WHAT IS CLAIMED IS:

1. Use of a composition in the preparation of a medicament for improving one, two, three, four, five, six or more (e.g., all) of erythrocyte function, turnover, or synthesis; hemoglobin function, turnover, or synthesis; or vascular function in a subject, the composition comprising:

a) a leucine amino acid entity,

b) a arginine amino acid entity,

c) glutamine amino acid entity; and

d) a N-acetylcysteine (NAC)-entity,

wherein the composition does not comprise a peptide of more than 20 amino acid residues in length (*e.g.*, whey protein), or if a peptide of more than 20 amino acid residues in length is present, the peptide is present at less than: 10 wt. % of the total wt. of the composition (*e.g.*, in dry form).

2. Use of a composition in the preparation of a medicament for the treatment of treating a hemoglobinopathy or a thalassemia in a subject, the composition comprising:

a) a leucine amino acid entity,

b) a arginine amino acid entity,

c) glutamine amino acid entity; and

d) a N-acetylcysteine (NAC)-entity

wherein the composition does not comprise a peptide of more than 20 amino acid residues in length (*e.g.*, whey protein), or if a peptide of more than 20 amino acid residues in length is present, the peptide is present at less than: 10 wt. % of the total wt. of the composition (*e.g.*, in dry form).

3. A composition for use in a method of improving one, two, three, four, five, six or more of erythrocyte function, turnover, or synthesis; hemoglobin function, turnover, or synthesis; or vascular function in a subject in need thereof, wherein the composition comprises an effective amount of:

a) a leucine amino acid entity,

b) an arginine amino acid entity,

c) glutamine amino acid entity; and

d) a N-acetylcysteine entity,

wherein the composition does not comprise a peptide of more than 20 amino acid residues in length, or if a peptide of more than 20 amino acid residues in length is present, the peptide is present at less than: 10 wt. % of the total wt. of the total components of the composition.

4. A composition for use in a method of treating a hemoglobinopathy or a thalassemia in a subject in need thereof, wherein the composition comprises an effective amount of:

a) a leucine amino acid entity,

b) a arginine amino acid entity,

c) glutamine amino acid entity; and

d) a N-acetylcysteine entity

wherein the composition does not comprise a peptide of more than 20 amino acid residues in length, or if a peptide of more than 20 amino acid residues in length is present, the peptide is present at less than: 10 wt. % of the total wt. of the total components of the composition.

5. The use of claim 1 or 2 or the composition for use of claim 3 or 4, wherein the composition further comprises: (e) one or both of a serine amino acid entity or a carnitine entity; and/or

one, two, three, or more of (f) a valine amino acid entity, (g) a histidine amino acid entity, (h) a lysine amino acid entity, or (i) a citrulline amino acid entity.

6. A composition comprising:

a) a leucine amino acid entity,

b) an arginine amino acid entity,

c) a glutamine amino acid entity,

d) a N-acetylcysteine entity,

e) a citrulline amino acid entity,

f) a carnitine entity,

g) a serine amino acid entity,

h) a valine amino acid entity,

i) a histidine amino acid entity, and

j) a lysine amino acid entity.

7. The use of claim 1 or 2, the composition for use of claim 3 or 4, or the composition of claim 6, wherein the composition does not comprise a peptide of more than 20 amino acid residues in length, or if a peptide of more than 20 amino acid residues in length is present, the peptide is present at less than: 10 wt. %, 9 wt. %, 8 wt. %, 7 wt. %, 6 wt. %, 5 wt. %, 4 wt. %, 3 wt. %, 2 wt. %, 1 wt. %, 0.5 wt. %, 0.1 wt. %, 0.05 wt. %, 0.01 wt. %, 0.001 wt. %, or less of the total wt. of the total components of the composition.

8. The use of claim 1 or 2, the composition for use of claim 3 or 4, or the composition of claim 6 or 7, wherein two, three, four, five, six, seven, eight, nine, ten, or more of (a)-(j) or (a)-(d) are in free amino acid form in the composition.

9. The use, the composition for use or the composition of claim 8, wherein at least: 42 wt. %, 45 wt. %, 50 wt. %, 55 wt. %, 60 wt. %, 65 wt. %, 70 wt. %, 75 wt. %, 80 wt. %, 85 wt. %, 90 wt. %, 95 wt. %, 97 wt. %, 98 wt. %, or more, of the total wt. of the composition is one, two, three, four, five, six, seven, eight, nine, or more of (a)-(j) or (a) – (d) in free amino acid form in the composition.

