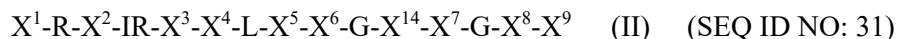


Claims:

1. An isolated peptide comprising an amino acid sequence of Formula II:



wherein X^1 is absent or is selected from D, (dD), E, (dE), K, (dK), R, (dR), H, (dH), N, (dN), Q, (dQ), S, (dS), T, (dT), Y, (dY), C, (dC), G, A, (dA), V, (dV), L, (dL), I, (dI), F, (dF), W, (dW), P, (dP), M and (dM); X^2 is selected from G, A, (dA), V, (dV), L, (dL), I, (dI), F, (dF), W, (dW), P, (dP), M and (dM); X^3 is selected from G, A, (dA), V, (dV), L, (dL), I, (dI), F, (dF), W, (dW), P, (dP), Nle, M and (dM); X^4 is selected from D, (dD), E, (dE), K, (dK), R, (dR), H, (dH), N, (dN), Q, (dQ), S, (dS), T, (dT), Y, (dY), C and (dC); X^5 is selected from D, (dD), E, (dE), K, (dK), R, (dR), H, (dH), N, (dN), Q, (dQ), S, (dS), T, (dT), Y, (dY), C, (dC), G, A, (dA), V, (dV), L, (dL), I, (dI), F, (dF), W, (dW), P, (dP), M and (dM); X^6 is selected from D, (dD), E, (dE), K, (dK), R, (dR), H, (dH), N, (dN), Q, (dQ), S, (dS), T, (dT), Y, (dY), C, (dC), G, A, (dA), V, (dV), L, (dL), I, (dI), F, (dF), W, (dW), P, (dP), M and (dM); X^7 is selected from D, (dD), E, (dE), K, (dK), R, (dR), H, (dH), N, (dN), Q, (dQ), S, (dS), T, (dT), Y, (dY), C, (dC), G, A, (dA), V, (dV), L, (dL), I, (dI), F, (dF), W, (dW), P, (dP), M and (dM); X^8 is selected from D, (dD), E, (dE), K, (dK), R, (dR), H, (dH), N, (dN), Q, (dQ), S, (dS), T, (dT), Y, (dY), C and (dC); and X^9 is absent or is $-X^{10}-X^{11}-X^{12}-X^{13}$, wherein X^{10} is selected from G, A, (dA), V, (dV), L, (dL), I, (dI), F, (dF), W, (dW), P, (dP), M and (dM); X^{11} is selected from G, A, (dA), V, (dV), L, (dL), I, (dI), F, (dF), W, (dW), P, (dP), M and (dM); X^{12} is absent or is selected from D, (dD), E, (dE), K, (dK), R, (dR), H, (dH), N, (dN), Q, (dQ), S, (dS), T, (dT), Y, (dY), C, (dC), G, A, (dA), V, (dV), L, (dL), I, (dI), F, (dF), W, (dW), P, (dP), M and (dM); and X^{13} is absent or is selected from D, (dD), E, (dE), K, (dK), R, (dR), H, (dH), N, (dN), Q, (dQ), S, (dS), T, (dT), Y, (dY), C and (dC); and X^{14} is selected from D, (dD), E, (dE), K, (dK), R, (dR), H, (dH), N, (dN), Q, (dQ), S, (dS), T, (dT), Y, (dY), C, (dC), G, A, (dA), V, (dV), L, (dL), I, (dI), F, (dF), W, (dW), P, (dP), M and (dM);

wherein the peptide is 6 to 20 amino acids in length;

or C-terminal acids or amides and/or N-acetyl derivatives thereof; or pharmaceutically acceptable salts thereof

2. The peptide of Claim 1 wherein X¹ is absent, K or M; X² is V or d(A); X³ is M, A or Nle; X⁴ is C or S; X⁵ is G or N; X⁶ is V or N; X⁷ is L, N or E; X⁸ is D or E; X⁹ is absent, -LAG, -L(dA)G, -L(dA)E, -L(dA)GK, -LAGK; or -L(dA); and X¹⁴ is N or L; or C-terminal acids or amides and/or N-acetyl derivatives thereof; or pharmaceutically acceptable salts thereof.

