and drawbacks of liposome-induced innate immune responses according to an embodiment herein; and

[0012] FIG. 2 illustrates an exemplary view of the immune response according to certain embodiments herein.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

[0013] The embodiments herein and the various features and advantageous details thereof are explained more fully with reference to the non-limiting embodiments that are illustrated in the accompanying drawings and detailed in the following description. Descriptions of well-known components and processing techniques are omitted so as to not unnecessarily obscure the embodiments herein. The examples used herein are intended merely to facilitate an understanding of ways in which the embodiments herein may be practiced and to further enable those of skill in the art to practice the embodiments herein. Accordingly, the examples should not be construed as limiting the scope of the embodiments herein.

[0014] Fig. 1 illustrates a method of analyzing the advantages and drawbacks of liposome-induced innate immune responses according to an embodiment herein.

[0015] According to aspects of the invention, liposomal spherical nucleic acids are

provided for use as multivalent immunomodulators. In some aspects, the invention is based on nanostructures comprising a liposome core having a lipid bilayer, wherein an immunostimulant or immunosuppressant is associated with the lipid bilayer, and an oligonucleotide located outside the liposome core.

[0016] In some embodiments, the nanostructure comprises a liposome core having a lipid bilayer, wherein an immunostimulant or immunosuppressant is associated with the lipid bilayer, and an oligonucleotide located outside the liposome core, wherein the oligonucleotide forms an oligonucleotide shell.

[0017] An unidentified mouse gene with significant structural homology to the catalytic domain of human oligoadenylate synthase, cyclic GMP-AMP synthase, was reported to be the enzyme involved in the production of STING-binding CDN in mammalian cells. It was Sun et al. , Science 339 (6121): 786-91, 2013. This enzyme, called cyclic GMP-AMP synthase (cGAS), catalyzes the synthesis of cGAMP from ATP and GTP in the presence of DNA. This cGAMP then functions as a second messenger, binds to STING and activates it. The CDNs produced by these cGASs were structurally different from the bacterially produced CDNs in that they have a unique phosphodiester bond.

[0018] In a first aspect, the present invention provides: When binding to interferon gene stimulator ("STING") and production of STING-dependent type I interferon is measured using at least one human (h) STING allele. , Bis-3 ′, 5′c-di-GMP (ie, 3′3 ′-(G) (G)), bis-3 ′, 5′c-di-AMP (ie, 3′3 ′-(A) (A) or CDA), or one or more of bis-3 ′, 5′c-GMP-AMP (ie 3′3 ′-(G) (A) or cGAMP) (preferably each of them). One or more mono- or di-fluoro substituted bis-3 ', 5' cyclic purine dinucleotides ("mono- or di-F-CDN compounds"), or their prods, which stimulate at a concentration at least 10 times lower than Tsu provided grayed,

pharmaceutically acceptable salts, pharmaceutically acceptable solvates, or a composition comprising a pharmaceutically acceptable hydrate. Preferably, this is described by Ishikawa, H .; , And Barber, G.

[0019] Although liposomes interact extensively with the immune system, and the immune system is a key player in both tumor progression and regression, the impact of liposome-induced immunomodulation on tumor growth has not been systematically studied. Our initial investigations revealed that a liposomal drug carrier, similar to that used for PLD, significant. Together, these results suggest that the protumoral effects of liposomes are dependent on tumor characteristics and not on the C57BL/6 background. Further investigations are warranted to determine the extent to which these findings are generalizable to other tumor models and to cancer patients, and to identify the relationship between the physicochemical parameters of liposomes and their immune-modulatory effects. These insights could have a major impact on the clinical development of liposomal drugs for the treatment of cancer.

[0020] The fate of drugs administered to a living organism varies according to several variables, including distribution, metabolism, and excretion. After a drug enters the systemic circulation, it is not distributed uniformly to the body’s tissues due to differences in organ blood perfusion, tissue affinity, local pH, and permeability of cell membrane. Thus, a significant amount of a given drug does not reach the target cell or organ. The consequence of the uneven distribution is a reduced concentration of drug reaching the target cells and the interaction of the drug with bystander targets. Increasing the dose of the drug helps reaching the therapeutic concentration at the target level and also increases the effects of the drug on other cells, concurring to amplify side or adverse events of drug administration.

[0021] Quinolones were shown to exert a condensing effect on the membrane bilayer and the condensing effect differed among the quinolones: even small differences in their chemical structure were shown to influence their lipophilicity, the consequent capacity to cross cell membranes and to accumulate intracellularly, and the eventual antimicrobial effect (18). Thus, the search of innovative approaches to increase drug transport across the cell membrane or to improve the permeability of small molecule, peptide, and/or protein–drugs to access the cytoplasm is a hot field in pharmacology.

