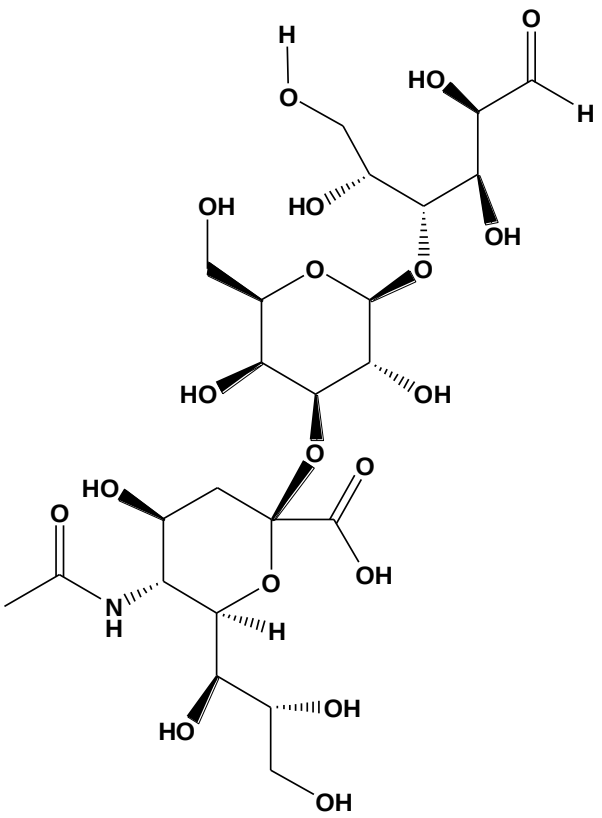
[0008a] In one aspect, the present disclosure refers to use of an oligosaccharide consisting of formula I(e), in the manufacture of a pharmaceutical composition for treating a subject having or suspected of having an inflammatory disease or an autoimmune disorder caused by or associated with macrophage driven chronic inflammation, wherein the oligosaccharide has a structure of Formula I(e):

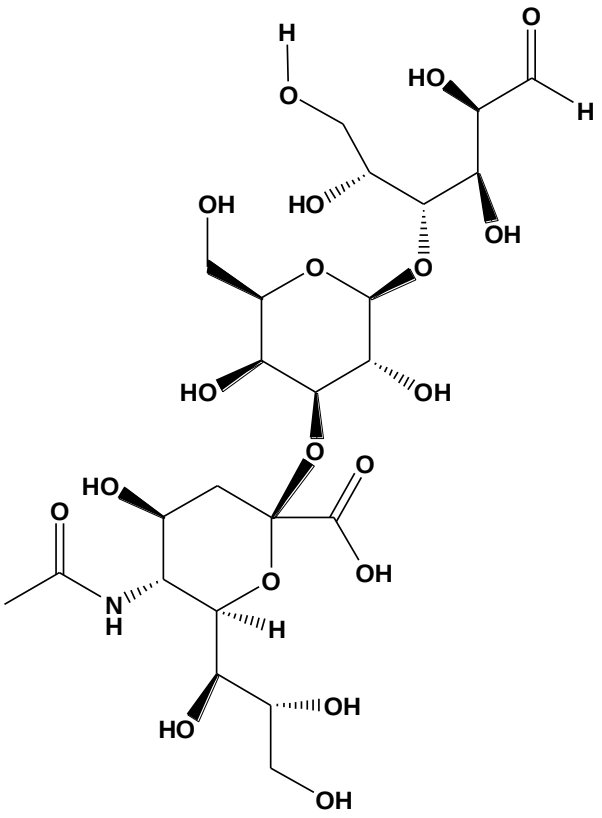


Formula I(e)