3. The peptide of Claim 1 or a dimer thereof, comprising or consisting of an amino acid sequence selected from SEQ ID NOs: 2-30; or C-terminal acids or amides and/or N-acetyl derivatives thereof; or pharmaceutically acceptable salts thereof.

4. An isolated peptide or peptide dimer comprising or consisting of an amino acid sequence selected from RVIRMCLGVLLGDL(dA)G (SEQ ID NO: 4); RVIRMCLNVGLLGEL(dA)G (SEQ ID NO: 5); RVIR(Nle)CLNVGLLGEL(dA)G (SEQ ID NO: 6); RVIRMSLVGLLGEL(dA)G (SEQ ID NO: 7); RVIR(Nle)SLNVGLLGEL(dA)G (SEQ ID NO: 8); RVIRMCLNNGLLGEL(dA)G (SEQ ID NO: 9); RVIRMCLNVGNLGEL(dA)G (SEQ ID NO: 10); RVIRMCLNVGLNGEL(dA)G (SEQ ID NO: 11); RVIRMCLNVGLLGEL(dA)E (SEQ ID NO: 12); RVIRMSLVGLEGEL(dA) (SEQ ID NO: 13); RVIR(Nle)SLNVGLEGEL(dA) (SEQ ID NO: 14); R(dA)IR(Nle)SLNVGLLGEL(dA) (SEQ ID NO: 15); {PEG12}KRVIRMCLGVLLGDLG (SEQ ID NO: 16); RVIRMCLGVLLGDLGK{PEG12} (SEQ ID NO: 17); {PEG12}KRVIRMCLNVGLLGEL(dA)E (SEQ ID NO: 18); RVIRMCLNVGLEGEL(dA) (SEQ ID NO: 19); RVIRMCLNVGLNGEL(dA)E (SEQ ID NO: 20); RVIRMCLNVGLNGE (SEQ ID NO: 21); RVIRMCLNNGLNGEL(dA)G (SEQ ID NO: 22); RVIRMCLNNGLNGEL(dA)E (SEQ ID NO: 23); {5-FAM}-RVIRMCLGVLLGDLG (SEQ ID NO: 24); {5-FAM}-RVIRMCLGVLLGDLGK{PEG12} (SEQ ID NO: 25); and RVIRACLVGLLGDL(dA)GK{PEG12} (SEQ ID NO: 29); or C-terminal acids or amides and/or N-acetyl derivatives thereof; or pharmaceutically acceptable salts thereof.

5. A dimer comprised of a peptide according to any one of claims 1-4 attached to a second peptide according to any one of claims 1-4; or C-terminal acids or amides and/or N-acetyl derivatives thereof; or pharmaceutically acceptable salts thereof.

6. The dimer according to claim 5 that is a homodimer; or C-terminal acids or amides and/or N-acetyl derivatives thereof; or pharmaceutically acceptable salts thereof.

7. The homodimer according to claim 6, comprising or consisting of

RVIRMCLGVGLLGDLAG

|
RVIRMCLGVGLLGDLAG (SEQ ID NO: 26); or

RVIRMCLNVGLLGEL(dA)G

|
RVIRMCLNVGLLGEL(dA)G (SEQ ID NO: 27); or

RVIRMCLGVGLLGDLAGK{PEG12}

|
RVIRMCLGVGLLGDLAGK{PEG12} (SEQ ID NO: 28); or

RVIRACLVGLLGDL(dA)GK{PEG12}

|
RVIRACLVGLLGDL(dA)GK{PEG12} (SEQ ID NO: 30);

or C-terminal acids or amides and/or N-acetyl derivatives thereof; or pharmaceutically acceptable salts thereof.

8. The peptide according to claim 4 comprising or consisting of an amino acid sequence

RVIRMCLGVGLLGDLAGK{PEG12} (SEQ ID NO: 17);

or C-terminal acids or amides and/or N-acetyl derivatives thereof; or pharmaceutically acceptable salts thereof.

9. The homodimer according to claim 7, comprising or consisting of

RVIRMCLGVGLLGDLAGK{PEG12}

|
RVIRMCLGVGLLGDLAGK{PEG12} (SEQ ID NO: 28).

10. The peptide according to claim 4 comprising or consisting of an amino acid sequence

RVIRACLVGLLGDL(dA)GK{PEG12} (SEQ ID NO: 29);

or C-terminal acids or amides and/or N-acetyl derivatives thereof; or pharmaceutically acceptable salts thereof.

