Claims

1. A hydrogel comprising a first peptide having the general formula

$$B^*\text{-}\ Z_p\text{-}(X)_m\text{-}(Y)_n\text{-}Z'_q \quad \text{or} \quad Z_p\text{-}(X)_m\text{-}(Y)_n\text{-}Z'_q\text{-}B^* \quad \text{or} \quad B^*\text{-}\ Z_p\text{-}(X)_m\text{-}(Y)_n\text{-}\ Z'_q\text{-}B^*$$

wherein

B* is a bioactive agent;

X is, at each occurrence, independently selected from an aliphatic amino acid, an aliphatic amino acid derivative and a glycine;

Y is, at each occurrence, independently selected from a polar amino acid and a polar amino acid derivative;

Z is an N-terminal protecting group;

Z' is a C-terminal protecting group;

m is an integer selected from 2 to 6;

n is selected from 1 or 2; and

p and q are independently selected from 0 or 1, wherein, preferably, p is 0,

wherein said hydrogel further comprises a second peptide having the general formula

$Z\text{-}(X)_m\text{-}(Y)_n\text{-}Z'_q$,

wherein said bioactive agent is covalently linked to the N-terminus and/or the C-terminus of said first peptide by means of a click chemistry reaction, and the release of the bioactive agent is triggered via hydrolysis of the hydrogel, wherein the covalent attachment of the bioactive agent to the first peptide and the release of the bioactive agent via hydrolysis are capable of achieving sustained or controlled release delivery of said bioactive agent, and wherein said second peptide is used as a matrix.

2. The hydrogel of claim 1, wherein said first peptide has the general formula

$$B^*\text{-}(X)_m\text{-}(Y)_n\text{-}Z'_q.$$

3. The hydrogel of any of the foregoing claims, wherein said bioactive agent is selected from the group consisting of nucleic acids, DNA, RNA, small RNAs, miRNA, mRNA, siRNA, rRNA, snRNA, snoRNA and analogs thereof, (poly)peptides, peptidomimetics, neutral or anionic or cationic polymers, virus particles, (poly)saccharides, oligosaccharides, glycans, vitamins, hormones, steroids, growth factors, sialic acids, antigens, antibiotics, anti-inflammatory

molecules, vaccines, drugs, prodrugs, catechols, biotin, lipids and lipid analogs, antibodies, nanoparticles, organometallic compounds and other organic or inorganic compounds, complexes, composites and nanomaterials; wherein optionally said bioactive agent is an anti-cancer therapeutic; preferably said anti-cancer therapeutic is selected from the group consisting of oxaliplatin, cisplatin, carboplatin, doxorubicin, daunorubicin, clyclophosphamide, 5-fluorouracile, chlorambucil, vincristine, methotrexate, hydroxyurea, bleomecyn, topotecan, irinotecan, dactinomycin, docetaxel, vinblastine, paclitaxel, gleevec, herceptin and other monoclonal or polyclonal antibodies.

4. The hydrogel of any of the foregoing claims, wherein said bioactive agent is covalently linked to the N-terminus and/or the C-terminus of said first peptide via a linking group comprising a moiety selected from the group consisting of a triazole group, a cyclohexene group, a thioether group, a succinimide group, an isoxazole group and analogs thereof, a isoxazolidine group and analogs thereof, and a pyrazoline group; wherein optionally said click chemistry reaction is a [3+2] cycloaddition reaction, a Diels-Alder reaction, a thiol-ene reaction, a thiol-Michael addition reaction, a thiol-vinylsulfone reaction, a Staudinger reaction, preferably a 1,3-dipolar cycloaddition reaction, more preferably a Cu(I)-catalyzed or a strained promoted 1,3-dipolar cycloaddition reaction.

5. The hydrogel of any of the foregoing claims, wherein the hydrophobicity decreases from the N-terminus to the C-terminus of said peptide; wherein optionally said aliphatic amino acid and aliphatic amino acid derivative are selected from the group consisting of alanine (Ala, A), homoallylglycine, homopropargylglycine, isoleucine (Ile, I), norleucine, leucine (Leu, L) and valine (Val, V), wherein preferably said aliphatic amino acid is selected from the group consisting of alanine (Ala, A), isoleucine (Ile, I), leucine (Leu, L) and valine (Val, V).

