SUMMARY

Provided herein is a composition (e.g., an Active Moiety) including amino acid entities that is useful for improving one, two, three, or more (e.g., all) of liver function, hyperammonemia, muscle mass, or muscle function in a subject, *e.g.*, a subject with a liver disease or disorder with one or both of hyperammonemia or muscle wasting. The composition can be used in a method of treating (*e.g.*, reversing, reducing, ameliorating, or preventing) a liver disease or disorder with one or both of hyperammonemia or muscle wasting (e.g., cirrhosis, e.g., cirrhotic sarcopenia, End Stage Liver Disease (ESLD), hepatic insufficiency, or hepatic encephalopathy) in a subject in need thereof (e.g, a human).

In one example, the disclosure features a composition comprising, consisting of, or consisting essentially of:

a) a Branched Chain Amino Acid (BCAA) entity chosen from a leucine amino acid entity, an isoleucine amino acid entity, a valine amino acid entity, or a combination of two or three BCAA entities;

b) a Urea Cycle Amino Acid (UCAA) entity chosen from an ornithine amino acid entity, an aspartate amino acid entity, or a combination of two UCAA entities; and

c) an essential amino acid (EAA) entity chosen from a histidine amino acid entity, a lysine amino acid entity, or a threonine amino acid entity or a combination of two or three EAA entities;

wherein at least one amino acid entity (e.g., two, three, four, five, six, seven, or eight amino acid entities) of (a)-(c) is not provided as a peptide of more than 20 amino acid residues in length.

In an aspect, there is provided a composition comprising:

a) a Branched Chain Amino Acid (BCAA) entity chosen from a leucine amino acid entity, an isoleucine amino acid entity, a valine amino acid entity, or a combination of two or three BCAA entities;

b) a Urea Cycle Amino Acid (UCAA) entity chosen from an ornithine amino acid entity chosen from L-ornithine or a salt thereof, citrulline, or a combination of either thereof; an aspartate amino acid entity; or a combination of two UCAA entities; and

c) an essential amino acid (EAA) entity chosen from a histidine amino acid entity, a lysine amino acid entity, or a threonine amino acid entity or a combination of two or three EAA entities;

wherein:

i) at least one amino acid entity of (a)-(c) is not provided as a peptide of more than 20 amino acid residues in length;

ii) the total weight (wt.) % of (a)-(c) is greater than the total wt. % of non-protein components or other protein components in the composition on a dry weight basis;

iii) one or two of tyrosine or glutamine, if present, is present at less than 1 wt. % of the total wt. of the composition on a dry weight basis; and

iv) two or three of phenylalanine, methionine, or tryptophan are absent from the composition.

In some examples, the ornithine amino acid entity is chosen from L-ornithine, ornithine α-ketoglutarate, ornithine HCl, citrulline, or a combination thereof.

In some examples, one, two, or all of phenylalanine, tyrosine, and glutamine are absent from the composition, or if present, are present at less than: 10 wt. %, 5 wt. %, 1 wt. %, 0.5 wt. %, 0.1 wt. %, 0.05 wt. %, 0.01 wt. %, 0.001 wt. %, or less, *e.g.*, of the total wt. of the composition (in dry form).

In some examples, the total wt. % of (a)-(c) (e.g., three, four, five, six, seven, or eight amino acid entities in (a)-(c)) is greater than the total wt. % of other protein components (e.g., whey protein) or non-protein components (or both) in the composition on a dry weight basis,

e.g., the total wt. % (a)-(c) is at least: 50 wt. %, 75 wt. %, or 90 wt. % of the total wt. of amino acid entities or total components in the composition (in dry form).

In some examples, three, four, five, six, seven, or eight amino acid entities in (a)-(c) are in one or both of free amino acid form or salt amino acid form in the composition, *e.g.*, at least: 35 wt. %, 40 wt. %, 42 wt. %, 45 wt. %, 50 wt. %, 75 wt. %, 80 wt. %, 90 wt. %, or more, of the total wt. of the composition (in dry form) is three, four, five, six, seven, or eight amino acid entities in (a)-(c) in one or both of free amino acid form or salt amino acid form in the composition.

