CLAIMS

1. A peptide comprising:

a first domain of the sequence X37-X5-X6-X7-G, and,

(i) a second domain of the formula I: -(X26-X27-X28-X29-X30-X31-X32-X33-X34-X35-X36)-(CterpolyD/E) directly linked at carboxy-terminal end of the first domain;

(ii) a second domain of the formula II: -(X13-X14-X15-X16-X17-X18-X19-X20-X21-X22-X23-X24-X25)-(CterGp) directly linked at carboxy-terminal end of the first domain; or

(iii) a second domain of the formula III: (NterGp)-(X8-X9-X10-X11-X12)- directly linked at amino-terminal end of the first domain;

wherein

X37 is Gly, L-Ser or D-Ser;

X5, X6 and X7 are independently any amino acid;

X8, X9, X10, X11 and X12 are independently any amino acid,

X13, X14, X15, X16, X17, X18, X19, X20, X21, X22, X23, X24 and X25 are independently any amino acid, wherein no more than 2 amino acids among X13, X14, X15, X16, X17, X18, X19, X20, X21, X22, X23, X24 and X25 are a charged amino acid;

X26, X27, X28, X29, X30, X31, X32, X33, X34, X35 and X36 are independently any amino acid, wherein no more than 2 amino acids among X26, X27, X28, X29, X30, X31, X32, X33, X34, X35 are a charged amino acid;

CterpolyD/E is a group of 4-10 amino acids including at least 2 negatively charged amino acids

NterGp is a group of 3-5 amino acids including at least 2 charged amino acids, and

CterGp is a group of 3-5 amino acids including at least 3 positively charged amino acids,

or a retro or retroinverso form thereof,

or a pharmaceutically acceptable salt thereof,

wherein the peptide does not comprise or consist of the sequence TLPAIVGIGGGGGLLLLVIVAVLIAYKRK (SEQ ID NO: 1).

2. The peptide of claim 1, wherein X5, X6 and X7 are aliphatic uncharged amino acids.

3. The peptide of claim 2, wherein X5, X6 and X7 are each independently Gly, D or L-Ala, D or L-Val, D or L-Leu and D or L-Ile.

4. The peptide of claim 3, wherein X5 is D-Leu, L-Leu, D-Ile or L-Ile; X6 is Gly, D-Val or L-Val; and/or X7 is Gly.

5. The peptide of claim 4, wherein X5 is L-Leu and/or X6 is L-Val.

6. The peptide of any one of claims 1 to 5, wherein X6 is Gly, D-Val or L-Val.

7. The peptide of any one of claims 1 to 6, wherein X37 is Gly.

8. The peptide of any one of claims 1 to 7, wherein X26 is an aliphatic uncharged amino acid; X27 is an aliphatic uncharged amino acid; X28 is an aliphatic uncharged amino acid; X29 is an aliphatic uncharged amino acid; X30 is an aliphatic uncharged amino acid; X31 is a negatively charged amino acid; X32 is an aliphatic uncharged amino acid; X33 is an aliphatic uncharged amino acid; X34 is an aliphatic uncharged amino acid; X35 is a negatively charged amino acid; and/or X36 is an aliphatic uncharged amino acid.

9. The peptide of claim 8, wherein X26 is Gly, D-Val or L-Val; X27 is Gly, D-Val or L-Val; X28 is D or L-Ala, D- or L-Val, D- or L-Leu, or D- or L-Ile; X29 is D- or L-Ala, D- or L-Val, D- or L-Leu, or D- or L-Ile; X30 is D- or L-Ala, D- or L-Val, D- or L-Leu, or D- or L-Ile; X31 is D or L-Glu; X32 is D- or L-Ala, D- or L-Val, D- or L-Leu, or D- or L-Ile; X33 is D- or L-Ala, D- or L-Val, D- or L-Leu, or D- or L-Ile; X34 is D- or L-Ala, D- or L-Val, D- or L-Leu, or D- or L-Ile; X35 is D or L-Glu; and/or X36 is D- or L-Ala, D- or L-Val, D- or L-Leu, or D- or L-Ile.

10. The peptide of claim 9, wherein X26 is L-Val; X27 is Gly; X28 is L-Leu; X29 is L-Leu; X30 is L-Leu; X31 is L-Glu; X32 is L-Val; X33 is L-Ile; X34 is L-Val; X35 is L-Glu; and/or X36 is L-Val.

11. The peptide of any one of claims 1 to 10, wherein X26-X27-X28-X29-X30-X31-X32-X33-X34-X35-X36 is VGLLLEVIVEV (SEQ ID NO: 91), GGELLLVIVE (SEQ ID NO: 92), VVLLLEVIVEV (SEQ ID NO: 93), VGLLVEVIVEV (SEQ ID NO:117), or VGLVLEVIVEV (SEQ ID NO:118).

12. The peptide of any one of claims 1 to 11, wherein CterpolyD/E comprises a sequence of -X”1-X”2-Z or -X”3-X”3bis-X”2-Z,
wherein

X”1 is a small amino acid,
X”2 is an aromatic amino acid,
X”3 and X”3bis are independently long aliphatic amino acids,
Z is from 2 to 10 D/L-Asp and/or D/L-Glu residues.

13. The peptide of claim 12, wherein: X”1 is D- or L-Ala.

14. The peptide of claim 12 or 13, wherein X”3 and X”3bis are independently D- or L-Leu, or D- or L-Ile.

15. The peptide of any one of claims 12 to 14, wherein Z is from 3 to 5 L-Glu residues.

16. The peptide of any one of claims 1 to 15, wherein the peptide comprises a second domain of formula I or II, and further comprises a third domain of 1 to 10 amino acids linked at the amino-terminal end of the first domain.