6. The hydrogel of any of the foregoing claims, wherein said polar amino acid and polar amino acid derivative are selected from the group consisting of aspartic acid (Asp, D), asparagine (Asn, N), glutamic acid (Glu, E), glutamine (Gln, Q), 5-N-ethyl-glutamine (theanine), citrulline, thio-citrulline, cysteine (Cys, C), homocysteine, methionine (Met, M), ethionine, selenomethionine, telluromethionine, serine (Ser, S), homoserine, arginine

(Arg, R), homoarginine, threonine (Thr, T), allo-threonine, lysine (Lys, K), hydroxylysine, N(6)-carboxymethyllysine, ornithine (Orn), 2,4-diaminobutyric acid (Dab), 2,4-diaminopropionic acid (Dap), histidine (His, H), azido-alanine, azido-homoalanine, azido-ornithine and azido-lysine; wherein preferably said polar amino acid and polar amino acid derivative are selected from the group consisting of aspartic acid (Asp, D), glutamic acid (Glu, E), cysteine (Cys, C), serine (Ser, S), threonine (Thr, T), lysine (Lys, K), ornithine (Orn), 2,4-diaminobutyric acid (Dab) and 2,4-diaminopropionic acid (Dap).

7. The hydrogel of any of the foregoing claims, wherein m is selected from 2 to 5; wherein optionally m + n is ≤ 7 or m + n is ≤ 6.

8. The hydrogel of any of the foregoing claims, wherein $(X)_m$-$(Y)_n$ is selected from the group consisting of

LIVAGDD	SEQ ID NO: 1
LIVAGDE	SEQ ID NO: 2
LIVAGED	SEQ ID NO: 3
LIVAGEE	SEQ ID NO: 4
LIVAGKC	SEQ ID NO: 5
LIVAGSC	SEQ ID NO: 6
AIVAGKC	SEQ ID NO: 7
AIVAGSC	SEQ ID NO: 8
LIVAGC	SEQ ID NO: 9
LIVAGD	SEQ ID NO: 10
ILVAGD	SEQ ID NO: 11
LIVAAD	SEQ ID NO: 12
LAVAGD	SEQ ID NO: 13
AIVAGD	SEQ ID NO: 14
LIVAGE	SEQ ID NO: 15
LIVAGK	SEQ ID NO: 16
LIVAGS	SEQ ID NO: 17
ILVAGS	SEQ ID NO: 18
AIVAGS	SEQ ID NO: 19

LIVAGT	SEQ ID NO: 20
AIVAGT	SEQ ID NO: 21
LIVAD	SEQ ID NO: 22
LIVGD	SEQ ID NO: 23
IVAD	SEQ ID NO: 24
IIID	SEQ ID NO: 25
IIIK	SEQ ID NO: 26
IVD	SEQ ID NO: 43
IID	SEQ ID NO: 44
LVE	SEQ ID NO: 45
IVE	SEQ ID NO: 46
LVD	SEQ ID NO: 47
VIE	SEQ ID NO: 48
VID	SEQ ID NO: 49
VLD	SEQ ID NO: 50
VLE	SEQ ID NO: 51
LLE	SEQ ID NO: 52
LLD	SEQ ID NO: 53
IIE	SEQ ID NO: 54
IVK	SEQ ID NO: 55
IV(Orn)	SEQ ID NO: 56
IV(Dab)	SEQ ID NO: 57
IV(Dap)	SEQ ID NO: 58
IVS	SEQ ID NO: 59
LVS	SEQ ID NO: 60
LVK	SEQ ID NO: 61
LV(Orn)	SEQ ID NO: 62
LV(Dab)	SEQ ID NO: 63
LV(Dap)	SEQ ID NO: 64
ILVAGK	SEQ ID NO: 27
ILVAG(Orn)	SEQ ID NO: 28
ILVAG(Dab)	SEQ ID NO: 29
ILVAG(Dap)	SEQ ID NO: 30