In some examples, the composition comprises a combination of 19 or fewer, 18 or fewer, 15 or fewer, 12 or fewer, or 10 or fewer amino acid entities. In some embodiments, the combination comprises at least: 42 wt. %, 75 wt. %, or 90 wt. % of the total wt. of amino acid entities or total components in the composition (in dry form).

In some examples, one, two, or more (*e.g.*, all) of phenylalanine, tyrosine, or glutamine is absent from the composition, or if present, are present at less than: 10 wt. %, 5 wt. %, 1 wt. %, 0.5 wt. %, 0.1 wt. %, 0.05 wt. %, 0.01 wt. %, 0.001 wt. %, or less, *e.g.*, of the total wt. of the composition (in dry form). In some embodiments, one, two, or more (*e.g.*, all) of phenylalanine, tyrosine, or glutamine, if present, are present in one or both of free amino acid form or salt amino acid.

In some examples, the wt. % of the BCAA entities is at least 37 wt. %, 38 wt. %, 39 wt. %, 40 wt. %, 41 wt. %, 42 wt. %, 43 wt. %, 44 wt. %, 45 wt. %, or more of the total wt. of amino acid entities or total components in the composition (in dry form).

In some examples, the wt. % of the UCAA entities is at least 25 wt. %, 26 wt. %, 27 wt. %, 28 wt. %, 29 wt. %, 30 wt. %, 31 wt. %, 32 wt. %, 33 wt. %, 34 wt. %, 35 wt. %, or more of the total wt. of amino acid entities or total components in the composition (in dry form).

In some examples, the wt. % of the EAA entities is at least 16 wt. %, 17 wt. %, 18 wt. %, 19 wt. %, 20 wt. %, or more of the total wt. of amino acid entities or total components in the composition (in dry form).

In some examples, 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 weight (wt.) %, 5 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 amino acid entities or total components of the composition (in dry form).

In some examples, the composition has one, two, or three of the following features:

d) the wt. % of the combination of three of the BCAA entities is greater than the wt. % of the UCAA entity or the combination of two of the UCAA entities, e.g., the wt. % of the combination of three of the BCAA entities is at least 5% greater than the wt. % of the UCAA entity or the combination of two of the UCAA entities; e.g., the wt. % of the combination of three of the BCAA entities is at least 10%, 15%, 20%, or more greater than the wt. % of the UCAA entity or the combination of two of the UCAA entities;

e) the wt. % of the combination of three of the BCAA entities is greater than the wt. % of the EAA entity or the combination of two or three of the EAA entities in (c); e.g., the wt. % of the combination of three of the BCAA entities is at least 30% greater than the wt. % of the EAA entity or the combination of two or three of the EAA entities in (c); e.g., the wt. % of the combination of three of the BCAA entities is at least 40%, 50%, or 55%, or more greater than the wt. % of the EAA entity or the combination of two or three of the EAA entities in (c);

f) the wt. % of the combination of the UCAA entity or two of the UCAA entities is greater than the wt. % of the EAA entity or the combination of two or three of the EAA entities in (c); e.g., the wt. % of the UAA entity or the combination of two of the UCAA entities is at least 25% greater than the wt. % of the EAA entity or the combination of two or three of the EAA entities in (c); e.g., the wt. % of the UCAA entity or the combination of two of the UCAA entities is at least 30%, 35%, 40%, or more greater than the wt. % of the EAA entity or the combination of two or three of the EAA entities in (c); or

g) a combination of two or three of (d)-(f).

In some examples, a wt. ratio of the BCAA entity or BCAA entities : the UCAA entity or UCAA entities : the EAA entity or EAA entities in (c) is 20+/- 15% : 15 +/- 15%: 9+/- 15%, where the ratios are determined based on an equivalent amount of each amino acid in free form.

