CLAIMS

1. A lipocalin mutein, or a fragment or a variant thereof, wherein the lipocalin mutein, fragment or variant is capable of increasing the bioavailability of iron in a subject in need thereof, for use in a method of treating, ameliorating or preventing a disorder comprising the step of administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising such lipocalin mutein, fragment or variant, and wherein said amount is sufficient to yield a satisfactory therapeutic readout in the subject.

2. A lipocalin mutein, or a fragment or a variant thereof according to the use of claim 1, wherein said composition is administered via a parenteral route or non-parenteral route.

3. A lipocalin mutein, or a fragment or a variant thereof according to the use of any one of the preceding claims, wherein said composition is administered via an enteral route.

4. A lipocalin mutein, or a fragment or a variant thereof according to the use of any one of the preceding claims, wherein said composition is administered up to twice daily, up to once daily, up to once every other day, up to once every third day, up to twice every week, up to once every week and up to once every other week and up to once every month.

5. A lipocalin mutein, or a fragment or a variant thereof according to the use of any one of the preceding claims, wherein said composition is administered to a subject in need thereof every time at a dosage level selected from the group consisting of: 0.1-1mg/kg, 0.1-40mg/kg, 1-20mg/kg, 1-10mg/kg, 3-20mg/kg and 1-3mg/kg.

6. A lipocalin mutein, or a fragment or a variant thereof according to the use of any one of the preceding claims, wherein the lipocalin mutein is capable of inhibiting binding of hepcidin to a hepcidin specific monoclonal antibody having the variable light chain region shown in SEQ ID No: 6 and the variable heavy chain region shown in SEQW ID No: 7.

7. A lipocalin mutein, or a fragment or a variant thereof according to the use of any one of the preceding claims, wherein the lipocalin mutein competes for binding to hepcidin

with an antibody having the variable light and heavy chain regions shown in SEQ ID NOs: 6 and 7, respectively.

8. A lipocalin mutein, or a fragment or a variant thereof according to the use of any one of the preceding claims, wherein the lipocalin mutein is with at least a 75% sequence identity or homology to SEQ ID NO: 1.

9. A lipocalin mutein, or a fragment or a variant thereof according to the use of any one of the preceding claims, wherein the lipocalin mutein is conjugated to a compound that extends the serum half-life of the mutein.

10. A lipocalin mutein, or a fragment or a variant thereof according to the use of claim 8, wherein the compound that extends the serum half-life is selected from the group consisting of a polyalkylene glycol molecule, a hydroethylstarch, a protein domain, a Fc part of an immunoglubolin, a CH3 domain of an immoglobulin, a CH4 domain of an immunoglubolin, an albumin-binding peptide, and an albumin-binding protein.

11. A conjugated lipocalin mutein, used in any method as defined in claim 9 or claim 10, which is capable of increasing the bioavailability of iron.

12. The conjugated mutein of claim 11, wherein the polyalkylene glycol is polyethylene (PEG) or an activated derivative thereof.

13. The conjugated of claim 12, wherein the polyethylene (PEG) is 30 kiloDalton in molecular weight.

14. A lipocalin mutein, or a fragment or a variant thereof as defined in any one of claims 1 o 13 for use in a method of treatment or diagnosis of anemia, anemia of inflammation, chronic inflammatory anemia, an iron-deficiency anemia, an iron loading anemia, sepsis, hereditary hemochromatosis, anemia associated with chronic kidney disease (CKD), anemia of cancer (AC), chemotherapy induced anemia (CIA), an anemia associated with ESA-resistance, ferroportin disease, hemochromatosis, end stage renal disorder, chronic kidney disease, inflammation, diabetes, rheumatoid arthritis, arteriosclerosis, vasculitis, systemic lupus erythematosus, and hemoglobinopathies.

15. A highly concentrated, stable pharmaceutical formulation of at least one lipocalin mutein which is capable of increasing the bioavailability of iron in a subject in need thereof, comprising:

a. about 50 to 350 mg/ml of the lipocalin mutein;
b. about 1 to 100 mM of a buffering agent providing a pH of 5.5 to 8;
c. about 1 to 500 mM of a stabilizer or a mixture of two or more stabilizers;
d. about 0.01 to 0.08% of a non-ionic surfactant; and
e. an effective amount of at least one hyaluronidase enzyme.

16. A formulation according to claim 15 for use in a method of treating a disorder which is amenable to treatment with a lipocalin mutein or fragments or variants thereof capable of increasing the bioavailability of iron in a subject in need thereof, comprising the step of administering to the subject an amount effective to treat the said disorder.

17. A kit comprising one or more vials containing the formulation according to claim 15 and an injection device for subcutaneous administration of the formulation to a patient.

