CLAIMS

1. A peptide derived from an antibody with reactivity against a GPI linkage epitope, or a functionally-equivalent ligand.

2. A peptide or functionally-equivalent ligand according to claim 1, wherein said antibody additionally has reactivity against epitopes selected from the group consisting of anti-TCR Vβ antibody, a phospholipid such as phosphatidyl inositol, phosphatidyl serine or cardiolipin (diacyl glycerol), a phospholipid glycan, single stranded DNA and double-stranded DNA.

3. A peptide or functionally-equivalent ligand according to claim 2, wherein said antibody additionally has reactivity against human pancreatic α cells, follicular cells of the thyroid, cells of the adrenal medulla, stomach and intestinal tract, salivary glands, ovary, striated muscle, connective tissue.

4. A peptide or functionally-equivalent ligand according to any of the preceding claims, which is a Fab, F(ab')2, Fv or scFv fragment.

5. A peptide or functionally-equivalent ligand according to any of the preceding claims, which is derived from the hypervariable region of said antibody.

6. A peptide comprising or consisting of an amino acid sequence selected from:

G-Y-x-F-T-x-x-x-x-x-W (SEQ ID NO:162)
x-A-S-x-x-x-x-x-x-x-x (SEQ ID NO:164)
x-x-S-x-x-x-S (SEQ ID NO:165)
Q-Q-x-x-x-x-P-x-x (SEQ ID NO:166)
G-Y-T-F-T-x-x-x-x-x-W (SEQ ID NO:167)
G-Y-x-F-x-x-Y-x-M-x-W (SEQ ID NO:168)
x-A-S-x-x-x-x-x-x-x-x (SEQ ID NO:171)
x-A-S-x-x-x-x-x-x-L-x (SEQ ID NO:172)
x-x-S-x-x-x-S (SEQ ID NO:173)
x-T-S-x-L-x-x (SEQ ID NO:174)
Q-Q-x-x-S-x-P-x-T (SEQ ID NO:175) and
Q-Q-x-N-x-x-P-x-x (SEQ ID NO:176)

wherein 'x' indicates any amino acid residue, '-' indicates a peptide bond and the peptides are shown in N to C terminal orientation.

7. A peptide comprising or consisting of an amino acid sequence selected from:

G-Y-[TA]-F-T-[RNS]-[YN]-[WGN]-[IM]-[NF]-W

[LKE]-[RG]-[GML]-[LTY]-[LTG]-[PGN]-[DY]-[YAF]

[KR]-A-S-[QS]-[NDS]-[VI]-[DSG]-[TNS]-[NY]-[VLY]-[ANL]

[SYR]-[AT]-S-[YRI]-[RL]-[YHA]-S

Q-Q-[YG]-[NS]-[TS]-[YFS]-P-[LTP]-[TF]

G-Y-T-F-T-[RNYSTDEG]-[NYF]-[WGAY]-[IMV]-[NGQH]-W

G-Y-[ATS]-F-[T/S]-[SDG]-Y-[NWV]-M-[FQHN]-W

[KR]-A-S-[QS]-[NSDT]-[VI]-[DGSR]-[TSYNK]-[NADY]-[VYGL]-[ALD]

[RK]-A-S-[QR]-[DSG]-[IV]-[SN]-[NSG]-[YW]-L-[NHA]

[SRW]-[AT]-S-[YIT]-[RL]-[YAE]-S

[YLDTK]-T-S-[RNKV]-L-[HAG]-[SP]

Q-Q-[YGWR]-[NSAG]-S-[YSDW]-P-[LPYI]-T and

Q-Q-[GNSTY]-N-[TES]-[FDWY]-P-[TYRF]-[FT]

wherein one of the amino acids shown in parentheses is selected at each position where relevant, and the peptides are shown in N to C terminal orientation.

