[0004] Tolerizing APCs to induce tolerance to a specific antigen is another approach to treat antigen-induced disorders. Such an approach may avoid the drawbacks of non-specific suppression of the immune system associated with immunosuppressants. However, one of the major limitations of tolerizing APCs for therapeutic treatment is the need to remove APCs from a subject's body and tolerize *ex vivo*, and the limited trafficking of these APCs to relevant disease tissues/sites once re-transplanted.

[0005] Thus, there is a need in the art for an immunomodulatory treatment that addresses the shortcomings of known approaches to modify a subject's immune response to a specific antigen, e.g. to treat, prevent and/or ameliorate antigen-induced disorders.

SUMMARY

[0006] The disclosure seeks to address one or more limitations of known art or to provide useful alternatives thereof.

[0006a] In one aspect, the present disclosure refers to an immunomodulatory combination comprising:a lipid conjugate comprising an immunomodulatory agent covalently linked to a lipophilic moiety by a cleavable linkage or through a cleavable linker; and an antigen and/or one or more nucleic acids that encode the antigen, wherein the antigen is a protein, polypeptide, peptide, lipoprotein, glycolipid, polynucleotide, or polysaccharide,wherein the lipid conjugate and the antigen and/or the one or more nucleic acids that encode the antigen are formulated in separate delivery vehicles or co-formulated in the same delivery vehicle.

[0006b] In another aspect, the present disclosure refers to the immunomodulatory combination as disclosed herein, for use in treatment of a subject having an antigen-induced disorder or undesired antigen-driven immune response, optionally wherein the antigen-induced disorder or undesired antigen-driven immune response is selected from: autoimmune diseases (T cell and/or antibody responses to self antigen), allergic diseases (T cell and IgE responses to environmental or food antigens), transplantation (T cell responses against major and minor histocompatibility antigens in donor tissue/organ/cell), anti-drug antibody responses (antibody responses that diminish efficacy of therapeutics), gene/protein replacement therapy (T cell/antibody response against proteins therapeutically replaced in genetic protein deficiencies), optionally wherein the antigen-induced disorder or undesired antigen-driven immune response is selected from: multiple sclerosis, rheumatoid arthritis, myelin oligodendrocyte glycoprotein antibody disorder, vitiligo, type 1 diabetes, primary biliary cholangitis, anti-GBM nephritis/Goodpasture's disease, celiac disease, psoriasis, myasthenia gravis, immune thrombocytopenia purpura, Grave's disease, neuromyelitis optica, pemphigus vulgaris, bullous pemphigoid, cicatricial pemphigoid, lupus including systemic lupus erythematosus SLE, autoimmune liver disease, myositis, Evan's syndrome, transverse myelitis, Guillain-Barré syndrome, warm autoimmune hemolytic anemia, chronic inflammatory demyelinating polyneuropathy, autoimmune dysautonomia, autoimmune angioedema, Hashimoto's thyroiditis, Lambert-Eaton syndrome, peanut/legume allergy, tree nut allergy (antigens from any of cashew, pistachio, hazelnut, walnut, almond), egg allergy, cow's milk allergy, soy allergy, fish allergy, shellfish allergy, sesame allergy, wheat allergy, allergic airway disease, and allergies caused by environmental allergens (antigens from pollen, dust, pet dander, mold and cockroaches).

[0006c] In another aspect, the present disclosure refers to use of the immunomodulatory combination as disclosed herein in the manufacture of a medicament for treating a subject having

