Claims

1. JNK inhibitor, selected from the group consisting of:

a) a JNK inhibitor, which comprises an inhibitory (poly-)peptide sequence according to the following general formula:

X1-X2-X3-R-X4-X5-X6-L-X7-L-X8 (SEQ ID NO: 1),

wherein X1 is an amino acid selected from amino acids R, P, Q and r,
wherein X2 is an amino acid selected from amino acids R, P, G and r,
wherein X3 is an amino acid selected from amino acids K, R, k and r,
wherein X4 is an amino acid selected from amino acids P and K,
wherein X5 is an amino acid selected from amino acids T, a, s, q, k or is absent,
wherein X6 is an amino acid selected from amino acids T, D and A,
wherein X7 is an amino acid selected from amino acids N, n, r and K; and
wherein X8 is an amino acid selected from F, f and w, and
wherein an amino acid residue given in capital letters indicates an L-amino acid, while an amino acid residue given in small letters indicates a D amino acid residue,

with the proviso that at least one of the amino acids selected from the group consisting of X1, X2, X3, X5, X7 and X8 is/are a D-amino acid(s), and

b) a JNK inhibitor which comprises an inhibitory (poly-)peptide sequence sharing at least at least 80% sequence identity with SEQ ID NO: 1 as defined in a),
with the proviso that with respect to SEQ ID NO: 1 such inhibitory (poly-)peptide sequence sharing sequence identity with SEQ ID NO: 1 maintains the L-arginine (R) residue of SEQ ID NO: 1 at position 4 and the two L-leucine (L) residues of SEQ ID NO: 1 at positions 8 and 10 and that at least one of the remaining amino acids in said sequence sharing at least at least 80% sequence identity with SEQ ID NO: 1 is a D-amino acid,

for use in a method of treatment of the human or animal body by therapy.

2. JNK inhibitor for use according to claim 1, wherein at least one of the amino acids selected from the group consisting of X3, X5, X7 and X8 is/are a D-amino acid(s).

3. JNK inhibitor for use according to claim 1 or 2, wherein the JNK inhibitor comprises an inhibitory (poly-)peptide sequence sharing at least 80% sequence identity with a sequence selected from any one of SEQ ID NOs: 2-27.

4. JNK inhibitor for use according to anyone of the preceding claims, wherein the inhibitory (poly-)peptide sequence is selected from anyone of SEQ ID NOs: 2-27.

5. JNK inhibitor for use according to anyone of the preceding claims, wherein the JNK inhibitor comprises SEQ ID NO: 8 or an inhibitory (poly-)peptide sequence sharing at least 80% sequence identity with SEQ ID NO: 8.

6. JNK inhibitor for use according to anyone of the preceding claims, wherein the JNK inhibitor comprises a transporter sequence.

7. JNK inhibitor for use according to claim 6, wherein the inhibitory (poly-)peptide sequence and the transporter sequence overlap.

8. JNK inhibitor for use according to claim 6 or 7, wherein the transporter sequence comprises a sequence of alternating D- and L-amino acids according to anyone of SEQ ID NOs: 28-30.

9. JNK inhibitor for use according to anyone of claims 6-8, wherein said transporter sequence is selected from any one of SEQ ID NOs: 31-170.

10. JNK inhibitor for use according to anyone of claims 6-9, wherein said transporter sequence is selected from any one of SEQ ID NOs: 31-34, 46, 47 and 52-151.

11. JNK inhibitor for use according to anyone of claims 6-10, wherein said transporter sequence is positioned directly N-terminal or directly C-terminal of the inhibitory (poly-)peptide sequence.

12. JNK inhibitor for use according to anyone of claims 6-11, wherein the JNK inhibitor comprises

    a) a sequence according to any one of SEQ ID NOs: 171-190, or

b) a sequence sharing at least 50% sequence identity with at least one of SEQ ID NOs: 171-190, with the proviso that said sequence sharing sequence identity anyone of SEQ ID NOs: 171-190:

i) maintains the L-arginine (R) residue on position 4 in its sequence stretch corresponding to SEQ ID NO: 1,

ii) maintains the two L-leucine (L) in its sequence stretch corresponding to SEQ ID NO: 1, and

iii) exhibits at least one D-amino acid at positions X1, X2, X3, X5, X7 or X8 in its sequence stretch corresponding to SEQ ID NO: 1.

