(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
8 May 2014 (08.05.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/066936 A1

(51) International Patent Classification:
C07K 7/02 (2006.01) *C07K 7/56* (2006.01)
C07K 5/023 (2006.01) *C07K 5/12* (2006.01)

(21) International Application Number:
PCT/AU2013/001252

(22) International Filing Date:
29 October 2013 (29.10.2013)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
2012904701 29 October 2012 (29.10.2012) AU

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ,

[Continued on next page]

(54) Title: SUPRAMOLECULAR STRUCTURE

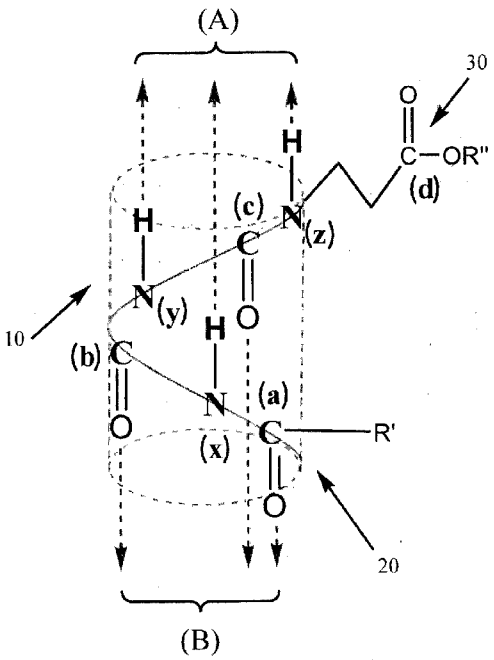


Figure 1

(57) Abstract: The present invention relates to a supramolecular structure comprising a plurality of peptide foldamer units, where each foldamer unit: (i) independently comprises at least three sequential ß-amino acid residues, one of which is N-acylated, and (ii) presents two complementary binding regions, each binding region comprising three sequential ß-amino acid residues, with one or both of the binding regions comprising the N-acylated ß-amino acid residue; wherein the foldamer units are associated through their complementary binding regions to provide the supramolecular structure.

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UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

SUPRAMOLECULAR STRUCTURE

Field of the Invention

The present invention relates in general to supramolecular structures and to a method of preparing the same. The supramolecular structures comprise peptide units, can develop filamentous character, and have a propensity to form higher order fibre structures. The supramolecular structures are well suited to forming such higher order fibre structures, and it will therefore be convenient to describe the invention with an emphasis toward this aspect. However, it is to be understood that the supramolecular structures according to the invention are not intended to be limited to any particular physical form.

Background of the Invention

Fibres, or networks of fibres (e.g. woven fibres), can provide structural strength to composite materials such as those originally developed for the aerospace and automotive industries.

Fibre technology is now applied in a diverse array of applications. For example, so called "smart textiles" are fibre structures where specific functionality on one or more fibres can provide for sensors and electronic circuits in a fabric, creating a wearable device, such as for monitoring heart rate, blood sugar or the presence of chemical agents. Advanced fibre technology is also increasingly being used in medical applications where features such as biocompatibility, strength, thickness and biodegradability or stability are often critical.

Both synthetic and natural fibres (e.g. carbon fibre and silk fibre, respectively) have shown some promise in such applications. However, suitable synthetic fibres often exhibit low biological compatibility and even toxicity, can be complex to manufacture, and may have limited potential for subsequent functionalisation. The

practical application of natural fibres can be constrained by a difficulty in facile mass production. Furthermore, the length and thickness of natural fibres typically depend on the organism that produces it, and such fibres are often coated with undesirable secretions from the production organism.

Supramolecular structures comprising peptides represent a unique source of biomaterial (Aida *et al.*, 2012, *Science*, **335**, 813-817; Boyle and Woolfson, 2011, *Chem. Soc. Rev.*, **40**, 4295-4306; Woolfson and Mahmoud, 2010, *Chem. Soc. Rev.*, **39**, 3464-3479; Lakshmanan *et al.*, 2012, *Trends in Biotechnology*, **30**, 2780-2790; Mahmoud *et al.*, 2010, *Biomaterials*, **31**, 7468-7474). Such biomaterial can offer advantages including biological compatibility, low toxicity, relative ease of preparation and potential for subsequent functionalisation. However, there remain several limitations and challenges in its practical application, particularly in the context of fibre technology. For example, the supramolecular structures can exhibit poor chemical, structural and metabolic stability, their rate of preparation can be relatively slow, and to date they have typically demonstrated limited ability to be formed into higher order fibre structures.

An opportunity therefore remains to develop new materials which can exhibit potential for fibre production and address or ameliorate one or more disadvantages or shortcomings associated with existing fibre forming materials and/or their methods of manufacture, or to at least provide a useful alternative to known fibre forming materials and their method of manufacture.

Summary of the Invention

The present invention therefore provides a supramolecular structure comprising a plurality of peptide foldamer units, where each foldamer unit:

(i) independently comprises at least three sequential ß-amino acid residues, one of which is N-acylated, and

(ii) presents two complementary binding regions, each binding region comprising three sequential ß-amino acid residues, with one or both of the binding regions comprising the N-acylated ß-amino acid residue;

wherein the foldamer units are associated through their complementary binding regions to provide the supramolecular structure.

The present invention further provides a method of preparing a supramolecular structure, the method comprising:

(i) providing a solution comprising a plurality of peptide foldamer units, where each foldamer unit:

(a) independently comprises at least three sequential ß-amino acid residues, one of which is N-acylated, and

(b) presents two complementary binding regions, each binding region comprising three sequential ß-amino acid residues, with one or both of the binding regions comprising the N-acylated ß-amino acid residue; and

(ii) allowing the peptide foldamer units to self-assemble through association of their complementary binding regions and form the supramolecular structure.

The supramolecular structure according to the present invention comprises a plurality of peptide foldamer units. Each peptide foldamer unit has a unique composition that provides for two complementary binding regions.

By the expression "two complementary binding regions" is meant that each peptide foldamer unit presents two regions, one of which has the potential to bind with the other region.

By presenting such complementary binding regions, a first peptide foldamer unit can bind to and associate with a second peptide foldamer unit through their complementary binding regions not dissimilar in principle to the way in which Lego® building blocks provide complementary binding regions that enable them to be coupled and form larger structural entities. Accordingly, at one level the peptide foldamer units in accordance with the invention can simplistically be viewed as

building blocks that can be associated through their complementary binding regions to form the supramolecular structure.

The unique composition of the peptide foldamer units not only enables association through respective complementary binding regions to form the supramolecular structure, but also provides for a surprisingly stable supramolecular structure that can be readily and rapidly produced.

Supramolecular structures according to the invention can also advantageously exhibit biological compatibility, low toxicity, good stability and potential for subsequent functionalisation.

Furthermore, the supramolecular structure can develop complex higher order structures. For example, supramolecular structures in accordance with the invention may develop into fibre structures.

The present invention therefore also provides fibre comprising one or more supramolecular structures in accordance with the invention.

An important feature of the invention relates to the nature of the peptide foldamer units. In one embodiment, the at least three sequential β-amino acid residues of the peptide foldamer units are β^3-amino acid residues.

In a further embodiment, each binding region of the peptide foldamer units has a helix conformation.

In yet a further embodiment, each binding region of the peptide foldamer units has a 14-helix conformation.

According to the method of the invention, the peptide foldamer units are provided in a solution and allowed to self-assemble and form the supramolecular structure. The solution can advantageously be an aqueous solution, and the peptide foldamer units

surprisingly self-assemble rapidly to form the supramolecular structure. Such attributes are believed to render the method according to the invention well suited for scale up and mass production of the supramolecular structures.

Further aspects and/or embodiments of the invention are discussed in more detail below.

Brief Description of the Drawings

The present invention will herein be described with reference to the following non-limiting drawings in which:

Figure 1 illustrates a schematic representation of a peptide foldamer unit according to the present invention in a helix conformation and having three sequential β-amino acid residues;

Figure 2 illustrates a schematic representation of a peptide foldamer unit according to the present invention in a helix conformation and having six sequential β-amino acid residues where in (a) intramolecular helix stabilisation hydrogen bonding is highlighted, and in (b) the complementary binding regions are highlighted;

Figure 3 illustrates a schematic representation of three peptide foldamer units according to the invention being associated to form a supramolecular structure, where each peptide foldamer unit has six sequential β-amino acid residues, and where both intramolecular helix stabilisation hydrogen bonding, association hydrogen bonding, and the complementary binding regions are highlighted;

Figure 4 illustrates images of supramolecular structures according to the invention in the form of fibres prepared using N-acetylated β^3-hexapeptide foldamer units (a-d), and N-acetylated β^3-tripeptide foldamer units (e and f). Panels (a) and (b) depict fibres formed from SEQ ID NO: 1, panel (c) is a fibre formed from SEQ ID NO: 4, panel (d) is a fibre formed from SEQ ID NO: 2; panel (e) is a fibre formed from SEQ

ID NO: 6 and panel (f) is a fibre formed from SEQ ID NO: 5;

Figure 5 illustrates atomic force microscopy (AFM) images of filaments of SEQ ID NO: 6. (a) large area scan; height scale is ~ 40 nm. (b) 3D rendered representation of the area outlined on (a). There is periodicity in the smaller filaments. (c, d) the same area; along the lines, height profiles have been measured and depicted below the images. Numbers correspond to the profile below each image; and

Figure 6 illustrates a schematic representation of (a) an axial view of a section of supramolecular structure SEQ ID NO: 4 in crystal form, (b) the intramolecular (light dashes) and intermolecular (dark dashes) H-bonding of supramolecular structure SEQ ID NO: 4 in crystal form , (c) a space-filling model of a section of supramolecular structure SEQ ID NO: 4 highlighting the axial self-assembly, (d) the associated helical β^3-peptide foldamer units providing for the supramolecular structure and showing the alignment and regular spacing or substituents along each face.

All figures have been filed in colour and are available on request.

Detailed Description of the Invention

The present invention provides for supramolecular structures. By the expression "supramolecular structure" is meant an assembly of molecular subunits or components that are associated and form together a larger unit object.

In the context of the present invention, the supramolecular structure comprises a plurality of peptide foldamer units. It is therefore an assembly of the peptide foldamer units that associate to form the supramolecular structure.

By the expression "peptide foldamer unit(s)" is meant a discreet chain molecule or oligomer comprising sequential amino acid residues that provide for a peptide sequence, and at least part, if not all, of which adopts a secondary structure stabilised by non-covalent interactions, for example hydrogen bonding. Further detail

concerning the form of the peptide foldamer units is provided below.

Each of the peptide foldamer units independently comprises at least three sequential β-amino acid residues. By having at least three sequential β-amino acid residues, those skilled in the art will appreciate that each foldamer unit presents a β-peptide sequence. Each foldamer unit may comprise the same or different at least three sequential β-amino acid residues, and each β-amino acid residue within the at least three sequential β-amino acid residues may be the same or different.

Provided that each foldamer unit comprises at least three sequential β-amino acid residues, and the folder units can associate as described herein, there is no particular limitation concerning the number of sequential β-amino acid residues that can be present.

In some embodiments, a given foldamer unit may comprise 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30 sequential β-amino acid residues. In other embodiments, the at least three sequential β-amino acid residues may be present in multiples of 3, for example, 3, 6, 9, 12, 15, 18, 21, 24, 27 or 30, or for example, 3, 6, 9 or 12, or for example, 3 or 6.

Provided that the at least three sequential β-amino acid residues and two complementary binding regions are present, each foldamer unit may comprise one or more linking groups. For example, a given peptide foldamer unit may comprise three sequential β-amino acid residues that are coupled through a linking group to a further and independent at least three sequential β-amino acid residues.

To further illustrate the nature of the peptide foldamer units, a given β-amino acid residue may be represented as "β-AA" and a linking group as "L". In that case, a peptide foldamer unit may be illustrated as comprising one of the following general formulae (I)-(III):

$$(\beta\text{-AA})_x \qquad (I)$$

$$(\beta\text{-AA})_x\text{-L-}(\beta\text{-AA})_y \qquad \text{(II)}$$

$$(\beta\text{-AA})_x\text{-L-}(\beta\text{-AA})_y\text{-L-}(\beta\text{-AA})_z \qquad \text{(III)}$$

where each β-amino acid residue β-AA may be the same or different, each linking group L may be the same or different, and x, y and z are each independently an integer equal to or greater than 3. For example, x, y and z may be an integer ranging from 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30. In one embodiment, x, y and z are each independently an integer selected from 3, 6, 9, 12, 15, 18, 21, 24, 27, or 30, or each an integer independently selected from 3, 6, 9, or 12, or each an integer independently selected from 3 or 6.

It will be appreciated that a given peptide foldamer unit may comprise more than 3 groups of at least three sequential β-amino acid residues that are each linked by a linking group L.

Provided that the peptide foldamer units can associate through their complementary binding regions to provide the supramolecular structure, there is no particular limitation regarding the nature of the linking group (L), if present.

In one embodiment, the linking group (L), before being coupled to at least three sequential β-amino acid residues, is a moiety comprising an acid (-COOH) group and an amine ($-NH_2$) group. In this way, the acid and amine groups of the linking group (L) can react with appropriate terminal groups of two at least three sequential β-amino acid residues, thereby coupling the two at least three sequential β-amino acid residues as depicted in formula (II) above. Upon coupling two at least three sequential β-amino acid residues the linking group (L) can of course be described as a moiety comprising acid group and an amine group residues (e.g. -C(O)- and -NH-, respectively). The linking group (L) may therefore be described as an amino acid residue. In that sense, it will be appreciated that that the linking group (L) will not be

a β-amino acid residue.

In one embodiment, the linking group (L) is one or more amino acid residues other than a β-amino acid residue. In that case, the linking group L may comprise one or more non-β-amino acid residues of general formula (IV):

$$-NR^z\text{-}A\text{-}C(O)- \qquad (IV)$$

where A is selected from optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, and optionally substituted heteroaryl, and R^z is selected from hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, and optionally substituted heteroaryl.

In one embodiment, the linking group L comprises one or more of an α-amino acid residue, γ-amino acid residue, δ-amino acid residue, ε-amino acid residue and ζ-amino acid residue.

In a further embodiment, the linking group L may be selected from amino hexanoic acid residue and 4-amino benzoic acid residue.

In another embodiment, L is or comprises a bioactive agent.

The expression "bioactive agent" is used herein to define any substance that is of medical or veterinary therapeutic, prophylactic or diagnostic utility capable of forming, or forming part of, the linking group L. For example a bioactive agent may be a drug or therapeutically active agent, including pharmacologically active agents (eg receptor binding agonist or antagonists, cytotoxic agents), pharmacologically inactive agents (eg antibiotics) and prodrugs thereof. The bioactive agent will generally be a substance (e.g. pharmaceutical substance) for therapeutic use whose

application (or one or more applications) involves: a chemical interaction, or physico-chemical interaction, with a subject's physiological system; or an action on an infectious agent, or on a toxin or other poison, in subject's body; or with biological material such as cells *in vitro*.

As used herein, a "therapeutic agent" refers to a bioactive agent that, when administered to a subject, will cure, or at least relieve to some extent, one or more symptoms of, a disease or disorder.

As used herein, a "prophylactic agent" refers to a bioactive agent that, when administered to a subject either prevents the occurrence of a disease or disorder or, if administered subsequent to a therapeutic agent, prevents or retards the recurrence of the disease or disorder.

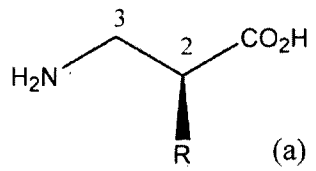
The at least three sequential β-amino acid residues may present within the foldamer unit in a helix conformation. For example, the at least three sequential β-amino acid residues may present in the form of an 8-, 10-, 10/12- or 14- helix conformation. In one embodiment, the at least three sequential β-amino acid residues present in the form of a 14-helix conformation.

Depending upon its composition, the entire peptide foldamer unit may present in the form of a helix conformation as herein defined (e.g. in the form of an 8-, 10-, 10/12- or 14- helix conformation).