[0022] Thus, variants or derivatives include deletions (including truncations and fragments); insertions and additions such as conservative substitutions, site-specific mutations and allelic variants; and one or more covalently linked to the peptide Modifications including peptoids having non-aminoacyl groups (eg, sugars, lipids, etc.) and post-translational modifications are included. As used herein, the term "conserved amino acid substitution" or "conservative substitution" refers to the substitution of one amino acid with another amino acid at a given position of the peptide, where the substitution is It can be done without substantial loss of functionality. In making such changes, substitution of similar amino acid residues may be made based on the relative similarity of the side chain substituents, such as size, charge, hydrophobicity, hydrophilicity, etc. Such substitutions can be assayed for their effect on peptide function by routine testing.

[0023] FIG. 2 illustrates an exemplary view of the immune response according to certain embodiments herein. In other embodiments, the nanostructure comprises a liposome core having a lipid bilayer, wherein an immunostimulant or immunosuppressant is associated with the lipid bilayer, and an oligonucleotide located outside the liposome core, wherein the oligonucleotide forms an oligonucleotide shell, wherein the oligonucleotide shell comprises

at least one pattern recognition receptor modulating oligonucleotide, wherein the pattern recognition receptor modulating oligonucleotide is a TLR antagonist.

[0024] In another embodiment, the linker is one or more of the following linkers: tocopherols, sphingolipids such as sphingosine, sphingosine phosphate, methylated sphingosine and dihydrosphingosine, ceramides, ceramide phosphate, 1-0 acylceramide, dihydroceramide, 2-hydroxyceramide, sphingomyelin, glycosylated sphingolipids, sulfatides, gangliosides, sphingomyelin, and phytosphingosines and derivatives thereof of various lengths and saturation.

[0025] An oligonucleotide may be a nucleic acid that interacts with a molecule or complex of molecules that, when stimulated, generates an immune response in response to the interaction. The molecule or complex of molecules may be a receptor. In some embodiments, the oligonucleotide may be a Pattern Recognition Receptor (PRR) regulatory oligonucleotide. PRRs are the primitive part of the immune system that contains proteins expressed by cells of the innate immune system to identify pathogen-associated molecular patterns (PAMPs) associated with microbial pathogens or cellular stress, as well as damage-associated molecular patterns (DAMPs) associated with cellular components released during cellular damage. PRRs include, but are not limited to, membrane-bound PRRs, such as receptor kinases, toll-like receptors (TLRs), and C-type lectin receptors (CLRs) (mannose and asialoglycoprotein receptors); cytoplasmic PRRs such as RIG-I like receptor (RLR), RNA helicase, plant PRR and nnrd kinase; and a secreted PRR. PRR regulatory oligonucleotides include, but are not limited to, TLR agonists, agonists or antagonists of RIG-I, transcription factors, cellular translation machinery, cellular transcription machinery, nucleic acid acting enzymes, and autoantigens that bind nucleic acids.

CLAIMS

I/We Claim:

1. A method of analyzing the advantages and drawbacks of liposome-induced innate immune responses, wherein the method comprises:

a liposome core having a lipid bilayer, and an oligonucleotide located outside the liposome core, wherein an immunostimulant is bound to the lipid bilayer, the oligonucleotide comprising an oligonucleotide containing a B-class CpG motif;

pharmaceutically acceptable solvate or a pharmaceutically acceptable hydrate, wherein, R21 and R22 Are independently guanine or adenine bound to the structure via the N9 position, provided that R21 and R22 are not both guanines;

compounds having a 3'3'-RR- (2'F-A) (2'F-A), or it's of medical drugs acceptable salts, pharmaceutically acceptable solvates or pharmaceutically, Hydrate acceptable;

wherein the persistence of stealth liposomes in the circulation facilitated their accumulation in highly vascularized sites, including tumours or inflammatory sites;

the different moieties that can be covalently or non-covalently attached to the liposome surface, antibodies and antibody fragments are the most widely employed, producing immunoliposomes.

Dated 14th day of October 2022

Signature

ABSTRACT

AN ANALYSIS OF THE ADVANTAGES AND DRAWBACKS OF LIPOSOME-INDUCED INNATE IMMUNE RESPONSES

A method of analysing the advantages and drawbacks of liposome-induced innate immune responses. The method comprises a liposome core having a lipid bilayer, and an oligonucleotide located outside the liposome core, wherein an immunostimulant is bound to the lipid bilayer, the oligonucleotide comprising an oligonucleotide containing a B-class CpG motif. Thepharmaceutically acceptable solvate or a pharmaceutically acceptable hydrate, wherein, R21 and R22 Are independently guanine or adenine bound to the structure via the N9 position, provided that R21 and R22 are not both guanine. The plurality of compositions comprising a carrier comprising a continuous phase of liposomes, antigens, polyI: C polynucleotides and a hydrophobic material, and uses thereof.

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(57) Abstract :
The goal of this invention is to get a thorough knowledge of artificial intelligence (AI) capabilities and how they might be used to assess the danger to aerial targets. Software tools that contain AI components are referred to as AI tools. Distinct approaches might be utilised in the same tool and there are many distinct schools of thought on AI. Machine learning (ML) is a key component of many contemporary artificial intelligence techniques. The outcome of an AI tools integration with current infrastructure will then be looked at. The threat assessment procedure will be discussed together with the aspects of the AI tool that it may enhance.

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