Claims

1. A *depsipeptide*, capable of self-assembling and forming a hydrogel, having the general formula selected from:

$$Z_a\text{-}(X^{AHA})_b\text{-}(Y)_c\text{-}Z'_d$$

(I)

wherein

Z is an N-terminal protecting group;

a is at least 1,

X^{AHA} is, at each occurrence, independently selected from the group consisting of aliphatic amino acids and aliphatic amino acid derivatives and includes at least one α-hydroxy acid, wherein the α-hydroxy acid is at least one selected from the group consisting of lactic acid, glycolic acid, malic acid, 2,3-dihydroxypropanoic acid, lactobionic acid, and citric acid;

b is an integer selected from 2 to 7;

Y is selected from the group consisting of polar amino acids and polar amino acid derivatives;

c is 0, 1 or 2;

Z' is a C-terminal protecting group; and

d is 0 or 1, and

b + **c** is at least 3;

$$Z_a\text{-}(X)_{b1}\text{-}(AHA)_d\text{-}(X)_{b2}\text{-}(Y)_c\text{-}Z'_e$$

(II)

wherein

Z is an N-terminal protecting group;

a is at least 1;

X is, at each occurrence, independently selected from the group consisting of aliphatic amino acids and aliphatic amino acid derivatives;

with each of **b1** and **b2** being an integer selected from 0 to 7, under the proviso that **b1** + **b2** is 2 to 7,

AHA is, at each occurrence, independently selected from the group consisting of α-hydroxy acids, wherein the α-hydroxy acid is at least one selected from the group

consisting of lactic acid, glycolic acid, malic acid, 2,3-dihydroxypropanoic acid, lactobionic acid, and citric acid;

d is 1 or 2;

Y is selected from the group consisting of polar amino acids and polar amino acid derivatives;

c is 0, 1 or 2;

under the proviso that **b1** + **b2** + **c** + **d** ≤ 7,

Z' is a C-terminal protecting group; and

e is 0 or 1;

$$Z_a\text{-}(X)_{b'}\text{-}(Y)_c\text{-}(AHA)_d\text{-}Z'_e$$

(III)

wherein

Z is an N-terminal protecting group;

a is at least 1;

X is, at each occurrence, independently selected from the group consisting of aliphatic amino acids and aliphatic amino acid derivatives;

b' is an integer selected from 2 to 7;

Y is selected from the group consisting of polar amino acids and polar amino acid derivatives;

c is 0, 1 or 2;

AHA is, at each occurrence, independently selected from the group consisting of α-hydroxy acids, wherein the α-hydroxy acid is at least one selected from the group consisting of lactic acid, glycolic acid, malic acid, 2,3-dihydroxypropanoic acid, lactobionic acid, and citric acid;

d is 1 or 2;

Z' is a C-terminal protecting group; and

e is 0 or 1, and

b' + **c** is at least 2;

wherein all or a portion of said aliphatic amino acids are arranged in an order of decreasing amino acid size in the direction from N- to C-terminus, wherein the size of the aliphatic amino acids is defined as I = L > V > A > G,

and/or wherein the overall hydrophobicity decreases from N- to C-terminus.

2. The depsipeptide according to claim 1, wherein $(X^{AHA})_b$ of formula I or $(X)_{b1}$-$(AHA)_d$-$(X)_{b2}$ of formula II has a sequence selected from

LIVAG(AHA) (SEQ ID NO: 1),
LIVA(AHA) (SEQ ID NO: 2),
LIV(AHA)G (SEQ ID NO: 3),
ILVAG(AHA) (SEQ ID NO: 4),
ILVA(AHA) (SEQ ID NO: 5),
ILV(AHA)G (SEQ ID NO: 6),
IVLA(AHA) (SEQ ID NO: 7),
IVL(AHA)G (SEQ ID NO: 8),
AIVAG(AHA) (SEQ ID NO: 9),
AIVA(AHA) (SEQ ID NO: 10),
AIV(AHA)G (SEQ ID NO: 11),
IV(AHA),
IL(AHA),

wherein, optionally,

$(X^{AHA})_b$ of formula I or $(X)_{b1}$-$(AHA)_d$-$(X)_{b2}$ of formula II has a sequence selected from