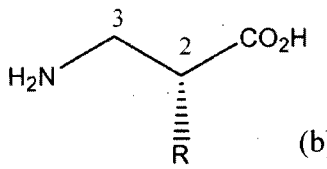
Those skilled in the art will appreciate that a helix conformation provided by the at least three sequential β-amino acid residues will typically be stabilised by intramolecular hydrogen bonding. The pitch of a given helix conformation will vary depending upon the size nomination of the helix. For example, a 14-helix β-peptide conformation will typically have a pitch of about 4.8 Å and about three β-amino acid residues per turn of the helix. The side chains of the β-amino acid residues in a 14-helix are typically aligned symmetrically along the faces of the helix.

An important feature of the present invention is that the supramolecular structure comprises at least three sequential β-amino acid residues. Those skilled in the art will readily appreciate what is meant by the general term "amino acid", and also by what is meant when this term is preceded by symbols such as "α", "β", "γ", "δ", "ε" and "ζ". Such terms/symbols used herein are intended to have their ordinary meaning within the art. The amino acids/amino acid residues may be naturally occurring or non-naturally occurring.

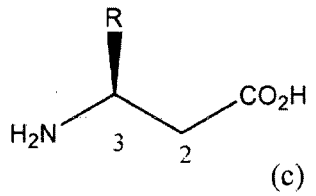
For example, the term "β-amino acid" refers to an amino acid that has two (2) carbon atoms separating the carboxyl terminus (C-terminus) and the amino terminus (N-terminus). As such, β-amino acids with a specific side chain can exist as the *R* or *S* enantiomers at either of the α (C2) carbon or the β (C3) carbon, resulting in a total of 4 possible isomers for any given side chain (see structures (a-d) below). The side chains may be the same as those of naturally occurring L-α-amino acids or may be the side chains of non-naturally occurring amino acids.



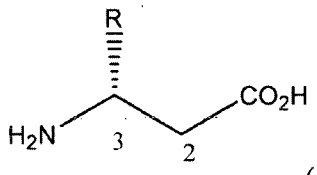
(a)



(b)



(c)



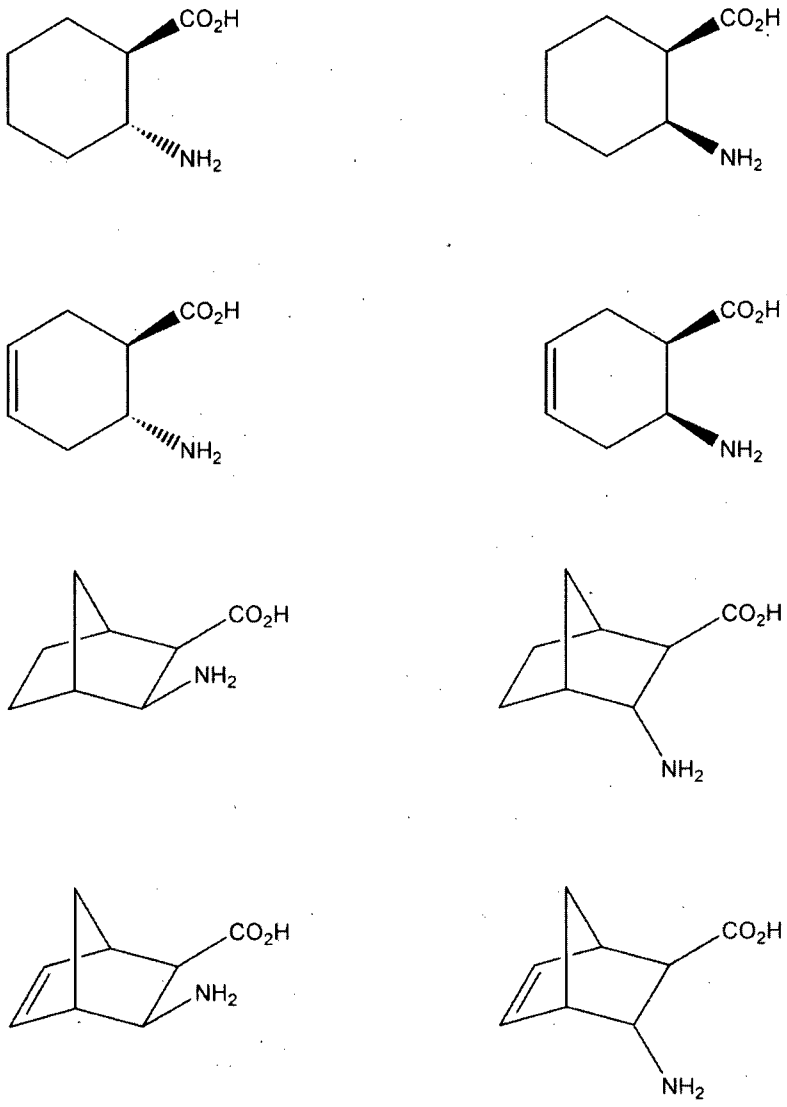
(d)

A β-amino acid may be mono-, di-, tri- or tetra-substituted. Mono-substitution may be at the C2 or C3 carbon atom. Di-substitution includes two substituents at the C2 carbon atom, two substituents at the C3 carbon atom or one substituent at each of the C2 and C3 carbon atoms. Tri-substitution includes two substituents at the C2 carbon atom and one substituent at the C3 carbon atom or two substituents at the C3 carbon

atom and one substituent at the C2 carbon atom. Tetra-substitution provides for two substituents at the C2 carbon atom and two substituents at the C3 carbon atom.

Suitable substituents for the β-amino acid include -C_1-C_6alkyl, -$(CH_2)_nCOR_1$, -$(CH_2)_nR_2$, -PO_3H, -$(CH_2)_n$heterocyclyl or -$(CH_2)_n$aryl where n is an integer ranging from 1 to 8, R_1 is -OH, -NH_2, -NHC_1-C_3alkyl, -OC_1-C_3alkyl or -C_1-C_3alkyl and R_2 is -OH, -SH, -SC_1-C_3alkyl, -OC_1-C_3alkyl, -C_3-C_{12}cycloalkyl, -NH_2, -NHC_1-C_3alkyl or -NHC(C=NH)NH_2, and where each alkyl, cycloalkyl, aryl or heterocyclyl group may be substituted with one or more groups selected from -OH, -NH_2, -NHC_1-C_3alkyl, -OC_1-C_3alkyl, -SH, -SC_1-C_3alkyl, -CO_2H, -CO_2C_1-C_3alkyl, -$CONH_2$ or -$CONHC_1$-C_3alkyl.

Other suitable β-amino acids include conformationally constrained β-amino acids. Cyclic β-amino acids are conformationally constrained and are generally not accessible to enzymatic degradation. Suitable cyclic β-amino acids include, but are not limited to, *cis*- and *trans*-2-aminocyclopropyl carboxylic acids, 2-aminocyclobutyl and cyclobutenyl carboxylic acids, 2-aminocyclopentyl and cyclopentenyl carboxylic acids, 2-aminocyclohexyl and cyclohexenyl carboxylic acids and 2-amino-norbornane carboxylic acids and their derivatives, some of which are shown below:



Suitable derivatives of β-amino acids include salts and may have functional groups protected by suitable protecting groups.

Those skilled in the art will appreciate that a peptide represents a series of two or more amino acids linked through a covalent bond formed between the carboxyl group of one amino acid and the amino group of another amino acid (i.e. the so called peptide bond). Accordingly, a "β-peptide" refers to a peptide that comprises β-amino acid residues. A β^3-peptide comprises β-amino acid residues that are substituted with one substituent at the C3 β carbon atom (i.e. a β^3-amino acid residue). A β^2-peptide comprises β-amino acid residues that are substituted with one substituent at the C2 α

carbon atom (i.e. a β^2-amino acid residue). The at least three sequential β-amino acid residues may therefore be described as a β-peptide sequence, or at least a β-tripeptide sequence of the foldamer unit.

In one embodiment, the at least three sequential β-amino acid residues of at least one peptide foldamer unit are β^2-amino acid residues.

In another embodiment, the at least three sequential β-amino acid residues of at least one peptide foldamer unit are β^3-amino acid residues.

In a further embodiment, the at least three sequential β-amino acid residues of at least one peptide foldamer unit are R-β^2-amino acid residues.

In another embodiment, the at least three sequential β-amino acid residues of at least one peptide foldamer unit are S-β^3-amino acid residues.

In a further embodiment, all β-amino acid residues in each peptide foldamer unit are β^2-amino acid residues.

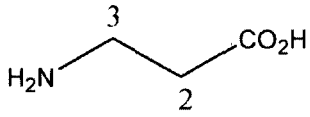
In another embodiment, all β-amino acid residues in each peptide foldamer unit are β^3-amino acid residues.

In a further embodiment, all β-amino acid residues in each peptide foldamer unit are R-β^2-amino acid residues.

In another embodiment, all β-amino acid residues in each peptide foldamer unit are S-β^2-amino acid residues.

Examples of β-amino acid residues that may provide for the at least three sequential β-amino acid residues include, but are not limited to, those set out in Table 1:

Table 1: β-amino acid residues



β-amino acid	**Structure of side chain**	**Position of side chain**
β^2-alanine	$-CH_3$	2
β^3-alanine	$-CH_3$	3
β^2-arginine	$-(CH_2)_3NHC(=NH)NH_2$	2
β^3-arginine	$-(CH_2)_3NHC(=NH)NH_2$	3
β^2-asparagine	$-CH_2CONH_2$	2
β^3-asparagine	$-CH_2CONH_2$	3
β^2-aspartic acid	$-CH_2CO_2H$	2
β^3-aspartic acid	$-CH_2CO_2H$	3
β^2-cysteine	$-CH_2SH$	2
β^3-cysteine	$-CH_2SH$	3
β^2-glutamine	$-(CH_2)_2CONH_2$	2
β^3-glutamine	$-(CH_2)_2CONH_2$	3
β^2-glutamic acid	$-(CH_2)_2CO_2H$	2
β^3-glutamic acid	$-(CH_2)_2CO_2H$	3
β-glycine	-	-
β^2-histidine	$-CH_2$(4-imidazole)	2
β^3-histidine	$-CH_2$(4-imidazole)	3
β^2-isoleucine	$-CH(CH_3)CH_2CH_3$	2
β^3-isoleucine	$-CH(CH_3)CH_2CH_3$	3
β^2-leucine	$-CH_2CH(CH_3)_2$	2
β^3-leucine	$-CH_2CH(CH_3)_2$	3
β^2-lysine	$-(CH_2)_4NH_2$	2
β^3-lysine	$-(CH_2)_4NH_2$	3
β^2-methionine	$-(CH_2)_2SCH_3$	2

β-amino acid	Structure of side chain	Position of side chain
β^3-methionine	$-(CH_2)_2SCH_3$	3
β^2-phenylalanine	$-CH_2Ph$	2
β^3-phenylalanine	$-CH_2Ph$	3
β^2-serine	$-CH_2OH$	2
β^3-serine	$-CH_2OH$	3
β^2-threonine	$-CH(CH_3)OH$	2
β^3-threonine	$-CH(CH_3)OH$	3
β^2-tryptophan	$-CH_2$(3-indolyl)	2
β^3-tryptophan	$-CH_2$(3-indolyl)	3
β^2-tyrosine	$-CH_2$(4-hydroxyphenyl)	2
β^3-tyrosine	$-CH_2$(4-hydroxyphenyl)	3
β^2-valine	$-CH(CH_3)_2$	2
β^3-valine	$-CH(CH_3)_2$	3
β^2-ornithine	$-(CH_2)_3NH_2$	2
β^3-ornithine	$-(CH_2)_3NH_2$	3
β^2-norleucine	$-(CH_2)_3CH_3$	2
β^3-norleucine	$-(CH_2)_3CH_3$	3
β^2-norvaline	$-(CH_2)_2CH_3$	2
β^3-norvaline	$-(CH_2)_2CH_3$	3
β^2-O-allylserine (βaSer)	$-CH_2OCH_2CH=CH_2$	2
β^3-O-allylserine (βaSer)	$-CH_2OCH_2CH=CH_2$	3
B^2-allylglycine	$-CH_2CH=CH_2$	2
B^3-allylglycine	$-CH_2CH=CH_2$	3

Cyclic β-amino acids such as β-proline, aminocyclopentane carboxylic acid (ACPC), and aminocyclohexane carboxylic acid (ACHC) may also be used:

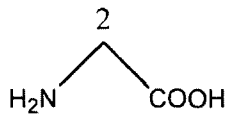
Similarly, the term "α-amino acid" as used herein refers to a compound having an amino group and a carboxyl group in which the amino group and the carboxyl group are separated by a single carbon atom, the α-carbon atom. An α-amino acid includes

naturally occurring and non-naturally occurring L-amino acids and derivatives thereof such as salts or derivatives where functional groups are protected by suitable protecting groups.

The α-amino acid may be substituted in the α-position with a group selected from -C_1-C_6alkyl, -$(CH_2)_nCOR_1$, -$(CH_2)_nR_2$, -PO_3H, -$(CH_2)_n$heterocyclyl or -$(CH_2)_n$aryl where n is an integer ranging from 1 to 8, R_1 is -OH, -NH_2, -NHC_1-C_3alkyl, -OC_1-C_3alkyl or -C_1-C_3alkyl and R_2 is -OH, -SH, -SC_1-C_3alkyl, -OC_1-C_3alkyl, -C_3-C_{12}cycloalkyl, -NH_2, -NHC_1-C_3alkyl or -NHC(C=NH)NH_2, and where each alkyl, cycloalkyl, aryl or heterocyclyl group may be substituted with one or more groups selected from -OH, -NH_2, -NHC_1-C_3alkyl, -OC_1-C_3alkyl, -SH, -SC_1-C_3alkyl, -CO_2H, -CO_2C_1-C_3alkyl, -$CONH_2$ or -$CONHC_1$-C_3alkyl.

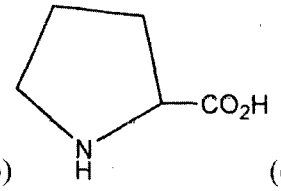
Examples of twenty naturally occurring α-amino acids are presented below in Table 2, together with their associated structural and letter abbreviations.

Table 2: α-amino acid residues



Amino Acid	**Three-letter Abbreviation**	**One-letter symbol**	**Structure of side chain at (2)**
Alanine	Ala	A	-CH_3
Arginine	Arg	R	-$(CH_2)_3NHC(=N)NH_2$
Asparagine	Asn	N	-CH_2CONH_2
Aspartic acid	Asp	D	-CH_2CO_2H
Cysteine	Cys	C	-CH_2SH
Glutamine	Gln	Q	-$(CH_2)_2CONH_2$
Glutamic acid	Glu	E	-$(CH_2)_2CO_2H$
Glycine	Gly	G	-H
Histidine	His	H	-CH_2(4-imidazolyl)

Amino Acid	Three-letter Abbreviation	One-letter symbol	Structure of side chain at (2)
Isoleucine	Ile	I	$-CH(CH_3)CH_2CH_3$
Leucine	Leu	L	$-CH_2CH(CH_3)_2$
Lysine	Lys	K	$-(CH_2)_4NH_2$
Methionine	Met	M	$-(CH_2)_2SCH_3$
Phenylalanine	Phe	F	$-CH_2Ph$
Proline	Pro	P	see formula (e) below for full structure
Serine	Ser	S	$-CH_2OH$
Threonine	Thr	T	$-CH(CH_3)OH$
Tryptophan	Trp	W	$-CH_2$(3-indolyl)
Tyrosine	Tyr	Y	$-CH_2$(4-hydroxyphenyl)
Valine	Val	V	$-CH(CH_3)_2$



Proline (Pro) (e)

The expression "non-naturally occurring amino acid" as used herein, refers to amino acids that do not occur in nature, for example amino acids having a side chain that does not occur in the naturally occurring L-α-amino acids such as those listed in Table 2.

Examples of non-naturally occurring amino acids are presented below in Table 3.