In some examples, three, four, five, six, seven, or eight amino acid entities in (a)-(c) is selected from Table 1.

In some examples, the composition (e.g., the Active Moiety) comprises, consists of, or consists essentially of: a) a leucine amino acid entity 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 (HMB) or a salt thereof; b) one or both of: i) an ornithine amino acid entity chosen from L-ornithine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-ornithine; or ii) an aspartate amino acid entity chosen from L-aspartate or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-aspartate; and c) an EAA entity chosen from: i) L-histidine or a salt thereof, ii) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-histidine, iii) L-lysine or a salt thereof, iv) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-lysine, v) L-threonine or a salt thereof, or vi) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-threonine. In some embodiments, the composition further comprises one or both of an isoleucine amino acid entity or a valine amino acid entity, wherein one or both of the isoleucine amino acid entity or the valine amino acid entity is not provided as a peptide of more than 20 amino acid residues in length.

In some examples, the isoleucine amino acid-entity is L-isoleucine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-isoleucine. In some embodiments, the valine amino acid-entity is L- valine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-valine.

In some examples, a wt. ratio of the leucine amino acid entity : the isoleucine amino acid entity : the valine amino acid entity : the ornithine amino acid entity : the aspartate amino acid entity : the histidine amino acid entity : the threonine amino acid entity : the lysine amino acid entity is 8+/- 20% : 4+/- 20% : 8 +/- 20% : 7.5+/- 20% : 7.5+/- 20% : 3+/- 20% : 3+/- 20% : 3+/- 20%, where the ratios are determined based on an equivalent amount of each amino acid in free form.

In some examples, the composition comprises, consists of, or consists essentially of: L-leucine or a salt thereof, L-isoleucine or a salt thereof, L-valine or a salt thereof, L-ornithine or a salt thereof, L-aspartate or a salt thereof, L-histidine or a salt thereof, L-threonine or a salt thereof, and L-lysine or a salt thereof (e.g., L-lysine acetate).

In some examples, the composition (e.g., the Active Moiety) is formulated with a pharmaceutically acceptable carrier. In some embodiments, the composition (e.g., the Active Moiety) is formulated as a dietary composition. In some embodiments, the dietary composition is chosen from a medical food, a functional food, or a supplement.

In another aspect, there is provided a composition comprising: a) a Branched Chain Amino Acid (BCAA) entity chosen from a leucine amino acid entity, an isoleucine amino acid entity, a valine amino acid entity, or a combination of two or three BCAA entities; b) a Urea Cycle Amino Acid (UCAA) entity chosen from an ornithine amino acid entity chosen from L-ornithine or salt thereof, citrulline, or a combination of either thereof; an aspartate amino acid entity; or a combination of two UCAA entities; and c) an essential amino acid (EAA) entity chosen from a histidine amino acid entity, a lysine amino acid entity, or a threonine amino acid entity or a combination of two or three EAA entities; wherein: i) at least one amino acid entity of (a)-(c) is not provided as a peptide of more than 20 amino acid residues in length; ii) the total weight (wt.) % of (a)-(c) is greater than the total wt. % of non-protein components or other protein components in the composition on a dry weight basis; iii) two or more of phenylalanine, tyrosine, or glutamine is absent from the composition, or if present, is present at less than 1 wt. % of the total wt. of the composition on a dry weight basis; and iv) wherein a wt. ratio of the BCAA entity or BCAA entities:the UCAA entity or UCAA entities:the EAA entity or EAA entities is 20+/-15%: 15+/-15%: 9+/-15%, where the ratios are determined based on an equivalent amount of each amino acid in free form.

