CLAIMS

What is claimed is:

1. A peptide having the following structural formula I

R^1-X-Y-R^2 (I) (SEQ ID NO:12)

or a pharmaceutically acceptable salt or solvate thereof, wherein:

R^1 is hydrogen, a C1-C6 alkyl, a C6-C12 aryl, a C6-C12 aryl C1-C6 alkyl, a C1-C20 alkanoyl or pGlu;

R^2 is -NH_2 or -OH;

X is a peptide sequence having the formula (Ic)

X1-Thr-His-X4-X5-Cys-Ile-X8-Phe-X10 (Ic) (SEQ ID NO:3)

wherein:

X1 is Asp, Ida, or absent;

X4 is Phe or Dpa;

X5 is Pro;

X8 is Ile, Lys, Glu, Phe, Gln, or Arg; and

X10 is Lys or absent;

and

Y is absent or Y is a peptide sequence having the formula (IIa)

Y1-Y2-Y3-Y4-Y5-Y6-Y7-Y8-Y9-Y10-Y11-Y12-Y13-Y14-Y15 (IIa) (SEQ ID NO:5)

wherein

Y1 is Gly, Glu, Lys, Ser, or absent;

Y2 is Pro, Ala, Cys, Gly, or absent;

Y3 is Arg, Lys, Ala, or absent;

Y4 is Ser, Ala, or absent;

Y5 is Lys, Arg, or absent;

Y6 is Gly, Ser, Lys, Ile, Arg, Ala, Pro, Val, or absent;

Y7 is Trp, Val, or absent;
Y8 is Val, Thr, Tyr, Ala, Glu, Lys, Asp, or absent;
Y9 is Cys, Tyr, or absent;
Y10 is Met, Lys, Arg, Tyr, or absent;
Y11 is Arg, Met, Cys, Lys, or absent;
Y12 is Arg, Lys, Ala, or absent;
Y13 is Arg, Cys, Lys, Val, or absent;
Y14 is Arg, Lys, Pro, Cys, Thr, or absent; and
Y15 is Thr, Arg, or absent,
wherein the peptide of formula (I) comprises two or more cysteine residues; optionally wherein the peptide is conjugated to one or more additional chemical moieties; and

wherein the peptide or pharmaceutically acceptable salt or solvate thereof has hepcidin activity.

2. The peptide or pharmaceutically acceptable salt or solvate thereof according to claim 1, wherein the peptide comprises two cysteine residues linked via a disulfide bond.

3. The peptide or pharmaceutically acceptable salt or solvate thereof according to claim 1 or claim 2, wherein R^1 is hydrogen, isovaleric acid, isobutyric acid or acetyl.

4. The peptide or pharmaceutically acceptable salt or solvate thereof according to any one of claims 1-3, wherein the peptide is conjugated to one or more additional chemical moieties, optionally wherein the one or more additional chemical moieties are lipophilic substituents and/or polymeric moieties.

5. The peptide or pharmaceutically acceptable salt or solvate thereof according to any one of claims 1-4, wherein

X is a peptide sequence having the formula (Id)

X1-Thr-His-Phe-X5-Cys-Ile-X8-Phe-X10 (Id) (SEQ ID NO:4)

wherein
X1 is Asp or Ida;

X5 is Pro;
X8 is Ile, Lys, or Phe; and
X10 is absent.

6. The peptide or pharmaceutically acceptable salt or solvate thereof of any one of claims 1-5, wherein

Y is a peptide sequence having the formula (IIg)

Y1-Pro-Y3-Ser-Y5-Y6-Y7-Y8-Cys-Y10 (IIg) (SEQ ID NO:11)

wherein:
Y1 is Glu or Lys;
Y3 is Arg or Lys;
Y5 is Arg or Lys;
Y6 is Gly, Ser, Lys, Ile or Arg;
Y7 is Trp or absent;
Y8 is Val or absent; and
Y10 is Lys or absent.

7. The peptide or pharmaceutically acceptable salt or solvate thereof according to claim 1, wherein:
X1 is Asp or IDA, X4 is Phe, or X8 is Lys.

8. The peptide or pharmaceutically acceptable salt or solvate thereof according to claim 1, wherein:
X1 is Asp or IDA, X4 is Phe, and X8 is Lys.

9. The peptide or pharmaceutically acceptable salt or solvate thereof according to claim 1, wherein the peptide comprises a sequence set forth in any of SEQ ID NOs: 204-207, 210-226, 237, 241-255, 261-265, 270-276, 286, 288, 289, 369, 370 or 372-375.