Table 3: non-naturally occurring amino acids

Non-conventional amino acid	Code	Non-conventional amino acid	Code
α-aminobutyric acid	Abu	L-N-methylalanine	Nmala
α-amino-α-methylbutyrate	Mgabu	L-N-methylarginine	Nmarg

Non-conventional amino acid	Code	Non-conventional amino acid	Code
aminocyclopropane-carboxylate	Cpro	L-N-methylasparagine	Nmasn
		L-N-methylaspartic acid	Nmasp
aminoisobutyric acid	Aib	L-N-methylcysteine	Nmcys
aminonorbornyl-carboxylate	Norb	L-N-methylglutamine	Nmgln
		L-N-methylglutamic acid	Nmglu
cyclohexylalanine	Chexa	L-N-methylhistidine	Nmhis
cyclopentylalanine	Cpen	L-N-methylisoleucine	Nmile
D-alanine	Dal	L-N-methylleucine	Nmleu
D-arginine	Darg	L-N-methyllysine	Nmlys
D-aspartic acid	Dasp	L-N-methylmethionine	Nmmet
D-cysteine	Dcys	L-N-methylnorleucine	Nmnle
D-glutamine	Dgln	L-N-methylnorvaline	Nmnva
D-glutamic acid	Dglu	L-N-methylornithine	Nmorn
D-histidine	Dhis	L-N-methylphenylalanine	Nmphe
D-isoleucine	Dile	L-N-methylproline	Nmpro
D-leucine	Dleu	L-N-methylserine	Nmser
D-lysine	Dlys	L-N-methylthreonine	Nmthr
D-methionine	Dmet	L-N-methyltryptophan	Nmtrp
D-ornithine	Dorn	L-N-methyltyrosine	Nmtyr
D-phenylalanine	Dphe	L-N-methylvaline	Nmval
D-proline	Dpro	L-N-methylethylglycine	Nmetg
D-serine	Dser	L-N-methyl-t-butylglycine	Nmtbug
D-threonine	Dthr	L-norleucine	Nle
D-tryptophan	Dtrp	L-norvaline	Nva
D-tyrosine	Dtyr	α-methyl-aminoisobutyrate	Maib
D-valine	Dval	α-methyl-aminobutyrate	Mgabu
D-α-methylalanine	Dmala	α-methylcyclohexylalanine	Mchexa
D-α-methylarginine	Dmarg	α-methylcylcopentylalanine	Mcpen
D-α-methylasparagine	Dmasn	α-methyl-α-napthylalanine	Manap
D-α-methylaspartate	Dmasp	α-methylpenicillamine	Mpen

Non-conventional amino acid	Code	Non-conventional amino acid	Code
D-α-methylcysteine	Dmcys	N-(4-aminobutyl)glycine	Nglu
D-α-methylglutamine	Dmgln	N-(2-aminoethyl)glycine	Naeg
D-α-methylhistidine	Dmhis	N-(3-aminopropyl)glycine	Norn
D-α-methylisoleucine	Dmile	N-amino-α-methylbutyrate	Nmaabu
D-α-methylleucine	Dmleu	α-napthylalanine	Anap
D-α-methyllysine	Dmlys	N-benzylglycine	Nphe
D-α-methylmethionine	Dmmet	N-(2-carbamylethyl)glycine	Ngln
D-α-methylornithine	Dmorn	N-(carbamylmethyl)glycine	Nasn
D-α-methylphenylalanine	Dmphe	N-(2-carboxyethyl)glycine	Nglu
D-α-methylproline	Dmpro	N-(carboxymethyl)glycine	Nasp
D-α-methylserine	Dmser	N-cyclobutylglycine	Ncbut
D-α-methylthreonine	Dmthr	N-cycloheptylglycine	Nchep
D-α-methyltryptophan	Dmtrp	N-cyclohexylglycine	Nchex
D-α-methyltyrosine	Dmty	N-cyclodecylglycine	Ncdec
D-α-methylvaline	Dmval	N-cyclododecylglycine	Ncdod
D-N-methylalanine	Dnmala	N-cyclooctylglycine	Ncoct
D-N-methylarginine	Dnmarg	N-cyclopropylglycine	Ncpro
D-N-methylasparagine	Dnmasn	N-cycloundecylglycine	Ncund
D-N-methylaspartate	Dnmasp	N-(2,2-diphenylethyl)glycine	Nbhm
D-N-methylcysteine	Dnmcys	N-(3,3-diphenylpropyl)glycine	Nbhe
D-N-methylglutamine	Dnmgln	N-(3-guanidinopropyl)glycine	Narg
D-N-methylglutamate	Dnmglu	N-(1-hydroxyethyl)glycine	Nthr
D-N-methylhistidine	Dnmhis	N-(hydroxyethyl))glycine	Nser
D-N-methylisoleucine	Dnmile	N-(imidazolylethyl))glycine	Nhis
D-N-methylleucine	Dnmleu	N-(3-indolylyethyl)glycine	Nhtrp
D-N-methyllysine	Dnmlys	N-methyl-γ-aminobutyrate	Nmgabu
N-methylcyclohexylalanine	Nmchexa	D-N-methylmethionine	Dnmmet
D-N-methylornithine	Dnmorn	N-methylcyclopentylalanine	Nmcpen
N-methylglycine	Nala	D-N-methylphenylalanine	Dnmphe
N-methylaminoisobutyrate	Nmaib	D-N-methylproline	Dnmpro

Non-conventional amino acid	Code	Non-conventional amino acid	Code
N-(1-methylpropyl)glycine	Nile	D-N-methylserine	Dnmser
N-(2-methylpropyl)glycine	Nleu	D-N-methylthreonine	Dnmthr
D-N-methyltryptophan	Dnmtrp	N-(1-methylethyl)glycine	Nval
D-N-methyltyrosine	Dnmtyr	N-methylnapthylalanine	Nmanap
D-N-methylvaline	Dnmval	N-methylpenicillamine	Nmpen
γ-aminobutyric acid	Gabu	N-(*p*-hydroxyphenyl)glycine	Nhtyr
L-*t*-butylglycine	Tbug	N-(thiomethyl)glycine	Ncys
L-ethylglycine	Etg	penicillamine	Pen
L-homophenylalanine	Hphe	L-α-methylalanine	Mala
L-α-methylarginine	Marg	L-α-methylasparagine	Masn
L-α-methylaspartate	Masp	L-α-methyl-*t*-butylglycine	Mtbug
L-α-methylcysteine	Mcys	L-methylethylglycine	Metg
L-α-methylglutamine	Mgln	L-α-methylglutamate	Mglu
L-α-methylhistidine	Mhis	L-α-methylhomophenyl alanine	Mhphe
L-α-methylisoleucine	Mile	N-(2-methylthioethyl)glycine	Nmet
L-α-methylleucine	Mleu	L-α-methyllysine	Mlys
L-α-methylmethionine	Mmet	L-α-methylnorleucine	Mnle
L-α-methylnorvaline	Mnva	L-α-methylornithine	Morn
L-α-methylphenylalanine	Mphe	L-α-methylproline	Mpro
L-α-methylserine	Mser	L-α-methylthreonine	Mthr
L-α-methyltryptophan	Mtrp	L-α-methyltyrosine	Mtyr
L-α-methylvaline	Mval	L-N-methylhomophenyl alanine	Nmhphe
N-(N-(2,2-diphenylethyl) carbamylmethyl)glycine	Nnbhm	N-(N-(3,3-diphenylpropyl) carbamylmethyl)glycine	Nnbhe
1-carboxy-1-(2,2-diphenyl-ethylamino)cyclopropane	Nmbc		

Further examples of non-naturally occurring amino acids and derivatives thereof include, but are not limited to, norleucine, 4-aminobenzoic acid, 4-amino butyric acid, 4-amino-3-hydroxy-5-phenylpentanoic acid, 6-aminohexanoic acid, *t*-butylglycine,

norvaline, phenylglycine, ornithine, citrulline, sarcosine, 4-amino-3-hydroxy-6-methylheptanoic acid, 2-thienyl alanine and/or D-isomers of amino acids.

An important feature of the present invention is that one of the at least three sequential β-amino acid residues is N-acylated. By being "N-acylated", those skilled in the art will appreciate that it will be a terminal nitrogen atom (N-terminus) of the at least three sequential β-amino acid residues that will be acylated.

To further illustrate the nature of the peptide foldamer units in accordance with the invention, formulae (I)–(III) from above are reproduced below in more detail as new formulae (V)–(VII) showing the presence of the N-acyl group (here R^x-C(O)-).

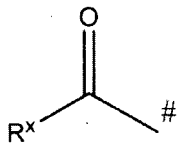
$$R^x\text{-}C(O)\text{-}(\beta\text{-}AA)_x \qquad (V)$$

$$R^x\text{-}C(O)\text{-}(\beta\text{-}AA)_x\text{-}L\text{-}(\beta\text{-}AA)_y \qquad (VI)$$

$$R^x\text{-}C(O)\text{-}(\beta\text{-}AA)_x\text{-}L\text{-}(\beta\text{-}AA)_y\text{-}L\text{-}(\beta\text{-}AA)_z \qquad (VII)$$

where β-AA, L, x, y and z are as herein defined, and R^x is selected from optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, and optionally substituted heteroaryl.

Accordingly, in one embodiment the N-acyl group of the at least three sequential β-amino acid residues is represented by formula (VIII):



(VIII)

where R^x is selected from optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, and optionally substituted heteroaryl, and # designates the point of attachment to the N-terminal nitrogen atom of the at least three sequential β-amino acid residues.

In one embodiment, R^x of formula (VIII) is selected from optionally substituted -C_{1-6}alkyl, optionally substituted -C_{1-6}haloalkyl, optionally substituted -C_{2-6}alkenyl, optionally substituted -C_{3-6}cycloalkyl, optionally substituted phenyl, optionally substituted -C_{1-3}alkylC_{3-6}cycloalkyl and optionally substituted -C_{1-3}alkylphenyl.

In a further embodiment, R^x of formula (VIII) is selected from -C_{1-3}alkyl, -C_{1-3}haloalkyl and -C_{2-3}alkenyl, especially methyl, ethyl, propyl, isopropyl, trifluoromethyl, difluoromethyl, allyl, 1-propenyl and 2-propenyl.

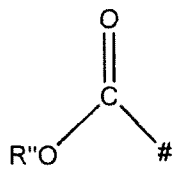
Without wishing to be limited by theory, the N-acyl group of the at least three sequential ß-amino acid residues is believed to a play role in establishing the complementary binding regions of the peptide foldamer units. In particular, association of the peptide foldamer units through their complementary binding regions is believed to occur via hydrogen bonding. The hydrogen bonding is in turn believed to be facilitated by each peptide foldamer unit presenting three appropriately orientated hydrogen bond acceptor groups that provide for the first complementary binding region, and three appropriately orientated hydrogen bond donor groups that provide for the second complementary binding region. The hydrogen bond acceptor groups are believed to be -NH groups provided by amide groups derived from the at least three sequential ß-amino acid residues, and the hydrogen bond donor groups are believed to be -C(O)- groups provided by amide groups derived from the at least three sequential ß-amino acid residues. The presence of the N-acyl amide group is believed to facilitate providing the appropriately orientated three hydrogen bond acceptor groups and three hydrogen bond donor groups, which in turn give rise to the two complementary binding regions.

Each foldamer unit in accordance with the invention independently comprises at least three sequential ß-amino acid residues. In this context, the term "residues" refers to the condensed residues of the at least three sequential ß-amino acids that give rise at least a tripeptide sequence. In other words, the at least three sequential ß-amino acid residues are directly coupled to each other to provide for a peptide sequence.

As previously noted, one of the at least three sequential ß-amino acid residues is N-acylated. Accordingly the terminal nitrogen atom of the peptide sequence derived from the at least three sequential ß-amino acid residues will be acylated, for example with an acyl group represented by general formula (VIII) defined herein.

Those skilled in the art will appreciate that in addition to having a N-terminus (which is acylated according to the present invention), the peptide sequence derived from the at least three sequential ß-amino acid residues will also have a C-terminus. Provided that the peptide foldamer units present the two complementary binding regions and can associate to provide for the supramolecular structure, there is no particular limitation concerning the molecular form of the C-terminus.

In one embodiment, the peptide sequence derived from the at least three sequential ß-amino acid residues has a C-terminus of general formula (IX):



(IX)

where R" is selected from hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, and optionally substituted heteroaryl, and # designates the point of attachment to the α-carbon atom of one of the at least three sequential ß-amino acid residues.

In one embodiment, R" of formula (IX) is selected from hydrogen, optionally

substituted -C_{1-6}alkyl, optionally substituted -C_{1-6}haloalkyl, optionally substituted -C_{2-6}alkenyl, optionally substituted -C_{3-6}cycloalkyl, optionally substituted phenyl, optionally substituted -C_{1-3}alkylC_{3-6}cycloalkyl and optionally substituted -C_{1-3}alkylphenyl.

In a further embodiment, R'' of formula (IX) is selected from hydrogen, -C_{1-3}alkyl, -C_{1-3}haloalkyl and -C_{2-3}alkenyl, especially methyl, ethyl, propyl, isopropyl, trifluoromethyl, difluoromethyl, allyl, 1-propenyl and 2-propenyl.

To assist with further describing the nature of the peptide foldamer units, reference can be made to Figure 1. Thus, Figure 1 illustrates a schematic representation of a peptide foldamer unit (10) in accordance with the invention. The peptide foldamer unit (10) in this instance consists of only three sequential ß-amino acid residues, one of which is N-acylated. The three sequential ß-amino acid residues present in the form of a helix conformation. R' represents an organic substituent of the N-acyl group (20), and R'' represents a hydrogen atom or organic substituent of the C-terminus group (30). The acylated nitrogen atom of the relevant ß-amino acid residue is designated (x), with the remaining two nitrogen atoms of the three sequential ß-amino acid residues designated (y) and (z), respectively. Each of the nitrogen atoms (x-z) form part of a corresponding amide group, which for convenience are designated amide groups (x-y), respectively. Each of the nitrogen atoms (x-y) have a hydrogen atom covalently attached thereto and provide for three hydrogen bond acceptor groups (-N-H). Each of the three hydrogen bond acceptor groups are orientated in an axial direction relative to the helix structure and collectively provide for one of the two complementary binding regions designated (A).

Each of the three amide groups (x-y) provide for carbonyl moieties -C(O)- (a-c), respectively, which are each orientated in an axial direction relative to the helix structure and opposite to the orientation of the three -N-H bonds (x-y). The three carbonyl moieties (a-c) present as hydrogen bond donor groups and collectively form the second complementary binding region designated (B). The fourth carbonyl moiety (d) forms part of the C-terminus group (30).

Those skilled in the art will appreciate that binding region (A) has the potential to bind with a complementary binding region (B).

By presenting only three sequential ß-amino acid residues, the acyl amide group (20) provides both a -N-H acceptor group (x) that forms part of the binding region (A), and a -C(O)- donor group (a) that forms part of binding region (B). Accordingly, in this case, both binding regions (A) and (B) comprise the N-acylated ß-amino acid residue. Furthermore, each binding region can be seen to comprise the three sequential ß-amino acid residues.

As outlined above, it is believed that the presence of the N-acylated ß-amino acid residue provides for the appropriately orientated hydrogen bond donor and acceptor groups which in turn give rise to the respective complementary binding regions.

To further illustrate the nature of the peptide foldamer unit, reference is further made to Figure 2 (a) and (b). Thus, Figure 2 (a) illustrates a schematic representation of a peptide foldamer unit in accordance with the invention (illustrated with less detail than in Figure 1 for clarity). The peptide foldamer unit in this case consists of six sequential ß-amino acid residues (1-6), one of which is N-acylated. In this illustration, only intramolecular hydrogen bond donor and acceptor interactions are highlighted.

Figure 2 (b) represents the same peptide foldamer unit illustrated in Figure 2 (a) but instead only highlights the oppositely axial orientated (i) -N-H acceptor groups (providing for binding region A), and (ii) -C(O)- donor groups (providing for binding region B). In contrast with the peptide foldamer unit illustrated in Figure 1, only one of the binding regions, in this case binding region B, comprises the N-acylated ß-amino acid residue. In other words, the -C(O)- moiety of the N-acyl group provides for one of the three -C(O)- donor groups that gives rise to binding region B, but the -N-H moiety of the associated amide group does not provide for one of the three -N-H acceptor groups that gives rise to binding region A. Instead, this -N-H moiety of the associated amide group provides for intramolecular hydrogen bonding as illustrated in

Figure 2(a). Accordingly, in this case only one of the binding regions comprises the N-acylated ß-amino acid residue.