In another aspect, there is provided a composition comprising: (a) a leucine amino acid entity 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) .beta.-hydroxy-.beta.-methylbutyrate (HMB) or a salt thereof; (b) an isoleucine amino acid entity chosen from: (i) L-isoleucine or a salt thereof, or (ii) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-isoleucine; (c) a valine amino acid entity chosen from: (i) L-valine or a salt thereof, or (ii) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-valine; (d) an ornithine amino acid entity chosen from: (i) L-ornithine or a salt thereof, (ii) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-ornithine, (iii) L-citrulline or a salt thereof, or (iv) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-citrulline; and (e) an essential amino acid (EAA) entity chosen from: (i) L-histidine or a salt thereof, (ii) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-histidine, (iii) L-lysine or a salt thereof, (iv) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-lysine, (v) L-threonine or a salt thereof, (vi) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-threonine, or (vii) or a combination of

one, two, or three EAA entities, and (f) an aspartate amino acid entity chosen from: (i) L-aspartate or a salt thereof, or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-aspartate, (ii) fumarate, (iii) adenylosuccinate, or (iv) a combination thereof, wherein: (g) the total weight (wt.) % of (a)-(f) is greater than the total wt. % of non-protein components or other protein components in the composition on a dry weight basis; (h) glutamine, if present, is present at less than 1 wt. % of the total wt. of the composition on a dry weight basis; and (i) a wt. ratio of the leucine amino acid entity:the isoleucine amino acid entity:the valine amino acid entity:the ornithine amino acid entity:the aspartate amino acid entity:the L-histidine or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-histidine:the L-threonine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-threonine:the L-lysine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-lysine is 8+/-20%:4+/-20%:8+/-20%:7.5+/-20%:7.5+/-20%:3+/-20%:3+/-20%:3+/-20%, where the ratios are determined based on an equivalent amount of each amino acid in free form.

In another aspect, there is provided a composition comprising: (a) L-leucine or a salt thereof; (b) L-isoleucine or a salt thereof; (c) L-valine or a salt thereof; (d) L-ornithine or a salt thereof; (e) L-histidine or a salt thereof; (f) L-lysine or a salt thereof; (g) L-threonine or a salt thereof; and (h) L-aspartate or a salt thereof, wherein: (h) the total weight (wt.) % of (a)-(h) is greater than the total wt. % of non-protein components or other protein components in the composition on a dry weight basis; and (i) two or three of phenylalanine, methionine, and tryptophan is absent from the composition.

In another examples, the disclosure features a method of improving one, two, three, or more (e.g., all) of liver function, hyperammonemia, muscle mass, or muscle function, comprising administering to a subject with cirrhosis an effective amount of a composition (e.g., an Active Moiety) of any of the examples disclosed herein, thereby improving one, two, three, or more (e.g., all) of liver function, hyperammonemia, muscle mass, or muscle function.

Another examples of the disclosure features a method of improving or treating a symptom selected from one, two, three, four, five, six, seven, eight, nine, 10, 11, 12, 13, 14, 15, 16, 17, or more (e.g., all) of hyperammonemia, ascites or complications associated with ascites, variceal bleeding, infection, hepatic encephalopathy, ammonia toxicity, hepatic insufficiency, decreased urea synthesis, inflammation of hepatic tissue, fibrosis, cirrhosis, muscle wasting, muscle catabolism, muscle atrophy, hypoalbuminemia, malnutrition, frailty, or coagulopathy, comprising administering to a subject in need thereof an effective amount of a composition (e.g., an Active Moiety) of any of the examples disclosed herein, thereby improving or treating the symptom in the subject.

In another example, the disclosure features a method for treating or preventing a liver disease or disorder characterized by one or both of hyperammonemia or muscle wasting, comprising administering to a subject in need thereof an effective amount of a composition (e.g., an Active Moiety) of any of the examples disclosed herein, thereby treating the liver disease or disorder or muscle wasting in the subject.

In some examples, the subject has cirrhosis. In some embodiments, the subject has cirrhotic sarcopenia. In some embodiments, the subject has hepatic insufficiency. In some embodiments, the subject has End Stage Liver Disease. In some embodiments, the subject has hepatic encephalopathy.