11. The homodimer according to claim 7, comprising or consisting of

RVIRACLVGVLGDL(dA)GK{PEG12}

|
RVIRACLVGVLGDL(dA)GK{PEG12} (SEQ ID NO: 30);

or C-terminal acids or amides and/or N-acetyl derivatives thereof; or pharmaceutically acceptable salts thereof.

12. An isolated peptide comprising an amino acid sequence having at least about 90% sequence identity with a peptide according to any one of claims 1-4; or C-terminal acids or amides and/or N-acetyl derivatives thereof; or pharmaceutically acceptable salts thereof.

13. A peptide or peptide dimer comprising an amino acid sequence having a deletion, insertion, or substitution of one to six amino acids compared to a reference peptide that comprises an amino acid sequence a peptide selected from

MRVIRMCLGVLLGDLG (SEQ ID NO: 2);

RVIRMCLGVLLGDLG (SEQ ID NO: 3);

RVIRMCLGVLLGDL(dA)G (SEQ ID NO: 4);

RVIRMCLNVLLGEL(dA)G (SEQ ID NO: 5);

RVIR(Nle)CLNVLLGEL(dA)G (SEQ ID NO: 6);

RVIRMSLVLLGEL(dA)G (SEQ ID NO: 7);

RVIR(Nle)SLNVLLGEL(dA)G (SEQ ID NO: 8);

RVIRMCLNGLLGEL(dA)G (SEQ ID NO: 9);

RVIRMCLNVGNLGEL(dA)G (SEQ ID NO: 10);

RVIRMCLNVGLNGEL(dA)G (SEQ ID NO: 11);

RVIRMCLNVLLGEL(dA)E (SEQ ID NO: 12);

RVIRMSLVGLEGEL(dA) (SEQ ID NO: 13);

RVIR(Nle)SLNVGLEGEL(dA) (SEQ ID NO: 14);

R(dA)IR(Nle)SLNVLLGEL(dA) (SEQ ID NO: 15);

{PEG12}KRVIRMCLGVLLGDLG (SEQ ID NO: 16);

RVIRMCLGVLLGDLGK{PEG12} (SEQ ID NO: 17);

{PEG12}KRVIRMCLNVLLGEL(dA)E (SEQ ID NO: 18);

RVIRMCLNVGLEGEL(dA) (SEQ ID NO: 19);

RVIRMCLNVGLNGEL(dA)E (SEQ ID NO: 20);
 RVIRMCLNVGLNGE (SEQ ID NO: 21);
 RVIRMCLNNGLNGEL(dA)}G (SEQ ID NO: 22);
 RVIRMCLNNGLNGEL(dA)E (SEQ ID NO: 23);
 {5-FAM}-RVIRMCLGVGLLGDLAG (SEQ ID NO: 24);
 {5-FAM}-RVIRMCLGVGLLGDLAGK{PEG12} (SEQ ID NO: 25);
 RVIRMCLGVGLLGDLAG
 |
 RVIRMCLGVGLLGDLAG (SEQ ID NO: 26);
 RVIRMCLNVGLLGEL(dA)G
 |
 RVIRMCLNVGLLGEL(dA)G (SEQ ID NO: 27)
 RVIRMCLGVGLLGDLAGK{PEG12}
 |
 RVIRMCLGVGLLGDLAGK{PEG12} (SEQ ID NO: 28);
 RVIRACLGVGLLGDLD(dA)GK{PEG12} (SEQ ID NO: 29); and
 RVIRACLGVGLLGDLD(dA)GK{PEG12}
 |
 RVIRACLGVGLLGDLD(dA)GK{PEG12} (SEQ ID NO: 30);

or C-terminal acids or amides and/or N-acetyl derivatives thereof; or pharmaceutically acceptable salts thereof.

14. A peptide or peptide dimer of Claim 13, wherein the peptide or dimer comprises substitution with at least one amino acid selected from (i) an amino acid having a D-configuration, and (ii) a non-naturally occurring amino acid residue; or C-terminal acids or amides and/or N-acetyl derivatives thereof; or pharmaceutically acceptable salts thereof.

15. A peptide or peptide dimer of any one of claims 1-14, further comprising a duration enhancing moiety, attached to the peptide, and optionally further comprising a metabolically cleavable linker coupling the peptide to the duration enhancing moiety.

