anti-IL-18 receptor monoclonal antibodies, but these reagents suppress IL-1β or IL-18, not NLRP3 and ASC.

[0007] Therefore, there is still a need in the art for specific methods and compounds which are able to suppress NLRs or ASC and to inhibit the formation of inflammasome complex.

SUMMARY OF THE INVENTION

[0008] The inventors of the present invention found that diacerein and its analogs are excellent inhibitors of the expression of ASC and NLRs (especially NLRP3), and accordingly are able to decrease the formation of inflammasome complex. Therefore, diacerein and its analogs can be used for treating and/or preventing disorders mediated by ASC and/or NLRs.

[0009] The primary objective of this disclosure is to provide a method of inhibiting ASC expression, NLRP3 expression, and/or formation of NLRP3 inflammasome complex in a cell, comprising contacting the cell with a compound selected from the group consisting of diacerein, rhein, monoacetylrhein, salts, esters and prodrugs thereof (hereinafter referred to as "diacerein or its analogs").

[00010] Another objective is to provide a method of inhibiting ASC expression, NLRP3 expression, and/or formation of NLRP3 inflammasome complex in a subject in need thereof, comprising administering diacerein or its analogs to said subject.

[00011] Yet a further objective is to provide a method for treatment and/or prevention of a disorder mediated by ASC and/or NLRP3, and/or by formation of NLRP3 inflammasome

complex in a subject in need thereof, comprising administering diacerein or its analogs to said subject.

In one aspect, there is provided the use of a compound selected from the group consisting of diacerein, rhein, monoacetylrhein, salts, esters, and prodrugs thereof, in the manufacture of a medicament for inhibiting ASC expression in a subject in need thereof.

In another aspect, there is disclosed the use of a compound selected from the group consisting of diacerein, rhein, monoacetylrhein, salts, esters, and prodrugs thereof, in the manufacture of a medicament, for inhibiting NLRP3 expression in a subject in need thereof.

In another aspect, there is disclosed the use of a compound selected from the group consisting of diacerein, rhein, monoacetylrhein, salts, esters, and prodrugs thereof, in the manufacture of a medicament, for inhibiting the formation of NLRP3 inflammasome complex in a subject in need thereof.

In another aspect, there is disclosed the use of a therapeutically effective amount of a compound selected from the group consisting of diacerein, rhein, monoacetylrhein, and therapeutically acceptable salts, esters, and prodrugs thereof, in the manufacture of a medicament, for the treatment and/or prevention of a disorder mediated by ASC and/or NLRP3 in a subject in need thereof.

In another aspect, there is disclosed the use of a therapeutically effective amount of a compound selected from the group consisting of diacerein, rhein, monoacetylrhein, and therapeutically acceptable salts, esters, and prodrugs thereof, in the

manufacture of a medicament, for the treatment and/or prevention of a disorder mediated by the formation of NLRP3 inflammasome complex in a subject in need thereof.

[00012] The detailed technology and preferred embodiments implemented for this invention are described in the following paragraphs accompanying the appended drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[00013] **FIG. 1** shows images of ASC and NLRP3 from a fluorescence confocal microscopy after THP-1 cells were stimulated by monosodium urate (MSU) and treated with various doses of rhein;

[00014] **FIG. 2** is a statistical bar graph showing the ASC stain area after THP-1 cells were stimulated by MSU and treated with various dose of rhein; and

[00015] **FIG. 3** is a statistical bar graph showing the NLRP3 stain area after THP-1 cells were stimulated by MSU and treated with various dose of rhein.

DETAILED DESCRIPTION OF THE INVENTION

[00016] The term "therapeutically effective amount," as used herein, refers to an amount that alleviates or reduces one or more symptoms of a disease.

[00017] The term "diacerein or its analogs," as used herein, refers to diacerein, rhein, monoacetylrhein, or a salt or ester or a prodrug thereof.

[00018] The term "prodrug," as used herein, refers to any compound that can be converted into rhein and exerts its physiological function in form of rhein within the body.

What is claimed is:

1. Use of a compound selected from the group consisting of diacerein, rhein, monoacetylrhein, salts, esters, and prodrugs thereof, in the manufacture of a medicament for inhibiting ASC expression in a subject in need thereof.

2. The use of Claim 1, wherein the subject is a human.

3. Use of a compound selected from the group consisting of diacerein, rhein, monoacetylrhein, salts, esters, and prodrugs thereof, in the manufacture of a medicament, for inhibiting NLRP3 expression in a subject in need thereof.

4. The use of Claim 3, wherein the subject is a human.

5. Use of a compound selected from the group consisting of diacerein, rhein, monoacetylrhein, salts, esters, and prodrugs thereof, in the manufacture of a medicament, for inhibiting the formation of NLRP3 inflammasome complex in a subject in need thereof.