In some examples, administration of the composition results in one, two, three, four, five, six, seven, eight, nine, ten, or more (e.g., all) of: a) increased level of BCAAs; b) decreased level of aromatic amino acids (AAAs); c) decreased level of ammonia; d) increased level of protein, e.g., increased protein synthesis; e) increased activation of mTORC1; f) decreased level of myostatin; g) decreased level of creatinine; h) increased level of albumin; i) decreased level of bilirubin; j) increased Fischer's ratio (e.g., increased level of BCAAs relative to the level of AAAs); or k) an increased level of valine relative to a level of phenylalanine.

WHAT IS CLAIMED IS:

1. A composition comprising:

a) a Branched Chain Amino Acid (BCAA) entity chosen from a leucine amino acid entity, an isoleucine amino acid entity, a valine amino acid entity, or a combination of two or three BCAA entities;

b) a Urea Cycle Amino Acid (UCAA) entity chosen from an ornithine amino acid entity chosen from L-ornithine or a salt thereof, citrulline, or a combination of either thereof; an aspartate amino acid entity; or a combination of two UCAA entities; and

c) an essential amino acid (EAA) entity chosen from a histidine amino acid entity, a lysine amino acid entity, or a threonine amino acid entity or a combination of two or three EAA entities;

wherein:

i) at least one amino acid entity of (a)-(c) is not provided as a peptide of more than 20 amino acid residues in length;

ii) the total weight (wt.) % of (a)-(c) is greater than the total wt. % of non-protein components or other protein components in the composition on a dry weight basis;

iii) one or two of tyrosine or glutamine, if present, is present at less than 1 wt. % of the total wt. of the composition on a dry weight basis; and

iv) two or three of phenylalanine, methionine, or tryptophan are absent from the composition.

2. The composition of claim 1, wherein two, three, four, five, six, seven, or eight amino acid entities of (a)-(c) is not provided as a peptide of more than 20 amino acid residues in length.

3. The composition of claim 1, 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 amino acid entities in the composition in dry form.

4. The composition of claim 1, wherein three, four, five, six, seven, or eight amino acid entities in (a)-(c) are in one or both of free amino acid form or salt amino acid form in the composition in dry form.

5. The composition of claim 4, wherein at least 35 wt. % of the total wt. of the composition in dry form is three, four, five, six, seven, or eight amino acid entities in (a)-(c) in one or both of free amino acid form or salt amino acid form.

6. The composition of claim 1, wherein:

i) the wt. % of the BCAA entities is at least 37 wt. % of the total wt. of amino acid entities in the composition in dry form;

ii) the wt. % of the UCAA entities is at least 25 wt. % of the total wt. of amino acid entities in the composition in dry form; or

iii) the wt. % of the EAA entities is at least 16 wt. % of the total wt. of amino acid entities in the composition in dry form.

7. The composition of claim 1, wherein a wt. ratio of the BCAA entity or BCAA entities : the UCAA entity or UCAA entities : the EAA entity or EAA entities is 20+/- 15% : 15 +/- 15%: 9+/- 15%, where the ratios are determined based on an equivalent amount of each amino acid in free form.

8. The composition of claim 1, wherein three, four, five, six, or seven amino acid entities in (a)-(c) are selected as follows:

i) the leucine amino acid entity is selected from: L-Leucine, Oxo-leucine (Alphaketoisocaproate (KIC)), HMB (betahydroxy-betamethylbutyrate), Isovaleryl-CoA, or N-Acetyl-Leucine;

ii) the isoleucine amino acid entity is selected from: L-Isoleucine, 2-Oxo-3-methyl-valerate (Alpha-ketobetamethylvaleric acid (KMV)), Threonine, Methylbutyrl-CoA, or N-Acetyl-Isoleucine;