13. JNK inhibitor for use according to anyone of claims 6-12, wherein the JNK inhibitor comprises

a) the sequence of SEQ ID NO: 172 or

b) a sequence sharing 50% sequence identity with SEQ ID NO: 172, with the proviso that said sequence sharing 50% sequence identity with SEQ ID NO: 172

i) maintains the L-arginine (R) residue on position 4 in its sequence stretch corresponding to SEQ ID NO: 1,

ii) maintains the two L-leucine (L) in its sequence stretch corresponding to SEQ ID NO: 1, and

iii) exhibits at least one D-amino acid at positions X1, X2, X3, X5, X7 or X8 in its sequence stretch corresponding to SEQ ID NO: 1.

14. JNK inhibitor comprising:

a) an inhibitory (poly-)peptide comprising a sequence selected from the group of sequences consisting of RPTTLNLF (SEQ ID NO: 191), KRPTTLNLF (SEQ ID NO: 192), RRPTTLNLF and/or RPKRPTTLNLF (SEQ ID NO: 193), and

b) a transporter sequence selected from SEQ ID NOs: 31-34 and 46-151,

for use in a method for treatment of the human or animal body by therapy.

15. JNK inhibitor comprising the sequence of SEQ ID NO: 194 or 195 for use in a method for treatment of the human or animal body by therapy.

16. JNK inhibitor for use according to any one of claims 1 to 61, wherein said method is for treatment of the human body by therapy.

17. JNK inhibitor for use according to any one of claims 1 to 61, wherein said JNK inhibitor is administered intravenously, intramuscularly, subcutaneously, intradermally, transdermally, enterally, orally, rectally, topically, nasally, locally, intranasally, epidermally, by patch delivery, by instillation, intravitreally, subconjunctivally and/or intratympanically.

18. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of diseases and/or disorders selected from inflammatory diseases, diseases of the eye, diseases of the bone, neural diseases, neuronal diseases, neurodegenerative diseases, diseases of the skin, immune and/or autoimmune diseases, diseases of the eye, diseases of the mouth, metabolic diseases, cardiovascular diseases, proliferative diseases, diseases of the ear, diseases of the intestine, and/or diseases of the respiratory system.

19. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of diseases and/or disorders selected from inflammatory diseases, acute inflammation, chronic inflammation, inflammation in the eye, inflammation in the mouth, inflammation of the respiratory system, inflammation of the lung, inflammation of the skin, inflammation within the cardiovascular system, inflammation of the brain, inflammation in the ear, mucositis, stomatitis, peri-implantitis, retinitis, chorioiditis, keratoconjunctivitis sicca, inflammatory bowel diseases (IBD), uveitis, anterior uveitis, intermediate uveitis, posterior uveitis, periodontitis, COPD, asthma, pulpitis, rheumatoid arthritis, osteoarthritis, Crohn's disease, psoriatic arthritis, vasculitis, interstitial cystitis; acute inflammation at a site of infection or wound, meningitis, encephalitis, pneumonia, pharyngitis, tonsillitis, otitis, otitis media, vasculitis, synovitis, enteritis, Crohn's disease, ulcerative colitis and graft rejection.

20. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of diseases and/or disorders selected from ear diseases, diseases of the inner ear, hearing loss, acute hearing loss, damaged hair cell stereocilia, hair cell apoptosis, noise trauma, otitis and otitis media.

21. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of diseases and/or disorders selected from metabolic disorders, diabetes, diabetes type 1, diabetes type 2, Fabry disease, Gaucher disease, hypothermia, hyperthermia, hypoxia, lipid histiocytosis, lipidoses, metachromatic leukodystrophy, mucopolysaccharidosis, Niemann Pick disease, obesity, and Wolman's disease.

22. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of diseases and/or disorders selected from Alexander disease, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), apoplexy, Ataxia Telangiectasia, cut or otherwise disrupted axons, axotomy, brain lesions, CMT (Charcot-Marie-Tooth), corticobasal degeneration, dementia, diseases or disorders of the nervous system, dystonia, epilepsy, Farber's disease, Friedreich ataxia (SCA), gangliosidoses, Guillain-Barré syndrome, hereditary spastic paraplegia, Hirschsprung's disease, human immunodeficiency virus dementia, Huntington's disease, infarct of the brain, ischemic stroke, Krabbe disease, Lennox Gastaut Syndrome, lissencephaly, multiple sclerosis, myelodysplastic syndromes, myelopathy, AIDS-related neurodegenerative diseases, neurofibromatosis type 2 (NF-2), neurolatyerism, neuronal apoptosis, neuronal death, neuropathic pain, neuropathy, chemotherapy induced neuropathy, diabetes induced neuropathy, NMDA-induced neurotoxicity, pain, Parkinson's disease, parkinsonism, Pick's Disease, polyneuropathy, progressive supranuclear palsy, Sandhoff disease, spina bifida, stroke, Tay Sachs, TBI (diffuse axonal injury), treatment of dark neurone induced for example by an inflammatory pain, West Syndrome and spinal muscular atrophy.

23. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of diseases and/or disorders selected from autoimmune diseases of the CNS, auto-inflammatory diseases, Celiac disease; Sjogren's syndrome and systemic lupus erythematosus.

24. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of diseases and/or disorders selected from arthritis, disc herniation, fibrodysplasia ossificans progressiva (FOP), osteoarthritis, osteopetrosis, osteoporosis, diabetes induced osteoporosis, Paget's Disease and rheumatoid arthritis.

25. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of diseases and/or disorders selected from psoriasis and lupus erythematosus.

26. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of diseases and/or disorders selected from age-related macular degeneration (AMD); angioid streaks; anterior ischemic optic neuropathy; anterior uveitis; cataract, in particular age related cataract; central exudative chorioretinopathy; central serous chorioretinopathy; chalazion; chorioderemia; chorioiditis; choroidal sclerosis; conjunctivitis; cyclitis; diabetic retinopathy; dry eye syndrome; endophthalmitis;

episcleritis; eye infection; fundus albipunctatus; gyrate atrophy of choroid and retina; hordeolum; inflammatory diseases of the blephara; inflammatory diseases of the choroid; inflammatory diseases of the ciliary body; inflammatory diseases of the conjunctiva; inflammatory diseases of the cornea; inflammatory diseases of the iris; inflammatory diseases of the lacrimal gland; inflammatory diseases of the orbital bone; inflammatory diseases of the sclera; inflammatory diseases of the vitreous body; inflammatory diseases of the uvea; inflammatory diseases of the retina; intermediate uveitis; irititis; keratitis; Leber's disease; multifocal choroiditis; myositis of the eye muscle; neovascular maculopathy (e.g. caused by high myopia, tilted disc syndrome, choroidal osteoma or the like); NMDA induced retinotoxicity; non-chronic or chronic inflammatory eye diseases; Oguchi's disease; optic nerve disease; orbital phlegmon; panophtalmitis; panuveitis; post caspule opacification; posterior capsule opacification (PCO) (a cataract after-surgery complication); posterior uveitis; proliferative vitreoretinopathy; retinal artery occlusion; retinal detachment, retinal diseases; retinal injuries; retinal macroaneurysm; retinal pigment epithelium detachment; retinal vein occlusion; retinitis; retinitis pigmentosa; retinitis punctata albescens; retinopathy, in particular retinopathy of prematurity and diabetic retinopathy; scleritis; Stargardt's disease; treatment of inflamed ocular wounds and/or ocular wound edges; treatment of intraocular inflammation after eye surgery or trauma; uveitis; and vitelliform macular dystrophy.

27. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of diseases and/or disorders selected from periodontitis, in particular chronic periodontitis; mucositis, oral desquamative disorders, oral liquen planus, pemphigus vulgaris, peri-implantitis, pulpitis; stomatitis; and temporomandibular joint disorder.

28. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of diseases and/or disorders selected from cancer and tumor diseases, acusticus neurinoma lung carcinomas; acute lymphocytic leukemia (L1, L2, L3); acute lymphoid leukaemia (ALL); acute myelogenous leukemia (AML); adenocarcinomas; anal carcinoma; bronchial carcinoma; cervix carcinoma; cervical cancer; astrocytoma; basalioma; cancer with Bcr-Abl transformation; bladder cancer; blastomas; bone cancer; brain metastases; brain tumours; breast cancer; Burkitt's lymphoma; carcinoids; cervical cancer; chronic lymphocytic leukaemia (CLL); chronic myeloid leukaemia (CML); colon cancer; colon carcinoma; corpus carcinoma; craniopharyngeomas; CUP syndrome; virus-induced tumours; EBV-induced B cell lymphoma; endometrium carcinoma; erytholeukemia (M6); esophagus cancer; gallbladder cancer; gastrointestinal cancer; gastrointestinal stromal