6. The use of Claim 5, wherein the subject is a human.

7. Use of a therapeutically effective amount of a compound selected from the group consisting of diacerein, rhein, monoacetylrhein, and therapeutically acceptable salts, esters, and prodrugs

thereof, in the manufacture of a medicament, for the treatment and/or prevention of a disorder mediated by ASC and/or NLRP3 in a subject in need thereof.

8. The use of Claim 7, wherein the disorder is selected from the group consisting of gout, pseudogout, gout flare prophylaxis, obesity-induced insulin resistance, type 2 diabetes, Alzheimer's Disease (AD), age-related macular degeneration (AMD), atherosclerosis, inflammatory bowel disease (IBD), rheumatoid arthritis (RA), cancer, systemic lupus erythematosus (SLE), asthma, allergic asthma, contact hypersensitivity, sunburn, UVB-induced skin damage, essential hypertension, cryopyrin-associated periodic syndromes (CAPS), Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndromes (FCAS), neonatal onset multi-systemic inflammatory disease/chronic infantile neurological cutaneous and articular syndrome (NOMD/CINCA), B-cell non-Hodgkin's lymphoma, acute myocardial infarction, myocardial infarction, allergic rhinitis, nasal polyposis, autoimmune encephalomyelitis (EAE), multiple sclerosis (MS), skin fibrosis in human systemic sclerosis (SSc), hyperhomocysteinemia (hHcys)-associated glomerular sclerosis, end-stage renal disease (ESRD), atherosclerosis, hepatic fibrosis, renal fibrosis, pulmonary fibrosis, chronic pulmonary fibrotic disorders, idiopathic pulmonary fibrosis (IPF), fibrotic lung disease, cystic fibrosis (CF), cardiac fibrosis, pancreatic islet fibrosis, chronic kidney disease (CKD), crystalline nephropathies, chronic obstructive pulmonary disease (COPD), ocular Bechet's disease, uvetitis,

psoriasis, asbestosis, silicosis, malaria, Dengue, bacterial infection, allergic dermatitis, hyperoxic lung injury, conjunctivitis, keratitis, atopic dermatitis, psoriatic arthritis, vitiligo, Crohn's disease, metabolic syndromes linked with obesity, inflammation-associated cancers, hypersensitivity dermatitis, familial Mediterranean fever (FMF), familial Hibernian Fever (FHF), familial cold urticarial (FCU), pyogenic sterile arthritis, pyoderma gangrenosum, acne (PAPA), systemic onset juvenile arthritis, mevalonate kinase deficiency (MKD), Epidermolysis bullosa (EB), Epidermolytic ichthyosis (EI), and Schnitzler's syndrome (SS).

9. The use of Claim 7, wherein the disorder is selected from the group consisting of allergic asthma, contact hypersensitivity, sunburn, UVB-induced skin damage, essential hypertension, cryopyrin-associated periodic syndromes (CAPS), Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndromes (FCAS), neonatal onset multi-systemic inflammatory disease/chronic infantile neurological cutaneous and articular syndrome (NOMD/CINCA), B-cell non-Hodgkin's lymphoma, acute myocardial infarction, myocardial infarction, allergic rhinitis, nasal polyposis, autoimmune encephalomyelitis (EAE), multiple sclerosis (MS), skin fibrosis in human systemic sclerosis (SSc), hyperhomocysteinemia (hHcys)-associated glomerular sclerosis, end-stage renal disease (ESRD), atherosclerosis, hepatic fibrosis, renal fibrosis, pulmonary fibrosis, chronic pulmonary fibrotic disorders, idiopathic pulmonary fibrosis (IPF), fibrotic lung disease, cystic

fibrosis (CF), cardiac fibrosis, pancreatic islet fibrosis, chronic kidney disease (CKD), crystalline nephropathies, chronic obstructive pulmonary disease (COPD), ocular Bechet's disease, uvetitis, psoriasis, asbestosis, silicosis, malaria, Dengue, bacterial infection, allergic dermatitis, hyperoxic lung injury, conjunctivitis, keratitis, atopic dermatitis, psoriatic arthritis, vitiligo, Crohn's disease, metabolic syndromes linked with obesity, inflammation-associated cancers, hypersensitivity dermatitis, familial Mediterranean fever (FMF), familial Hibernian Fever (FHF), familial cold urticarial (FCU), pyogenic sterile arthritis, pyoderma gangrenosum, acne (PAPA), systemic onset juvenile arthritis, mevalonate kinase deficiency (MKD), Epidermolysis bullosa (EB), Epidermolytic ichthyosis (EI), and Schnitzler's syndrome (SS).

10. The use of Claim 7, wherein the medicament causes a decrease in ASC expression and/or NLRP3 expression in the subject.