Despite both binding regions not comprising the N-acylated ß-amino acid residue, it can be seen that the peptide foldamer unit made up of six sequential ß-amino acid residues provides for similar complementary binding regions as one that is made up of three sequential ß-amino acid residues (i.e. as illustrated in Figure 1). Furthermore, it will be appreciated that each binding region nevertheless still comprises three sequential ß-amino acid residues.

To assist with describing how it is believed the peptide foldamer units associate to provide for the supramolecular structure, reference is made to Figure 3. Thus, Figure 3 illustrates a schematic representation of a supramolecular structure (10) in accordance with the invention. The supramolecular structure (10) is made up of three peptide foldamer units (20) having a similar structure to the peptide foldamer unit illustrated in Figure 2 (i.e. made of six sequential ß-amino acid residues, one of which is N-acylated). The peptide foldamer units (20) are associated through their complementary binding regions A and B at position (30). The association at position (30) is provided for by binding region A of one peptide foldamer unit coupling with binding region B of a second peptide foldamer unit, the coupling being maintained through hydrogen bond donor and acceptor interactions (40). Stabilisation of the supramolecular structure is believed to be facilitated by intramolecular (i.e. relative to each peptide foldamer unit) hydrogen bond donor/acceptor interactions (50).

The supramolecular structure (10) may be extended in the axial direction relative to the helix conformation through further association of one or more peptide foldamer units (20) at exposed binding regions A and/or B. In this way, a large number of peptide units may be associated to facilitate formation of higher order fibre structures.

Without wishing to be limited by theory, it is believed that presenting each of the two complementary binding regions in a helix conformation may facilitate association of the peptide foldamer units to provide the supramolecular structure.

In one embodiment, each foldamer unit presents two complementary binding regions, each binding region having a helix conformation and comprising three sequential ß-amino acid residues, with one or both of the binding regions comprising the N-acylated ß-amino acid residue.

The helix conformation may be in the form of an 8-, 10-, 10/12- or 14-helix conformation.

In another embodiment, each of the two complementary binding regions present in the form of a 14-helix conformation.

In a further embodiment, one of the complementary binding regions comprises hydrogen bond acceptor groups, and the other binding region comprises hydrogen bond donor groups.

In another embodiment, -N-H groups present as the hydrogen bond acceptor groups. In a further embodiment, -C(O)- groups present as the hydrogen bond donor groups.

In yet a further embodiment, the hydrogen bond acceptor groups are each orientated in an opposite direction to each of the hydrogen bond donor groups, and each of the hydrogen bond donor and acceptor groups are orientated in an axial direction relative to the helix.

By selecting particular ß-amino acids or linking groups (L) (if present) for a given peptide foldamer unit it will be appreciated that properties of that foldamer unit, such as its hydrophobicity, hydrophilicity, reactivity for further functionalisation or reactivity for covalent bonding with other amino acid residues, either intramolecularly or intermolecularly, can be varied. Tailoring such properties will of course consequently result in tailoring of the properties of the resulting supramolecular structure.

In the context of at least amino acid residues within the peptide foldamer units, such properties can advantageously be tailored by the judicious selection of the amino acid side chains. Those skilled in the art will appreciate the various properties that may be imparted by particular amino acid side chains to the peptide foldamer units or supramolecular structure.

In some embodiments, an amino acid residue side chain present in a peptide foldamer unit may be covalently coupled with an amino acid residue side chain present in the same or different peptide foldamer unit. For example, a peptide sequence in a peptide foldamer unit may present as a cyclic peptide in which two amino acid residue side chains are covalently coupled to form a macrocycle. In that case, the amino acid residue side chains may be covalently coupled to one another by any suitable means, for example through an amide bond or a carbon-carbon single or double bond. Particular examples of such side chain coupling include coupling through an amide bond where the side chains of, for example, ß-lysine or ß-ornithine couple with a side chain of, for example, ß-glutamic acid or ß-aspartic acid. Alternatively, side chain coupling may be through a carbon-carbon double bond formed by ring closing metathesis of two amino acid residue side chains that each include a double bond capable of undergoing ring closing metathesis. In that case, the double bond formed in the ring closure may be used for subsequent reaction or functionalisation.

Where two amino acid side chains derived from a peptide sequence within a given peptide foldamer unit are coupled so as to form a macrocycle, the coupling may be defined as an intramolecular coupling. Where a side chain from an amino acid residue derived from a given peptide sequence couples with an amino acid residue side chain derived from a separate peptide sequence or foldamer unit, the coupling may be described as an intermolecular coupling. In that case, the intermolecular coupling may couple one peptide foldamer unit with a second and associated peptide foldamer unit within the supramolecular structure, or it may couple a first supramolecular structure to a second supramolecular structure.

Examples of peptide foldamer units according to the invention include those listed in

Table 4.

Table 4

SEQ ID NO:	Peptide Sequence
1	Ac-β³Trp-β³Lys-β³Leu-β³Trp-β³Glu-β³Leu-OH
2	Ac-β³Phe-β³Lys-β³Leu-β³Phe-β³Glu-β³Leu-OH
3	Ac-β³Trp-β³aSer-β³Trp- β³Trp-β³aSer-β³Trp-OH
4	Ac-β³Val-β³aSer-β³Leu-β³Val-β³aSer-β³Leu-OH
5	Ac-β³Leu-β³Ile-β³Ala -OH
6	Ac-β³Leu-β³Ile-β³Ala -OH
7	Ac- β³Trp-β³Ser-β³Ile -OH
8	Ac-β³Leu-β³Ile-β³Ala -OH
9	Ac- β³Trp-β³Ser-β³Ile -OH
10	Ac- β³Trp-β³Ser-β³Trp -OH
11	Ac- β³Trp-β³Ile-β³Trp -OH
12	Ac- β³Lys-β³Ser-β³Ile -OH
13	Ac- β³aSer-β³Leu- β³Val-β³Ser- OH
14	Ac-β³Ser-β³Leu-β³Ile-β³Ala -OH
16	Ac-β³Ala-β³Leu-β³Ile-β³Ala -OH
17	Ac-β³Lys-β³Leu-β³Ile-β³Glu -OH
18	Ac-β³Ile-β³Trp-β³Ser-β³Ile -OH
19	Ac-β³Trp-β³Leu-β³Ile-β³Trp -OH
20	Ac-β³Trp-β³Ile-β³Trp-β³Ser-β³Ile-OH
21	Ac-β³Lys-β³Ile-β³Trp-β³Ser-β³Ile- OH
23	Ac-β³Tyr-β³Lys-β³Leu-β³Tyr-β³Glu-β³Leu-OH
24	Ac-β³Val-β³aSer-β³Leu-β³Val-β³aSer-β³Leu-OH
25	Ac-β³Trp-β³Lys-β³Trp-β³Trp-β³Glu-β³Trp-OH
26	Ac-β³Trp-β³Lys-β³Leu-AHx-β³Trp-β³Glu-β³Leu-OH
27	Ac-β³Trp-β³Lys-β³Leu-PABA-β³Trp-β³Glu-β³Leu-OH

The peptide foldamer units in accordance with the invention may be prepared using standard synthetic techniques, including standard peptide synthetic techniques such as solution or solid phase synthesis known in the art. For example, the at least three sequential ß-amino acid residues that provide for the at least tripeptide sequence may be prepared using appropriately protected ß-amino acids which are commercially available, or may be synthesised from unprotected ß-amino acids that are also commercially available. As a case in point, Fmoc-O-allyl-β^3-serine may be prepared as described by Bergman *et al.*, Tetrahedron Asymmetry, 2008, 19(24), 2861-2863. Side chains may be protected and deprotected as required and as known in the art, for example, as described by Green & Wutz, Protective Groups in Organic Synthesis, third edition, Wiley-Interscience, 1999.

According to the method of the invention, the supramolecular structure is prepared by providing a solution comprising a plurality of peptide foldamer units. Provided that the peptide foldamer units can be solvated, there is no particular limitation regarding the nature of the solvent that can be used.

Examples of solvents that may be used to provide the solution comprising the plurality of peptide foldamer units include aqueous solutions and polar solvents such as water miscible alcohols (e.g. methanol and ethanol).

In one embodiment, the method comprises providing an aqueous solution comprising the plurality of the peptide foldamer units.

Provided the supramolecular structure can form, the solution comprising the plurality of peptide foldamer units may further comprise one or more additives.

Upon providing the solution comprising the plurality of peptide foldamer units, the peptide foldamer units self-assemble through association of their complementary binding regions to form the supramolecular structure.

Surprisingly, the peptide foldamer units in solution have been found to readily and spontaneously self-assemble to form the supramolecular structure. This is in contrast with techniques where self assembly of peptides has been shown to occur.

The method of forming the supramolecular structure in accordance with the invention is particularly simple and believed to be well suited for mass production of the supramolecular structures.

As the peptide foldamer units self assemble the resulting supramolecular structure continues to grow and can develop into higher order fibre structures. Such fibre structures will typically be made up of multiple intra- and/or inter-twined supramolecular structures. In that case, the supramolecular structures can be viewed as forming assembled filaments that intra- and/or inter-twine to develop the fibre structure.

In one embodiment, one or more supramolecular structures are intertwined and/or intratwined to form a fibre structure.

The fibre structure may be a nanofibre (i.e. a fibre having a diameter of less than 1,000 nm), a microfiber (i.e. a fibre that measures less than one denier) or a macrofibre (i.e. a fibre that measures equal to or greater than one denier).

The present invention therefore also provides a fibre comprising one or more supramolecular structures in accordance with the invention.

In one embodiment, the fibre is a nanofibre.

In a further embodiment the fibre is a microfiber.

In yet a further embodiment the fibre is a macrofibre.

In some embodiments, the supramolecular structure presents one or more functional groups, where the one or more functional groups are selected for a particular desired purpose. For example, the functional groups may be selected to provide conductivity, or bio-activity. Such functional groups may be attached to a side chain of one or more amino acid residues of the peptide foldamer unit.

Suitable functional groups that may be used to confer conductability include but are not limited to porphyrins, and thallocenes.

Suitable functional groups with bio-activity that may be conjugated to an amino acid residue side chain that forms part of the peptide foldamer unit or supramolecular structure include those herein described such as drugs or pharmaceutically active agents (e.g. antibiotics, antibodies, antigens, lipids, sugars or carbohydrates, proteins and the like).

In some embodiments, the supramolecular structures may be formed into three dimensional structures. For example, supramolecular structures may be provided in the form of fibres and the fibres formed into a felted fabric or woven fabric.

In other embodiments, the supramolecular structure, for example in the form of fibres, may be incorporated into a composition, such as a pharmaceutical composition further comprising a pharmaceutically acceptable carrier, diluent or excipient. Such a pharmaceutical composition may be useful in drug delivery where the supramolecular structure further comprises a biologically active agent such as a drug conjugated thereto. Such pharmaceutical compositions may also be useful in delivering the supramolecular structure to a specific location where they may support tissue repair after damage by injury or disease. Supramolecular structures used as scaffolds for tissue repair may further comprise biologically active compounds such as those that allow attachment of cells to a surface, differentiation of cells or growth and proliferation of cells.

The present invention therefore also provides a composite material comprising the supramolecular structure of the invention.

In some embodiments, the composite material includes the supramolecular structure attached to a surface. The surface may be any surface including plastic, glass, metal or organic materials such as fabric or wood, and the like.

The supramolecular structures of the invention may be applied in a variety of applications and industries.

Fibres formed form the supramolecular structures have been found to exhibit excellent physical and mechanical properties. For example, the fibres proved sufficiently strong and flexible such that they could be handled like a common thread.

In some embodiments, the fibres may be woven to provide textiles.

In some embodiments, the fibres may be used as an implantable tissue scaffold for cells such as stem cells, in the regeneration of damaged or diseased tissue. Optionally, the fibres may be conjugated to biologically active molecules that assist with attachment, differentiation, growth and/or proliferation of the new cells.

As used herein, the term "alkyl", used either alone or in compound words denotes straight chain, branched or cyclic alkyl, preferably C_{1-20} alkyl, e.g. C_{1-10} or C_{1-6}. Examples of straight chain and branched alkyl include methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, *sec*-butyl, *t*-butyl, *n*-pentyl, 1,2-dimethylpropyl, 1,1-dimethyl-propyl, hexyl, 4-methylpentyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, 1,1-dimethylbutyl, 2,2-dimethylbutyl, 3,3-dimethylbutyl, 1,2-dimethylbutyl, 1,3-dimethylbutyl, 1,2,2-trimethylpropyl, 1,1,2-trimethylpropyl, heptyl, 5-methylhexyl, 1-methylhexyl, 2,2-dimethylpentyl, 3,3-dimethylpentyl, 4,4-dimethylpentyl, 1,2-dimethylpentyl, 1,3-dimethylpentyl, 1,4-dimethyl-pentyl, 1,2,3-trimethylbutyl, 1,1,2-trimethylbutyl, 1,1,3-trimethylbutyl, octyl, 6-methylheptyl, 1-methylheptyl, 1,1,3,3-tetramethylbutyl, nonyl, 1-, 2-, 3-, 4-, 5-, 6- or 7-methyloctyl, 1-, 2-, 3-, 4- or 5-

ethylheptyl, 1-, 2- or 3-propylhexyl, decyl, 1-, 2-, 3-, 4-, 5-, 6-, 7- and 8-methylnonyl, 1-, 2-, 3-, 4-, 5- or 6-ethyloctyl, 1-, 2-, 3- or 4-propylheptyl, undecyl, 1-, 2-, 3-, 4-, 5-, 6-, 7-, 8- or 9-methyldecyl, 1-, 2-, 3-, 4-, 5-, 6- or 7-ethylnonyl, 1-, 2-, 3-, 4- or 5-propyloctyl, 1-, 2- or 3-butylheptyl, 1-pentylhexyl, dodecyl, 1-, 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9- or 10-methylundecyl, 1-, 2-, 3-, 4-, 5-, 6-, 7- or 8-ethyldecyl, 1-, 2-, 3-, 4-, 5- or 6-propylnonyl, 1-, 2-, 3- or 4-butyloctyl, 1-2-pentylheptyl and the like. Examples of cyclic alkyl include mono- or polycyclic alkyl groups such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclononyl, cyclodecyl and the like. Where an alkyl group is referred to generally as "propyl", butyl" etc, it will be understood that this can refer to any of straight, branched and cyclic isomers where appropriate. An alkyl group may be optionally substituted by one or more optional substituents as herein defined.

The term "alkenyl" as used herein denotes groups formed from straight chain, branched or cyclic hydrocarbon residues containing at least one carbon to carbon double bond including ethylenically mono-, di- or polyunsaturated alkyl or cycloalkyl groups as previously defined, preferably C_{2-20} alkenyl (e.g. C_{2-10} or C_{2-6}). Examples of alkenyl include vinyl, allyl, 1-methylvinyl, butenyl, iso-butenyl, 3-methyl-2-butenyl, 1-pentenyl, cyclopentenyl, 1-methyl-cyclopentenyl, 1-hexenyl, 3-hexenyl, cyclohexenyl, 1-heptenyl, 3-heptenyl, 1-octenyl, cyclooctenyl, 1-nonenyl, 2-nonenyl, 3-nonenyl, 1-decenyl, 3-decenyl, 1,3-butadienyl, 1,4-pentadienyl, 1,3-cyclopentadienyl, 1,3-hexadienyl, 1,4-hexadienyl, 1,3-cyclohexadienyl, 1,4-cyclohexadienyl, 1,3-cycloheptadienyl, 1,3,5-cycloheptatrienyl and 1,3,5,7-cyclooctatetraenyl. An alkenyl group may be optionally substituted by one or more optional substituents as herein defined.