8. A peptide comprising or consisting of an amino acid sequence selected from:

G-Y-T-F-T-R-[YN]-W-[IM]-N-W

L-[RG]-G-L-L-P-[DY]-Y

K-A-S-Q-N-V-[DSG]-T-N-V-A

S-A-S-Y-R-Y-S

Q-Q-Y-N-S-Y-P-L-T

G-Y-T-F-T-[RNS]-Y-W-[IM]-N-W

G-Y-T-F-T-S-Y-W-M-H-W

K-A-S-Q-N-V-S-T-N-V-A

R-A-S-Q-S-I-S-N-Y-L-[NA]

S-A-S-Y-R-Y-S

Y-T-S-N-L-A-S

Q-Q-Y-N-S-Y-P-L-T and

Q-Q-N-N-E-D-P-[YR]-T

wherein one of the amino acids shown in parentheses is selected at each position where relevant, and the peptides are shown in N to C terminal orientation.

9. A peptide comprising the amino acid sequence recited in any one of SEQ ID NOs:6, 10, 12, 14, 16, 22, 26, 28, 30, 32, 38, 42, 44, 46, 48, 54, 58, 60, 62, 64, 70, 74, 76, 78,

80, 86, 90, 92, 94 or 96, preferably comprising the amino acid sequence recited in SEQ ID NO:10 or 16.

10. A peptide according to claim 9, comprising or consisting of the amino acid sequence recited in any one of SEQ ID NOs:2, 4, 6, 10, 12, 14, 16, 18, 20, 22, 26, 28, 30, 32, 34, 36, 38, 42, 44, 46, 48, 50, 52, 54, 58, 60, 62, 64, 66, 68, 70, 74, 76, 78, 80, 82, 84, 86, 90, 92, 94 or 96, or a functional equivalent or fragment thereof.

11. A peptide which comprises two or more peptides according to any of the preceding claims linked together.

12. A peptide according to claim 11, which comprises two or more peptides comprising the amino acid sequence recited in SEQ ID NO:10 or SEQ ID NO:16 linked together.

13. A peptide according to claim 12, which is a homodimer of monomer peptides, the monomer peptides consisting of the amino acid sequence recited in SEQ ID NO:160 or SEQ ID NO:161.

14. A peptide or functionally-equivalent ligand according to any of the preceding claims, which is chemically-modified, bound to a biological or synthetic substance, or which is conjugated to an enzyme, an indicator compound, a drug, a toxin or a radioactive label.

15. An antibody or antibody fragment comprising a peptide or functionally-equivalent ligand according to any of the preceding claims.

16. The antibody or antibody fragment of claim 15, which comprises 1, 2, 3, 4, 5 or 6 of the sequences recited in SEQ ID NOs:6, 10, 12, 14, 16, 22, 26, 28, 30, 32, 38, 42, 44, 46, 48, 54, 58, 60, 62, 64, 70, 74, 76, 78, 80, 86, 90, 92, 94 and 96.

17. An antibody, or functionally-equivalent ligand, which exhibits reactivity against a peptide according to any of claims 1 to 14.

18. A nucleic acid molecule encoding a peptide according to any of claims 1-14, an antibody or antibody fragment according to claim 15 or 16, or an antibody or functionally-equivalent ligand according to claim 17.

19. A vector incorporating a nucleic acid molecule according to claim 17.

20. A host cell incorporating a nucleic acid molecule according to claim 17 or a vector according to claim 19.

21. A method of expressing a peptide according to any of claims 1-14, an antibody or antibody fragment according to claim 15 or 16, an antibody or equivalent ligand according to claim 17, said method comprising expressing a nucleic acid molecule according to claim 18 or a vector according to claim 19 in a host cell.

22. A method of treating a disease in a patient comprising administering to the patient a peptide according to any of claims 1-14, an antibody or antibody fragment according to claim 15 or 16, or an antibody or equivalent ligand according to claim 17, a nucleic acid molecule according to claim 18, a vector according to claim 19, or a host cell according to claim 20.

