Only a very limited number of aptamers which could be used to regulate TLR 9 activation in, for example, autoimmune diseases is available at present and their effectiveness and harmlessness for the application in human patients remains to be confirmed. The availability of additional oligonucleotide sequences which inhibit or suppress TLR 9 activation is therefore desired.

Accordingly, it is an object of the present invention to provide new antagonists for the use in therapy of a subject by inhibiting or suppressing the activation of TLR9 in a cell.

Furthermore, it is another object of the present invention to provide a method for inhibiting or suppressing TLR9 activation employing new TLR9 antagonists.

It is also an object of the present invention to provide a pharmaceutical composition and a kit comprising new TLR 9 antagonists.

It is a further object of the present invention to provide a use of novel TLR 9 antagonists for inhibiting or suppressing TLR9 activation.

Summary

This object is solved by the aspects of the present disclosure as specified hereinafter.

In one aspect, the present disclosure refers to use of an aptamer in the manufacture of a medicament for treating a disease or disorder by inhibiting or suppressing the activation of TLR9 in a cell in a subject, wherein the aptamer comprises a nucleic acid sequence of SEQ ID No. 1 (GGT TGG TGT GGT TGG) and/or a nucleic acid sequence being at least 80% identical to SEQ ID No. 1 and wherein the aptamer inhibits or suppresses TLR9 activation, wherein the disease or disorder is characterized by overexpression and/or overactivity of TLR-9 mediated signalling and is selected from an autoimmune disorder, an inflammatory disorder, an autoimmune connective tissue disease (ACTD) and/or a neurodegenerative disorder, preferably the disease or disorder is selected from psoriasis, rheumatoid arthritis, alopecia universalis, acute disseminated encephalomyelitis, Addison's disease, allergy, ankylosing spondylitis, antiphospholipid antibody syndrome, arteriosclerosis, atherosclerosis, autoimmune hemolytic anemia, autoimmune hepatitis, Bullous pemphigoid, Chagas’ disease, chronic obstructive pulmonary disease, coeliac disease, cutaneous lupus erythematosus (CLE), dermatomyositis, diabetes, dilated cardiomyopathy (DCM), endometriosis, Goodpasture's syndrome, Graves' disease, Guillain-Barre syndrome, Hashimoto's disease,

hidradenitis suppurativa, idiopathic thrombocytopenic purpura, inflammatory bowel disease, interstitial cystitis, morphea, multiple sclerosis (MS), myasthenia gravis, myocarditis, narcolepsy, neuromyotonia, pemphigus, pernicious anaemia, polymyositis, primary biliary cirrhosis, rheumatoid arthritis (RA), schizophrenia, Sjogren's syndrome, systemic lupus erythematosus (SLE), systemic sclerosis, temporal arteritis, vasculitis, vitiligo, vulvodynia, Wegener's granulomatosis, traumatic pain, neuropathic pain and acetaminophen toxicity, alternatively wherein the subject is having tumour/cancer, preferably wherein the tumour/cancer is selected from the group consisting of breast cancer, cervical squamous cell carcinoma, gastric carcinoma, glioma, hepatocellular carcinoma, lung cancer, melanoma, prostate cancer, recurrent glioblastoma, recurrent non-Hodgkin lymphoma, colorectal cancer

In another aspect, the present disclosure refers to a method of inhibiting or suppressing the activation of TLR9 in a cell comprising contacting a cell expressing TLR9 with an aptamer, wherein the method is carried out *in vitro/ex vivo* and wherein the aptamer comprises a nucleic acid sequence of SEQ ID No. 1 (GGT TGG TGT GGT TGG) and/or a nucleic acid sequence being at least 80% identical to SEQ ID No. 1 and wherein the aptamer inhibits or suppresses TLR9 activation.