an antigen-induced disorder or undesired antigen-driven immune response, wherein the medicament is to be administered to the subject, wherein the antigen, or the one or more nucleic acids encoding the antigen, and the lipid conjugate are to be administered together or sequentially,optionally wherein the antigen-induced disorder or undesired antigen-driven immune response is selected from: autoimmune diseases (T cell and/or antibody responses to self antigen), allergic diseases (T cell and IgE responses to environmental or food antigens), transplantation (T cell responses against major and minor histocompatibility antigens in donor tissue/organ/cell), anti-drug antibody responses (antibody responses that diminish efficacy of therapeutics), or gene/protein replacement therapy (T cell/antibody response against proteins therapeutically replaced in genetic protein deficiencies), optionally wherein the antigen-induced disorder is: multiple sclerosis, rheumatoid arthritis, myelin oligodendrocyte glycoprotein antibody disorder, vitiligo, type 1 diabetes, primary biliary cholangitis, anti-GBM nephritis/Goodpasture's disease, celiac disease, psoriasis, myasthenia gravis, immune thrombocytopenia purpura, Grave's disease, neuromyelitis optica, pemphigus vulgaris, bullous pemphigoid, cicatricial pemphigoid, lupus including systemic lupus erythematosus SLE, autoimmune liver disease, myositis, Evan's syndrome, transverse myelitis, Guillain-Barré syndrome, warm autoimmune hemolytic anemia, chronic inflammatory demyelinating polyneuropathy, autoimmune dysautonomia, autoimmune angioedema, Hashimoto's thyroiditis, Lambert-Eaton syndrome, peanut/legume allergy, tree nut allergy (antigens from any of cashew, pistachio, hazelnut, walnut, almond), egg allergy, cow's milk allergy, soy allergy, fish allergy, shellfish allergy, sesame allergy, wheat allergy, allergic airway disease, or allergies caused by environmental allergens (antigens from pollen, dust, pet dander, mold and cockroaches).

[0007] Various examples disclosed herein relate to an immunomodulatory combination comprising: a lipid conjugate comprising an immunomodulatory agent covalently linked to a lipophilic moiety by a cleavable linkage or through a cleavable linker; and an antigen and/or one or more nucleic acids that encode the antigen, wherein the antigen is a protein, polypeptide, peptide, lipoprotein, glycolipid, polynucleotide, or polysaccharide, wherein the lipid conjugate and the antigen and/or the one or more nucleic acids that encode the antigen are formulated in separate delivery vehicles or co-formulated in the same delivery vehicle. In some examples, the delivery vehicles are lipid nanoparticles and/or liposomes. In some of these examples, the delivery vehicles are lipid nanoparticles that deliver to antigen presenting cells (APCs). In some examples, the antigen or the one or more nucleic acids encoding the antigen is entrapped within a lipid nanoparticle or liposome and has a net charge that is opposite a net charge of a lipid in the lipid nanoparticle, or the antigen is lipophilic and incorporated into a lipid compartment of a lipid nanoparticle or liposome. In other examples, the antigen is hydrophilic and entrapped in a liposome containing an aqueous core.

[0008] In some examples, the lipid conjugate is co-formulated in the same delivery vehicle as the antigen or the one or more nucleic acids that encode the antigen. The immunomodulatory combination may comprise two or more (e.g. two, three, or more than three) lipid conjugates. In

some examples, the lipid conjugate is a first lipid conjugate, and the immunomodulatory combination further comprises a second lipid conjugate, wherein the second lipid conjugate comprises an immunomodulatory agent covalently linked to a lipophilic moiety by a cleavable linkage or through a cleavable linker, wherein the immunomodulatory agent of the second lipid conjugate is different from the immunomodulatory agent of the first lipid conjugate, wherein the first lipid conjugate and the second lipid conjugate are formulated in separate delivery vehicles or are co-formulated in the same delivery vehicle. In some such examples, the immunomodulatory agent of the second lipid conjugate targets a different immune pathway than the immunomodulatory agent of the first lipid conjugate. In some examples, the first lipid conjugate and the second lipid conjugate are co-formulated in the same delivery vehicle.

[0009] In various examples, the immunomodulatory combinations disclosed herein may be used in treatment of a subject having an antigen-induced disorder or undesired antigen-driven immune response, or for use in manufacture of a medicament for treating the subject. This disclosure therefore provides a method for treating a subject having an antigen-induced disorder or undesired antigen-specific immune response comprising administering an immunomodulatory combination defined herein to the subject, wherein the antigen, or the one or more nucleic acids encoding the antigen, and the lipid conjugate are administered together or sequentially.

