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.

2. JNK inhibitor 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 according to claim 1 or 2, wherein the inhibitory (poly-)peptide sequence is selected from anyone of SEQ ID NOs: 2-27.

4. JNK inhibitor 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.

5. JNK inhibitor 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 NOs: 8.

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

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

8. JNK inhibitor 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 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 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 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 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 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.

15. JNK inhibitor comprising the sequence of SEQ ID NO: 194 or 195.

16. (Poly-)peptide comprising a transporter sequence selected from the group of sequences consisting of rKKRrQRr (SEQ ID NO: 148), rKKRrQRrK (SEQ ID NO: 149), and/or rKKRrQRrR (SEQ ID NO: 150).

17. Method of immunizing a non-human animal with a JNK inhibitor according to anyone of claims 1-14, the method comprising the following step:

- contacting (immunizing) a non-human animal suitable for antibody production, in particular a non-human mammal,

more preferably an animal selected from goat and rodents such as mouse, rat, and rabbit

with a JNK inhibitor according to anyone of claims 1-14,

more preferably with a JNK inhibitor comprising a (poly-)peptide having a sequence selected from any one of SEQ ID NOs: 1-27.

18. Method of producing an (polyclonal) antibody recognizing a JNK inhibitor according to anyone of claims 1-14, the method comprising the step of:

- Isolating from a non-human animal suitable for antibody production,

in particular a non human mammal,

more preferably an animal selected from goat and rodents such as mouse, rat, and rabbit,

which has been contacted (immunized) previously with a JNK inhibitor according to anyone of claims 1-14,

more preferably with a JNK inhibitor consisting of a (poly-)peptide having a sequence selected from any one of SEQ ID NOs: 1-27,

an (polyclonal) antibody recognizing said JNK inhibitor.

19. Method of isolating a cell producing an antibody recognizing a JNK inhibitor according to anyone of claims 1-14, the method comprising the step of:

- Isolating from a non-human animal suitable for antibody production,

in particular a non human mammal,

more preferably an animal selected from goat and rodents such as mouse, rat, and rabbit,

which has been contacted (immunized) previously with a JNK inhibitor according to anyone of claims 1-14,

more preferably with a JNK inhibitor consisting of a (poly-)peptide having a sequence selected from any one of SEQ ID NOs: 1-27,

a cell producing said antibody recognizing said JNK inhibitor, and

optionally immortalizing said cell.

20. Method of producing a (monoclonal) antibody recognizing a JNK inhibitor according to anyone of claims 1-14, the method comprising the step of:

Isolating an antibody recognizing a JNK inhibitor according to anyone of claims 1-14,

more preferably recognizing a JNK inhibitor consisting of a (poly-)peptide having a sequence selected from any one of SEQ ID NOs: 1-27,

from the cell culture supernatant of a cell producing said antibody, the cell being optionally immortalized.

21. Antibody producible with anyone of the methods according to claim 18 or 20, wherein the antibody recognizes at least one (poly-)peptide selected from any one of SEQ ID NOs: 1-27, but does not recognize the essentially same (poly-)peptide with L-amino acids in place of the D-amino acids.

22. Cell producible with the method according to claim 19, wherein the cell produces an antibody according to claim 21.

Claims

1. A JNK inhibitor comprising an inhibitory polypeptide sequence sharing at least 80% sequence identity with SEQ ID NO: 8.

2. The JNK inhibitor according to claim 1, wherein the inhibitory polypeptide sequence is SEQ ID NO: 8.

3. The JNK inhibitor of claim 1, wherein the inhibitory polypeptide sequence sharing at least 80% sequence identity with SEQ ID NOs: 8 has a D-Ala residue at a position corresponding to position 6 of SEQ ID NO: 8.

4. The JNK inhibitor of claim 1, wherein the JNK inhibitor further comprises a transporter sequence.

5. The JNK inhibitor according to claim 4, wherein the inhibitory polypeptide sequence and the transporter sequence overlap.

6. The JNK inhibitor according to claim 4, wherein the transporter sequence comprises a sequence of alternating D- and L-amino acids according to anyone of SEQ ID NOs: 28-30.

7. The JNK inhibitor of claim 4, wherein said transporter sequence is SEQ ID NO: 46.

8. The JNK inhibitor of claim 4, wherein said transporter sequence is selected from any one of SEQ ID NOs: 31-34, 46, 47 and 52-151.

9. The JNK inhibitor of claim 4, wherein said transporter sequence is positioned directly N-terminal or directly C-terminal of the inhibitory polypeptide sequence.

10. The JNK inhibitor of claim 4, wherein the JNK inhibitor comprises a sequence selected from SEQ ID NOs: 171-173, 176-177 and 182-187.

11. The JNK inhibitor of claim 4, wherein the JNK inhibitor comprises the sequence of SEQ ID NO: 172.

12. The JNK inhibitor of claim 1, wherein the L arginine (R) residue at position 4 and the L-leucine (L) residue at positions 8 and 10 of SEQ ID NO: 8 cannot be changed, and wherein at least one other amino acid of the inhibitory polypeptide sequence is in the D conformation.

13. The JNK inhibitor of claim 12, wherein the amino acid corresponding to position 1 of SEQ ID NO: 8 is selected from the group consisting of R, P, Q and r, the amino acid corresponding to position 2 of SEQ ID NO: 8 is selected from the group consisting of R, P, G and r, the amino acid corresponding to position 3 of SEQ ID NO: 8 is selected from the group consisting of K, R, k and r, the amino acid corresponding to position 5 of SEQ ID NO: 8 is selected from the group consisting of P and K, the amino acid corresponding to position 6 of SEQ ID NO: 8 is absent or is selected from the group consisting of T, a, s, q, k, the amino acid corresponding to position 7 of SEQ ID NO: 8 is selected from the group consisting of T, D and A, the amino acid corresponding to position 9 of SEQ ID NO: 8 is selected from the group consisting of N, n, r and K, and the amino acid corresponding to position 11 of SEQ ID NO: 8 is selected from the group consisting of F, f and w, wherein an amino acid residue in a capital letter indicates an L-amino acid, and an amino acid residue in a lower case letter indicates a D amino acid residue.

14. The JNK inhibitor of claim 1, wherein the inhibitory polypeptide sequence sharing at least 80% sequence identity with SEQ ID NOs: 8 has a D-Lys residue at a position corresponding to position 3 of SEQ ID NO: 8.

15. The JNK inhibitor of claim 1, wherein the inhibitory polypeptide sequence sharing at least 80% sequence identity with SEQ ID NOs: 8 has a D-Phe residue at a position corresponding to position 11 of SEQ ID NO: 8.