As used herein the term "alkynyl" denotes groups formed from straight chain, branched or cyclic hydrocarbon residues containing at least one carbon-carbon triple bond including ethylenically mono-, di- or polyunsaturated alkyl or cycloalkyl groups as previously defined. Unless the number of carbon atoms is specified the term preferably refers to C_{2-20} alkynyl (e.g. C_{2-10} or C_{2-6}). Examples include ethynyl, 1-propynyl, 2-propynyl, and butynyl isomers, and pentynyl isomers. An alkynyl group

may be optionally substituted by one or more optional substituents as herein defined.

The term "halogen" ("halo") denotes fluorine, chlorine, bromine or iodine (fluoro, chloro, bromo or iodo).

The term "aryl" (or "carboaryl") denotes any of single, polynuclear, conjugated and fused residues of aromatic hydrocarbon ring systems(e.g. C_{6-24} or C_{6-18}). . Examples of aryl include phenyl, biphenyl, terphenyl, quaterphenyl, naphthyl, tetrahydronaphthyl, anthracenyl, dihydroanthracenyl, benzanthracenyl, dibenzanthracenyl, phenanthrenyl, fluorenyl, pyrenyl, idenyl, azulenyl, chrysenyl. Preferred aryl include phenyl and naphthyl. An aryl group may or may not be optionally substituted by one or more optional substituents as herein defined. The term "arylene" is intended to denote the divalent form of aryl.

The term "carbocyclyl" includes any of non-aromatic monocyclic, polycyclic, fused or conjugated hydrocarbon residues, preferably C_{3-20} (e.g. C_{3-10} or C_{3-8}). The rings may be saturated, e.g. cycloalkyl, or may possess one or more double bonds (cycloalkenyl) and/or one or more triple bonds (cycloalkynyl). Particularly preferred carbocyclyl moieties are 5-6-membered or 9-10 membered ring systems. Suitable examples include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclononyl, cyclodecyl, cyclopentenyl, cyclohexenyl, cyclooctenyl, cyclopentadienyl, cyclohexadienyl, cyclooctatetraenyl, indanyl, decalinyl and indenyl. A carbocyclyl group may be optionally substituted by one or more optional substituents as herein defined. The term "carbocyclylene" is intended to denote the divalent form of carbocyclyl.

The term "heteroatom" or "hetero" as used herein in its broadest sense refers to any atom other than a carbon atom which may be a member of a cyclic organic group. Particular examples of heteroatoms include nitrogen, oxygen, sulfur, phosphorous, boron, silicon, selenium and tellurium, more particularly nitrogen, oxygen and sulfur.

The term "heterocyclyl" when used alone or in compound words includes any of

monocyclic, polycyclic, fused or conjugated hydrocarbon residues, preferably C_{3-20} (e.g. C_{3-10} or C_{3-8}) wherein one or more carbon atoms are replaced by a heteroatom so as to provide a non-aromatic residue. Suitable heteroatoms include O, N, S, P and Se, particularly O, N and S. Where two or more carbon atoms are replaced, this may be by two or more of the same heteroatom or by different heteroatoms. The heterocyclyl group may be saturated or partially unsaturated, i.e. possess one or more double bonds. Particularly preferred heterocyclyl are 5-6 and 9-10 membered heterocyclyl. Suitable examples of heterocyclyl groups may include azridinyl, oxiranyl, thiiranyl, azetidinyl, oxetanyl, thietanyl, 2H-pyrrolyl, pyrrolidinyl, pyrrolinyl, piperidyl, piperazinyl, morpholinyl, indolinyl, imidazolidinyl, imidazolinyl, pyrazolidinyl, thiomorpholinyl, dioxanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyrrolyl, tetrahydrothiophenyl, pyrazolinyl, dioxalanyl, thiazolidinyl, isoxazolidinyl, dihydropyranyl, oxazinyl, thiazinyl, thiomorpholinyl, oxathianyl, dithianyl, trioxanyl, thiadiazinyl, dithiazinyl, trithianyl, azepinyl, oxepinyl, thiepinyl, indenyl, indanyl, 3H-indolyl, isoindolinyl, 4H-quinolazinyl, chromenyl, chromanyl, isochromanyl, pyranyl and dihydropyranyl. A heterocyclyl group may be optionally substituted by one or more optional substituents as herein defined. The term "heterocyclylene" is intended to denote the divalent form of heterocyclyl.

The term "heteroaryl" includes any of monocyclic, polycyclic, fused or conjugated hydrocarbon residues, wherein one or more carbon atoms are replaced by a heteroatom so as to provide an aromatic residue. Preferred heteroaryl have 3-20 ring atoms, e.g. 3-10. Particularly preferred heteroaryl are 5-6 and 9-10 membered bicyclic ring systems. Suitable heteroatoms include, O, N, S, P and Se, particularly O, N and S. Where two or more carbon atoms are replaced, this may be by two or more of the same heteroatom or by different heteroatoms. Suitable examples of heteroaryl groups may include pyridyl, pyrrolyl, thienyl, imidazolyl, furanyl, benzothienyl, isobenzothienyl, benzofuranyl, isobenzofuranyl, indolyl, isoindolyl, pyrazolyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolizinyl, quinolyl, isoquinolyl, phthalazinyl, 1,5-naphthyridinyl, quinozalinyl, quinazolinyl, quinolinyl, oxazolyl, thiazolyl, isothiazolyl, isoxazolyl, triazolyl, oxadialzolyl, oxatriazolyl, triazinyl, and furazanyl. A heteroaryl group may be optionally substituted by one or more optional substituents

as herein defined. The term "heteroarylene" is intended to denote the divalent form of heteroaryl.

The term "acyl" either alone or in compound words denotes a group containing the moiety C=O (and not being a carboxylic acid, ester or amide) Preferred acyl includes C(O)-R^e, wherein R^e is hydrogen or an alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocyclyl, or heterocyclyl residue. Examples of acyl include formyl, straight chain or branched alkanoyl (e.g. C_{1-20}) such as acetyl, propanoyl, butanoyl, 2-methylpropanoyl, pentanoyl, 2,2-dimethylpropanoyl, hexanoyl, heptanoyl, octanoyl, nonanoyl, decanoyl, undecanoyl, dodecanoyl, tridecanoyl, tetradecanoyl, pentadecanoyl, hexadecanoyl, heptadecanoyl, octadecanoyl, nonadecanoyl and icosanoyl; cycloalkylcarbonyl such as cyclopropylcarbonyl cyclobutylcarbonyl, cyclopentylcarbonyl and cyclohexylcarbonyl; aroyl such as benzoyl, toluoyl and naphthoyl; aralkanoyl such as phenylalkanoyl (e.g. phenylacetyl, phenylpropanoyl, phenylbutanoyl, phenylisobutylyl, phenylpentanoyl and phenylhexanoyl) and naphthylalkanoyl (e.g. naphthylacetyl, naphthylpropanoyl and naphthylbutanoyl]; aralkenoyl such as phenylalkenoyl (e.g. phenylpropenoyl, phenylbutenoyl, phenylmethacryloyl, phenylpentenoyl and phenylhexenoyl and naphthylalkenoyl (e.g. naphthylpropenoyl, naphthylbutenoyl and naphthylpentenoyl); aryloxyalkanoyl such as phenoxyacetyl and phenoxypropionyl; arylthiocarbamoyl such as phenylthiocarbamoyl; arylglyoxyloyl such as phenylglyoxyloyl and naphthylglyoxyloyl; arylsulfonyl such as phenylsulfonyl and napthylsulfonyl; heterocycliccarbonyl; heterocyclicalkanoyl such as thienylacetyl, thienylpropanoyl, thienylbutanoyl, thienylpentanoyl, thienylhexanoyl, thiazolylacetyl, thiadiazolylacetyl and tetrazolylacetyl; heterocyclicalkenoyl such as heterocyclicpropenoyl, heterocyclicbutenoyl, heterocyclicpentenoyl and heterocyclichexenoyl; and heterocyclicglyoxyloyl such as thiazolyglyoxyloyl and thienylglyoxyloyl. The R^e residue may be optionally substituted as described herein.

The term "sulfoxide", either alone or in a compound word, refers to a group $-S(O)R^f$ wherein R^f is selected from hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, heterocyclyl, carbocyclyl, and aralkyl. Examples of preferred R^f include C_{1-20}alkyl,

phenyl and benzyl.

The term "sulfonyl", either alone or in a compound word, refers to a group $S(O)_2$-R^f, wherein R^f is selected from hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, heterocyclyl, carbocyclyl and aralkyl. Examples of preferred R^f include C_{1-20}alkyl, phenyl and benzyl.

The term "sulfonamide", either alone or in a compound word, refers to a group $S(O)NR^fR^f$ wherein each R^f is independently selected from hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, heterocyclyl, carbocyclyl, and aralkyl. Examples of preferred R^f include C_{1-20}alkyl, phenyl and benzyl. In one embodiment at least one R^f is hydrogen. In another embodiment, both R^f are hydrogen.

The term, "amino" is used here in its broadest sense as understood in the art and includes groups of the formula NR^aR^b wherein R^a and R^b may be any independently selected from hydrogen, alkyl, alkenyl, alkynyl, aryl, carbocyclyl, heteroaryl, heterocyclyl, arylalkyl, and acyl. R^a and R^b, together with the nitrogen to which they are attached, may also form a monocyclic, or polycyclic ring system e.g. a 3-10 membered ring, particularly, 5-6 and 9-10 membered systems. Examples of "amino" include NH_2, NHalkyl (e.g. C_{1-20}alkyl), NHaryl (e.g. NHphenyl), NHaralkyl (e.g. NHbenzyl), NHacyl (e.g. $NHC(O)C_{1-20}$alkyl, NHC(O)phenyl), Nalkylalkyl (wherein each alkyl, for example C_{1-20}, may be the same or different) and 5 or 6 membered rings, optionally containing one or more same or different heteroatoms (e.g. O, N and S).

The term "amido" is used here in its broadest sense as understood in the art and includes groups having the formula $C(O)NR^aR^b$, wherein R^a and R^b are as defined as above. Examples of amido include $C(O)NH_2$, C(O)NHalkyl (e.g. C_{1-20}alkyl), C(O)NHaryl (e.g. C(O)NHphenyl), C(O)NHaralkyl (e.g. C(O)NHbenzyl), C(O)NHacyl (e.g. $C(O)NHC(O)C_{1-20}$alkyl, C(O)NHC(O)phenyl), C(O)Nalkylalkyl (wherein each alkyl, for example C_{1-20}, may be the same or different) and 5 or 6 membered rings, optionally containing one or more same or different heteroatoms

(e.g. O, N and S).

The term "carboxy ester" is used here in its broadest sense as understood in the art and includes groups having the formula CO_2R^g, wherein R^g may be selected from groups including alkyl, alkenyl, alkynyl, aryl, carbocyclyl, heteroaryl, heterocyclyl, aralkyl, and acyl. Examples of carboxy ester include CO_2C_{1-20}alkyl, CO_2aryl (e.g.. CO_2phenyl), CO_2aralkyl (e.g. CO_2 benzyl).

As used herein, the term "aryloxy" refers to an "aryl" group attached through an oxygen bridge. Examples of aryloxy substituents include phenoxy, biphenyloxy, naphthyloxy and the like.

As used herein, the term "acyloxy" refers to an "acyl" group wherein the "acyl" group is in turn attached through an oxygen atom. Examples of "acyloxy" include hexylcarbonyloxy (heptanoyloxy), cyclopentylcarbonyloxy, benzoyloxy, 4-chlorobenzoyloxy, decylcarbonyloxy (undecanoyloxy), propylcarbonyloxy (butanoyloxy), octylcarbonyloxy (nonanoyloxy), biphenylcarbonyloxy (eg 4-phenylbenzoyloxy), naphthylcarbonyloxy (eg 1-naphthoyloxy) and the like.

As used herein, the term "alkyloxycarbonyl" refers to a "alkyloxy" group attached through a carbonyl group. Examples of "alkyloxycarbonyl" groups include butylformate, sec-butylformate, hexylformate, octylformate, decylformate, cyclopentylformate and the like.

As used herein, the term "arylalkyl" refers to groups formed from straight or branched chain alkanes substituted with an aromatic ring. Examples of arylalkyl include phenylmethyl (benzyl), phenylethyl and phenylpropyl.

As used herein, the term "alkylaryl" refers to groups formed from aryl groups substituted with a straight chain or branched alkane. Examples of alkylaryl include methylphenyl and isopropylphenyl.

In this specification "optionally substituted" is taken to mean that a group may or may not be substituted or fused (so as to form a condensed polycyclic group) with one, two, three or more of organic and inorganic groups, including those selected from: alkyl, alkenyl, alkynyl, carbocyclyl, aryl, heterocyclyl, heteroaryl, acyl, aralkyl, alkaryl, alkheterocyclyl, alkheteroaryl, alkcarbocyclyl, halo, haloalkyl, haloalkenyl, haloalkynyl, haloaryl, halocarbocyclyl, haloheterocyclyl, haloheteroaryl, haloacyl, haloaryalkyl, hydroxy, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, hydroxycarbocyclyl, hydroxyaryl, hydroxyheterocyclyl, hydroxyheteroaryl, hydroxyacyl, hydroxyaralkyl, alkoxyalkyl, alkoxyalkenyl, alkoxyalkynyl, alkoxycarbocyclyl, alkoxyaryl, alkoxyheterocyclyl, alkoxyheteroaryl, alkoxyacyl, alkoxyaralkyl, alkoxy, alkenyloxy, alkynyloxy, aryloxy, carbocyclyloxy, aralkyloxy, heteroaryloxy, heterocyclyloxy, acyloxy, haloalkoxy, haloalkenyloxy, haloalkynyloxy, haloaryloxy, halocarbocyclyloxy, haloaralkyloxy, haloheteroaryloxy, haloheterocyclyloxy, haloacyloxy, nitro, nitroalkyl, nitroalkenyl, nitroalkynyl, nitroaryl, nitroheterocyclyl, nitroheteroayl, nitrocarbocyclyl, nitroacyl, nitroaralkyl, amino (NH_2), alkylamino, dialkylamino, alkenylamino, alkynylamino, arylamino, diarylamino, aralkylamino, diaralkylamino, acylamino, diacylamino, heterocyclamino, heteroarylamino, carboxy, carboxyester, amido, alkylsulphonyloxy, arylsulphenyloxy, alkylsulphenyl, arylsulphenyl, thio, alkylthio, alkenylthio, alkynylthio, arylthio, aralkylthio, carbocyclylthio, heterocyclylthio, heteroarylthio, acylthio, sulfoxide, sulfonyl, sulfonamide, aminoalkyl, aminoalkenyl, aminoalkynyl, aminocarbocyclyl, aminoaryl, aminoheterocyclyl, aminoheteroaryl, aminoacyl, aminoaralkyl, thioalkyl, thioalkenyl, thioalkynyl, thiocarbocyclyl, thioaryl, thioheterocyclyl, thioheteroaryl, thioacyl, thioaralkyl, carboxyalkyl, carboxyalkenyl, carboxyalkynyl, carboxycarbocyclyl, carboxyaryl, carboxyheterocyclyl, carboxyheteroaryl, carboxyacyl, carboxyaralkyl, carboxyesteralkyl, carboxyesteralkenyl, carboxyesteralkynyl, carboxyestercarbocyclyl, carboxyesteraryl, carboxyesterheterocyclyl, carboxyesterheteroaryl, carboxyesteracyl, carboxyesteraralkyl, amidoalkyl, amidoalkenyl, amidoalkynyl, amidocarbocyclyl, amidoaryl, amidoheterocyclyl, amidoheteroaryl, amidoacyl, amidoaralkyl, formylalkyl, formylalkenyl, formylalkynyl, formylcarbocyclyl, formylaryl, formylheterocyclyl, formylheteroaryl, formylacyl, formylaralkyl, acylalkyl,

acylalkenyl, acylalkynyl, acylcarbocyclyl, acylaryl, acylheterocyclyl, acylheteroaryl, acylacyl, acylaralkyl, sulfoxidealkyl, sulfoxidealkenyl, sulfoxidealkynyl, sulfoxidecarbocyclyl, sulfoxidearyl, sulfoxideheterocyclyl, sulfoxideheteroaryl, sulfoxideacyl, sulfoxidearalkyl, sulfonylalkyl, sulfonylalkenyl, sulfonylalkynyl, sulfonylcarbocyclyl, sulfonylaryl, sulfonylheterocyclyl, sulfonylheteroaryl, sulfonylacyl, sulfonylaralkyl, sulfonamidoalkyl, sulfonamidoalkenyl, sulfonamidoalkynyl, sulfonamidocarbocyclyl, sulfonamidoaryl, sulfonamidoheterocyclyl, sulfonamidoheteroaryl, sulfonamidoacyl, sulfonamidoaralkyl, nitroalkyl, nitroalkenyl, nitroalkynyl, nitrocarbocyclyl, nitroaryl, nitroheterocyclyl, nitroheteroaryl, nitroacyl, nitroaralkyl, cyano, sulfate, phosphate, triarylmethyl, triarylamino, oxadiazole, and carbazole groups. Optional substitution may also be taken to refer to where a $-CH_2-$ group in a chain or ring is replaced by a group selected from -O-, -S-, $-NR^a-$, -C(O)- (i.e. carbonyl), -C(O)O- (i.e. ester), and $-C(O)NR^a-$ (i.e. amide), where R^a is as defined herein.