[0010] According to another example of the disclosure, there is provided a vaccine formulation comprising: at least one prodrug comprising an immunomodulatory agent that is conjugated to a lipid moiety; and at least one antigen and/or a nucleic acid that encodes the antigen, wherein the at least one antigen is a protein, polypeptide, peptide, lipoprotein, glycolipid, polynucleotide, or polysaccharide, wherein the at least one prodrug and the antigen and/or the nucleic acid that encodes the antigen are formulated in separate delivery vehicles or co-formulated in the same delivery vehicles in the formulation.

[0011] According to another example of the disclosure, there is provided a method for treating a subject having an antigen-induced disorder or undesired antigen-driven immune response comprising: administering at least one prodrug comprising an immunomodulatory agent that is conjugated to a lipophilic moiety; and administering at least one antigen and/or a nucleic acid that encodes the antigen, wherein the at least one antigen is a protein, polypeptide, peptide, lipoprotein, glycolipid, polynucleotide, or polysaccharide, wherein the at least one prodrug and the antigen

and/or the nucleic acid that encodes the antigen are formulated separately in delivery vehicles or co-formulated in the same delivery vehicle, and wherein the at least one prodrug and the at least one antigen and/or nucleic acid that encodes the antigen are administered together or sequentially.

[0012] According to another example of the disclosure, there is provided use a prodrug comprising an immunomodulatory agent that is conjugated to a lipophilic moiety to treat a subject having an antigen-induced disorder or undesired antigen-driven immune response in combination with at least one antigen and/or a nucleic acid that encodes the at least one antigen, wherein the at least one antigen is a protein, polypeptide, peptide, lipoprotein, glycolipid, polynucleotide, or polysaccharide, and wherein the at least one prodrug and the antigen and/or the nucleic acid that encodes the antigen are (i) co-formulated in the same delivery vehicles in an at least one formulation, or (ii) formulated in separate delivery vehicles for sequential administration or co-administration to the subject.

[0013] According to another example of the disclosure, there is provided a combination of a prodrug comprising an immunomodulatory agent that is conjugated to a lipophilic moiety and at least one antigen and/or a nucleic acid that encodes the at least one antigen to treat a subject having an antigen-induced disorder or undesired antigen-driven immune response, wherein the at least one antigen is a protein, polypeptide, peptide, lipoprotein, glycolipid, polynucleotide, or polysaccharide, and wherein the at least one prodrug and the antigen and/or the nucleic acid that encodes the antigen are (i) co-formulated in a delivery vehicle, or (ii) formulated in separate delivery vehicles for sequential administration or co-administration to the subject.

[0014] According to a further example of the disclosure, there is provided a formulation comprising: at least two prodrugs comprising an immunomodulatory agent that is conjugated to a lipophilic moiety, wherein the at least two prodrugs are formulated in separate delivery vehicles or co-formulated in the same delivery vehicles in the formulation, and wherein the at least two prodrugs are targeting different immune pathways. Optionally the formulation comprises at least one antigen and/or a nucleic acid that encodes the antigen, wherein the at least one antigen is a protein, polypeptide, peptide, lipoprotein, glycolipid, polynucleotide, or polysaccharide. The antigen or nucleic acid that encodes the antigen may be formulated in a delivery vehicle, including co-formulated with the two prodrugs in one delivery vehicle or formulated in a separate delivery vehicles thereof.

[0015] According to any one of the foregoing aspects of the disclosure, the delivery vehicles may be lipid nanoparticles.

[0016] According to any one of the foregoing aspects or examples of the disclosure, the at least one prodrug may be co-formulated in the same delivery vehicles with the antigen or the nucleic acid that encodes the antigen.

[0017] According to any one of the foregoing aspects or examples of the disclosure, two prodrugs may be present in the formulation and formulated separately or co-formulated in the same delivery vehicles.

[0018] According to any one of the foregoing aspects or examples of the disclosure, the immunomodulatory agent may be a tolerogenic or anti-inflammatory agent.