10. The use of claim 1 or 2, the composition for use of claim 3 or 4, or the composition of any of claims 6-9, wherein the total wt. % of (a)-(j) or (a)-(d) is greater than the total wt. % of one, two, or three of other amino acid entity components, non-amino acid entity protein components, or non-protein components in the composition .

11. The use, the composition for use or the composition of claim 10, wherein (a)-(j) or (a)-(d) is at least: 50 wt. %, 55 wt. %, 60 wt. %, 65 wt. %, 70 wt. %, 75 wt. %, 80 wt. %, 85 wt. %, 90 wt. %, 95 wt. %, 97 wt. %, 98 wt. %, or more, of the total wt. of one, two, or three of other

amino acid entity components, non-amino acid entity protein components, or total components in the composition.

12. The use of claim 1 or 2, the composition for use of claim 3 or 4, or the composition of any of claims 6-11, wherein the composition comprises a combination of 18 or fewer, 17 or fewer, 16 or fewer, 15 or fewer, 14 or fewer, 13 or fewer, 12 or fewer, or 11 or fewer amino acid entities.

13. The use of claim 1 or 2, the composition for use of claim 3 or 4, or the composition of any of claims 6-12, wherein the composition comprises:

a) the leucine amino acid entity is chosen from:

i) L-leucine or a salt thereof,

ii) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-leucine, or

iii) β-hydroxy-β-methylbutyrate or a salt thereof;

b) the arginine amino acid entity is chosen from:

i) L-arginine or a salt thereof,

ii) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-arginine,

iii) creatine or a salt thereof, or

v) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising creatine;

c) the glutamine amino acid entity is L-glutamine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-glutamine;

d) the N-acetylcysteine entity is N-acetylcysteine or a salt thereof or a dipeptide or salt thereof comprising N-acetylcysteine;

e) the citrulline amino acid entity, if present, is L-citrulline or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-citrulline;

f) the carnitine entity, if present, is L-carnitine or a salt thereof, or a dipeptide or salt thereof, comprising L-carnitine;

g) the serine amino acid entity, if present, is L-serine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-serine;

h) the valine amino acid entity, if present, is L-valine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-valine;

i) the histidine amino acid entity, if present, is L-histidine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-histidine; and

j) the lysine amino acid entity, if present, is L-lysine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-lysine.

14. The use of claim 1 or 2, the composition for use of claim 3 or 4, or the composition of any of claims 6-13, wherein the composition comprises:

a) L-leucine or a salt thereof,

b) L-arginine or a salt thereof,

c) L-glutamine or a salt thereof,

d) NAC or a salt thereof,

e) L-citrulline or a salt thereof,

f) L-carnitine or a salt thereof,

g) L-serine or a salt thereof,

h) L-valine or a salt thereof,

i) L-histidine or a salt thereof, and

j) L-lysine or a salt thereof.

15. Use of the composition of any one of claims 6-14 in the preparation of a medicament for the improvement of one, two, three, four, five, six, seven, eight, or more (e.g., all) of erythrocyte function, turnover, or synthesis; hemoglobin function, turnover, or synthesis; vascular function; oxidative stress (e.g., one or both of blood or systemic oxidative stress); or inflammation.

16. Use of the composition of any one of claims 6-14 in the preparation of a medicament for the treatment of a hemoglobinopathy or a thalassemia.

17. A composition for use in a method of improving one, two, three, four, five, six, seven, eight, or more of erythrocyte function, turnover, or synthesis; hemoglobin function, turnover, or synthesis; vascular function; oxidative stress; or inflammation, comprising an effective amount of a composition of any of claims 6-14.

18. A composition for use in a method of treating a hemoglobinopathy or a thalassemia, comprising an effective amount of a composition of any of claims 6-15.

19. The use of claim 1 or 2 or the composition for use of claim 3 or 4, wherein the subject is at risk of, or has been diagnosed with a hemoglobinopathy or a thalassemia optionally wherein the hemoglobinopathy or thalassemia is chosen from: a sickle cell disease, α-thalassemia, or β-thalassemia.

20. The use or composition for use of claim 19, wherein the sickle cell disesase is selected from sickle cell anemia, Hemoglobin SC disease, sickle β^+-thalassemia, sickle β^0-thalassemia, hemoglobin SE disease, hemoglobin SD disease, or hemoglobin SO disease.

21. The use of claim 1 or 2, the composition for use of claim 3 or 4, or composition of any of the foregoing claims, wherein the composition is formulated with a pharmaceutically acceptable carrier.

22. The use of claim 1 or 2, the composition for use of claim 3 or 4, or composition of any of the foregoing claims, wherein the composition is formulated as a dietary composition.