iii) the valine amino acid entity is selected from: L-Valine, 2-Oxo-valerate (alphaketoisovalerate (KIV)), Isobutryl-CoA, or N-Acetyl-Valine;

iv) the ornithine amino acid entity is selected from: L-ornithine or salt thereof, or citrulline;

v) the aspartate amino acid entity is selected from: L-Aspartate, Fumarate, or Adenylosuccinate;

vi) the histidine amino acid entity is selected from: L-Histidine, Histidinol, Histidinal, Ribose-5-phosphate, Carnosine, Histamine, Urocanate, or N-Acetyl-Histidine;

vii) the lysine amino acid entity is selected from: L-Lysine, Diaminopimelate, Aspartate Trimethylhistidine, Carnitine, Saccharopine, N-Acetyl-Lysine, or L-Lysine Acetate; or

viii) the threonine amino acid entity is selected from: L-Threonine, Homoserine, O-PhosphoHomoserine, Oxobutyrate, or N-Acetyl-Threonine.

9. The composition of claim 1, 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 (HMB) or a salt thereof;

b) one or both of:

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

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

c) the EAA entity is chosen from:

i) L-histidine or a salt thereof,

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

iii) L-lysine or a salt thereof,

iv) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-lysine,

v) L-threonine or a salt thereof, or

vi) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-threonine.

10. The composition of claim 9, wherein the composition further comprises one or both of an isoleucine amino acid entity or a valine amino acid entity.

11. The composition of claim 10, wherein the isoleucine amino acid-entity is L-isoleucine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-isoleucine.

12. The composition of claim 10, wherein the valine amino acid entity is L-valine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-valine.

13. The composition of claim 10, wherein a wt. ratio of the leucine amino acid entity : the isoleucine amino acid entity : the valine amino acid entity : the ornithine amino acid entity : the aspartate amino acid entity : the histidine amino acid entity : the threonine amino acid entity : the lysine amino acid entity is 8+/- 20% : 4+/- 20% : 8 +/- 20% : 7.5+/- 20% : 7.5+/- 20% : 3+/- 20% : 3+/- 20% : 3+/- 20%, where the ratios are determined based on an equivalent amount of each amino acid in free form.

14. The composition of claim 1, wherein the composition comprises: L-leucine or a salt thereof, L-isoleucine or a salt thereof, L-valine or a salt thereof, L-ornithine or a salt thereof, L-aspartate or a salt thereof, L-histidine or a salt thereof, L-threonine or a salt thereof, and L-lysine or a salt thereof.

15. The composition of claim 1, wherein the composition is formulated with a pharmaceutically acceptable carrier.

16. The composition of claim 1, wherein the composition is formulated as a dietary composition.

17. The composition of claim 1, wherein the composition comprises: (a) a leucine amino acid entity 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) .beta.-hydroxy-.beta.-methylbutyrate

(HMB) or a salt thereof; (b) an isoleucine amino acid entity chosen from: (i) L-isoleucine or a salt thereof, or (ii) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-isoleucine; (c) a valine amino acid entity chosen from: (i) L-valine or a salt thereof, or (ii) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-valine; (d) an ornithine amino acid entity chosen from: (i) L-ornithine or a salt thereof, (ii) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-ornithine, (iii) L-citrulline or a salt thereof, or (iv) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-citrulline; and (e) an essential amino acid (EAA) entity chosen from: (i) L-histidine or a salt thereof, (ii) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-histidine, (iii) L-lysine or a salt thereof, (iv) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-lysine, (v) L-threonine or a salt thereof, (vi) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-threonine, or (vii) or a combination of one, two, or three EAA entities, wherein: (f) the total weight (wt.) % of (a)-(e) is greater than the total wt. % of non-protein components or other protein components in the composition on a dry weight basis; (g) glutamine, if present, is present at less than 1 wt. % of the total wt. of the composition on a dry weight basis; and (h) two or three of phenylalanine, methionine, or tryptophan are absent from the composition.

