Therefore, in one aspect, the present disclosure refers to the use of a composition comprising apotransferrin (Apo-Tf) and holo-transferrin (holo-Tf), in the manufacture of a medicament for treating a Hypoxia Inducible Factor (HIF)-related pathological condition selected from the group consisting of: a condition associated with organ transplantation; a condition associated with ischemia or oxygen deprivation in a patient prior to surgery; ischemia due to cardiac arrest, thrombotic clots, or traumatic injury; an interruption of blood flow during a surgical intervention; and a condition due to a neurodegenerative disease.

Also disclosed herein is a method of treatment of Hypoxia Inducible Factor (HIF)-related conditions comprising the administration of a composition comprising transferrin. The present disclosure also refers to a method of treatment of Hypoxia Inducible Factor (HIF)-related conditions wherein the administered composition further comprises a combination of a transferrin and an iron chelator.

As used herein, the term “transferrin” and its plural refers to ApoTf alone, or HoloTf alone or a mixture thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention is further described with reference to the following drawings, in which:

Figure 1 shows that compositions of majority ApoTf and majority HoloTf induce HIF-1α protein under normoxic and hypoxic conditions 6 hrs post treatment.

Figure 2 shows that compositions of majority ApoTf and majority HoloTf induce HIF-1α protein under normoxic conditions 24 hrs post treatment.

Figure 3 shows that mixtures of ApoTf and HoloTf induce HIF-1α protein 6 hrs post treatment.

Figure 4A shows mRNA expression levels of Glut1 under normoxic and hypoxic conditions in the presence of HSA,

CLAIMS

1. Use of a composition comprising apotransferrin (Apo-Tf) and holo-transferrin (holo-Tf), in the manufacture of a medicament for treating a Hypoxia Inducible Factor (HIF)-related pathological condition selected from the group consisting of: a condition associated with organ transplantation; a condition associated with ischemia or oxygen deprivation in a patient prior to surgery; ischemia due to cardiac arrest, thrombotic clots, or traumatic injury; an interruption of blood flow during a surgical intervention; and a condition due to a neurodegenerative disease.

2. The use of claim 1, wherein the composition further comprises either an iron chelator or PHD2 enzyme inhibitor.

3. The use of claim 1, wherein the HIF-related pathological condition is a condition associated with organ transplantation, and wherein the organ has been treated with a composition comprising transferrin in preparation for transplantation into the recipient.

4. The use of claim 3, where the organ has been treated with a composition comprising transferrin and iron chelator or PHD2 enzyme inhibitor in preparation for transplantation into the recipient.

5. The use of claim 1, wherein the HIF-related pathological condition is a condition due to a neurodegenerative disease, and wherein the neurodegenerative disease is selected from the group consisting of Alzheimer’s disease, Parkinson’s disease, Huntington’s disease and Amylotrophic Lateral Sclerosis.

6. The use of claim 1, wherein said Apo-Tf and Holo-Tf are recombinant.

7. The use of claim 1, wherein said Apo-Tf and Holo-Tf are modified by pegylation, glycosylation, polysialylation, or other physical modifications to extend plasma half-life of the protein, including covalent fusion to domains that extend half-life in blood, such as the Fc domain of immunoglobulin, albumin, glucagon-like peptide-1, exendin-4, XTEN, etc.

8. The use of claim 1, wherein said Apo-Tf and Holo-Tf are protein conjugates between Apo-Tf and Holo-Tf with any other protein, protein fragment, or peptide.

9. The use of claim 1, wherein said Apo-Tf and Holo-Tf are modified to increase metal binding affinity.

10. The use of claim 1, wherein said Apo-Tf and Holo-Tf are derivatives of transferrin comprising more than 50% similarity with SEQ ID NO: 1.

11. The use of claim 1, wherein said composition is a mixture of apotransferrin (Apo-Tf) and holo-transferrin (Holo-Tf), in a ratio of 99% Apo-Tf:1% Holo-Tf to 30% Apo- Tf:70% Holo-Tf, or the proportion that is most comparable to a fraction obtained or purified from biological fluids.

12. The use of claim 2, wherein said iron chelator is M30, deferoxamine (DFO), Deferasirox, deferiprone, deferitrin, L1NAl1, CP363, CP502, or Ethylenediaminetetraacetic acid (EDTA).

13. The use of claim 2, wherein said PHD2 enzyme inhibitor is IOX2, IOX3, dimethyloxallyl glycine or other 2-oxoglutarate binding site molecules.