23. The use of claim 1 or 2, the composition for use of claim 3 or 4, or composition of any of the foregoing claims, wherein the composition is a dry blended preparation.

24. A method of manufacturing a dry blended preparation, comprising at least 4 pharmaceutical grade amino acid entities, said method comprising:

forming a combination of at least 4 pharmaceutical grade amino acid entities and blending the combination for a time sufficient to achieve a dry blended preparation, wherein the dry blended preparation, comprises:

a) a leucine amino acid entity,

b) a arginine amino acid entity,

c) glutamine amino acid entity; and

d) a N-acetylcysteine entity.

25. The method of claim 24, wherein the dry blended preparation, e.g., PGDBP, further comprises one, two, three, four, five, or more of:

e) a citrulline amino acid entity,

f) a carnitine entity,

g) a serine amino acid entity,

h) a valine amino acid entity,

i) a histidine amino acid entity, and

j) a lysine amino acid entity.

26. The method of any of claims 24-25, wherein:

(i) blending occurs at a temperature lower than 40 °C;

(ii) blending comprises blending or mixing in a blender or mixer at a speed of less than 1000 rpm; or

(iii) the method further comprises one, two, or three of direct blending, roller compaction, or wet granulation of the dry blended preparation.

27. A composition comprising:

a) an arginine amino acid entity,

b) a citrulline amino acid entity; and

c) a N-acetylcysteine entity,

wherein:

(i) the composition does not comprise a peptide of more than 20 amino acid residues in length, or if a peptide of more than 20 amino acid residues in length is present, the peptide is present at less than: 10 wt. % of the total wt. of the composition;

(ii) at least 50 wt. % of the total wt. of the composition is one or more amino acid entities in free form; and

(iii) the wt. % of the citrulline amino acid entity is greater than the wt. % of the N-acetylcysteine entity.

28. The composition of claim 27, wherein

i) the arginine amino acid entity is L-arginine or a salt thereof, a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-arginine, creatine or a salt thereof, or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising creatine;

ii) the citrulline amino acid entity is L-citrulline or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-citrulline; and

iii) the N-acetylcysteine entity is N-acetylcysteine or a salt thereof or a dipeptide or salt thereof comprising N-acetylcysteine.

29. The composition of claim 27 or 28, wherein one, two, or three of the following:

(i) the wt. % of the citrulline amino acid entity in the composition is at least 50% greater than the wt. % of the N-acetylcysteine entity, *e.g.*, the wt. % of the citrulline amino acid entity is at least 60%, 65%, 70%, 75%, or 80% greater than the wt. % of the N-acetylcysteine entity;

(ii) the wt. % of the arginine amino acid entity, the citrulline amino acid entity, and the N-acetylcysteine entity is at least: 20 wt. %, 25 wt. %, 30 wt. %, or 35 wt. % of the amino acid entity components or total components in the composition, but not more than 80 wt. % of the amino acid entity components or total components in the composition; or

(iii) the wt. % of the citrulline amino acid entity is at least: 5 wt. %, 10 wt. %, 11 wt. %, 12 wt. %, 13 wt. %, or more of the amino acid entity components in the composition, but not more than 60 wt. % of the amino acid entity components in the composition.

30. The composition of any one of claims 27-29, wherein the composition further comprises one or both of: (d) a carnitine amino acid entity; or (e) a glutamine amino acid entity.

31. A composition comprising:

a) an arginine amino acid entity,

b) a citrulline amino acid entity,

c) a N-acetylcysteine (NAC) entity,

d) a carnitine entity, and

e) a glutamine amino acid entity.

32. The composition of claim 31, wherein

i) the arginine amino acid entity is L-arginine or a salt thereof, a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-arginine, creatine or a salt thereof, or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising creatine;

ii) the citrulline amino acid entity is L-citrulline or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-citrulline;

iii) the N-acetylcysteine entity is N-acetylcysteine or a salt thereof or a dipeptide or salt thereof comprising N-acetylcysteine;

iv) the carnitine entity is L-carnitine or a salt thereof, or a dipeptide or salt thereof, comprising L-carnitine; and

v) the glutamine amino acid entity is L-glutamine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-glutamine.

33. The composition of claim 30, wherein the wt. % of the citrulline amino acid entity is greater than the wt. % of the N-acetylcysteine entity.