LIVAg (SEQ ID NO: 12),
LIVaG (SEQ ID NO: 13),
LIVAm (SEQ ID NO: 14),
LIVAGm (SEQ ID NO: 15),
ILVAg (SEQ ID NO: 16),
ILVaG (SEQ ID NO: 17),
ILVAm (SEQ ID NO: 18),
ILVAGm (SEQ ID NO: 19),
IVLAg (SEQ ID NO: 20),
IVLaG (SEQ ID NO: 21),
AIVAg (SEQ ID NO: 22),
AIVaG (SEQ ID NO: 23),
AIVAGm (SEQ ID NO: 24),
IVa,
ILa,
IVm,

wherein "g" refers to glycolic acid, "a" refers to lactic acid and "m" refers to malic acid, or wherein $(X)_{b'}$ of formula III has a sequence selected from

IV,

or wherein $(X)_{b'}$ of formula III has a sequence selected from

LIVAG (SEQ ID NO: 25),
ILVAG (SEQ ID NO: 26),
LIVAA (SEQ ID NO: 27),
LAVAG (SEQ ID NO: 28),
AIVAG (SEQ ID NO: 29)
GIVAG (SEQ ID NO: 30)
VIVAG (SEQ ID NO: 31)
ALVAG (SEQ ID NO: 32)
GLVAG (SEQ ID NO: 33)
VLVAG (SEQ ID NO: 34)
IVAG (SEQ ID NO: 35)
LIVA (SEQ ID NO: 36)
LIVG (SEQ ID NO: 37) and
IVA,

wherein, optionally,
in formula I **b** is an integer from 2 to 7,
in formula II **b1** + **b2** is 2 to 7, and
in formula III **b'** is an integer from 2 to 7.

3. The depsipeptide according to claim 1 or 2, wherein i) **c** is 2 and said polar amino acids are identical amino acids,
or wherein **c** is 1 and said polar polar amino acid comprises any one of aspartic acid, asparagine, glutamic acid, glutamine, serine, threonine, cysteine, methionine, lysine, ornithine, 2,4-diaminobutyric acid (Dab) and histidine,
optionally wherein ii) $(Y)_c$ has a sequence selected from Asp, Asn, Glu, Gln, Ser, Thr, Cys, Met, Lys, Orn, Dab, His, Asn-Asn, Asp-Asp, Glu-Glu, Gln-Gln, Asn-Gln, Gln-Asn, Asp-Gln, Gln-Asp, Asn-Glu, Glu-Asn, Asp-Glu, Glu-Asp, Gln-Glu, Glu-Gln, Asp-Asn, Asn-Asp Thr-Thr, Ser-Ser, Thr-Ser, Ser-Thr, Asp-Ser, Ser-Asp, Ser-Asn, Asn-Ser, Gln-Ser, Ser-Gln, Glu-Ser, Ser-Glu, Asp-Thr, Thr-Asp, Thr-Asn, Asn-Thr, Gln-Thr, Thr-Gln, Glu-Thr, Thr-Glu,

Cys-Asp, Cys-Lys, Cys-Ser, Cys-Thr, Cys-Orn, Cys-Dab, Cys-Dap, Lys-Lys, Lys-Ser, Lys-Thr, Lys-Orn, Lys-Dab, Lys-Dap, Ser-Lys, Ser-Orn, Ser-Dab, Ser-Dap, Orn-Lys, Orn-Orn, Orn-Ser, Orn-Thr, Orn-Dab, Orn-Dap, Dab-Lys, Dab-Ser, Dab-Thr, Dab-Orn, Dab-Dab, Dab-Dap, Dap-Lys, Dap-Ser, Dap-Thr, Dap-Orn, Dap-Dab, Dap-Dap; optionally

wherein $(X^{AHA})_b$-$(Y)_c$ of formula I or $(X)_{b1}$-$(AHA)_d$-$(X)_{b2}$-$(Y)_c$ of formula II has a sequence selected from the group consisting of