17. The peptide of claim 16, wherein the third domain is of the formula IV: X38-X39-X40-X41-X42-X43, wherein:
X38 is D-Thr or L-Thr, or is absent;
X39 is D- or L-Leu, D- or L-Ile, or is absent;
X40 is Pro, D- or L-Ile, or is absent;
X41 is D- or L-Ala, D- or L-Val, or is absent;
X42 is D- or L-Leu, D- or L-Ile, or is absent; and
X43 is D- or L-Val, D-Thr or L-Thr.

18. The peptide of any one of claims 1 to 17, which comprises 35 amino acid or less.

19. The peptide of any one of claims 1 to 18, which comprises one of the following sequences:
AITGLVGGVGLLLEVIVEVAYEEEEE (SEQ ID NO: 16);
TGLVGGVGLLLEVIVEVAYEEEEE (SEQ ID NO: 17);
GLVGGVGLLLEVIVEVAYEEEEE (SEQ ID NO: 18);
TLPAIVGIGGGGGELLLVIVEVLIYEEEEE (SEQ ID NO: 19);
TLPAITGLVGGVGLLLEVIVEVAYEEEEE (SEQ ID NO: 20);
TLPAIVSIGGGVVLLLEVIVEVAYEEEEE (SEQ ID NO: 21);
TLPAITGLVGGVGLLLEVIVEVAYEEE (SEQ ID NO: 97);
TLPAITGLVGGVGLLLEVIVEVAYEE (SEQ ID NO: 98);
TLPAITGLVGGVGLLLEVIVEVAYDDDDD (SEQ ID NO: 99);
TLPAITGLVGGVVLLLEVIVEVAYEEEEE (SEQ ID NO: 100);

TLPAITGLVGGVGLVLEVIVEVAYEEEEE (SEQ ID NO: 101);
TLPAITGLVGGVGLLLEVIVEVVYEEEEE (SEQ ID NO: 105);
$_{d}E_{d}E_{d}E_{d}E_{d}Y_{d}A_{d}V_{d}E_{d}V_{d}I_{d}V_{d}E_{d}L_{d}L_{d}LG_{d}VGG_{d}V_{d}LG_{d}T_{d}I_{d}A_{d}P_{d}L_{d}T$ (SEQ ID NO: 106);
TLPAITGLVGGVGLLLEVIVEVAYDD (SEQ ID NO: 107);
TLPAITGLVGGVGLLLEVIVEVAYDEDED (SEQ ID NO: 108);
$_{d}$TLPAITGLVGGVGLLLEVIVEVAYEEEEE (SEQ ID NO: 111);
TLPAITGLVGGVGLLLEVIV$_{d}$EVAYEEEEE (SEQ ID NO: 112); or
TLPAITGLVGGVGLLVEVIVEVAYEEEEE (SEQ ID NO: 113).

20. The peptide of claim 19, which comprises one of the following sequences:
TLPAITGLVGGVGLLLEVIVEVAYEEEEE (SEQ ID NO: 20);
TLPAITGLVGGVVLLLEVIVEVAYEEEEE (SEQ ID NO: 100);
TLPAITGLVGGVGLLLEVIVEVAYDEDED (SEQ ID NO: 108); or
TLPAITGLVGGVGLLVEVIVEVAYEEEEE (SEQ ID NO: 113).

21. A pharmaceutical composition comprising the peptide, retro or retroinverso form thereof, or pharmaceutically acceptable salt thereof according to any one of claims 1 to 20, and a pharmaceutically acceptable carrier.

22. Use of the peptide, retro or retroinverso form thereof, or pharmaceutically acceptable salt thereof according to any one of claims 1 to 20, or the pharmaceutical composition according to claim 21, for the manufacture of a medicament for the treatment of a demyelinating disease in a subject.

23. The use according to claim 22, wherein the demyelinating disease is a demyelinating autoimmune disease

24. The use according to claim 22 or 23, wherein the demyelinating disease is multiple sclerosis, transverse myelitis, neuromyelitis optica (Devic's disease), acute hemorrhagic leukoencephalitis, acute disseminated encephalomyelitis (ADEM), diffuse cerebral sclerosis of Schilder, adrenoleukodystrophy, Alexander disease, Canavan disease, Krabbe disease, Balo's disease, Charcot-Marie-Tooth disease (CMT), HIV encephalitis, HTLV-I Associated Myelopathy (HAM), Binswanger's disease (subcortical leukoencephalopathy and subcortical arteriosclerotic encephalopathy (SAE)), globoid cell leukodystrophy, metachromatic leukodystrophy, Pelizaeus-Merzbacher disease, progressive multifocal

leukoencephalopathy, Marchiafava-Bignami disease, central pontine myelinolysis, polyradiculonueropathy, or demyelinating diseases caused by antineoplastic agents, carbon monoxide, vitamin B12 deficiency, mercury intoxication, alcohol or tobacco amblyopia, hypoxia or irradiation.

25. The use according to claim 24, wherein the demyelinating disease is multiple sclerosis.

26. The use according to any one of claims 22 to 25, wherein the medicament is for use in combination with one or more additional therapeutic agents.

27. The use according to claim 26, wherein the one or more additional therapeutic agents comprise fingolimod.