or a pharmaceutically acceptable salt, or solvate thereof, wherein the autoimmune disease is selected from the group consisting of autoimmune myocarditis, Dressler's syndrome, postpericardiotomy syndrome, subacute bacterial endocarditis, anti-glomerular basement membrane nephritis, interstitial cystitis, lupus nephritis, autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, antisynthetase syndrome, alopecia areata, autoimmune angioedema, autoimmune progesterone dermatitis, autoimmune urticaria, bullous pemphigoid, cicatricial pemphigoid, dermatitis herpetiformis, discoid lupus erythematosus, epidermolysis bullosa acquisita, erythema nodosum, gestational pemphigoid, hidradenitis suppurativa, lichen planus, lichen sclerosus, linear IgA disease, morphea, pemphigus vulgaris, pityriasis lichenoides et varioliformis acuta, Mucha-Habermann disease, psoriasis, Systemic scleroderma, vitiligo, Addison's disease, autoimmune polyendocrine syndrome type 1, autoimmune polyendocrine syndrome type 2, autoimmune polyendocrine syndrome type 3, autoimmune pancreatitis, diabetes mellitus type 1, autoimmune thyroiditis, Ord's thyroiditis, Graves' disease, autoimmune Oophoritis, endometriosis, Sjögren syndrome,

autoimmune enteropathy, antiphospholipid syndrome, aplastic anemia, autoimmune hemolytic anemia, autoimmune lymphoproliferative syndrome, autoimmune neutropenia, autoimmune thrombocytopenic purpura, cold agglutinin disease, essential mixed cryoglobulinemia, Evans syndrome, pernicious anemia, pure red cell aplasia, thrombocytopenia, adiposis dolorosa, adult-onset Still's disease, ankylosing spondylitis, CREST syndrome, drug-induced lupus, enthesitis-related arthritis, eosinophilic fasciitis, Felty syndrome, IgG4-related disease, juvenile arthritis, chronic Lyme disease, mixed connective tissue disease, palindromic rheumatism, Parry Romberg syndrome, Parsonage-Turner syndrome, psoriatic arthritis, reactive arthritis, relapsing polychondritis, retroperitoneal fibrosis, rhematic fever, rheumatoid arthritis, sarcoidosis, Schnitzler syndrome, systemic lupus erythematosus, undifferentiated connective tissue disease, dermatomyositis, fibromyalgia, inclusion body myositis, myositis, myasthenia gravis, neuromyotonia, paraneoplastic cerebellar degeneration, polymyositis, acute disseminated encephalomyelitis, acute motor axonal neuropathy, anti-N-methyl-D-aspartate receptor encephalitis, Balo concentric sclerosis, Bickerstaff's encephalitis, chronic inflammatory demyelinating polyneuropathy, Guillain-Barrè syndrome, Hashimoto's encephalopathy, idiopathic inflammatory demyelinating diseases, Lambert-Eaton myasthenic syndrome, multiple sclerosis, Oshtoran syndrome, pediatric autoimmune neuropsychiatric disorder associated with Streptococcus, progressive inflammatory neuropathy, restless leg syndrome, stiff person syndrome, sydenham chorea, transverse myelitis, autoimmune retinopathy, autoimmune uveitis, Cogan syndrome, Graves ophthalmopathy, intermediate uveitis, ligneous conjunctivitis, Mooren's ulcer, neuromyelitis optica, opsoclonus myoclonus syndrome, autoimmune inner ear disease, Ménière's disease, Behçet's disease, eosinophilic granulomatosis with polyangiitis, IgA vasculitis, Kawasaki's disease, leukocytoclastic vasculitis, lupus vasculitis, rheumatoid vasculitis, microscopic polyangiitis, polyarteritis nodosa, polymyalgia rheumatica, urticarial vasculitis, vasculitis, and primary immune deficiency, and wherein the inflammatory disease is selected from the group consisting of ankylosing spondylitis, antiphospholipid antibody syndrome, gout, myositis, rheumatoid arthritis, scleroderma, systemic lupus erythematosus, vasculitis, Sjögren's syndrome, asthma, tuberculosis, chronic periodontitis, chronic sinusitis, chronic active hepatitis, Alzheimer's, Parkinson's disease, nephritis, fibromyalgia, atherosclerosis, psoriatic arthritis, eczema, gastritis, sinusitis, seborrheic dermatitis, and Wegener's granulomatosis.