LIVA(AHA)K (SEQ ID NO: 38),
LIV(AHA)GK (SEQ ID NO: 39),
LIVA(AHA)D (SEQ ID NO: 40),
LIV(AHA)GD (SEQ ID NO: 41),
LIVA(AHA) (SEQ ID NO: 2),
LIVAG(AHA) (SEQ ID NO: 1),
ILVA(AHA)K (SEQ ID NO: 42),
ILV(AHA)GK (SEQ ID NO: 43),
ILVA(AHA) (SEQ ID NO: 5),
ILVAG(AHA) (SEQ ID NO: 4),
IVLA(AHA)K (SEQ ID NO: 44),
IVL(AHA)GK (SEQ ID NO: 45),
AIVA(AHA)S (SEQ ID NO: 46),
AIV(AHA)GS (SEQ ID NO: 47),
AIVAG(AHA) (SEQ ID NO: 9),
IV(AHA)D (SEQ ID NO: 48),
IV(AHA), and
IL(AHA),

wherein AHA refers to α-hydroxy acid; optionally

wherein $(X^{AHA})_b$-$(Y)_c$ of formula I or $(X)_{b1}$-$(AHA)_d$-$(X)_{b2}$-$(Y)_c$ of formula II has a sequence selected from the group consisting of

LIVAgK (SEQ ID NO: 49),
LIVaGK (SEQ ID NO: 50),
ILVAgK (SEQ ID NO: 51),
ILVaGK (SEQ ID NO: 52),
IVLAgK (SEQ ID NO: 53),
IVLaGK (SEQ ID NO: 54),
LIVAgD (SEQ ID NO: 55),

LIVaGD (SEQ ID NO: 56),
AIVAgS (SEQ ID NO: 57)
AIVaGS (SEQ ID NO: 58)
IVaD (SEQ ID NO: 59)
LIVAm (SEQ ID NO: 14),
ILVAm (SEQ ID NO: 18),
AIVAGm (SEQ ID NO: 24),
IVa,
IVm, and
ILa,

wherein "g" refers to glycolic acid, "a" refers to lactic acid and "m" refers to malic acid.

4. The depsipeptide according to any one of claims 1 to 3, wherein $(X)_b$-$(Y)_c$-$(AHA)_d$ of formula III has a sequence selected from the group consisting of

IVD(AHA) (SEQ ID NO: 60),
IVK(AHA) (SEQ ID NO: 61),
ILVAGK(AHA) (SEQ ID NO: 62),
ILVAGD(AHA) (SEQ ID NO: 63),
ILVAGS(AHA) (SEQ ID NO: 64),
LIVAGK(AHA) (SEQ ID NO: 65),
LIVAGD(AHA) (SEQ ID NO: 66),
LIVAGS(AHA) (SEQ ID NO: 67), and
AIVAGS(AHA) (SEQ ID NO: 68),

wherein AHA refers to α-hydroxy acid; optionallywherein $(X)_b$-$(Y)_c$-$(AHA)_d$ of formula III has a sequence selected from the group consisting of

IVDa (SEQ ID NO: 69),
IVKa (SEQ ID NO: 70),

wherein "a" refers to lactic acid.

5. The depsipeptide according to any one of the foregoing claims, wherein **a** is 1 and said N-terminal protecting group ***Z*** has the general formula –C(O)–R, wherein R is selected from the group consisting of H, unsubstituted or substituted alkyls, and unsubstituted or substituted aryls; optionally wherein said N-terminal protecting group ***Z*** is an acetyl group; optionally

wherein said N-terminal protecting group ***Z*** is a peptidomimetic molecule, including natural and synthetic amino acid derivatives, wherein the N-terminus of said peptidomimetic molecule may be modified with a functional group selected from the group consisting of carboxylic acid, amide, alcohol, aldehyde, amine, imine, nitrile, an urea analog, phosphate, carbonate, sulfate, nitrate, maleimide, vinyl sulfone, azide, alkyne, alkene, carbohydrate, imide, peroxide, ester, aryl, ketone, sulphite, nitrite, phosphonate, and silane.