16. A peptide or peptide dimer of any one of claims 1-15, wherein the peptide or dimer is derivatized via acetylation, pegylation, biotinylation or acylation.

17. The peptide or dimer of claim 16 wherein the derivative is PEG12, acetyl, biotin or palmityl.

18. A pharmaceutical composition comprising a peptide or dimer or C-terminal acids or amides and/or N-acetyl derivatives thereof or pharmaceutically acceptable salts thereof of any one of claims 1-17.

19. An isolated nucleic acid that comprises a nucleotide sequence that encodes a peptide of any one of claims 1-4 and 8, 10, and 12-17 that is comprised of naturally occurring amino acids.

20. A vector or expression vector that comprises an isolated nucleic acid according to claim 19.

21. A host cell that comprises a nucleic acid according to claim 19 or a vector or expression vector according to claim 20.

22. The peptide or peptide analog or dimer of any one of claims 1-17, or the composition according to claim 18, for use in treating fibrosis.

23. Use of the peptide or peptide analog or dimer of any one of claims 1-17, the composition according to claim 18, in the manufacture of a medicament for treating fibrosis.

24. The peptide or dimer of any of claims 1-17, or the composition according to claim 18, for use as a medicament for one or more of the following: (a) modulating cell viability; (b) treating cancer; (c) modulating cell proliferation; (d) treating an apoptotic disease (e) treating a metabolic disease; and providing cytoprotection.

25. The peptide or peptide analog or dimer or the composition of claim 22, or the use of claim 23, wherein the fibrosis is any of cirrhosis of the liver; pulmonary fibrosis, idiopathic pulmonary fibrosis; fibrosis following myocardial infarction; CNS fibrosis following a stroke, or neurodegenerative disorders (eg Alzheimer's Disease, multiple sclerosis); proliferative vitreoretinopathy (PVR) and arthritis; adhesions, eg in the digestive tract, abdomen, pelvis, spine; nephrogenic systemic fibrosis; myocardial fibrosis; liver/hepatic fibrosis; epidural fibrosis (failed back surgery syndrome); endomyocardial fibrosis; tubulointerstitial fibrosis; renal interstitial fibrosis; mediastinal fibrosis; retroperitoneal fibrosis; penile fibrosis; oral submucous; kidney fibrosis; idiopathic pulmonary upper lobe fibrosis (Amitani disease); congenital hepatic fibrosis;

postlaminotomy fibrosis; painful disc fibrosis; graft fibrosis; atrial fibrosis; corneal subepithelial fibrosis; congenital orbital fibrosis; bone fibrosis; peritoneal fibrosis; nephrogenic systemic fibrosis; non-cirrhotic portal fibrosis; pulmonary tuberculosis, disease-related pulmonary apical fibrosis in ankylosing spondylitis; colorectal fibrosis; periglomerular fibrosis/atubular glomeruli; basal fibrosis syndrome (emphysema/ fibrosis syndrome); tissue fibrosis; and massive neck fibrosis.

26. The use of Claim 25 wherein the fibrosis is idiopathic pulmonary fibrosis.

27. The use of Claim 25 wherein the fibrosis is scleroderma or systemic sclerosis.

28. The peptide or peptide analog or dimer or the composition of claim 22, or the use of claim 23, wherein the peptide or peptide analog or dimer has a sequence

RVIRMCLGVGLLGDLAGK{PEG12} (SEQ ID NO: 17); or

RVIRMCLGVGLLGDLAGK{PEG12}

RVIRMCLGVGLLGDLAGK{PEG12} (SEQ ID NO: 28).

29. The peptide or peptide analog or dimer or the composition of claim 22, or the use of claim 23, wherein the peptide or peptide analog or dimer has a sequence

RVIRACLGVGLLGDL(dA)GK{PEG12} (SEQ ID NO: 29); or

RVIRACLGVGLLGDL(dA)GK{PEG12}

RVIRACLGVGLLGDL(dA)GK{PEG12} (SEQ ID NO: 30).

30. The peptide or peptide analog or dimer or the composition of claim 22, or the use of claim 23, wherein the fibrosis is fibrosis of the eye.

31. The peptide or peptide analog or dimer of any one of claims 1-17, or the composition according to claim 18, for use in treating retinopathy.

32. Use of the peptide or peptide analog or dimer of any one of claims 1-17, the composition according to claim 18, in the manufacture of a medicament for treating retinopathy.