CLAIMS

1. A peptide ligand specific for plasma kallikrein comprising a polypeptide comprising at least three cysteine residues, separated by at least two loop sequences, and a molecular scaffold selected from TBMB or a derivative thereof, which forms covalent bonds with the cysteine residues of the polypeptide such that at least two polypeptide loops are formed on the molecular scaffold, in which the peptide ligand comprises a peptide sequence of:

(a) -C_i-N-X-W-N-P-W-C_{ii}-O/U-X-X-X-O/J-X-C_{iii}- (SEQ ID NO: 1)

or a pharmaceutically acceptable salt, thereof;

in which:

C_i, C_{ii} and C_{iii} represent first, second and third cysteine residues, respectively;

X represents any amino acid residue;

O represents a non-polar aliphatic amino acid residue selected from G, A, I, L, P and V;

J represents a non-polar aromatic amino acid residue selected from F, W and Y; and

U represents a polar, uncharged amino acid residue selected from N, C, Q, M, S and T.

2. A peptide ligand according to Claim 1, in which the peptide of formula (a) comprises a sequence selected from -C_i-N-X-W-N-P-W-C_{ii}-O/U-X-X-X-O-X-C_{iii}- (SEQ ID NO: 7), such as -C_i-N-T/H/Y-W-N-P-W-C_{ii}-G/S/P-A/V/W/D/S-D/E/V/T/P-A/G/P/I/R/D-G/P/Y/I-F/I/L/V/R/G/D-C_{iii}- (SEQ ID NO: 8), in particular -C_i-N-T/H/Y-W-N-P-W-C_{ii}-G/S/P-A/V/W-D/E/V-A/G/P-G/P-F/I/L/V-C_{iii}- (SEQ ID NO: 9).

3. A peptide ligand according to Claim 1 or 2, in which the peptide of formula (a) comprises a sequence selected from:

-C_i-N-T-W-N-P-W-C_{ii}-G-W-V-G-G-F-C_{iii}- (06-259) (SEQ ID NO: 10);

-C_i-N-H-W-N-P-W-C_{ii}-S-V-E-P-P-V-C_{iii}- (06-259-01) (SEQ ID NO: 11);

-C_i-N-T-W-N-P-W-C_{ii}-P-W-D-A-P-L-C_{iii}- (06-259-02) (SEQ ID NO: 12);

-C_i-N-H-W-N-P-W-C_{ii}-S-A-D-P-P-I-C_{iii}- (06-259-03) (SEQ ID NO: 13);

-C_i-N-Y-W-N-P-W-C_{ii}-P-W-D-A-P-L-C_{iii}- (06-259-04) (SEQ ID NO: 14);

-C_i-N-H-W-N-P-W-C_{ii}-S-A-D-P-P-R-C_{iii}- (06-259-F1) (SEQ ID NO: 15);

-C_i-N-H-W-N-P-W-C_{ii}-P-A-D-I-P-V-C_{iii}- (06-259-E2) (SEQ ID NO: 16);

-C_i-N-H-W-N-P-W-C_{ii}-S-D-D-P-Y-I-C_{iii}- (06-259-H3) (SEQ ID NO: 17);

-C_i-N-H-W-N-P-W-C_{ii}-S-S-D-P-P-V-C_{iii}- (06-259-H4) (SEQ ID NO: 18);

-C_i-N-Y-W-N-P-W-C_{ii}-S-D-T-R-I-G-C_{iii}- (06-259-A6) (SEQ ID NO: 19); and

-C_i-N-T-W-N-P-W-C_{ii}-S-W-P-D-I-D-C_{iii}- (06-259-F2) (SEQ ID NO: 20);

such as -C_i-N-H-W-N-P-W-C_{ii}-S-V-E-P-P-V-C_{iii}- (06-259-01) (SEQ ID NO: 11);

-C_i-N-T-W-N-P-W-C_{ii}-P-W-D-A-P-L-C_{iii}- (06-259-02) (SEQ ID NO: 12);

-C_i-N-H-W-N-P-W-C_{ii}-S-A-D-P-P-I-C_{iii}- (06-259-03) (SEQ ID NO: 13); and

-C_i-N-Y-W-N-P-W-C_{ii}-P-W-D-A-P-L-C_{iii}- (06-259-04) (SEQ ID NO: 14).