23. A peptide according to any of claims 1-14, an antibody or antibody fragment according to claim 15 or 16, an antibody or equivalent ligand according to claim 17, a nucleic acid molecule according to claim 18, a vector according to claim 19, or a host cell according to claim 20, for use in therapy or diagnosis of disease.

24. A method or use according to claim 22 or claim 23, wherein said disease is characterised by the presence of autoantibodies with reactivity against a GPI linkage epitope, and is also reactive against epitopes in anti-TCR Vβ antibodies, molecules with signalling capacity, phospholipids including phosphatidyl inositol, phosphatidyl serine and cardiolipin (diacyl glycerol), and phospholipid glycans, second messengers of insulin action, single and double-stranded DNA and elements of the GPI-linkage.

25. A method or use according to claim 22 or claim 23, wherein said disease is selected from the group consisting of IDDM, NIDDM, or organ or non-organ specific autoimmune disease, cardiovascular disease, cancer cachexia and cancer or any other diseases where anti-phospholipid antibodies and/or hyperinsulinaemia and/or hyperglucagonaemia and/or insulin resistance and/or glucose intolerance are present.

26. A method according to claim 25, wherein said other diseases where anti-phospholipid antibodies and/or hyperinsulinaemia, insulin resistance and glucose intolerance are present are selected from the group consisting of psoriasis, eczema, vitiligo, acanthosis nigricans, skin ageing, alopecia areata, alzheimer's disease, schizophrenia, depression, parkinson's disease, migraine, multiple sclerosis, myasthenia gravis, amyotrophic lateral sclerosis and related diseases, motoneuron and related diseases, thyroid disease,

cushing's syndrome and addison's disease, polycystic overy syndrome, hypogonadism and premature baldness in men, obesity, syndrome x, diseases related to antiphospholipid and lupus anticoagulant antibodies, coeliac disease, gastritis, inflammatory bowel disease, arthritis and related diseases, asthma, cystic fibrosis, osteoporosis and osteopenia, lichen planus and leukoplakia, anaemia, paroxysmal nocturnal haemoglobinuria, sleep apnoea, insomnia, cancer, HIV, infection and dysfunctions in immunoregulation.

27. A method or use according to claim 22 or claim 23, wherein said disease is a disease associated with glucose intolerance or a disease associated with loss or deterioration of auto-glycaemic regulation.

28. A pharmaceutical composition comprising a peptide according to any of claims 1-14, an antibody or antibody fragment according to claim 15 or 16, an antibody or equivalent ligand according to claim 17, a nucleic acid molecule according to claim 18, a vector according to claim 19, or a host cell according to claim 20, in conjunction with a pharmaceutically-acceptable carrier.

29. A vaccine composition comprising a peptide according to any of claims 1-14.

30. A vaccine composition according to claim 29, which includes an adjuvant.

31. A method of vaccinating an individual against a disease or disorder, comprising administering to the individual a peptide according to any of claims 1 to 14, or a vaccine composition according to either of claims 29 or 30 into an individual.

32. A method according to claim 31, wherein antibodies against the peptide are formed in the individual.

33. A method of diagnosing an individual for the presence of or levels of autoimmune antibodies, said method comprising contacting a blood, plasma or serum sample or other body fluid with a peptide according to any of claims 1-14 in the presence of a target for said autoimmune antibodies and assessing the amount of said naturally-occurring autoantibody that binds specifically to the target.

34. A method according to claim 33, wherein said target is an anti-TCR Vβ polyclonal or monoclonal immunoglobulin molecule or any part thereof that identifies at least one epitope on a T cell receptor Vβ chain.

35. The method of claim 33 or 34, wherein said peptide, antibody and/or target is labelled.

36. An array of peptides, at least one of which is a peptide according to any of claims 1-14.

CLAIMS

1. A dimer or multimer which comprises or consists of two or more monomer peptides linked together by a non-antibody linker, wherein each of the monomer peptides:

(a) consists of the amino acid sequence:

LRGLLPDY (SEQ ID NO:10); or
KGMTTGYA (SEQ ID NO:26); or
EGLYGNYF (SEQ ID NO:42),

wherein the peptide is shown in N to C terminal orientation;

(b) is an extended variant of a peptide of (a) which includes up to 5 additional amino acid residues at the C terminal and/or N terminal; or

(c) is a truncated variant of a peptide of (a) which includes one amino acid deletion at the C terminal and/or N terminal,

and wherein the dimer or multimer is not an antibody.