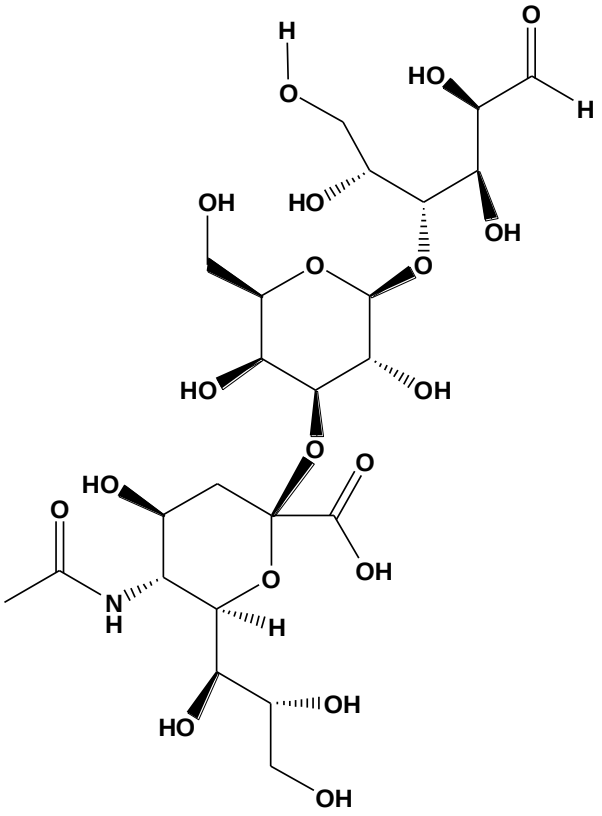
[0008b] In another aspect, the present disclosure refers to use of an oligosaccharide consisting of Formula I(e) in the manufacture of a pharmaceutical composition for attenuating macrophage inflammation and/or suppressing the secretion of pro-inflammatory cytokines in a subject in need thereof, wherein Formula I(e) is:



Formula I(e)

or a pharmaceutically acceptable salt, or solvate thereof.

[0008c] In another aspect, the present disclosure refers to a nutritional supplement consisting of the oligosaccharide of Formula I(e):



Formula I(e)

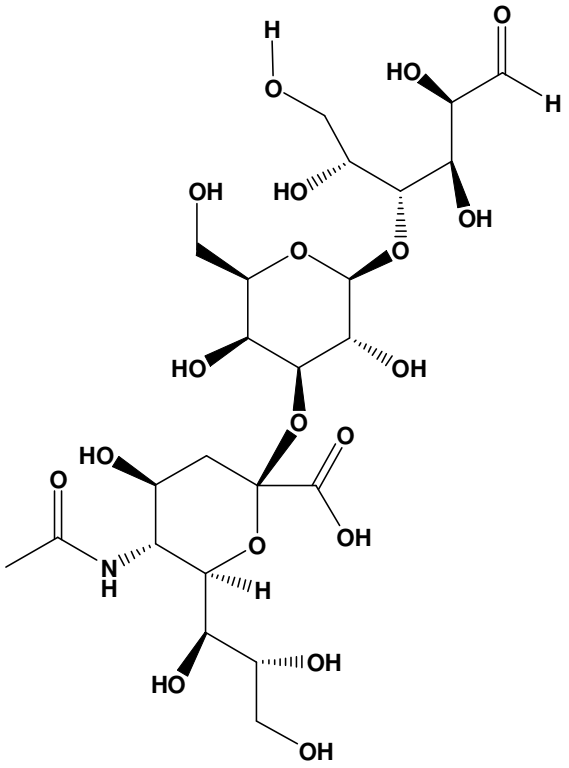
or a pharmaceutically acceptable salt, or solvate thereof, the nutritional supplement having 145 mg/L or greater of the oligosaccharide of Formula I(e).

DESCRIPTION OF DRAWINGS

[0009] **Figure 1A-C** demonstrates that 3'-sialyllactose (3'SL) reduces IL-6 and IL-1β mRNA expression in LPS-activated macrophages. RAW246.7 cells were exposed to LPS either alone or in combination with either pooled human milk oligosaccharides (HMOs), or 3'-sialyllactose (3'SL) or 2'-fucosyllactose (2'FL). After 6 hours, IL-6 **(A)** and IL-1β **(B)** mRNA levels were measured by RT-PCR and are plotted as mean ± standard deviation (n=8) relative the respective

WHAT IS CLAIMED IS:

1. Use of an oligosaccharide consisting of formula I(e), in the manufacture of a pharmaceutical composition for treating a subject having or suspected of having an inflammatory disease or an autoimmune disorder caused by or associated with macrophage driven chronic inflammation, wherein the oligosaccharide has a structure of Formula I(e):