Preferred optional substituents include alkyl, (e.g. C_{1-6} alkyl such as methyl, ethyl, propyl, butyl, cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl), hydroxyalkyl (e.g. hydroxymethyl, hydroxyethyl, hydroxypropyl), alkoxyalkyl (e.g. methoxymethyl, methoxyethyl, methoxypropyl, ethoxymethyl, ethoxyethyl, ethoxypropyl etc) alkoxy (e.g. C_{1-6} alkoxy such as methoxy, ethoxy, propoxy, butoxy, cyclopropoxy, cyclobutoxy), halo, trifluoromethyl, trichloromethyl, tribromomethyl, hydroxy, phenyl (which itself may be further substituted e.g., by C_{1-6} alkyl, halo, hydroxy, hydroxyC_{1-6} alkyl, C_{1-6} alkoxy, haloC_{1-6}alkyl, cyano, nitro $OC(O)C_{1-6}$ alkyl, and amino), benzyl (wherein benzyl itself may be further substituted e.g., by C_{1-6} alkyl, halo, hydroxy, hydroxyC_{1-6}alkyl, C_{1-6} alkoxy, haloC_{1-6} alkyl, cyano, nitro $OC(O)C_{1-6}$ alkyl, and amino), phenoxy (wherein phenyl itself may be further substituted e.g., by C_{1-6} alkyl, halo, hydroxy, hydroxyC_{1-6} alkyl, C_{1-6} alkoxy, haloC_{1-6} alkyl, cyano, nitro $OC(O)C_{1-6}$ alkyl, and amino), benzyloxy (wherein benzyl itself may be further substituted e.g., by C_{1-6} alkyl, halo, hydroxy, hydroxyC_{1-6} alkyl, C_{1-6} alkoxy, haloC_{1-6} alkyl, cyano, nitro $OC(O)C_{1-6}$ alkyl, and amino), amino, alkylamino (e.g. C_{1-6} alkyl, such as methylamino, ethylamino, propylamino etc), dialkylamino (e.g. C_{1-6} alkyl, such as dimethylamino, diethylamino, dipropylamino), acylamino (e.g. $NHC(O)CH_3$), phenylamino (wherein

phenyl itself may be further substituted e.g., by C_{1-6} alkyl, halo, hydroxy, hydroxyC_{1-6} alkyl, C_{1-6} alkoxy, haloC_{1-6} alkyl, cyano, nitro $OC(O)C_{1-6}$ alkyl, and amino), nitro, formyl, -C(O)-alkyl (e.g. C_{1-6} alkyl, such as acetyl), O-C(O)-alkyl (e.g. C_{1-6}alkyl, such as acetyloxy), benzoyl (wherein the phenyl group itself may be further substituted e.g., by C_{1-6} alkyl, halo, hydroxy hydroxyC_{1-6} alkyl, C_{1-6} alkoxy, haloC_{1-6} alkyl, cyano, nitro $OC(O)C_{1-6}$alkyl, and amino), replacement of CH_2 with C=O, CO_2H, CO_2alkyl (e.g. C_{1-6} alkyl such as methyl ester, ethyl ester, propyl ester, butyl ester), CO_2phenyl (wherein phenyl itself may be further substituted e.g., by C_{1-6} alkyl, halo, hydroxy, hydroxyl C_{1-6} alkyl, C_{1-6} alkoxy, halo C_{1-6} alkyl, cyano, nitro $OC(O)C_{1-6}$ alkyl, and amino), $CONH_2$, CONHphenyl (wherein phenyl itself may be further substituted e.g., by C_{1-6} alkyl, halo, hydroxy, hydroxyl C_{1-6} alkyl, C_{1-6} alkoxy, halo C_{1-6} alkyl, cyano, nitro $OC(O)C_{1-6}$ alkyl, and amino), CONHbenzyl (wherein benzyl itself may be further substituted e.g., by C_{1-6} alkyl, halo, hydroxy hydroxyl C_{1-6} alkyl, C_{1-6} alkoxy, halo C_{1-6} alkyl, cyano, nitro $OC(O)C_{1-6}$ alkyl, and amino), CONHalkyl (e.g. C_{1-6} alkyl such as methyl ester, ethyl ester, propyl ester, butyl amide) CONHdialkyl (e.g. C_{1-6} alkyl) aminoalkyl (e.g., HN C_{1-6} alkyl-, C_{1-6}alkylHN-C_{1-6} alkyl- and $(C_{1-6}$ alkyl$)_2$N-C_{1-6} alkyl-), thioalkyl (e.g., HS C_{1-6} alkyl-), carboxyalkyl (e.g., HO_2CC_{1-6} alkyl-), carboxyesteralkyl (e.g., C_{1-6} alkylO_2CC_{1-6} alkyl-), amidoalkyl (e.g., $H_2N(O)CC_{1-6}$ alkyl-, $H(C_{1-6}$ alkyl$)N(O)CC_{1-6}$ alkyl-), formylalkyl (e.g., $OHCC_{1-6}$alkyl-), acylalkyl (e.g., C_{1-6} alkyl$(O)CC_{1-6}$ alkyl-), nitroalkyl (e.g., O_2NC_{1-6} alkyl-), sulfoxidealkyl (e.g., $R(O)SC_{1-6}$ alkyl, such as C_{1-6} alkyl$(O)SC_{1-6}$ alkyl-), sulfonylalkyl (e.g., $R(O)_2SC_{1-6}$ alkyl- such as C_{1-6} alkyl$(O)_2SC_{1-6}$ alkyl-), sulfonamidoalkyl (e.g., $_2HRN(O)SC_{1-6}$ alkyl, $H(C_{1-6}$ alkyl$)N(O)SC_{1-6}$ alkyl-), triarylmethyl, triarylamino, oxadiazole, and carbazole.

Many modifications will be apparent to those skilled in the art without departing from the scope of the present invention.

Certain embodiments of the invention will now be described with reference to the following examples which are intended for the purpose of illustration only and are not intended to limit the scope of the generality hereinbefore described.

EXAMPLES

Example 1: Peptide preparation

1.1 General information

Fmoc-protected β-amino acids were purchased from PepTech (Cambridge, MA, USA). Fmoc-O-allyl-β^3-serine was prepared as described by Bergman *et al.*, Tetrahedron Asymmetry, 2008, 19(24), 2861-2863. 2-(1H-7-Azabenzotriazol-1-yl)-1,1,3,3-tetramethyl uronium hexafluorophosphate (HATU), *O*-benzotriazole-*N*,*N*,*N*',*N*'-tetramethyl-uronium-hexafluorophosphate (HBTU), *N*-hydroxybenzotriazole (HOBt), and Wang resin were purchased from GL Biochem (Shanghai, China). Dimethylformamide (DMF, stored over 4Å MS), *N*-methyl-2-pyrrolidone (NMP), dichloromethane (CH_2Cl_2, distilled from P_2O_5 and stored over 4Å MS), and piperidine were purchased from Merck (Darmstadt, Germany). Trifluoroacetic acid (TFA) and diisopropylethylamine (DIPEA) were purchased from Auspep (Melbourne, Australia). All other reagents were purchased from Sigma-Aldrich.

1.2 β^3-Peptide preparation

All β^3-Peptides were synthesized on a 100 μmol scale using standard Fmoc chemistry on Wang resin (0.9 mmol/g loading, GL Biochem, Shanghai, China). The resin was washed (3 x 30 sec) with NMP and the Fmoc-protected β-amino acid (3.1 eq. to resin loading) was dissolved in NMP along with HBTU (3 eq. to resin loading), HOBt (3 eq. to resin loading) and DIPEA (4.5 eq. to resin loading). 4-Dimethylaminopyridine (0.1 eq. to resin loading) in NMP was added dropwise and the reaction proceeded overnight. At this stage peptide synthesis of all peptides proceeded as normal. Thus, following the overnight coupling, the resin was washed with NMP (5 x 30 sec) and CH_2Cl_2 (5 x 30 sec) and peptide synthesis was continued. One cycle of peptide elongation consisted of the following steps. The loaded resin was first washed with

NMP (3 x 30 sec) and the terminal Fmoc protecting group was removed with 20% piperidine/DMF (2 x 15 min). The deprotected resin was then washed with NMP (5 x 30 sec) and treated for 90 min with a solution containing 3.1 eq. of the appropriate β-amino acid, 3 eq. HATU, and 4.5 eq. DIPEA. The resin was then washed three times with NMP (3 x 30 sec), unreacted amino groups were acetylated upon treatment with 10% v/v acetic anhydride and 1% v/v DIPEA in NMP (2 x 20 min), and the capped resin washed with NMP (3 x 30 sec). These steps were repeated until the β-peptide sequence was complete. Once the final Fmoc-protecting group had been removed, the resin was treated with 10% v/v acetic anhydride and 1% v/v DIPEA in NMP (2 x 20 min) to afford an acetyl-capped N-terminus. The resin was subsequently washed with NMP (5 x 30 s) and CH_2Cl_2 (5 x 30 sec), dried for 20 min under vacuum, and then treated for 90 min with a cleavage solution containing 2.5% v/v water and 2.5% v/v triisopropylsilane in TFA. The cleaved resin was washed twice with the cleavage solution (2 x 30 sec) and the cleaved β^3-peptide in TFA was collected. The TFA was evaporated under a stream of N_2 and the peptide was precipitated by the addition of diethyl ether. The precipitate was filtered and reconstituted in H_2O/acetonitrile (1:1) for lyophilization.

Foldamer units comprising a non-β-amino acid linking group such as amino-caproic acid were also prepared in this manner using Fmoc-derivatives, for example Fmoc-amino-caproic acid.

Example 2: Ring-closing Metathesis

Ring-closing metathesis

Ring closing metathesis (RCM) of peptides comprising two O-allyl-β-serine amino acid residues was performed on Fmoc-protected peptides on Wang resin prior to N-acetylation of the N-terminus and removal from the resin. The resin was swelled in TFE:CH_2Cl_2 (4:1 ratio, 10 mM) and Hoveyda-Grubbs II generation catalyst (35 mol%) was added to the solution and the reaction was allowed to proceed for 48 h (monitored by HPLC and ESI-MS upon cleaving a small sample off resin). The resin

was then washed in a solution of DMSO:DMF (1:1) overnight. Final deprotection (and acetylation) and subsequent cleavage of the peptide from the resin was performed using the protocol described in Example 1.

Example 3: Synthesis of Peptide of SEQ ID NO: 4

The synthesis of this peptide has been described previously (Gopalan *et al.*, Organic & Biomolecular Chemistry, 2012, Doi: 10.1039/c2ob06617c). Briefly, a mixture of acetone/water/*t*-BuOH (17:1.5:1) was added to the acetylated, ring-closed peptide prepared in Example 2 on Wang resin (50 mg, 19.88 mol). *N*-Methylmorpholine *N*-oxide (10 mg, 1.17 mol) and potassium osmate dihydrate (3 mg, 1.1mol) was added and the reaction was sealed and stirred overnight under a stream of Ar. The resin was washed with DMF, DCM and ether and cleavage of the peptide from the resin was performed as described in Example 1.

Equivalent non-acetylated peptides were prepared by the above methods, only without the acetic anhydride treatment.

Example 4: Purification and analysis of Peptides

Peptide purification and analysis

Mass spectra were acquired with an Agilent 1100 MSD SL ion trap mass spectrometer. Reverse-phase HPLC was performed using an Agilent HP1200 system fitted with a VydacTM analytical (C18, 300 Å, 5 μm, 4.6 mm x 150 mm) or preparative (C18, 300 Å, 5 μm, 10 mm x 250 mm) columns. Preparative HPLC columns were heated to 60 °C in a water bath. The eluents were 0.1% aqueous TFA and 0.1% TFA in acetonitrile.

The success of each synthesis was assessed first by HPLC and ESI-MS analysis of the crude reaction mixture. β-Peptides were then purified to homogeneity by reverse-phase HPLC. The identities and purities of purified β-peptides were assessed by

analytical HPLC and mass spectrometry (Table 5). HPLC retention times were observed following analytical HPLC with a solvent gradient of 0-70% 0.1% acetonitrile over 40 min.

Table 5: Analytical data for β-peptides

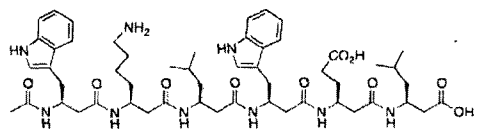
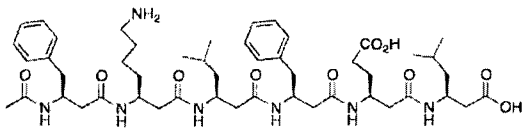
Peptide Sequence	SEQ ID NO:	HPLC RT(min)	MS calc	MS obtained
Ac-β³Trp-β³Lys-β³Leu-β³Trp-β³Glu-β³Leu-OH	SEQ ID NO: 1	17.307	1000.2	500.5#
Ac-β³Phe-β³Lys-β³Leu-β³Phe-β³Glu-β³Leu-OH	SEQ ID NO: 2	19.782	922.2	461.5#
Ac-β³Trp-β³aSer-β³Trp-β³Trp-β³aSer-β³Trp-OH	SEQ ID NO: 3	24.972	1114.5	1113.3
Ac-β³Val-β³aSer-β³Leu-β³Val-β³aSer-β³Leu-OH	SEQ ID NO: 4	27.406	955.3	954.3
Ac-β³Leu-β³Ile-β³Ala -OH	SEQ ID NO: 5	15.613	399.5	398.1
Ac- β³Trp-β³Ser-β³Ile -OH	SEQ ID NO: 6	20.980	488.2	489.2

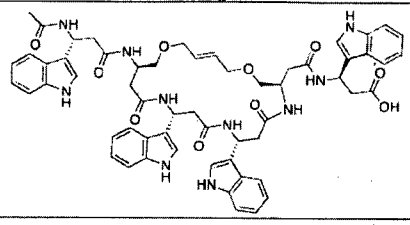
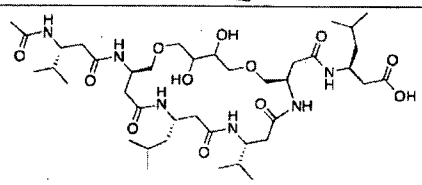
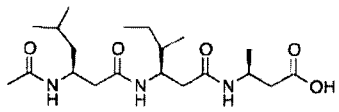
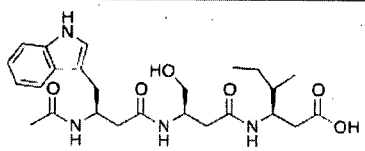
2+ peaks observed

Example 5: Self-assembly of β^3-peptides

Each acetylated β^3-peptide was dissolved in either methanol (MeOH) or water as shown in Table 6.