11. The use of Claim 7, wherein the compound is to be administered at a dose of about 5 to 500 mg per day.

12. The use of Claim 7, wherein the subject is a human.

13. Use of a therapeutically effective amount of a compound selected from the group consisting of diacerein, rhein, monoacetylrhein, and therapeutically acceptable salts, esters, and prodrugs

thereof, in the manufacture of a medicament, for the treatment and/or prevention of a disorder mediated by the formation of NLRP3 inflammasome complex in a subject in need thereof.

14. The use of Claim 13, wherein the disorder is selected from the group consisting of gout, pseudogout, gout flare prophylaxis, obesity-induced insulin resistance, type 2 diabetes, Alzheimer's Disease (AD), age-related macular degeneration (AMD), atherosclerosis, inflammatory bowel diease (IBD), rheumatoid arthritis (RA), cancer, systemic lupus erythematosus (SLE), asthma, allergic asthma, contact hypersensitivity, sunburn, UVB-induced skin damage, essential hypertension, cryopyrin-associated periodic syndromes (CAPS), Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndromes (FCAS), neonatal onset multi-systemic inflammatory disease/chronic infantile neurological cutaneous and articular syndrome (NOMD/CINCA), B-cell non-Hodgkin's lymphoma, acute myocardial infarction, myocardial infarction, allergic rhinitis, nasal polyposis, autoimmune encephalomyelitis (EAE), multiple sclerosis (MS), skin fibrosis in human systemic sclerosis (SSc), hyperhomocysteinemia (hHcys)-associated glomerular sclerosis, end-stage renal disease (ESRD), atherosclerosis, hepatic fibrosis, renal fibrosis, pulmonary fibrosis, chronic pulmonary fibrotic disorders, idiopathic pulmonary fibrosis (IPF), fibrotic lung disease, cystic fibrosis (CF), cardiac fibrosis, pancreatic islet fibrosis, chronic kidney disease (CKD), crystalline nephropathies, chronic obstructive pulmonary disease (COPD), ocular Bechet's disease, uvetitis,

psoriasis, asbestosis, silicosis, malaria, Dengue, bacterial infection, allergic dermatitis, hyperoxic lung injury, conjunctivitis, keratitis, atopic dermatitis, psoriatic arthritis, vitiligo, Crohn's disease, metabolic syndromes linked with obesity, inflammation-associated cancers, hypersensitivity dermatitis, familial Mediterranean fever (FMF), familial Hibernian Fever (FHF), familial cold urticarial (FCU), pyogenic sterile arthritis, pyoderma gangrenosum, acne (PAPA), systemic onset juvenile arthritis, mevalonate kinase deficiency (MKD), Epidermolysis bullosa (EB), Epidermolytic ichthyosis (EI), and Schnitzler's syndrome (SS).

15. The use of Claim 13, wherein the disorder is selected from the group consisting of allergic asthma, contact hypersensitivity, sunburn, UVB-induced skin damage, essential hypertension, cryopyrin-associated periodic syndromes (CAPS), Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndromes (FCAS), neonatal onset multi-systemic inflammatory disease/chronic infantile neurological cutaneous and articular syndrome (NOMD/CINCA), B-cell non-Hodgkin's lymphoma, acute myocardial infarction, myocardial infarction, allergic rhinitis, nasal polyposis, autoimmune encephalomyelitis (EAE), multiple sclerosis (MS), skin fibrosis in human systemic sclerosis (SSc), hyperhomocysteinemia (hHcys)-associated glomerular sclerosis, end-stage renal disease (ESRD), atherosclerosis, hepatic fibrosis, renal fibrosis, pulmonary fibrosis, chronic pulmonary fibrotic disorders, idiopathic pulmonary fibrosis (IPF), fibrotic lung disease, cystic

fibrosis (CF), cardiac fibrosis, pancreatic islet fibrosis, chronic kidney disease (CKD), crystalline nephropathies, chronic obstructive pulmonary disease (COPD), ocular Bechet's disease, uvetitis, psoriasis, asbestosis, silicosis, malaria, Dengue, bacterial infection, allergic dermatitis, hyperoxic lung injury, conjunctivitis, keratitis, atopic dermatitis, psoriatic arthritis, vitiligo, Crohn's disease, metabolic syndromes linked with obesity, inflammation-associated cancers, hypersensitivity dermatitis, familial Mediterranean fever (FMF), familial Hibernian Fever (FHF), familial cold urticarial (FCU), pyogenic sterile arthritis, pyoderma gangrenosum, acne (PAPA), systemic onset juvenile arthritis, mevalonate kinase deficiency (MKD), Epidermolysis bullosa (EB), Epidermolytic ichthyosis (EI), and Schnitzler's syndrome (SS).

16. The use of Claim 13, wherein the medicament causes a decrease in ASC expression and/or NLRP3 expression in the subject.

17. The use of Claim 13, wherein the compound is to be administered at a dose of about 5 to 500 mg per day.

18. The use of Claim 13, wherein the subject is a human.