Formula I(e)

or a pharmaceutically acceptable salt, or solvate thereof, wherein the autoimmune disease is selected from the group consisting of autoimmune myocarditis, Dressler's syndrome, postpericardiotomy syndrome, subacute bacterial endocarditis, anti-glomerular basement membrane nephritis, interstitial cystitis, lupus nephritis, autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, antisynthetase syndrome, alopecia areata, autoimmune angioedema, autoimmune progesterone dermatitis, autoimmune urticaria, bullous pemphigoid, cicatricial pemphigoid, dermatitis herpetiformis, discoid lupus erythematosus, epidermolysis bullosa acquisita, erythema nodosum, gestational pemphigoid, hidradenitis

suppurativa, lichen planus, lichen sclerosus, linear IgA disease, morphea, pemphigus vulgaris, pityriasis lichenoides et varioliformis acuta, Mucha-Habermann disease, psoriasis, Systemic scleroderma, vitiligo, Addison's disease, autoimmune polyendocrine syndrome type 1, autoimmune polyendocrine syndrome type 2, autoimmune polyendocrine syndrome type 3, autoimmune pancreatitis, diabetes mellitus type 1, autoimmune thyroiditis, Ord's thyroiditis, Graves' disease, autoimmune Oophoritis, endometriosis, Sjögren syndrome, autoimmune enteropathy, antiphospholipid syndrome, aplastic anemia, autoimmune hemolytic anemia, autoimmune lymphoproliferative syndrome, autoimmune neutropenia, autoimmune thrombocytopenic purpura, cold agglutinin disease, essential mixed cryoglobulinemia, Evans syndrome, pernicious anemia, pure red cell aplasia, thrombocytopenia, adiposis dolorosa, adult-onset Still's disease, ankylosing spondylitis, CREST syndrome, drug-induced lupus, enthesitis-related arthritis, eosinophilic fasciitis, Felty syndrome, IgG4-related disease, juvenile arthritis, chronic Lyme disease, mixed connective tissue disease, palindromic rheumatism, Parry Romberg syndrome, Parsonage-Turner syndrome, psoriatic arthritis, reactive arthritis, relapsing polychondritis, retroperitoneal fibrosis, rhematic fever, rheumatoid arthritis, sarcoidosis, Schnitzler syndrome, systemic lupus erythematosus, undifferentiated connective tissue disease, dermatomyositis, fibromyalgia, inclusion body myositis, myositis, myasthenia gravis, neuromyotonia, paraneoplastic cerebellar degeneration, polymyositis, acute disseminated encephalomyelitis, acute motor axonal neuropathy, anti-N-methyl-D-aspartate receptor encephalitis, Balo concentric sclerosis, Bickerstaff's encephalitis, chronic inflammatory demyelinating polyneuropathy, Guillain-Barrè syndrome, Hashimoto's encephalopathy, idiopathic inflammatory demyelinating diseases, Lambert-Eaton myasthenic syndrome, multiple sclerosis, Oshtoran syndrome, pediatric autoimmune neuropsychiatric disorder associated with Streptococcus, progressive inflammatory neuropathy, restless leg syndrome, stiff person syndrome, sydenham chorea, transverse myelitis, autoimmune retinopathy, autoimmune uveitis, Cogan syndrome, Graves ophthalmopathy, intermediate uveitis, ligneous conjunctivitis, Mooren's ulcer, neuromyelitis optica, opsoclonus

myoclonus syndrome, autoimmune inner ear disease, Ménière's disease, Behçet's disease, eosinophilic granulomatosis with polyangiitis, IgA vasculitis, Kawasaki's disease, leukocytoclastic vasculitis, lupus vasculitis, rheumatoid vasculitis, microscopic polyangiitis, polyarteritis nodosa, polymyalgia rheumatica, urticarial vasculitis, vasculitis, and primary immune deficiency, and wherein the inflammatory disease is selected from the group consisting of ankylosing spondylitis, antiphospholipid antibody syndrome, gout, myositis, rheumatoid arthritis, scleroderma, systemic lupus erythematosus, vasculitis, Sjögren's syndrome, asthma, tuberculosis, chronic periodontitis, chronic sinusitis, chronic active hepatitis, Alzheimer's, Parkinson's disease, nephritis, fibromyalgia, atherosclerosis, psoriatic arthritis, eczema, gastritis, sinusitis, seborrheic dermatitis, and Wegener's granulomatosis.