4. A peptide ligand according to Claim 1, 2 or 3, in which the peptide of formula (a) comprises a sequence -C_i-N-T-W-N-P-W-C_{ii}-P-W-D-A-P-L-C_{iii}- (06-259-02) (SEQ ID NO: 12).

5. A peptide ligand according to any preceding claim, which additionally comprises one or more modifications selected from: N-terminal and/or C-terminal modifications; replacement of one or more amino acid residues with one or more non-natural amino acid residues (such as replacement of one or more polar amino acid residues with one or more isosteric or isoelectronic amino acids; replacement of one or more hydrophobic amino acid residues with other non-natural isosteric or isoelectronic amino acids); addition of a spacer group; replacement of one or more L-amino acid residues with one or more D-amino acid residues; N-alkylation of one or more amide bonds within the bicyclic peptide ligand; replacement of one or more peptide bonds with a surrogate bond; peptide backbone length modification; substitution of the hydrogen on the α-carbon of one or more amino acid residues with another chemical group, and post-synthetic bioorthogonal modification of amino acids such as cysteine, lysine, glutamate and tyrosine with suitable amine, thiol, carboxylic acid and phenol-reactive reagents.

6. A peptide ligand according to Claim 5, in which the one or more modifications comprise N-terminal modification, such as an N-terminal acetyl group, in particular in which the N-terminal cysteine group (C_i) is capped with acetic anhydride.

7. A peptide ligand according to Claim 5, in which the one or more modifications comprise a C-terminal modification, such as a C-terminal amide group, in particular amidation of the C-terminal cysteine group (C_{iii}).

8. A peptide ligand according to Claim 5, in which the one or more modifications comprise replacement of one or more amino acid residues with one or more non-natural amino acid residues, such as replacement of a proline residue with an L-azetidine carboxylic acid residue and/or replacement of an arginine residue with an N-α-methyl arginine or L-homoarginine residue.

9. A peptide ligand according to Claim 5, in which the one or more modifications comprise the addition of a spacer group, such as addition of a spacer group to the N-terminal cysteine (C_i) and/or the C-terminal cysteine (C_{iii}).

10. A peptide ligand according to Claim 9, in which the spacer group comprises one or more sarcosine groups (suitably 3 sarcosine groups) linked to two or more D-arginine residues (suitably 2 D-arginine residues).

11. A peptide ligand according to Claim 9 or 10, which is a peptide having a sequence selected from -C_i-N-T-W-N-P-W-C_{ii}-P-W-D-A-P-L-C_{iii}-Sar_3-$(D\text{-}Arg)_2$ ((06-259-02 (Sar_3-$(D\text{-}Arg)_2$) (SEQ ID NO: 61); in which Sar_3 represents 3 sarcosine spacers and $(D\text{-}Arg)_2$ represents 2 D-arginine residues.

12. A peptide ligand according to any preceding claim, in which the pharmaceutically acceptable salt is selected from a hydrochloride or acetate salt.

13. A peptide ligand according to any preceding claim which is specific for human, rat and/or rabbit plasma kallikrein, such as human and/or rat plasma kallikrein, in particular human plasma kallikrein.

14. A pharmaceutical composition comprising a peptide ligand according to any preceding claim in combination with one or more pharmaceutically acceptable excipients.

15. A peptide ligand according to any of Claims 1 to 13, for use in preventing, suppressing or treating inflammatory states, allergic hypersensitivity, cancer, bacterial or viral infection, ophthalmic disorders and autoimmune disorders.