[0019] According to any one of the foregoing aspects or examples of the disclosure, the immunomodulatory agent may be an immunostimulant or an immunosuppressant.

[0020] Furthermore, according to any one of the foregoing aspects or examples of the disclosure, the immunomodulatory agent of the at least one prodrug may be selected from prednisone, budesonide, prednisolone, methylprednisolone, hydrocortisone, cortisone, betamethasone, budesonide, triamcinolone, flunisolide, beclomethasone, fluticasone, mometasone, fludrocortisone, flumethasone, triamcinolone acetonide, isoflupredone, corticosterone, desoxycortone acetate, desoxycortone enanthate, 11-deoxycorticosterone, 11-deoxycortisol, aldosterone, dexamethasone, calcitriol, acetylsalicylic acid, salicylate, mycophenolic acid, sirolimus, tacrolimus, cholecalciferol, calcifediol, alfacalcidol, calcipotriol, falecalcitriol, maxacalcitol, paricalcitol, doxercalciferol, 22-oxacalcitriol, tacalcitol, eldecalcitol, elocalcitol, inecalcitol, becocalcidiol, seocalcital, ergocalciferol, lexacalcitol, retinoic acid, cyclophosphamide (nitrogen mustards), filgotinib, baricitinib, tofacitinib, ruxolitinib, upadacitinib, oclacitinib, peficitinib, fedratinib, delgocitinib, deucravacitinib, abrocitinib, auranofin, apremilast, azathioprine, chloroquine, hydroxychloroquine, ciclosporin, leflunomide, methotrexate, minocycline, sulfasalazine, salicylic acid, diflunisal, salsalate, naproxen, ibuprofen, oxaprozin, loxoprofen, zaltoprofen, indomethacin, tolmetin, sulindac, etodolac, ketorolac, diclofenac, aceclofenac, bromfenac, nabumetone, piroxicam, meloxicam, tenoxicam, droxicam, lornoxicam, isoxicam, phenylbutazone, celecoxib, firocoxib, parecoxib, etoricoxib, clonixin,

licofelone, MCC950, glyburide, CY-09, tranilast, oridonin, BOT-4-one (2-cyclohexylimino-6-methyl-6,7-dihydro-5H-benzo[1,3]oxathiol-4-one), INF39 (Ethyl 2-(2-chlorobenzyl)acrylate), MNS (3,4-Methylenedioxy-β-nitrostyrene), fenamic acid, beta-hydroxybutyric acid, quercetin, JC-171, ibrutinib, OLT1177, FC11A-2, INF58, JC124, Ethyl 2-((2-chlorophenyl) (hydroxy)methyl)acrylate, or combinations thereof.

[0021] According to any one of the foregoing aspects or examples of the disclosure, two or more antigens and/or nucleic acid encoding the antigens may be present in the formulation and formulated separately or co-formulated in the same delivery vehicles.

[0022] According to any one of the foregoing aspects or examples of the disclosure, the antigen may be a peptide, polypeptide or protein.

[0023] Other objects, features, and advantages of the present disclosure will be apparent to those of skill in the art from the following detailed description and figures.

BRIEF DESCRIPTION OF THE DRAWINGS

[0024] FIG. 1A shows gated plots (gated on live cells) from pancreatic lymph nodes of mice assessed for APC markers, CD11b and CD11c, by flow cytometry 48 hours post-administration of DiO (3,3'-Dioctadecyloxacarbocyanine Perchlorate) labelled lipid nanoparticles (LNPs, DSPC/Chol/DSPE-PEG at 54/45/1 mol:mol). Mice received 2 injections, 24 hours apart, of LNP injected at a dose of 600 mg/kg i.p.

[0025] FIG. 1B shows counts of the DiO positive APCs (gated on CD11b+CD11c+ cells) in the pancreatic lymph nodes of the mice injected with the DiO-labelled LNPs.

[0026] FIG. 1C shows gated plots (gated on live cells) from pancreatic islets of the mice assessed for APC markers, CD11b and CD11c, by flow cytometry 48 hours post-administration of DiO-labelled lipid nanoparticles (DSPC/Chol/DSPE-PEG at 54/45/1 mol:mol).