Table 6

SEQ ID NO:	B^3-Peptide	Solvent
SEQ ID NO: 1		H_2O
SEQ ID NO: 2		H_2O

SEQ ID NO:	B^3-Peptide	Solvent
SEQ ID NO: 3		MeOH
SEQ ID NO: 4		MeOH
SEQ ID NO: 5		MeOH
SEQ ID NO: 6		MeOH

After discussion of each peptide, the solutions were visualized under a light microscope. For microscopic imaging a Nikon TS100 inverted optical microscope was used. Fibres were imaged in solution, in the sample vial; thus the fibres were not flattened and, consequently, parts of the fibres were occasionally out of focus. This way of imaging was chosen to avoid any alteration to the fibre structure due to mechanical stress. Bright field and phase contrast imaging modes were used depending on which provided better contrast.

All solutions containing N-acetylated β^3-peptides exhibited rapid fibre formation (Figure 2). Fibres from either Peptide of SEQ ID NO: 1 or SEQ ID NO: 3 grew from several millimetres up to three centimetres in length all within one hour and were of approximately 0.25 mm in diameter (Figures 2a and 2b). Remarkably, these fibres could be easily removed from solution and proved strong and flexible enough to be handled like common thread (Figures 2a and 2b). For example, these fibres can be bent and/or stretched without damage retaining their original shape. The critical role played by the *N*-acetyl group in promoting axial self-assembly and fibre growth was

dramatically demonstrated by the complete absence of fibre formation by any of the β^3-peptides with a free N-terminus.

The relative thickness of the fibres suggests a higher order hierarchical self-assembly. However, the substructure of the large fibres could not be resolved by light microscopy. Hexa-β^3-peptides of SEQ ID NO: 3 and SEQ ID NO: 4 and tri-β^3-peptides of SEQ ID NO: 5 and SEQ ID NO: 6 formed thinner fibres which proved amenable to light microscopy imaging. Images of these fibres clearly revealed a twisted ribbon-like morphology (Figure 2). Moreover the presence of sub-micron fibrils, as revealed by fraying of the ends, provides evidence of hierarchical self-assembly (Figures 2c and 2e).

Higher resolution analysis of tri-β^3-peptides of SEQ ID NO: 5 by atomic force microscopy (AFM) revealed the initial stages of self-assembly as shown in Figure 3. The smallest unit visible is a helical fibril of ~10 nm diameter. These fibrils assemble to form larger helical, rope-like structures with the largest fibre approximately 35 nm in diameter. If it is assumed that one nanorod is approximately 0.5 nm in diameter, the fibrils designated 1 and 2 are likely to arise from the assembly of two/three individual nanorods. The fibrils also exhibited a surface periodicity which was measured to be approximately 50 nm for fibrils 1 and 2 and is indicative of a helical structure. The largest fibre visible was 35 nm in diameter and also exhibited a surface periodicity of 100 nm. The presence of the different sized fibres with helical periodicity suggests a mechanism of hierarchical self-assembly that follows a multi-step "self-twining" process via the formation of consecutively higher order rope-like nanofibres from individual fibrils.

Atomic Force Microscopy imaging was performed on an NT-MDT Ntegra platform, in intermittent contact mode, using high spring constant MikroMasch and NT-MDT probes with a nominal apex radius of 10 nm. Typical probe resonances were in the range of 200-400 kHz; 10-50 nm probe amplitudes were used. The AFM was used in scan-by-sample configuration with a 150 (closed loop) or 15 μm tube scanner. 2 μl of the peptide solution (in MeOH or water) was applied to freshly cleaved mica surface

using a positive displacement glass capillary pipette. The sample was covered with a petri dish to slow down evaporation. After 15min incubation the petri dish was removed and the surface dried under a gentle stream of N_2 or Ar gas. Samples were then imaged immediately. AFM images were processed using Gwyddion software (www.gwyddion.net) with a sequence of plane fit, median line fit and flattening along paths.

Example 6: Self assembly of other β^3-peptides

Other N-acetylated β^3-peptides were prepared including dipeptides, tripeptides, tetrapeptides, pentapeptides and hexapeptides and dissolved in methanol or water and allowed to self-assemble.

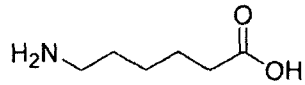
The N-acetylated peptides that formed fibres upon dissolution in solvent are shown in Table 7.

Table 7

Peptide Sequence	MS calc	MS obtained	Purified >95%	solvent	SEQ ID NO:
Ac-β³Ser-β³Ile -OH	288.2	289.1	Yes	MeOH	7
Ac-β³Leu-β³Ile-β³Ala -OH	399.5	398.1	Yes	MeOH	8
Ac-β³Trp-β³Ser-β³Ile -OH	488.2	489.2	Yes	MeOH	9
Ac-β³Trp-β³Ser-β³Trp -OH	561.2	562.2	Yes	MeOH	10
Ac-β³Trp-β³Ile-β³Trp -OH	586.3	587.2	Yes	MeOH	11
Ac-β³Lys-β³Ser-β³Ile -OH	431.1	432.2	Yes	Water	12
Ac-β³aSer-β³Leu-β³Val-β³Ser- OH	554.3	553.2	Yes	MeOH	13
Ac-β³Ser-β³Leu-β³Ile-β³Ala -OH	500.6	499.4	Yes	MeOH	14
Ac-β³Ala-β³Leu-β³Ile-β³Ala -OH	484.6	483.4	Yes	MeOH	16
Ac-β³Lys-β³Leu-β³Ile-β³Glu -OH	599.7	598.5	Yes	water	17
Ac-β³Ile-β³Trp-β³Ser-β³Ile -OH	616.3	617.2	Yes	MeOH	18
Ac-β³Trp-β³Leu-β³Ile-β³Trp -OH	715.4	716.5	Yes	MeOH	19
Ac-β³Trp-β³Ile-β³Trp-β³Ser-β³Ile-OH	816.2	816.9	Yes	MeOH	20
Ac-β³Lys-β³Ile-β³Trp-β³Ser-β³Ile- OH	758.1	759.0	Yes	water	21
Ac-β³Tyr-β³Lys-β³Leu-β³Tyr-β³Glu-β³Leu-OH	954.1	477.5#	Yes	water	23
Ac-β³Val-β³aSer-β³Leu-β³Val-β³aSer-β³Leu-OH	955.3	954.3	Yes	MeOH	24
Ac-β³Trp-β³Lys-β³Trp-β³Trp-β³Glu-β³Trp-OH	1146.3	1145.5	Yes	MeOH	25
Ac-β³Trp-β³Lys-β³Leu-AHx-β³Trp-β³Glu-β³Leu-OH	1113.2	556.5#	Yes	MeOH	26

* formed a hydrogel

AHx = amino hexanoic acid



Example 7: Crystal Structures of SEQ ID NOs: 4 and 6

Crystals of SEQ ID NO: 4 were initially examined using a standard laboratory X-ray diffractometer (Bruker ApexII CCD using MoKa radiation, *T* 123K) which gave very weak data and no structure solution could be obtained. Subsequently data were collected for all samples using either the MX1 or MX2 beamlines at the Australian synchrotron, Victoria, Australia. For each sample a very small colourless, crystal was mounted on a cryoloop and then flash cooled to 100 K. Data were collected using a single wavelength (see Table 8). The MX1 end station comprised a phi goniostat and ADSC Quantum 210r 210×210 mm large area detector. Due to hardware constraints (fixed detector angle), the maximum available data resolution on MX1 was limited to approximately 0.80 Å at the detector edges. The MX2 end station has a larger ADSC Quantum 310r 315×315 mm detector enabling better resolution. For compound **4c** (SEQ ID NO: 6), initial data indicated that the sample was twinned with a doubled *c* axis. The final dataset was collected by focusing a narrow beam onto a relatively single domain within the crystal. Data were collected using the Blu Ice [1] GUI and processed with the XDS (McPhillips, T. M., McPhillips, S. E., Chiu, H. J., Cohen, A. E., Deacon, A. M., Ellis, P. J., Garman, E., Gonzalez, A., Sauter, N. K., Phizackerley, R. P., Soltis, S. M., Kuhn, P. Blu-Ice and the Distributed Control System: software for data acquisition and instrument control at macromolecular crystallography beamlines. *J. Synchrotron Rad.* **2002**, *9*, 401-406. 3) software package. Anomalous scattering coefficients *f'* and *f''* were calculated for individual wavelengths (Kabsch, W. *J. Appl. Cryst.* **1993**, *26*, 795-800). Structure solution and refinement were performed with SHELX-97(Brennan, S. and Cowan, P. L. A suite of programs for calculating X-ray absorption, reflection and diffraction performance for a variety of materials at arbitrary wavelengths. *Rev. Sci. Instrum.* **1992**, *63*, 850).

The structures were solved in the space group *P*21 by direct methods and refined with anisotropic thermal parameter forms. Hydrogen atoms attached to carbon were placed in calculated positions and refined using a riding model. Subsequent difference Fourier maps revealed plausible locations of the acidic hydrogen atoms which were refined with restrained N-H and O-H distances and U(H)iso = 1.2×U(N/O)eq. The

absolute configurations were inferred from the syntheses; for the final refinement cycles, Friedel opposites were merged. The structure of compound of SEQ ID NO: 4 was modelled with the *trans*-diol moiety C(25-28),O(11),O(12) disordered over two positions (refined occupancies 0.62:0.38) and the disordered atoms were refined with isotropic thermal parameter forms only. Crystal data and refinement details are listed in Table 8 with selected hydrogen bond distances and torsion angles listed in Table 9.

Table 8: Crystal and refinement data for SEQ ID NOs: 4 and 6

	SEQ ID NO:4	**SEQ ID NO:6**
Empirical	$C_{40}H_{72}N_6O_{12}$	$C_{25}H_{36}N_4O_6$
Formula weight	829.04	488.26
Crystal system	Monoclinic	Monoclinic
Space group	*P*21	P21
Wavelength (Å)	0.77342	1.54178
Unit cell		
a [Å]	9.983(2)	4.9978(5)
b [Å]	21.542(4)	14.5143(12)
c [Å]	10.539(2)	16.8630(13)
β[deg]	95.64(2)	90.433(8)
Volume [Å3]	2255.5(8)	1223.20(18)
Z	2	2
ρ (calc.) [g.cm-3]	1.221	1.327
Theta range [deg]	2.23 to 26.57	2.62 to 66.75
*N*total	24685	12211
N (*R*int)a	3690 (0.056)	4228 (0.066)
*N*obs [I>2σ(I)]	3534	4228
Params/restraints	543/8	342/7
R indices		
*R*1	0.045	0.0443
w*R*2	0.117	0.0945
R indices (all		
*R*1	0.047	0.0613
w*R*2	0.119	0.1037
GoF(on *F*2)	1.059	1.059
a Friedel opposites were merged for the final refinement.		

b Amine N-H geometries were restrained.
c Non-hydrogen atoms were refined with isotropic thermal parameters only.

Table 9:
Selected hydrogen bond distances (Å) and torsion angles (°).

	SEQ ID NO: 4	SEQ ID NO: 6
N(1)-H_O(4)	1.99(1)	2.04(2)
N(2)-H_O(5)	2.13(2)	2.04(2)
N(3)-H_O(6)	2.10(2)	2.01(3)
O(8)-H_O(5)i	1.84(-)	1.89(4)
N(4)-H_O(1)ii	2.23(3)	2.18(3)
N(5)-H_O(1)iia	2.15(3)	2.18(3)
N(5)-H_O(2)iia	2.50(4)	2.49(4)
N(6)-H_O(3)ii	2.14(2)	2.10(2)
N(1)-C(3)-C(4)-C(5)	63.6(3)	64.7(3)
N(2)-C(6)-C(7)-C(8)	61.0(4)	47.7(4)
N(3)-C(9)-C(10)-C(11)	63.1(3)	62.5(3)
N(4)-C(12)-C(13)-C(14)	38.5(4)	38.2(4)
N(5)-C(15)-C(16)-C(17)	75.8(4)	76.7(3)
N(6)-C(18)-C(19)-C(20)	169.5(3)	164.4(3)
ai –x,y+½,2-z		
aii 1+x,y,z		
a N(5)-H bonds to both O(1)ii and O(2)ii.		

The proposed model of axial self-assembly was confirmed by X-ray crystallographic analysis of SEQ ID NO: 4 and 6. The peptides of SEQ ID NO: 4 exhibit a typical left-handed 14-helical structure of approximately two turns, internally supported by three *i,i+3* intamolecular N-H – O hydrogen bonds between N(1), N(2) and N(3), and O(4), O(5) and O(6) respectively (Figure 6b). The amino acid side chains aligned along three faces of the helix (Figure 6a and 6d). The first three residues form hydrogen bonds from their backbone NH to the carbonyl of residue i+3 in a manner typically of a 14-helix[1] (Figure 6b – light H-bonds). There was a slight distortion to the third hydrogen bond due to the orientation of the C-terminal carboxylic acid. Self-assembly arises when the second three residues form equivalent *inter*molecular hydrogen bonds

to the first three residues of the axially proximal peptide (Figure 6b – dark H-bonds). The pitch of the helix is approximately 5.0Å and is the same for both intramolecular and intermolecular rotations with an internal radius of approximately 1.8Å. X-ray crystal structure of the β^3-tripeptide of SEQ ID NO: 6 also shows a 3-point intermolecular H-bond motif equivalent to the motif found in β^3-hexapeptide of SEQ ID NO: 4. Each residue forms a H-bond from the backbone NH to the carbonyl of the same amino acid residue of the axially proximal peptide, therefore each peptide has 6 intermolecular H-bonds to drive the self-assembly. The acetyl cap provides a crucial role in the formation of the 3-point H-bond motif in this case as well. As shown in Figure 6c, a space filling model of crystalline peptides of SEQ ID NO: 4 highlights the axial self-assembly of individual nanorods.

Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" and "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as an acknowledgment or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

CLAIMS

1. A supramolecular structure comprising a plurality of peptide foldamer units, where each foldamer unit:

(i) independently comprises at least three sequential ß-amino acid residues, one of which is N-acylated, and

(ii) presents two complementary binding regions, each binding region comprising three sequential ß-amino acid residues, with one or both of the binding regions comprising the N-acylated ß-amino acid residue;

wherein the foldamer units are associated through their complementary binding regions to provide the supramolecular structure.

2. The supramolecular structure according to claim 1, wherein the at least three sequential ß-amino acid residues are present in multiples of 3.

3. The supramolecular structure according to claim 1 or 2, wherein a foldamer unit comprises a structure $(\beta\text{-AA})_x\text{-L-}(\beta\text{-AA})_y$, where each β-amino acid residue β-AA may be the same or different, L is a linking group, and x and y are each independently an integer equal to or greater than 3.

4. The supramolecular structure according to claim 3, wherein L is an amino acid residue other than a β-amino acid residue.

5. The supramolecular structure according to claim 3, wherein L is a bioactive agent.

6. The supramolecular structure according to any one of claims 1 to 5, wherein the at least three sequential β-amino acid residues present in the form of an 8-, 10-, 10/12- or 14- helix conformation.

7. The supramolecular structure according to any one of claims 1 to 6, wherein all β-amino acid residues in each peptide foldamer unit are R-β^2-amino acid residues.

8. The supramolecular structure according to any one of claims 1 to 6, wherein all β-amino acid residues in each peptide foldamer unit are S-β^2-amino acid residues.

9. A fibre comprising supramolecular structure according to any one of claims 1 to 8.

10. The fibre according to claim 9, wherein one or more supramolecular structures are intertwined and/or intratwined to form the fibre.

11. The fibre according to claim 9 or 10 in the form of a microfibre.

12. A fabric comprising a fibre according to any one of claims 9 to 11.

13. A method of preparing a supramolecular structure, the method comprising:

(i) providing a solution comprising a plurality of peptide foldamer units, where each foldamer unit:

(a) independently comprises at least three sequential ß-amino acid residues, one of which is N-acylated, and

(b) presents two complementary binding regions, each binding region comprising three sequential ß-amino acid residues, with one or both of the binding regions comprising the N-acylated ß-amino acid residue; and

(ii) allowing the peptide foldamer units to self-assemble through association of their complementary binding regions and form the supramolecular structure.

14. The method according to claim 13, wherein the solution comprising the peptide foldamer units is an aqueous solution.

15. The method according to claim 13 or 14, wherein the so formed supramolecular structures self-assemble into filaments that intra- and/or inter-twine to form a fibre structure.