10. The peptide or pharmaceutically acceptable salt or solvate thereof according to claim 1, wherein the peptide comprises one of the following sequences or structures:

Isovaleric acid-DTHFPCIIFGPRSKGWVCK-NH_2 (SEQ ID NO:38);

Isovaleric acid-DTHFPCIIFEPRSKGWVCK-NH_2 (SEQ ID NO:128);

Isovaleric acid-DTHFPCIIFGPRSKGWACK-NH_2 (SEQ ID NO:164);

Isovaleric acid-DTHFPCIIFEPRSKGWVCK-NH_2 (SEQ ID NO:165);

Isovaleric acid-DTHFPCIIFGPRSKGWVCKK-NH_2 (SEQ ID NO:168);

Isovaleric acid-DTHFPCI-K(PEG8)-FGPRSKGWVCK-NH_2 (SEQ ID NO:172);

Isovaleric acid-DTHFPCIKF-K(PEG8)-PRSKGWVCK-NH_2 (SEQ ID NO:173);

Isovaleric acid-DTHFPCIIFGPRSRGWVC-K(PEG8)-NH_2(SEQ ID NO:201);

Isovaleric acid-DTHFPCIIFGPRSRGWVC-K(PEG4)-NH_2 (SEQ ID NO:202;;

Isovaleric acid-DTHFPCIIFGPRSRGWVC-K(PEG2)-NH_2 (SEQ ID NO:203;;

Isovaleric acid-DTHFPCI-K(Palm)-FGPRSKGWVCK-NH_2 (SEQ ID NO:183);

Isobutyric acid-DTHFPCIKFGPRSKGWVCK-NH_2 (SEQ ID NO: 185);

Cyclohexanoic acid-DTHFPCIKFGPRSKGWVCK-NH_2 (SEQ ID NO: 191);

Isovaleric acid-DTHFPCIKF-K(Palm)-PRSKGWVCK-NH_2 (SEQ ID NO:217);

Isovaleric acid-DTHFPCIKFGP-K(Palm)-SKGWVCK-NH_2 (SEQ ID NO:219);

Isovaleric acid-DTHFPCIKFGPRS-K(Palm)-GWVCK-NH_2 (SEQ ID NO:220);

Isovaleric acid-DTHFPCIKFGPRSKGWVC-K(Palm)-NH_2 (SEQ ID NO:221);

Isovaleric acid-DTHFPCI-K(PEG3-Palm)-FGPRSKGWVCK-NH_2 (SEQ ID NO:222);

Isovaleric acid-DTHFPCIKF-K(PEG3-Palm)-PRSKGWVCK-NH_2 (SEQ ID NO:223);

Isovaleric acid-DTHFPCIKFGP-K(PEG3-Palm)-SKGWVCK-NH_2 (SEQ ID NO:224);

Isovaleric acid-DTHFPCIKFGPRS-K(PEG3-Palm)-GWVCK-NH_2 (SEQ ID NO:225);

Isovaleric acid-DTHFPCIKFGPRSKGWVC-K(PEG3-Palm)-NH_2 (SEQ ID NO:226);

Isovaleric acid-DTHFPCIKFGPRSKGWVC-K(PEG8)-NH_2 (SEQ ID NO:176);

Isovaleric acid-DTHFPCI-K(isoGlu-Palm)-FEPRSKGCK-NH_2 (SEQ ID NO:241);

Isovaleric acid-DTHFPCIKF-K(isoGlu-Palm)-PRSKGCK-NH_2 (SEQ ID NO:242);

Isovaleric acid-DTHFPCIKFEP-K(isoGlu-Palm)-SKGCK-NH_2 (SEQ ID NO:243);

Isovaleric acid-DTHFPCIKFEPK(isoGlu-Palm)-SKGWECK-NH_2 (SEQ ID NO:265);

Isovaleric acid-DTHFPCIKFEPRS-K(isoGlu-Palm)-GCK-NH_2 (SEQ ID NO:244);

Isovaleric acid-DTHFPCIKFEPRSK-K(isoGlu-Palm)-CK-NH_2 (SEQ ID NO:245);

Isovaleric acid-DTHFPCIKFEPRSKGCK-K(isoGlu-Palm)-NH_2 (SEQ ID NO:246);

Isovaleric acid-DTHFPCI-K(Dapa-Palm)-FEPRSKGCK-NH_2 (SEQ ID NO:248);

Isovaleric acid-DTHFPCIKF-K(Dapa-Palm)-PRSKGCK-NH_2 (SEQ ID NO:249);

Isovaleric acid-DTHFPCIKFEP-K(Dapa-Palm)-SKGCK-NH_2 (SEQ ID NO:250);

Isovaleric acid-DTHFPCIKFEPRS-K(Dapa-Palm)-GCK-NH_2 (SEQ ID NO:251);

Isovaleric acid-DTHFPCIKFEPRSK-K(Dapa-Palm)-CK-NH_2 (SEQ ID NO:252);

Isovaleric acid-DTHFPCIKFEPRSKGC-K(Dapa-Palm)-K-NH_2 (SEQ ID NO:253);

Isovaleric acid-DTHFPCIKFEPRSKGCK-K(Dapa-Palm)-NH_2 (SEQ ID NO:254);