6. The depsipeptide according to any one of the foregoing claims, wherein said C-terminal protecting group ***Z'*** is an amide group or an ester group; optionally wherein said C-terminal protecting group ***Z'*** is an amide group and the C-terminus of the depsipeptide has the formula -CONHR or -CONRR', with R and R' being selected from the group consisting of H, unsubstituted or substituted alkyls, and unsubstituted or substituted aryls; or
wherein said C-terminal protecting group ***Z'*** is an ester group and the C-terminus of the depsipeptide has the formula $-CO_2R$, with R being selected from the group consisting of H, unsubstituted or substituted alkyls, and unsubstituted or substituted aryls.

7. The depsipeptide according to any one of claims 1 to 5, wherein said C-terminal protecting group ***Z'*** is a peptidomimetic molecule, including natural and synthetic amino acid derivatives, wherein the C-terminus of said peptidomimetic molecule may be modified with a functional group selected from the group consisting of carboxylic acid, amide, alcohol, aldehyde, amine, imine, nitrile, an urea analog, thiol, phosphate, carbonate, sulfate, nitrate, maleimide, vinyl sulfone, azide, alkyne, alkene, carbohydrate, imide, peroxide, ester, thioester, aryl, ketone, sulphite, nitrite, phosphonate and silane.

8. A *method of preparing a hydrogel*, the method comprising dissolving at least one depsipeptide as defined in any one of claims 1 to 7 in an aqueous solution.

9. A *method of preparing a co-gel or co-hydrogel*, the method comprising
(a) dissolving at least one depsipeptide as defined in any one of claims 1 to 7 in an aqueous solution,
(b) dissolving at least one peptide which has the same sequence as the depsipeptide of step (a), but includes no AHA ("parent peptide"), in an aqueous solution,
(c) mixing the solutions of (a) and (b) and gelating,
(d) obtaining the co-gel or co-hydrogel.

10. A *hydrogel* comprising at least one depsipeptide as defined in any one of claims 1 to 7

11. A *co-gel* or *co-hydrogel* comprising
at least one depsipeptide as defined in any one of claims 1 to 7, and
at least one parent peptide, i.e. a peptide which has the same sequence as the depsipeptide, but includes no AHA.

12. A *pharmaceutical and/or cosmetic composition* and/or a *biomedical device* and/or a *surgical implant* comprising
at least one depsipeptide of any one of claims 1 to 7,
a hydrogel of claim 10, or
a co-gel or co-hydrogel of claim 11.

13. A *kit of parts*, the kit comprising
a first container with at least one depsipeptide of any one of claims 1 to 7, and
a second container with an aqueous solution.

14. A depsipeptide of any one of claims 1 to 7, a hydrogel of claim 10, a co-gel or co-hydrogel of claim 11, or a pharmaceutical and/or cosmetic composition and/or a biomedical device and/or a surgical implant of claim 12, for use in at least one selected from the group consisting of:

- regenerative medicine and tissue regeneration or tissue replacement,
- implantable scaffold
- disease model
- wound treatment and/or wound healing,
- 2D and 3D synthetic cell culture substrate,
- stem cell therapy,
- drug delivery
- injectable therapies,
- treatment of degenerative diseases of the skeletal system,
- biosensor development,
- high-throughput screening,
- biofunctionalized surfaces,

- biofabrication, such as bio-printing,
- cosmetic use;
and
- gene therapy.

15. An *in vitro* or *ex vivo method of tissue regeneration or tissue replacement* comprising the steps:

a) providing a hydrogel according to claim 10, or
a co-gel or co-hydrogel according to claim 11;

b) exposing said hydrogel or co-gel or co-hydrogel to cells which are to form regenerated tissue;

c) allowing said cells to grow on or in said hydrogel;

wherein the tissue is at least one selected from the group consisting of skin tissue, nucleus pulposus in the intervertebral disc, cartilage tissue, synovial fluid and submucosal connective tissue in the bladder neck, and adipose tissue.