2. The dimer or multimer according to claim 1, wherein each monomer peptide comprises the amino acid sequence recited in SEQ ID NO:10, SEQ ID NO:26 or SEQ ID NO:42.

3. The dimer or multimer according to claim 1, wherein each monomer peptide consists of the amino acid sequence recited in SEQ ID NO:10, SEQ ID NO:26 or SEQ ID NO:42.

4. The dimer or multimer according to claim 1, which is a homodimer or a homomultimer.

5. The dimer or multimer according to claim 1, which is a homodimer that comprises monomer peptides linked together by a cysteine residue at the N terminal or C terminal of each monomer peptide.

6. The dimer or multimer according to claim 1, which is chemically-modified, bound to a biological or synthetic substance, or which is conjugated to an enzyme, an indicator compound, a drug, a toxin or a radioactive label.

7. The dimer or multimer according to claim 2, wherein each monomer peptide comprises the amino acid sequence recited in SEQ ID NO: 160.

8. The dimer or multimer according to claim 3, wherein each monomer peptide consists of the amino acid sequence recited in SEQ ID NO: 160.

9. A pharmaceutical composition comprising the dimer or multimer according to claim 1 and a pharmaceutically-acceptable carrier.

10. A dimer or multimer which comprises or consists of two or more monomer peptides linked together by a non-antibody linker, wherein each of the monomer peptides:

(a) consists of the amino acid sequence:

QQYNSYPLT (SEQ ID NO:16); or

QQGNTFPTF (SEQ ID NO:32); or

QQGSSSPLT (SEQ ID NO:64); or

QQYNSYPPT (SEQ ID NO:80),

wherein the peptide is shown in N to C terminal orientation;

(b) is a variant of a peptide according to (a) which includes 1 or 2 amino acid substitutions, and which consists of the amino acid sequence:

Q-Q-x-x-x-x-P-x-x (SEQ ID NO:166),

wherein 'x' indicates any amino acid residue, '-' indicates a peptide bond and the peptides are shown in N to C terminal orientation;

(c) is an extended variant of a peptide of (a) or (b) which includes up to 5 additional amino acid residues at the C terminal and/or N terminal; or

(d) is a truncated variant of a peptide of (a) or (b) which includes one amino acid deletion at the C terminal and/or N terminal,

and wherein the dimer or multimer is not an antibody.

11. The dimer or multimer according to claim 10, wherein each monomer peptide comprises the amino acid sequence recited in SEQ ID NO:16, SEQ ID NO:32, SEQ ID NO:64 or SEQ ID NO:80.

12. The dimer or multimer according to claim 10, wherein each monomer peptide consists of the amino acid sequence recited in SEQ ID NO:16, SEQ ID NO:32, SEQ ID NO:64 or SEQ ID NO:80.

13. The dimer or multimer according to claim 10, which is a homodimer or a homomultimer.

14. The dimer or multimer according to claim 10, which is a homodimer that comprises monomer peptides linked together by a cysteine residue at the N terminal or C terminal of each monomer peptide.

15. The dimer or multimer according to claim 10, which is chemically-modified, bound to a biological or synthetic substance, or which is conjugated to an enzyme, an indicator compound, a drug, a toxin or a radioactive label.

16. The dimer or multimer according to claim 11, wherein each monomer peptide comprises the amino acid sequence recited in SEQ ID NO: 161.

17. The dimer or multimer according to claim 12, wherein each monomer peptide consists of the amino acid sequence recited in SEQ ID NO: 161.

18. A pharmaceutical composition comprising the dimer or multimer according to claim 10 and a pharmaceutically-acceptable carrier.