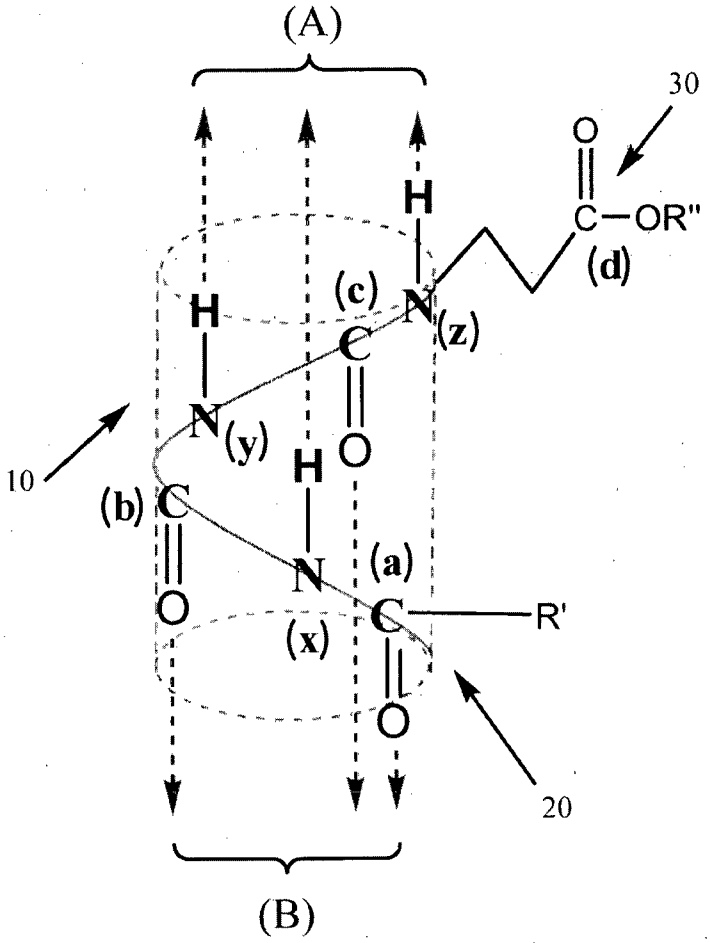
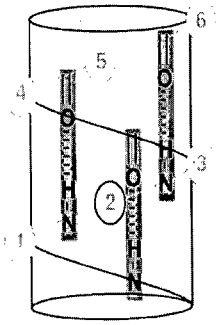
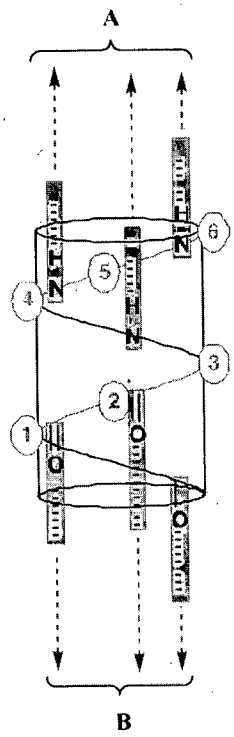


Figure 1



(a)



(b)

Figure 2

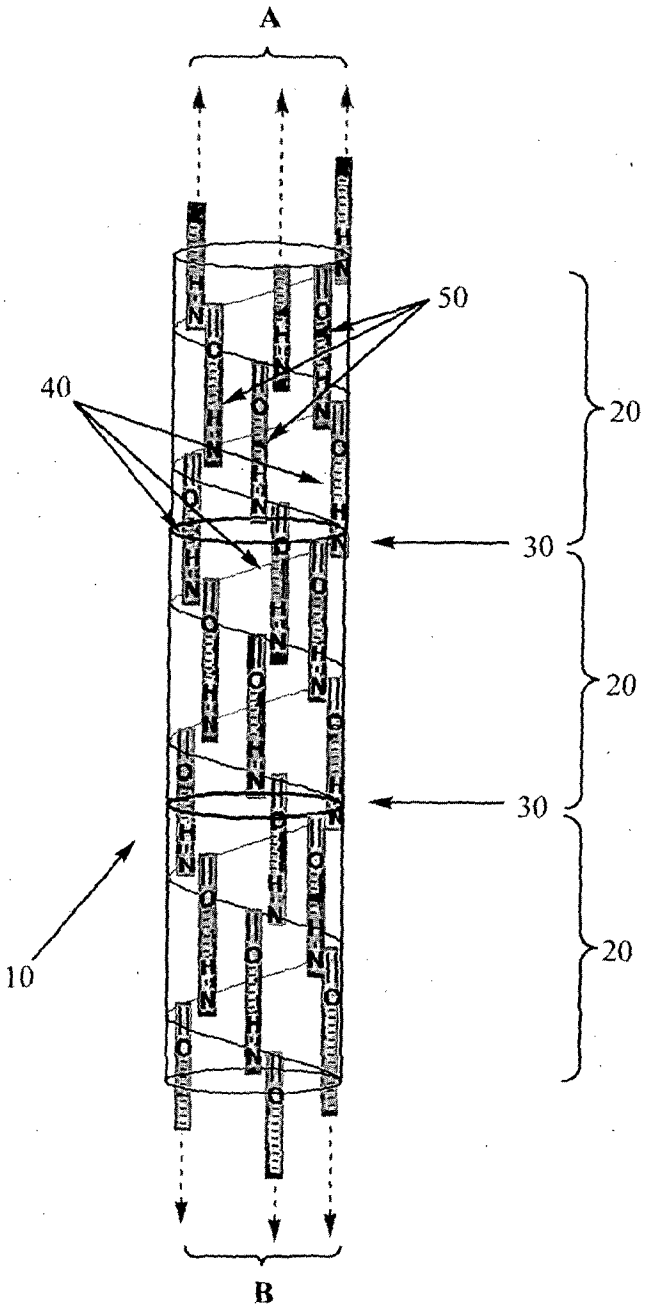


Figure 3

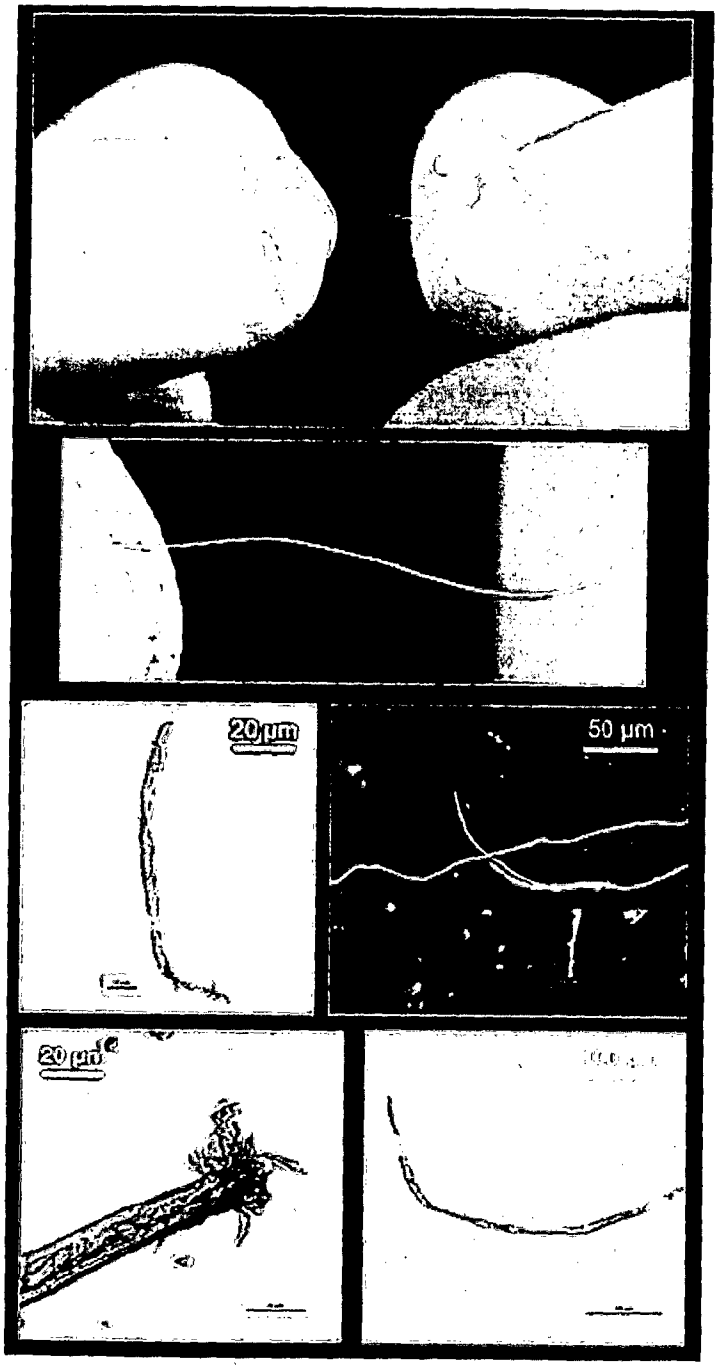


Figure 4

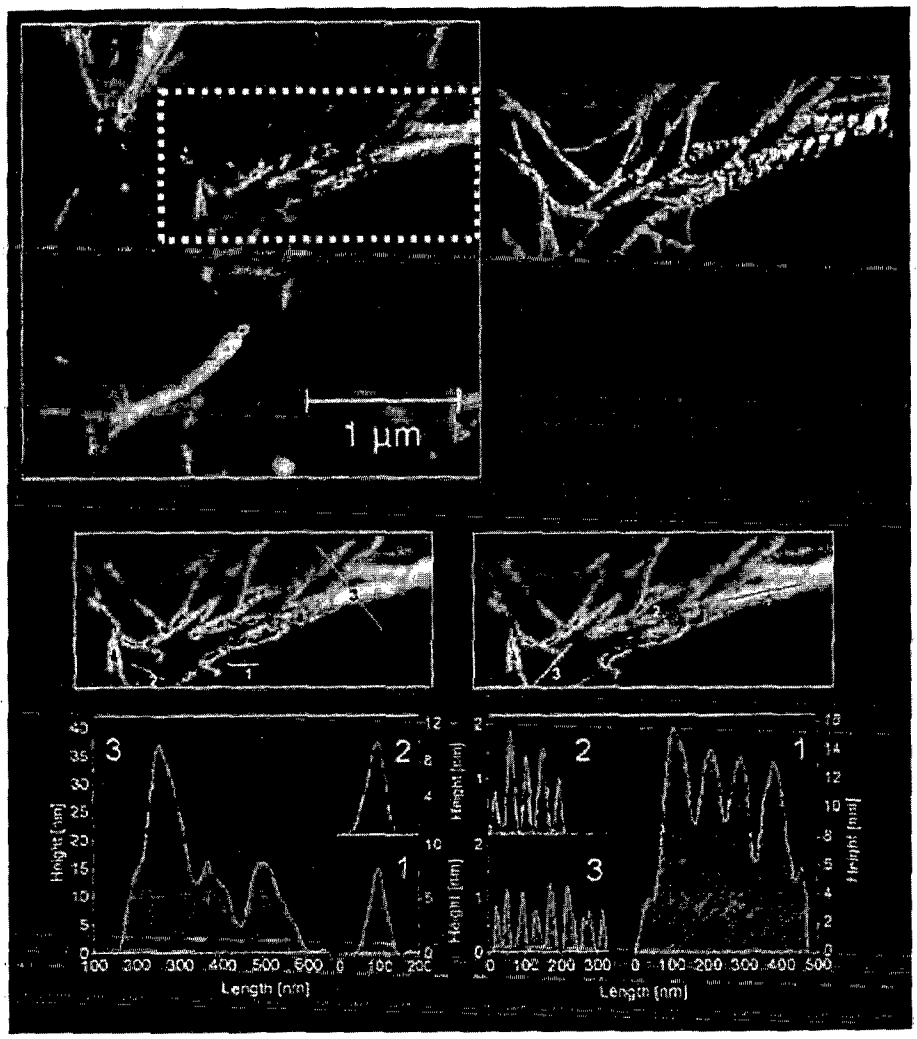


Figure 5

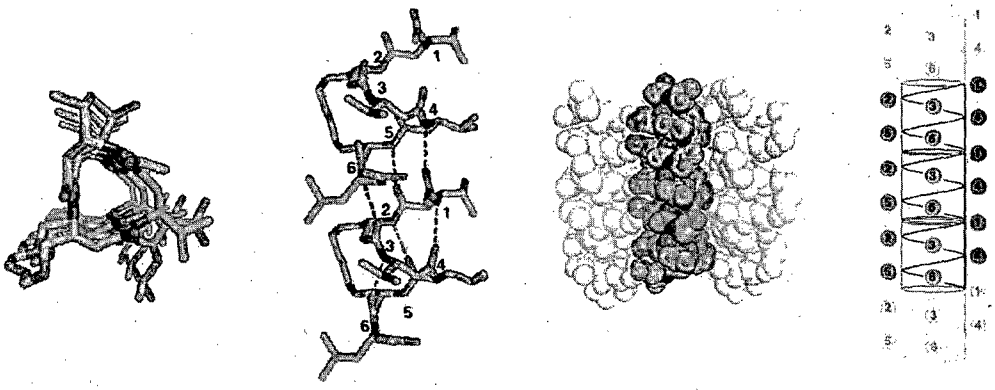


Figure 6

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU2013/001252

A. CLASSIFICATION OF SUBJECT MATTER

C07K 7/02 (2006.01) C07K 5/023 (2006.01) C07K 7/56 (2006.01) C07K 5/12 (2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CA Registry: Chemical structure search based on structure of peptide foldamers.
Google scholar search: keywords self assembly peptide foldamer and like terms

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	Documents are listed in the continuation of Box C	

[X] Further documents are listed in the continuation of Box C [ ] See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 November 2013	29 November 2013

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INTERNATIONAL SEARCH REPORT C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		International application No. **PCT/AU2013/001252**
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Gopalan, R. D. et al., "Conformational stability studies of a stapled hexa-β^3 -peptide library", *Organic & Biomolecular Chemistry*, 2012, 10, 1802-1806. Scheme 1 (especially peptide a), figure 2, page 1802 right column - page 1803 left column	1-2, 6, 9-11, 13-15
X	Del Borgo, M. P. et al., "Supramolecular Self-Assembly of *N*-Acetyl-Capped β-Peptides Leads to Nano- to Macroscale Fiber Formation", *Angewandte Chemie International Edition*, 2013, 52, 8266-8270. Table 1, page 8267 left column, page 8270 right column	5
X	Beke, T. et al, "A Theoretical Comparison of Self-Assembling α- and β-Peptide Nanostructures: Toward Design of β -Barrel Frameworks", *ACS Nano,* 2008, 2(3), 545-553 Figures 1-2, table 2, page 550, page 551 left column, page 552 left column	1-5, 7-8, 13-14
X	Beke, T. et al, "Theoretical Study on Tertiary Structural Elements of β-peptides: Nanotubes Formed from Parallel-Sheet-Derived Assemblies of β-Peptides", *Journal of the American Chemical Society*, 2006, 128 (15), 5158-5167 Scheme 1, figures 2-3, pages 5162-5264, page 5166 right column	1-5, 7-8, 13-14
A	Hart, S. A. et al., "Helix Macrodipole Control of β^3-Peptide 14-Helix Stability in Water", *Journal of the American Chemical Society,* 2003, 125 (14), 4022-4023 Page 4023 left column	
A	Martinek, T. A. et al., "Secondary Structure Dependent Self-Assembly of β-Peptides into Nanosized Fibrils and Membranes", *Angewandte Chemie International Edition*, 2006, 45, 2396-2400 Page 2397 left column	
A	Kwon, S. et al., "Unprecedented Molecular Architectures by the Controlled Self-Assembly of a β-Peptide Foldamer", *Angewandte Chemie International Edition*, 2010, 49, 8232-8236 Page 8232 left column	
P,X	Del Borgo, M. P. et al., "Supramolecular Self-Assembly of *N*-Acetyl-Capped β-Peptides Leads to Nano- to Macroscale Fiber Formation", *Angewandte Chemie International Edition*, 2013, 52, 8266-8270. The whole document	1-4, 6-15