CLAIMS

1. A lipocalin mutein, or a fragment or a variant thereof having binding affinity to hepcidin, wherein the lipocalin mutein, fragment or variant is capable of increasing the bioavailability of iron in a subject in need thereof, for use in a method of treating, ameliorating or preventing a disorder comprising the step of administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising such lipocalin mutein, fragment or variant, and wherein said amount is sufficient to yield a satisfactory therapeutic readout in the subject.

2. A lipocalin mutein, or a fragment or a variant thereof according to claim 1, wherein said composition is administered via a parenteral route or non-parenteral route.

3. A lipocalin mutein, or a fragment or a variant thereof according to any one of the preceding claims, wherein said composition is administered via an enteral route.

4. A lipocalin mutein, or a fragment or a variant thereof according to any one of the preceding claims, wherein said composition is administered up to twice daily, up to once daily, up to once every other day, up to once every third day, up to twice every week, up to once every week and up to once every other week and up to once every month.

5. A lipocalin mutein, or a fragment or a variant thereof according to any one of the preceding claims, wherein said composition is administered to a subject in need thereof every time at a dosage level selected from the group consisting of: 0.1-1mg/kg, 0.1-40mg/kg, 1-20mg/kg, 1-10mg/kg, 3-20mg/kg and 1-3mg/kg.

6. A lipocalin mutein, or a fragment or a variant thereof according to any one of the preceding claims, wherein the lipocalin mutein is capable of inhibiting binding of hepcidin to a hepcidin specific monoclonal antibody having the variable light chain region shown in SEQ ID No: 6 and the variable heavy chain region shown in SEQ ID No: 7.

7. A lipocalin mutein, or a fragment or a variant thereof according to any one of the preceding claims, wherein the lipocalin mutein competes for binding to hepcidin with

an antibody having the variable light and heavy chain regions shown in SEQ ID NOs: 6 and 7, respectively.

8. A lipocalin mutein, or a fragment or a variant thereof according to any one of the preceding claims, wherein the lipocalin mutein is with at least a 75% sequence identity or homology to SEQ ID NO: 1.

9. A lipocalin mutein, or a fragment or a variant thereof according to any one of the preceding claims, wherein the lipocalin mutein is conjugated to a compound that extends the serum half-life of the mutein.

10. A lipocalin mutein, or a fragment or a variant thereof according to claim 9, wherein the compound that extends the serum half-life is selected from the group consisting of a polyalkylene glycol molecule, a hydroethylstarch, a protein domain, a Fc part of an immunoglubolin, a CH3 domain of an immoglobulin, a CH4 domain of an immunoglubolin, an albumin-binding peptide, and an albumin-binding protein.

11. A conjugated lipocalin mutein, used in any method as defined in claim 9 or claim 10, which is capable of increasing the bioavailability of iron.

12. The conjugated mutein of claim 11, wherein the polyalkylene glycol is polyethylene (PEG) or an activated derivative thereof.

13. The conjugated mutein of claim 12, wherein the polyethylene (PEG) is 30 kiloDalton in molecular weight.

14. A lipocalin mutein, or a fragment or a variant thereof as defined in any one of claims 1 to 13 for use in a method of treatment or diagnosis of anemia, anemia of inflammation, chronic inflammatory anemia, an iron-deficiency anemia, an iron loading anemia, sepsis, hereditary hemochromatosis, anemia associated with chronic kidney disease (CKD), anemia of cancer (AC), chemotherapy induced anemia (CIA), an anemia associated with ESA-resistance, ferroportin disease, hemochromatosis, end stage renal disorder, chronic kidney disease, inflammation, diabetes, rheumatoid arthritis, arteriosclerosis, vasculitis, systemic lupus erythematosus, or hemoglobinopathies.

15. A highly concentrated, stable pharmaceutical formulation of at least one lipocalin mutein according to any one of claims 1-14, which is capable of increasing the bioavailability of iron in a subject in need thereof, comprising:

a. about 50 to 350 mg/ml of the lipocalin mutein;
b. about 1 to 100 mM of a buffering agent providing a pH of 5.5 to 8;
c. about 1 to 500 mM of a stabilizer or a mixture of two or more stabilizers;
d. about 0.01 to 0.08% of a non-ionic surfactant; and
e. an effective amount of at least one hyaluronidase enzyme.

16. A formulation according to claim 15 for use in a method of treating a disorder which is amenable to treatment with a lipocalin mutein or fragments or variants thereof capable of increasing the bioavailability of iron in a subject in need thereof, comprising the step of administering to the subject an amount effective to treat the said disorder.

17. A kit comprising one or more vials containing the formulation according to claim 15 and an injection device for subcutaneous administration of the formulation to a patient.