In yet another aspect, the present disclosure refers to use of a pharmaceutical composition comprising an aptamer and at least one pharmaceutically acceptable excipient in the manufacture of a medicament for treating a disease or disorder by inhibiting or suppressing the activation of TLR9 in a cell in a subject, wherein the aptamer comprises a nucleic acid sequence of SEQ ID No. 1 (GGT TGG TGT GGT TGG) and/or a nucleic acid sequence being at least 80% identical to SEQ ID No. 1 and wherein the aptamer inhibits or suppresses TLR9 activation, and wherein the disease or disorder is characterized by overexpression and/or overactivity of TLR-9 mediated signalling and is selected from an autoimmune disorder, an inflammatory disorder, an autoimmune connective tissue disease (ACTD) and/or a neurodegenerative disorder, preferably the disease or disorder is selected from psoriasis, rheumatoid arthritis, alopecia universalis, acute disseminated encephalomyelitis, Addison's disease, allergy, ankylosing spondylitis, antiphospholipid antibody syndrome, arteriosclerosis, atherosclerosis, autoimmune hemolytic anemia, autoimmune hepatitis, Bullous pemphigoid, Chagas' disease, chronic obstructive pulmonary disease, coeliac disease, cutaneous lupus erythematosus (CLE), dermatomyositis, diabetes, dilated cardiomyopathy (DCM), endometriosis, Goodpasture's syndrome, Graves' disease, Guillain-Barre syndrome, Hashimoto's disease, hidradenitis suppurativa, idiopathic thrombocytopenic purpura, inflammatory bowel disease, interstitial cystitis, morphea, multiple sclerosis (MS), myasthenia gravis, myocarditis, narcolepsy, neuromyotonia, pemphigus, pernicious anaemia, polymyositis, primary biliary cirrhosis, rheumatoid arthritis (RA), schizophrenia, Sjogren's syndrome, systemic lupus erythematosus (SLE), systemic sclerosis, temporal arteritis, vasculitis, vitiligo, vulvodynia, Wegener's granulomatosis, traumatic pain, neuropathic pain and acetaminophen toxicity, alternatively wherein the subject is having tumour/cancer, preferably wherein the tumour/cancer is selected from the group consisting of breast cancer, cervical squamous cell carcinoma, gastric carcinoma, glioma, hepatocellular carcinoma, lung cancer, melanoma, prostate cancer, recurrent glioblastoma, recurrent non-Hodgkin lymphoma, colorectal cancer.

According to the first example of the present disclosure, an aptamer is provided for use in therapy of a subject by inhibiting or suppressing the activation of TLR9 in a cell.

Claims

1. Use of an aptamer in the manufacture of a medicament for treating a disease or disorder by inhibiting or suppressing the activation of TLR9 in a cell in a subject, wherein the aptamer comprises a nucleic acid sequence of SEQ ID No. 1 (GGT TGG TGT GGT TGG) and/or a nucleic acid sequence being at least 80% identical to SEQ ID No. 1 and wherein the aptamer inhibits or suppresses TLR9 activation, wherein the disease or disorder is characterized by overexpression and/or overactivity of TLR-9 mediated signalling and is selected from an autoimmune disorder, an inflammatory disorder, an autoimmune connective tissue disease (ACTD) and/or a neurodegenerative disorder, preferably the disease or disorder is selected from psoriasis, rheumatoid arthritis, alopecia universalis, acute disseminated encephalomyelitis, Addison's disease, allergy, ankylosing spondylitis, antiphospholipid antibody syndrome, arteriosclerosis, atherosclerosis, autoimmune hemolytic anemia, autoimmune hepatitis, Bullous pemphigoid, Chagas' disease, chronic obstructive pulmonary disease, coeliac disease, cutaneous lupus erythematosus (CLE), dermatomyositis, diabetes, dilated cardiomyopathy (DCM), endometriosis, Goodpasture's syndrome, Graves' disease, Guillain-Barre syndrome, Hashimoto's disease, hidradenitis suppurativa, idiopathic thrombocytopenic purpura, inflammatory bowel disease, interstitial cystitis, morphea, multiple sclerosis (MS), myasthenia gravis, myocarditis, narcolepsy, neuromyotonia, pemphigus, pernicious anaemia, polymyositis, primary biliary cirrhosis, rheumatoid arthritis (RA), schizophrenia, Sjogren's syndrome, systemic lupus erythematosus (SLE), systemic sclerosis, temporal arteritis, vasculitis, vitiligo, vulvodynia, Wegener's granulomatosis, traumatic pain, neuropathic pain and acetaminophen toxicity, alternatively wherein the subject is having tumour/cancer, preferably wherein the tumour/cancer is selected from the group consisting of breast cancer, cervical squamous cell carcinoma, gastric carcinoma, glioma, hepatocellular carcinoma, lung cancer, melanoma, prostate cancer, recurrent glioblastoma, recurrent non-Hodgkin lymphoma, colorectal cancer.