DTHFPCIIFGPRSKGWVCK;
DTHFPCIIFEPRSKGWVCK;
DTHFPCIIFGPRSKGWACK;
DTHFPCIIFGPRSKGWVCKK;
DTHFPCIKFGPRSKGWVCK;
DTHFPCIKFGPRSKGWVCK;
DTHFPCIKFKPRSKGWVCK;
DTHFPCIIFGPRSRGWVCK;
DTHFPCIKFGPKSKGWVCK;
DTHFPCIKFEPRSKGCK;
DTHFPCIKFEPKSKGWECK;
DTHFPCIKFEPRSKKCK;
DTHFPCIKFEPRSKGCKK;
DTHFPCIKFKPRSKGCK; or
DTHFPCIKFEPKSKGCK.

11. The peptide or pharmaceutically acceptable salt or solvate thereof of claim 1, wherein the peptide comprises the following sequence:

DTHFPCIKFEPRSKGCK,

DTHFPCIKFKPRSKGCK, or

DTHFPCIKFGPRSKGWVCK.

12. The peptide or pharmaceutically acceptable salt or solvate thereof of claim 1, wherein the peptide comprises the following structure:

Isovaleric acid-DTHFPCI-K(isoGlu-Palm)-FEPRSKGCK-NH_2 (SEQ ID NO:241)

and wherein there is a disulfide bond between the two Cys residues.

13. The peptide or pharmaceutically acceptable salt or solvate thereof of claim 1, wherein the peptide comprises the following structure:

Isovaleric acid-DTHFPCIKF-K(isoGlu-Palm)-PRSKGCK-NH_2 (SEQ ID NO:242)

and wherein there is a disulfide bond between the two Cys residues.

14. The peptide or pharmaceutically acceptable salt or solvate thereof of claim 1, wherein the peptide comprises the following structure:

Cyclohexanoic acid-DTHFPCIKFGPRSKGWVCK-NH_2 (SEQ ID NO: 191)

and wherein there is a disulfide bond between the two Cys residues.

15. The peptide or pharmaceutically acceptable salt or solvate thereof according to claim 1, wherein,

Y1 is Gly, Glu, Ser, or absent ;
Y2 is Pro, Cys, or absent ;
Y3 is Arg, Lys, Ala, or absent;
Y4 is Ser, Ala, or absent;
Y5 is Lys, Arg, or absent;
Y6 is Gly, or absent;
Y7 is Trp, Val, or absent;
Y8 is Val, Thr, Ala, Glu, Lys, Asp, or absent;
Y9 is Cys or absent;
Y10 is Lys or absent;
Y11 is absent;
Y12 is absent;
Y13 is absent;
Y14 is absent; and
Y15 is absent.

16. A pharmaceutical composition comprising the peptide or pharmaceutically acceptable salt or solvate thereof according to any one of claims 1-15 and a pharmaceutically acceptable carrier or excipient.

17. A method of binding ferroportin or inducing ferroportin internalization and degradation in vitro, comprising contacting the ferroportin with the peptide or pharmaceutically acceptable salt or solvate thereof according to any one of claims 1-15 or the composition according to claim 16.

18. The peptide or pharmaceutically acceptable salt or solvate thereof according to any one of claims 1-15 or the composition according to claim 16 for use in the treatment of a disease of iron metabolism in a subject in need thereof, wherein the disease of iron metabolism is optionally selected from hereditary hemochromatosis, iron hemochromatosis, HFE mutation hemochromatosis, ferroportin mutation hemochromatosis, transferrin receptor 2 mutation hemochromatosis, hemojuvelin mutation hemochromatosis, hepcidin mutation hemochromatosis, juvenile hemochromatosis, neonatal hemochromatosis, hepcidin deficiency, transfusional iron overload, thalassemia, thalassemia intermedia, alpha thalassemia, and β-thalassemia.

19. The peptide or pharmaceutically acceptable salt or solvate thereof or composition for use according to claim 18, wherein the disease of iron metabolism is a thalassemia, optionally alpha thalassemia or β-thalassemia.

20. Use of the peptide or pharmaceutically acceptable salt or solvate thereof according to any one of claims 1-15 or the composition according to claim 16 in the manufacture of a medicament for the treatment of a disease of iron metabolism in a subject in need thereof, wherein the disease of iron metabolism is optionally selected from hemochromatosis, hereditary hemochromatosis, HFE mutation hemochromatosis, ferroportin mutation hemochromatosis, transferrin receptor 2 mutation hemochromatosis, hemojuvelin mutation hemochromatosis, hepcidin mutation hemochromatosis, juvenile hemochromatosis, neonatal hemochromatosis, hepcidin deficiency,

an iron overload disease, transfusional iron overload, thalassemia, thalassemia intermedia, alpha thalassemia, and β-thalassemia.