ILVAGS	SEQ ID NO: 31
ILVAGKC	SEQ ID NO: 32
AIVAGK	SEQ ID NO: 33
AIVAG(Orn)	SEQ ID NO: 34
AIVAG(Dab)	SEQ ID NO: 35
AIVAG(Dap)	SEQ ID NO: 36
LIVAG(Orn)	SEQ ID NO: 37
LIVAG(Dab)	SEQ ID NO: 38
LIVAG(Dap)	SEQ ID NO: 39
III(Orn)	SEQ ID NO: 40
III(Dab)	SEQ ID NO: 41 and
III(Dap)	SEQ ID NO: 42.

9. The hydrogel of any of the foregoing claims, wherein said N-terminal protecting group is selected from:

a) 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; wherein preferably said N-terminal protecting group is an acetyl group; or

b) 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, thiol, phosphate, carbonate, sulfate, nitrate, maleimide, vinyl sulfone, azide, alkyne, alkene, carbohydrate, imide, peroxide, ester, thioester, aryl, ketone, sulphite, nitrite, phosphonate and silane.

10. The hydrogel of any of the foregoing claims, wherein said C-terminal protecting group is selected from:

a) an amide group; preferably the C-terminus of said at least one peptide 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

b) an ester group; preferably the C-terminus of said at least one peptide has the formula –CO_2R , with R being selected from the group consisting of H, unsubstituted or substituted alkyls, and unsubstituted or substituted aryls; or

c) a peptidomimetic molecule, wherein the peptidomimetic molecule includes 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.

11. The hydrogel of any of the foregoing claims, wherein said first peptide and said second peptide is capable of forming said hydrogel via self-assembly, preferably via antiparallel self-assembly; wherein optionally the hydrogel is characterized by a storage modulus G' to loss modulus G'' ratio that is greater than 2 or optionally the hydrogel is characterized by a storage modulus G' in the range of from 100 Pa to 100,000 Pa at a frequency in the range of from 0.001 Hz to 16 Hz, preferably 0.01 Hz to 0.2 Hz.

12. The hydrogel of any of the foregoing claims, wherein the hydrogel is injectable and gels *in situ*.

13. The hydrogel of any of the foregoing claims, wherein the hydrogel comprises 10 wt% of the first peptide and 90 wt% of the second peptide.

14. Use of a hydrogel of any of the foregoing claims for delivery of said bioactive agent in vitro, preferably for sustained or controlled release delivery of said bioactive agent.

15. A device for drug delivery, preferably sustained or controlled release drug delivery, comprising a hydrogel of any of claims 1 to 13.

16. An implant comprising a hydrogel of any of claims 1 to 13.

17. A pharmaceutical or cosmetic composition comprising a hydrogel of any of claims 1 to 13.

18. Use of a hydrogel of any of claims 1-13 in the manufacture of a medicament for treatment of cancer, wherein said cancer is selected from the group consisting of prostate cancer, breast cancer, colorectal cancer, head and neck tumors, gliomas, liver cancer, bladder cancer, sarcomas, melanomas, non-small-cell lung cancer, genitourinary cancer and other solid tumors.

19. A kit comprising a first container with a first peptide as defined in any of claims 1 to 13 and a second container with an aqueous solution, wherein said first container further contains a second peptide as defined in any of claims 1 to 13, or wherein said kit further comprises a third container with a second peptide as defined in any of claims 1 to 13.

20. A method of preparing a hydrogel of any of claims 1 to 13, said method comprising the step of dissolving a first peptide as defined in any of claims 1 to 13 or a first peptide obtained by the method of claim 20 or 21 and a second peptide as defined in any of claims 1 to 13 in an aqueous solution and optionally
the method further comprising the step(s) of

- adding at least one buffer, preferably at least one physiologically acceptable buffer; and/or
- adding at least one compound acting as gelation enhancer.