[0027] FIG. 1D shows counts of the DiO positive APCs (gated on CD11b+CD11c+ cells) in the pancreatic islets of the mice injected with the DiO-labelled LNPs.

[0028] FIG. 2A shows the DiO positive cell counts in islet macrophages (CD11b+CD11c+) from mice injected with PBS control, DSPC/Chol/DSPE-PEG LNP (DSPC/Chol/DSPE-PEG at 54/45/1 mol:mol) or ionizable LNP (A002/DSPC/Chol/PEG-DMG at 50/10/38.5/1.5 mol:mol). Mice were

CLAIMS

1. An immunomodulatory combination comprising:

a lipid conjugate comprising an immunomodulatory agent covalently linked to a lipophilic moiety by a cleavable linkage or through a cleavable linker; and

an antigen and/or one or more nucleic acids that encode the antigen, wherein the antigen is a protein, polypeptide, peptide, lipoprotein, glycolipid, polynucleotide, or polysaccharide,

wherein the lipid conjugate and the antigen and/or the one or more nucleic acids that encode the antigen are formulated in separate delivery vehicles or co-formulated in the same delivery vehicle.

2. The immunomodulatory combination as claimed in claim 1, wherein the delivery vehicles are lipid nanoparticles and/or liposomes,

optionally wherein the delivery vehicles are lipid nanoparticles which deliver to antigen presenting cells (APCs).

3. The immunomodulatory combination as claimed in claim 2, wherein:

the antigen or the one or more nucleic acids encoding the antigen is entrapped within a lipid nanoparticle or liposome and has a net charge that is opposite a net charge of a lipid in the lipid nanoparticle, or

the antigen is lipophilic and incorporated into a lipid compartment of a lipid nanoparticle or liposome, or

wherein the antigen is hydrophilic and entrapped in a liposome containing an aqueous core.

4. The immunomodulatory combination as claimed in any one of claims 1 to 3, wherein the lipid conjugate is co-formulated in the same delivery vehicle as the antigen or the one or more nucleic acids that encode the antigen.

5. The immunomodulatory combination as claimed in any one of claims 1 to 4, wherein the lipid conjugate is a first lipid conjugate, and the immunomodulatory combination further comprises a second lipid conjugate, wherein the second lipid conjugate comprises an

immunomodulatory agent covalently linked to a lipophilic moiety by a cleavable linkage or through a cleavable linker, wherein the immunomodulatory agent of the second lipid conjugate is different from the immunomodulatory agent of the first lipid conjugate, wherein the first lipid conjugate and the second lipid conjugate are formulated in separate delivery vehicles or are co-formulated in the same delivery vehicle,

optionally wherein the immunomodulatory combination comprises a plurality of lipid conjugates, wherein the plurality of lipid conjugates comprise 3, 4, 5, 6, 7, 8, 9, or 10 immunomodulatory agents, wherein each immunomodulatory agent of the plurality of lipid conjugates is different, and wherein each lipid conjugate of the plurality of lipid conjugates is independently formulated in a separate delivery vehicle from the other components of the immunomodulatory combination or is co-formulated with one or more of the other components of the immunomodulatory combination.

6. The immunomodulatory combination as claimed in claim 5, wherein the immunomodulatory agent of the second lipid conjugate targets a different immune pathway than the immunomodulatory agent of the first lipid conjugate.

7. The immunomodulatory combination as claimed in claim 5 or 6, wherein the first lipid conjugate and the second lipid conjugate are co-formulated in the same delivery vehicle.

8. The immunomodulatory combination as claimed in any one of claims 1 to 7, wherein each immunomodulatory agent is a tolerogenic agent or anti-inflammatory agent.

9. The immunomodulatory combination as claimed in any one of claims 1 to 7, wherein each immunomodulatory agent is an immunostimulant or an immunosuppressant.