34. The composition of any one of claims 27-33, wherein one, two, three, or four of the following:

(i) the wt. % of the arginine amino acid entity, the citrulline amino acid entity, the NAC entity, the carnitine amino acid entity, and the glutamine amino acid entity is at least: 40 wt. %, 45 wt. %, 50 wt. %, 55 wt. %, or 60 wt. % of the amino acid entity components or total components in the composition;

(ii) the wt. % of the citrulline amino acid entity in the composition is greater than the wt. % of the carnitine amino acid entity, *e.g.*, the wt. % of the citrulline amino acid entity in the composition is at least 50% greater than the wt. % of the carnitine amino acid entity, *e.g.*, the wt. % of the citrulline amino acid entity is at least 60%, 65%, 70%, 75%, or 80% greater than the wt. % of the carnitine amino acid entity;

(iii) the wt. % of the glutamine amino acid entity in the composition is greater than the wt. % of the citrulline amino acid entity, *e.g.*, the wt. % of the glutamine amino acid entity in the composition is at least 40% greater than the wt. % of the citrulline amino acid entity, *e.g.*, the wt.

% of the glutamine amino acid entity is at least 60%, 45%, 50%, 55%, 60%, or 65 % greater than the wt. % of the citrulline amino acid entity; or

(iv) the wt. % of the citrulline amino acid entity and the arginine amino acid entity in combination in the composition is greater than the wt. % of the glutamine amino acid entity, *e.g.*, the wt. % of the citrulline amino acid entity in the composition is at least 20% greater than the wt. % of the carnitine amino acid entity, *e.g.*, the wt. % of the citrulline amino acid entity is at least 30%, 35%, 40%, 45%, or 50% greater than the wt. % of the carnitine amino acid entity.

35. The composition of any one of claims 27-34, wherein the composition further comprises one, two, or three of: (f) a leucine amino acid entity, (g) a serine amino acid entity, (h) a valine amino acid entity, (i) a histidine amino acid entity, or (j) a lysine amino acid entity.

36. Use of the composition of any one of claims 27-35 in the preparation of a medicament for the treatment of a hemoglobinopathy or a thalassemia.

37. A composition for use in a method of treating a hemoglobinopathy or a thalassemia, comprising an effective amount of a composition of any one of claims 27-35.

38. A composition for use in a method of treating a hemoglobinopathy or a thalassemia, comprising an effective amount of a composition of claim 31.

39. A composition for use in a method of improving one, two, three, four, five, six or more of erythrocyte function, turnover, or synthesis; hemoglobin function, turnover, or synthesis; or vascular function in a subject in need thereof, wherein the composition comprises an effective amount of:

a) an arginine amino acid entity,

b) a citrulline amino acid entity, and

c) a N-acetylcysteine (NAC) entity,

wherein the composition does not comprise a peptide of more than 20 amino acid residues in length, or if a peptide of more than 20 amino acid residues in length is present, the

peptide is present at less than: 10 wt. % of the total wt. of the total components of the composition.

40. The composition for use of claim 39, further comprising an effective amount of:

d) a carnitine entity, and

e) a glutamine amino acid entity.

41. The composition for use of claim 39 or 40, wherein

i) the arginine amino acid entity is L-arginine or a salt thereof, a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-arginine, creatine or a salt thereof, or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising creatine;

ii) the citrulline amino acid entity is L-citrulline or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-citrulline;

iii) the N-acetylcysteine entity is N-acetylcysteine or a salt thereof or a dipeptide or salt thereof comprising N-acetylcysteine;

iv) the carnitine entity is L-carnitine or a salt thereof, or a dipeptide or salt thereof, comprising L-carnitine; and

v) the glutamine amino acid entity is L-glutamine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-glutamine.

42. A composition for use in a method for improving vascular function in a subject in need thereof, wherein the composition comprises an effective amount of:

a) an arginine amino acid entity,

b) a citrulline amino acid entity, and

c) a N-acetylcysteine (NAC) entity,

wherein the composition does not comprise a peptide of more than 20 amino acid residues in length, or if a peptide of more than 20 amino acid residues in length is present, the peptide is present at less than: 10 wt. % of the total wt. of the total components of the composition.

43. The composition for use of claim 42, wherein the composition further comprises an effective amount of:

d) a carnitine entity, and

e) a glutamine amino acid entity.

44. The composition for use of claim 42 or 43, wherein the

i) arginine amino acid entity is L-arginine or a salt thereof, a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-arginine, creatine or a salt thereof, or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising creatine;

ii) citrulline amino acid entity is L-citrulline or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-citrulline;

iii) the N-acetylcysteine entity is N-acetylcysteine or a salt thereof or a dipeptide or salt thereof comprising N-acetylcysteine;

iv) the carnitine entity is L-carnitine or a salt thereof, or a dipeptide or salt thereof, comprising L-carnitine; and

v) the glutamine amino acid entity is L-glutamine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-glutamine.