2. The use of claim 1, wherein the pharmaceutical composition is to be orally administered to the subject.

3. The use of claim 2, wherein the pharmaceutical composition is formulated as a tablet or a capsule.

4. The use of claim 3, wherein the pharmaceutical composition comprises Formula I(e) at 145 mg/L or greater.

5. The use of claim 3, wherein the pharmaceutical composition comprises at least 9% of the oligosaccharide of Formula I(e) of the total oligosaccharides in the pharmaceutical composition.

6. The use of claim 1, wherein the inflammatory disease is selected from the group consisting of atherosclerosis, chronic obstructive pulmonary disease, insulin resistance, type-2 diabetes, obesity, and systemic juvenile idiopathic arthritis.

7. The use of claim 1, wherein the autoimmune disorder or inflammatory disease is rheumatoid arthritis.

8. The use of claim 1, wherein the pharmaceutical composition is to be administered with a therapeutic agent.

9. The use of claim 8, wherein the therapeutic agent is a nonsteroidal anti-inflammatory drug, a glucocorticoid, a biologic response modifier or an opioid.

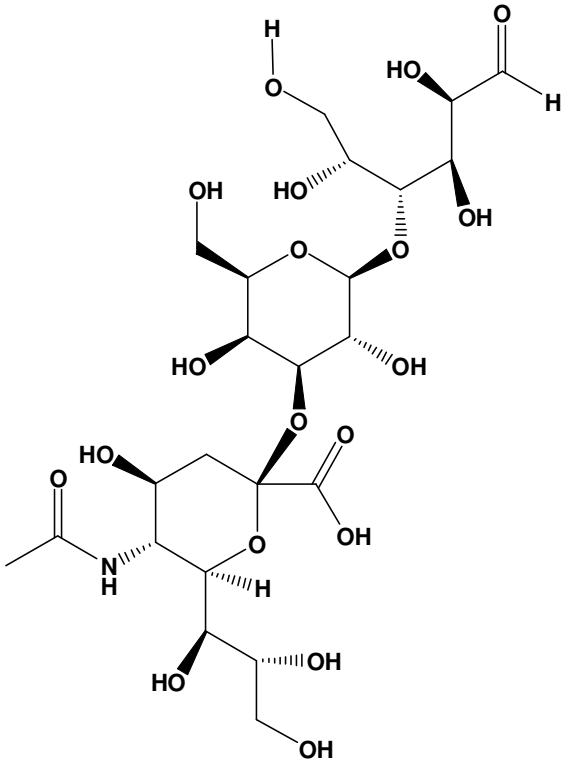
10. The use of claim 9, wherein the nonsteroidal anti-inflammatory drug is selected from the group consisting of Aminophenazone, Ampyrone, Azapropazone, Clofezone, Difenamizole, Famprofazone, Feprazone, Kebuzone, Metamizole, Mofebutazone, Morazone, Nifenazone, Oxyphenbutazone, Phenazone, Phenylbutazone, Propyphenazone, Sulfinpyrazone, Suxibuzone, Aspirin, Aloxiprin, Benorylate, Carbasalate, calcium Diflunisal, Dipyrocetyl, Ethenzamide, Guacetisal, Magnesium salicylate, Methyl salicylate, Salsalate, Salicin, Salicylamide, Salicylic acid (salicylate), Sodium salicylate, Aceclofenac, Acemetacin, Alclofenac, Amfenac, Bendazac, Bromfenac, Bumadizone, Bufexamac, Diclofenac, Difenpiramide, Etodolac, Felbinac, Fenclozic acid, Fentiazac, Indomethacin, Indomethacin farnesil, Isoxepac, Ketorolac, Lonazolac, Oxametacin, Prodolic acid, Proglumetacin, Sulindac, Tiopinac, Tolmetin, Zomepirac, Ampiroxicam, Droxicam, Isoxicam, Lornoxicam, Meloxicam, Piroxicam, Tenoxicam, Alminoprofen, Benoxaprofen, Carprofen, Dexibuprofen, Dexketoprofen, Fenbufen, Fenoprofen, Flunoxaprofen, Flurbiprofen, Ibuprofen, Ibuproxam, Indoprofen, Ketoprofen, Loxoprofen, Miroprofen, Naproxen, Oxaprozin, Pirprofen, Suprofen, Tarenflurbil, Tepoxalin, Tiaprofenic acid, Vedaprofen, Naproxcinod, Azapropazone, Clonixin, Etofenamate, Flufenamic acid, Flunixin, Meclofenamic acid, Mefenamic acid, Morniflumate, Niflumic acid, Tolfenamic acid, Flutiazin, Apricoxib, Celecoxib, Cimicoxib, Deracoxib, Etoricoxib, Firocoxib, Lumiracoxib, Mavacoxib, Parecoxib, Robenacoxib, Rofecoxib, Valdecoxib, Aminopropionitrile, Benzydamine, Chondroitin sulfate, Diacerein, Fluproquazone, Glucosamine, Glycosaminoglycan, Hyperforin, Nabumetone, Nimesulide, Oxaceprol, Proquazone, Superoxide dismutase/Orgotein, and Tenidap.