10. The immunomodulatory combination as claimed in any one of claims 1 to 9, wherein each immunomodulatory agent is independently: a non-steroidal anti-inflammatory drug (NSAID), an inflammasome inhibitor, a Janus kinase (JAK) inhibitor, a corticosteroid, an mTOR inhibitor, a DMARD (disease-modifying antirheumatic drug), a calcineurin inhibitor, or a vitamin D receptor agonist.

11. The immunomodulatory combination as claimed in any one of claims 1 to 9, wherein each immunomodulatory agent is independently prednisone, budesonide, prednisolone, methylprednisolone, hydrocortisone, cortisone, betamethasone, budesonide, triamcinolone,

flunisolide, beclomethasone, fluticasone, mometasone, fludrocortisone, flumethasone, triamcinolone acetonide, isoflupredone, corticosterone, desoxycortone acetate, desoxycortone enanthate, 11-deoxycorticosterone, 11-deoxycortisol, aldosterone, dexamethasone, calcitriol, acetylsalicylic acid, salicylate, mycophenolic acid, sirolimus, tacrolimus, cholecalciferol, calcifediol, alfacalcidol, calcipotriol, falecalcitriol, maxacalcitol, paricalcitol, doxercalciferol, 22-oxacalcitriol, tacalcitol, eldecalcitol, elocalcitol, inecalcitol, becocalcidiol, seocalcital, ergocalciferol, lexacalcitol, retinoic acid, cyclophosphamide (nitrogen mustards), filgotinib, baricitinib, tofacitinib, ruxolitinib, upadacitinib, oclacitinib, peficitinib, fedratinib, delgocitinib, deucravacitinib, abrocitinib, auranofin, apremilast, azathioprine, chloroquine, hydroxychloroquine, ciclosporin, leflunomide, methotrexate, minocycline, sulfasalazine, salicylic acid, diflunisal, salsalate, naproxen, ibuprofen, oxaprozin, loxoprofen, zaltoprofen, indomethacin, tolmetin, sulindac, etodolac, ketorolac, diclofenac, aceclofenac, bromfenac, nabumetone, piroxicam, meloxicam, tenoxicam, droxicam, lornoxicam, isoxicam, phenylbutazone, celecoxib, firocoxib, parecoxib, etoricoxib, clonixin, licofelone, MCC950, glyburide, CY-09, tranilast, oridonin, BOT-4-one (2-cyclohexylimino-6-methyl-6,7-dihydro-5H-benzo[1,3]oxathiol-4-one), INF39 (Ethyl 2-(2-chlorobenzyl)acrylate), MNS (3,4-Methylenedioxy-β-nitrostyrene), fenamic acid, beta-hydroxybutyric acid, quercetin, JC-171, ibrutinib, OLT1177, FC11A-2, INF58, JC124, or Ethyl 2-((2-chlorophenyl) (hydroxy)methyl)acrylate.

12. The immunomodulatory combination as claimed in any one of claims 1 to 11, wherein the antigen is a first antigen, and the immunomodulatory combination further comprises a second antigen or one or more nucleic acids encoding the second antigen, wherein the first antigen is different than the second antigen,

wherein the second antigen or the one or more nucleic acids encoding the second antigen is formulated in a separate delivery vehicle from the other components of the immunomodulatory combination or is co-formulated with one or more of the other components of the immunomodulatory combination,

optionally wherein the immunomodulatory combination comprises a plurality of antigens or comprises one or more nucleic acids encoding the plurality of antigens, or comprises a combination of antigens and antigen-encoding nucleic acid(s) for providing the plurality of antigens, wherein the plurality of antigens comprises 3, 4, 5, 6, 7, 8, 9, or 10 antigens, and each

antigen or antigen-encoding nucleic acid is independently formulated in a separate delivery vehicle from the other components of the immunomodulatory combination or is co-formulated with one or more of the other components of the immunomodulatory combination.

13. The immunomodulatory combination as claimed in claim 12, wherein the one or more nucleic acids encoding the first antigen and the one or more nucleic acids encoding the second antigen are comprised within a single nucleic acid and the first antigen and the second antigen are co-formulated in the same delivery vehicle.