18. The composition of claim 17, wherein the wt. % of the leucine amino acid entity, isoleucine amino acid entity, and valine amino acid entity is greater than the wt. % of the ornithine amino acid entity.

19. The composition of claim 17, wherein the wt. % of the leucine amino acid entity, isoleucine amino acid entity, valine amino acid entity, and ornithine amino acid entity is greater than the wt. % of the EAA or the combination or two or three EAAs.

20. The composition of claim 17, further comprising an aspartate amino acid entity chosen from L-aspartate or a salt thereof, or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-aspartate; fumarate; adenylosuccinate; or a combination thereof.

21. The composition of claim 20, wherein a wt. ratio of the leucine amino acid entity:the isoleucine amino acid entity:the valine amino acid entity:the ornithine amino acid entity:the

aspartate amino acid entity:the L-histidine or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-histidine:the L-threonine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-threonine:the L-lysine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-lysine is 8+/-20%:4+/-20%:8+/-20%:7.5+/-20%:7.5+/-20%:3+/-20%:3+/-20%:3+/-20%, where the ratios are determined based on an equivalent amount of each amino acid in free form.

22. The composition of claim 1, wherein methionine is absent from the composition.

23. The composition of claim 1, wherein tryptophan is absent from the composition.

24. The composition of claim 1, wherein methionine and tryptophan are absent from the composition.

25. The composition of claim 1, wherein methionine, phenylalanine, and tryptophan are absent from the composition.

26. A composition comprising: a) a Branched Chain Amino Acid (BCAA) entity chosen from a leucine amino acid entity, an isoleucine amino acid entity, a valine amino acid entity, or a combination of two or three BCAA entities; b) a Urea Cycle Amino Acid (UCAA) entity chosen from an ornithine amino acid entity chosen from L-ornithine or salt thereof, citrulline, or a combination of either thereof; an aspartate amino acid entity; or a combination of two UCAA entities; and c) an essential amino acid (EAA) entity chosen from a histidine amino acid entity, a lysine amino acid entity, or a threonine amino acid entity or a combination of two or three EAA entities; wherein: i) at least one amino acid entity of (a)-(c) is not provided as a peptide of more than 20 amino acid residues in length; ii) the total weight (wt.) % of (a)-(c) is greater than the total wt. % of non-protein components or other protein components in the composition on a dry weight basis; iii) two or more of phenylalanine, tyrosine, or glutamine is absent from the composition, or if present, is present at less than 1 wt. % of the total wt. of the composition on a dry weight basis; and iv) wherein a wt. ratio of the BCAA entity or BCAA entities:the UCAA

entity or UCAA entities:the EAA entity or EAA entities is 20+/-15%: 15+/-15%: 9+/-15%, where the ratios are determined based on an equivalent amount of each amino acid in free form.

27. A composition comprising: (a) a leucine amino acid entity 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) .beta.-hydroxy-.beta.-methylbutyrate (HMB) or a salt thereof; (b) an isoleucine amino acid entity chosen from: (i) L-isoleucine or a salt thereof, or (ii) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-isoleucine; (c) a valine amino acid entity chosen from: (i) L-valine or a salt thereof, or (ii) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-valine; (d) an ornithine amino acid entity chosen from: (i) L-ornithine or a salt thereof, (ii) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-ornithine, (iii) L-citrulline or a salt thereof, or (iv) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-citrulline; and (e) an essential amino acid (EAA) entity chosen from: (i) L-histidine or a salt thereof, (ii) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-histidine, (iii) L-lysine or a salt thereof, (iv) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-lysine, (v) L-threonine or a salt thereof, (vi) a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-threonine, or (vii) or a combination of one, two, or three EAA entities, and (f) an aspartate amino acid entity chosen from: (i) L-aspartate or a salt thereof, or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-aspartate, (ii) fumarate, (iii) adenylosuccinate, or (iv) a combination thereof, wherein: (g) the total weight (wt.) % of (a)-(f) is greater than the total wt. % of non-protein components or other protein components in the composition on a dry weight basis; (h) glutamine, if present, is present at less than 1 wt. % of the total wt. of the composition on a dry weight basis; and (i) a wt. ratio of the leucine amino acid entity:the isoleucine amino acid entity:the valine amino acid entity:the ornithine amino acid entity:the aspartate amino acid entity:the L-histidine or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-histidine:the L-threonine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-threonine:the L-lysine or a salt thereof or a dipeptide or salt thereof, or tripeptide or salt thereof, comprising L-lysine is 8+/-20%:4+/-20%:8+/-20%:7.5+/-20%:7.5+/-20%:3+/-20%:3+/-20%:3+/-20%, where the ratios are determined based on an equivalent amount of each amino acid in free form.