2. The use according to claim 1, wherein the subject is a mammal, preferably wherein the subject is a human.

3. The use according to any of the preceding claims, wherein the subject to be treated is showing TLR9 overexpression and/or overactivity of TLR9-mediated signaling, wherein TLR9 overexpression and/or overactivity of TLR9-mediated signalling in a subject is given if the TLR9-mediated production of TNFα is increased over a reference value for healthy subjects.

4. The use according to claim 3, wherein the value for the subject to be treated is determined using the method described in the description as “Determination of TLR9 overexpression and/or overactivity of TLR9-mediated signaling by using TLR9-mediated TNFα production as a surrogate parameter”, and is at least 50 pg/ml, preferably at least 75 pg/ml, more preferably at least 100 pg/ml, most preferably at least 125 pg/ml.

5. A method of inhibiting or suppressing the activation of TLR9 in a cell comprising contacting a cell expressing TLR9 with an aptamer, wherein the method is carried out *in vitro/ex vivo* and wherein the aptamer comprises a nucleic acid sequence of SEQ ID No. 1 (GGT TGG TGT GGT TGG) and/or a nucleic acid sequence being at least 80% identical to SEQ ID No. 1 and wherein the aptamer inhibits or suppresses TLR9 activation.

6. The method of claim 5, wherein the method additionally comprises a previous step of testing the cell for TLR9 overexpression and/or overactivity of TLR9-mediated signaling.

7. The method according to claim 5 or 6, wherein the cell is a mammalian cell, preferably wherein the cell is a human cell.

8. Use of a pharmaceutical composition comprising an aptamer and at least one pharmaceutically acceptable excipient in the manufacture of a medicament for treating a disease or disorder by inhibiting or suppressing the activation of TLR9 in a cell in a subject, wherein the aptamer comprises a nucleic acid sequence of SEQ ID No. 1 (GGT TGG TGT GGT TGG) and/or a nucleic acid sequence being at least 80% identical to SEQ ID No. 1 and wherein the aptamer inhibits or suppresses TLR9 activation, and wherein the disease or disorder is characterized by overexpression and/or overactivity of TLR-9 mediated signalling and is selected from an autoimmune disorder, an inflammatory disorder, an autoimmune connective tissue disease (ACTD) and/or a neurodegenerative disorder, preferably the disease or disorder is selected from psoriasis, rheumatoid arthritis, alopecia universalis, acute disseminated encephalomyelitis, Addison's disease, allergy, ankylosing spondylitis, antiphospholipid antibody syndrome, arteriosclerosis, atherosclerosis, autoimmune hemolytic anemia, autoimmune hepatitis, Bullous pemphigoid, Chagas’ disease, chronic obstructive pulmonary disease, coeliac disease, cutaneous lupus erythematosus (CLE), dermatomyositis, diabetes, dilated cardiomyopathy (DCM), endometriosis, Goodpasture's syndrome, Graves' disease, Guillain-Barre syndrome, Hashimoto's disease, hidradenitis suppurativa, idiopathic thrombocytopenic purpura, inflammatory bowel disease, interstitial cystitis, morphea, multiple sclerosis (MS), myasthenia gravis, myocarditis, narcolepsy, neuromyotonia,

pemphigus, pernicious anaemia, polymyositis, primary biliary cirrhosis, rheumatoid arthritis (RA), schizophrenia, Sjogren's syndrome, systemic lupus erythematosus (SLE), systemic sclerosis, temporal arteritis, vasculitis, vitiligo, vulvodynia, Wegener's granulomatosis, traumatic pain, neuropathic pain and acetaminophen toxicity, alternatively wherein the subject is having tumour/cancer, preferably wherein the tumour/cancer is selected from the group consisting of breast cancer, cervical squamous cell carcinoma, gastric carcinoma, glioma, hepatocellular carcinoma, lung cancer, melanoma, prostate cancer, recurrent glioblastoma, recurrent non-Hodgkin lymphoma, colorectal cancer.