11. The use of claim 9, wherein the glucocorticoid is selected from betamethasone or prednisone.

12. The use of claim 9, wherein the biological response modifier is selected from the group consisting of hydroxychloroquine, leflunomide, methotrexate, tofacitinib, abatacept, adalimumab, adalimumab-atto, anakinra, etanercept, etanercept-szzs, rituximab, infliximab-dyyb, golimumab, certolizumab pegol, tocilizumab, and sarilumab.

13. The use of claim 9, wherein the opioid is selected from the group consisting of tramadol, oxycontin, oxycodone, fentanyl, morphine, codeine, dihydrocodeine, and actiq.

14. Use of an oligosaccharide consisting of Formula I(e) in the manufacture of a pharmaceutical composition for attenuating macrophage inflammation and/or suppressing the secretion of pro-inflammatory cytokines in a subject in need thereof, wherein Formula I(e) is:



Formula I(e)

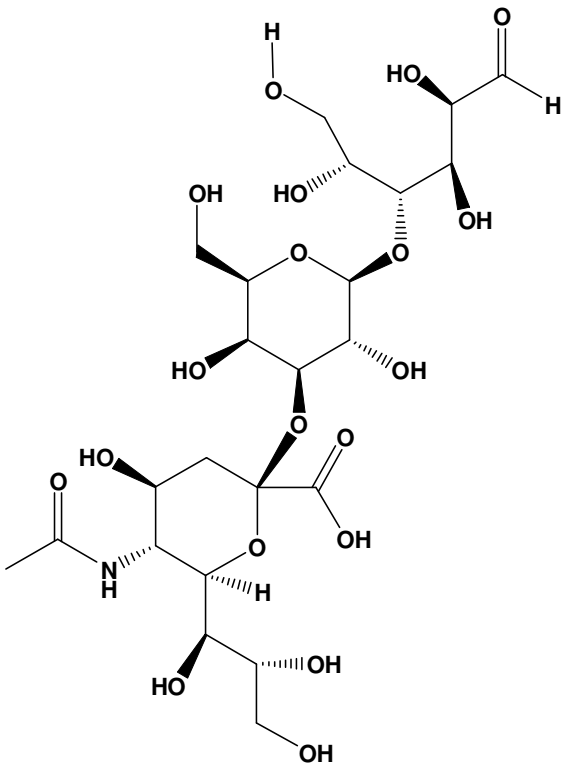
or a pharmaceutically acceptable salt, or solvate thereof.

15. The use of claim 14, wherein the pro-inflammatory cytokines comprise interleukin (IL)-1β and IL-6.

16. The use of claim 1 or 14, wherein the subject is a human subject that is 5 years of age or older.

17. The use of claim 16, wherein the subject is a human subject that 18 years of age or older.

18. A nutritional supplement consisting of the oligosaccharide of Formula I(e):



Formula I(e)

or a pharmaceutically acceptable salt, or solvate thereof, the nutritional supplement having 145 mg/L or greater of the oligosaccharide of Formula I(e).