28. A composition comprising: (a) L-leucine or a salt thereof; (b) L-isoleucine or a salt thereof; (c) L-valine or a salt thereof; (d) L-ornithine or a salt thereof; (e) L-histidine or a salt thereof; (f) L-lysine or a salt thereof; (g) L-threonine or a salt thereof; and (h) L-aspartate or a salt thereof, wherein: (h) the total weight (wt.) % of (a)-(h) is greater than the total wt. % of non-protein components or other protein components in the composition on a dry weight basis; and (i) two or three of phenylalanine, methionine, and tryptophan is absent from the composition.

29. The composition of claim 28, wherein the L-ornithine or a salt thereof is chosen from L-ornithine, L-ornithine L-aspartate (LOLA), ornithine .alpha.-ketoglutarate, or ornithine HCl.

30. The composition of claim 28, wherein the L-ornithine or a salt thereof in (d) and the L-aspartate or salt thereof in (h) are provided as L-ornithine L-aspartate (LOLA).

31. The composition of claim 28, wherein methionine, phenylalanine, and tryptophan are absent from the composition.

32. The composition of claim 1, wherein the L-ornithine or salt thereof is chosen from L-ornithine, L-ornithine L-aspartate (LOLA), ornithine .alpha.-ketoglutarate, or ornithine HCl.

33. The composition of claim 1, wherein the combination of two UCAA entities of b) comprises the ornithine amino acid entity and the aspartate amino acid entity.

34. The composition of claim 33, wherein the ornithine amino acid entity is L-ornithine or a salt thereof, and the aspartate amino acid entity is L-aspartate or a salt thereof.

35. The composition of claim 34, wherein the L-ornithine or a salt thereof and the L-aspartate or salt thereof are provided as L-ornithine L-aspartate (LOLA).

36. The composition of claim 26, wherein the combination of two UCAA entities of b) comprises the ornithine amino acid entity and the aspartate amino acid entity.

37. The composition of claim 36, wherein the ornithine amino acid entity is L-ornithine or a salt thereof, and the aspartate amino acid entity is L-aspartate or a salt thereof.

38. The composition of claim 37, wherein the L-ornithine or a salt thereof and the L-aspartate or salt thereof are provided as L-ornithine L-aspartate (LOLA).

39. The composition of claim 26, wherein the L-ornithine or salt thereof is chosen from L-ornithine, L-ornithine L-aspartate (LOLA), ornithine .alpha.-ketoglutarate, or ornithine HCl.

40. The composition of claim 27, wherein the ornithine amino acid entity comprises L-ornithine or a salt thereof and the aspartate amino acid entity comprises L-aspartate or a salt thereof.

41. The composition of claim 40, wherein the L-ornithine or a salt thereof and the L-aspartate or salt thereof are provided as L-ornithine L-aspartate (LOLA).

42. The composition of claim 27, wherein the L-ornithine or salt thereof is chosen from L-ornithine, L-ornithine L-aspartate (LOLA), ornithine .alpha.-ketoglutarate, or ornithine HCl.