14. The immunomodulatory combination as claimed in any one of claims 1 to 13, for use in treatment of a subject having an antigen-induced disorder or undesired antigen-driven immune response,

optionally wherein the antigen-induced disorder or undesired antigen-driven immune response is selected from: autoimmune diseases (T cell and/or antibody responses to self antigen), allergic diseases (T cell and IgE responses to environmental or food antigens), transplantation (T cell responses against major and minor histocompatibility antigens in donor tissue/organ/cell), anti-drug antibody responses (antibody responses that diminish efficacy of therapeutics), gene/protein replacement therapy (T cell/antibody response against proteins therapeutically replaced in genetic protein deficiencies),

optionally wherein the antigen-induced disorder or undesired antigen-driven immune response is selected from: multiple sclerosis, rheumatoid arthritis, myelin oligodendrocyte glycoprotein antibody disorder, vitiligo, type 1 diabetes, primary biliary cholangitis, anti-GBM nephritis/Goodpasture's disease, celiac disease, psoriasis, myasthenia gravis, immune thrombocytopenia purpura, Grave's disease, neuromyelitis optica, pemphigus vulgaris, bullous pemphigoid, cicatricial pemphigoid, lupus including systemic lupus erythematosus SLE, autoimmune liver disease, myositis, Evan's syndrome, transverse myelitis, Guillain-Barré syndrome, warm autoimmune hemolytic anemia, chronic inflammatory demyelinating polyneuropathy, autoimmune dysautonomia, autoimmune angioedema, Hashimoto's thyroiditis, Lambert-Eaton syndrome, peanut/legume allergy, tree nut allergy (antigens from any of cashew, pistachio, hazelnut, walnut, almond), egg allergy, cow's milk allergy, soy allergy, fish allergy, shellfish allergy, sesame allergy, wheat allergy, allergic airway disease, and allergies caused by environmental allergens (antigens from pollen, dust, pet dander, mold and cockroaches).

15. Use of the immunomodulatory combination as defined in any one of claims 1 to 13 in the manufacture of a medicament for treating a subject having an antigen-induced disorder or undesired antigen-driven immune response, wherein the medicament is to be administered to the subject, wherein the antigen, or the one or more nucleic acids encoding the antigen, and the lipid conjugate are to be administered together or sequentially,

optionally wherein the antigen-induced disorder or undesired antigen-driven immune response is selected from: autoimmune diseases (T cell and/or antibody responses to self antigen), allergic diseases (T cell and IgE responses to environmental or food antigens), transplantation (T cell responses against major and minor histocompatibility antigens in donor tissue/organ/cell), anti-drug antibody responses (antibody responses that diminish efficacy of therapeutics), or gene/protein replacement therapy (T cell/antibody response against proteins therapeutically replaced in genetic protein deficiencies),

optionally wherein the antigen-induced disorder is: multiple sclerosis, rheumatoid arthritis, myelin oligodendrocyte glycoprotein antibody disorder, vitiligo, type 1 diabetes, primary biliary cholangitis, anti-GBM nephritis/Goodpasture's disease, celiac disease, psoriasis, myasthenia gravis, immune thrombocytopenia purpura, Grave's disease, neuromyelitis optica, pemphigus vulgaris, bullous pemphigoid, cicatricial pemphigoid, lupus including systemic lupus erythematosus SLE, autoimmune liver disease, myositis, Evan's syndrome, transverse myelitis, Guillain-Barré syndrome, warm autoimmune hemolytic anemia, chronic inflammatory demyelinating polyneuropathy, autoimmune dysautonomia, autoimmune angioedema, Hashimoto's thyroiditis, Lambert-Eaton syndrome, peanut/legume allergy, tree nut allergy (antigens from any of cashew, pistachio, hazelnut, walnut, almond), egg allergy, cow's milk allergy, soy allergy, fish allergy, shellfish allergy, sesame allergy, wheat allergy, allergic airway disease, or allergies caused by environmental allergens (antigens from pollen, dust, pet dander, mold and cockroaches).