tumors; gastrointestinal tumours; genitourinary cancer; glaucoma; glioblastoma; gliomas; head/neck tumours; hepatitis B-induced tumours; hepatocell carcinomas; hepatomas; herpes virus-induced tumours; Hodgkin's syndrome; HTLV-1-induced lymphomas; HTLV-2-induced lymphomas; insulinomas; intestinal cancer; Kaposi's sarcoma; kidney cancer; kidney carcinomas; laryngeal cancer; leukemia; lid tumour; liver cancer; liver metastases; lung cancer; lymphoid cancer; lymphomas; malignant melanomas; mammary carcinomas; mantle cell lymphoma; medulloblastoma; megakaryoblastic leukemia (M7); melanoma, in particular malignant melanoma; meningioma; mesothelioma; monocytic leukemia (M5); multiple myeloma; mycosis fungoides; myeloblastic leukemia (M1); myeloblastic leukemia (M2); myelomonocytic leukemia (M4); neurinoma; non-Hodgkin's lymphomas; non-small cell carcinoma; non-small cell carcinoma of the lung; oesophageal cancer; oesophageal carcinoma; oligodendroglioma; ovarian cancer; ovarian carcinoma; pancreatic cancer; pancreatic carcinoma; papilloma virus-induced carcinomas; penis cancer; pituitary tumour; plasmocytoma; promyelocytic leukemia (M3); prostate cancer; prostate tumours; rectal tumours; rectum carcinoma; renal-cell carcinoma; retinoblastoma; sarcomas; Schneeberger's disease; small cell lung carcinomas; small intestine cancer; small intestine tumours; soft tissue tumours; spinalioma; squamous cell carcinoma; stomach cancer; testicular cancer; throat cancer; thymoma; thyroid cancer; thyroid carcinoma; tongue cancer; undifferentiated AML (M0); urethral cancer; uterine cancer; vaginal cancer; Von Hippel Lindau disease; vulval cancer; Wilms' Tumor; and Xeroderma pigmentosum.

29. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of diseases and/or disorders selected from arterial hypertension; arteriosclerosis; arteriosclerotic lesions; Behcet's syndrome; bifurcations of blood vessels; cardiac hypertrophy; cardiavascular hypertrophy; cardiomyopathies, in particular chemotherapy induced cardiomyopathies; cerebral ischemia; coronary heart diseases; dilatation of the abdominal aorta; focal cerebral ischemia; global cerebral ischemia; heart hypertrophy; infrarenal aneurism hypertension; ischemia; myocardial infarct, in particular acute myocardial infarction; myocarditis; reperfusion; restenosis; vasculitis; and Wegener's granulomatosis.

30. JNK inhibitor for use according to any one of claims 1 to 17, wherein the JNK inhibitor is used complementary to coronary artery bypass graft surgery (CABG surgery); percutaneous transluminal coronary angioplasty (PTCA); and/or stent treatment.

31. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of diseases and/or disorders selected from acute respiratory distress syndrome (ARDS); asthma; chronic illnesses involving the respiratory system; chronic obstructive pulmonary disease (COPD); cystic fibrosis; diseases of the lung; inflammatory lung diseases; pneumonia; pulmonary fibrosis; etc.

32. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of diseases and/or disorders selected from colitis, atypical colitis, chemical colitis; collagenous colitis, distal colitis, diversion colitis; fulminant colitis, indeterminate colitis, infectious colitis, ischemic colitis, lymphocytic colitis, microscopic colitis, Crohn's disease, gastroenteritis, Hirschsprung's disease, inflammatory digestive diseases; inflammatory bowel disease (IBD), Morbus Crohn, non-chronic or chronic digestive diseases, non-chronic or chronic inflammatory digestive diseases; regional enteritis and ulcerative colitis.

33. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of diseases and/or disorders selected from bacterial infectious diseases, viral infectious diseases, viral encephalitis; viral induced cancers and tumours, human immunodeficiency virus dementia, meningitis, meningoencephalitis, encephalomyelitis and tonsillitis.

34. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of diseases and/or disorders selected from Aarskog syndrome, acetaminophen hepatotoxicity; Alder-Reilly anomaly; alopecia areata; alpha-1-antitrypsin deficiency; anaphylaxis; apoptosis; apoptotic cell death; atypical hemolytic uremic syndrome; basopenia; basophilia; bipolar disorders; burns; cellular shear stress; Chedial-Higashi syndrome; DNA damage due to chemotherapeutic drugs; cholestasis; chromosome 11, Partial Monosomy 11q; chromosome 22, Trisomy Mosaic; chronic granulomatous disease; hepatitis, such as chronic or fulminant hepatitis; clinical depression; common variable hypogammaglobulinemia; congenital C3 deficiency; CTL protection from activation-induced cell death (AICD); deafness; depression and depressive disorders (in particular prevention of depressive disorders develop on a background of cytokine-induced sickness behaviour), DiGeorge's syndrome; diseases caused by defective apoptosis; diseases of the liver; diseases of the spine; diseases of the uterus; diseases states and symptoms due to exposure to DNA damaging agents and/or ionizing radiation and resulting cellular stress; Down Syndrome; Duchenne muscular dystrophy; ectodermal dysplasias; endometriosis;

eosinopenia; eosinophilia; exocitoxic cell death; fetal alcohol syndrome; fibrosis; fibrotic disease; formation of fibrous tissue; free radicals (leading to cellular stress); graft rejection; graft versus host disease; hair loss; hemolytic uremic syndrome; hepatotoxicity; hyperalgesia, such as diabetes induced hyperalgesia; hyperthermia; hypoglycemia; hypothyroidism; idiopathic hypereosinophilic syndrome; IgA nephropathy; infantile sex-linked agammaglobulinemia; inflammatory pain; infrarenal aneyrism; islet regeneration; islet transplantation; Job's syndrome (hyper-IgE); lazy leukocyte syndrome; leukocyte glucose-6-phosphate dehydrogenase deficiency; leukodystrophy; leukopenia; lymphocytic leukocytosis; lymphocytopenia; lymphocytosis; major depression; mania; maniac depression; Marfan syndrome; mastocytosis; May Hegglin Anomaly; membranoproliferative glomerulonephritis Type II; monocytopenia; monocytosis; myeloperoxidase deficiency-benign; myopathies; neutropenia; neutrophilia; Nezelof's syndrome; organ transplantation; oxidative stress injuries; Pelger-Huet anomaly; polycystic kidney diseases; post-dialysis syndrome; radiation syndromes; radiotherapy; renal diseases; renal failure; rescuing CTL from activation induced cell death; severe combined immunodeficiency disease; transplant rejection; transplantation; trisomy; unipolar depression; UV-induced injuries; Wiskott Aldrich syndrome and wound healing.

35. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of temporomandibular joint disorder.

36. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of mucositis.

37. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of stomatitis.

38. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of peri-implantitis.

39. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of oral liquen planus.

40. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of Pemphigus vulgaris.

41. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of periodontitis.

42. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of chronic periodontitis.

43. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of pulpitis.

44. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of uveitis, in particular of anterior uveitis, intermediate uveitis and/or posterior uveitis.

45. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of dry eye syndrome.

46. JNK inhibitor for use according to any one of claims 1 to 17, wherein the JNK inhibitor is administered in context of coronary artery bypass graft surgery.

47. JNK inhibitor for use according to any one of claims 1 to 17, wherein the JNK inhibitor is administered in context of percutaneous transluminal coronary angioplasty (PTCA).

48. JNK inhibitor for use according to any one of claims 1 to 17, wherein the JNK inhibitor is administered in context of stent placement.

49. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of acute myocardial infarction.

50. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of atherosclerosis.

51. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of COPD.

52. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of asthma.

53. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of rheumatoid arthritis.

54. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of osteoarthritis.

55. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of Crohn's disease.

56. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of inflammatory bowel disease (IBD).

57. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of psoriasis.

58. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of diabetes, in particular diabetes type 1.

59. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of stroke.

60. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of Parkinson's disease.

61. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of Alzheimer's disease.

62. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of systemic lupus erythematosus.

63. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of vasculitis, in particular Wegener's granulomatosis.

64. JNK inhibitor for use according to any one of claims 1 to 17, wherein said method is for treatment of acute hearing loss.

65. JNK inhibitor for use according to any one of the preceding claims, wherein the JNK inhibitor consists of the sequence of SEQ ID NO: 172.

66. Pharmaceutical composition comprising a JNK inhibitor as defined in any of claims 1 to 15 and a pharmaceutically acceptable carrier.

Claims

1. JNK inhibitor comprising the sequence of SEQ ID NO: 194 or 195 for use in a method for treatment of the human or animal body by therapy.