CLAIMS

WHAT IS CLAIMED IS:

1. A method of altering senescence-associated secretory phenotype (SASP) of a senescent cell in a subject in need thereof comprising administering to the subject a composition comprising alpha-ketoglutarate (AKG), wherein the AKG is administered in a therapeutically effect amount to delay SASP.

2. A method of altering senescence-associated secretory phenotype (SASP) of a senescent cell in a subject in need thereof comprising administering to the subject a composition comprising alpha-ketoglutarate (AKG), wherein the AKG is administered in a therapeutically effect amount to reduce SASP.

3. A method for re-growing hair on a subject, the method comprising administering to the subject a therapeutically effect amount of a composition comprising an AKG.

4. A method for increasing exercise endurance in a subject, the method comprising administering to the subject a therapeutically effect amount of a composition comprising an AKG.

5. A method for increasing exercise efficiency and/or metabolism in a subject, the method comprising administering to the subject a therapeutically effect amount of a composition comprising an AKG.

6. A method for improving gait in a subject, the method comprising administering to the subject a therapeutically effect amount of a composition comprising an AKG.

7. A method for improving locomotion in a subject, the method comprising administering to the subject a therapeutically effect amount of a composition comprising an AKG.

8. A method for improving balance in a subject, the method comprising administering to the subject a therapeutically effect amount of a composition comprising an AKG.

9. A method for treating sarcopenia in a subject, the method comprising administering to the subject a therapeutically effect amount of a composition comprising an AKG.

10. A method for increasing collagen synthesis in a subject, the method comprising administering to the subject a therapeutically effect amount of a composition comprising an AKG.

11. The method of any one of claims 1 to 10 wherein altering SASP comprises altering secretion of at least one SASP factor.

12. The method of any one of claims 1 to 10 wherein altering SASP comprises reducing secretion of at least one SASP factor.

13. The method of any one of claims 11 or 12 wherein the SASP factors comprise an interleukin (IL), a chemokine, an inflammatory factor, a growth factor, a protease, an extracellular matrix component, or a combination thereof.

14. The method of any one of claims 11 or 12 wherein the SASP factors comprise IL-1β, IL-3, IL-6, IL-7, MIP-1β, TNF-α, CCL2, MMP3, or a combination thereof.

15. The method of any one of claims 11 or 12 wherein at least one senescent marker comprises $p16^{INK4a}$.

16. The method of any one of claims 11 or 12 wherein at least one senescent marker comprises $p21^{WAF1}$.

17. The method of any one of claims 1 to 16 wherein altering SASP does not affect formation of senescent cells.

18. The method of any one of claims 1 to 15 wherein altering SASP does not affect number of senescent cells.

19. The method of any one of claims 1 to 18 wherein the composition does not kill senescent cells.

20. The method of any one of claims 1 to 19 wherein the composition is administered twice daily.

21. The method of any one of claims 1 to 20 wherein the composition is administered to the subject for at least 3 months.

22. The method of any one of claims 1 to 21 wherein the composition is formulated into an orally administered form.

23. The method of claim 22 wherein the orally administered form is a sustained release dosage form.

24. The method of any one of claims 1 to 21 wherein the composition is formulated into a topically administered form.

25. The method of any one of claims 1 to 21 wherein the composition is formulated into a hair care product.

26. The method of any one of claims 1 to 25 wherein the subject has at least 6 fold reduction in plasma AKG level compared to plasma AKG level in a control sample, where the

control sample is a serum sample from a control subject who is at least 2 years younger than the subject.

27. The method of any one of claims 1 to 26 wherein the composition alters the DNA methylation profile of the subject.

28. The method of any one of claims 1 to 27 wherein the composition consists essentially of a AKG.

29. The method of any one of claims 1 to 28 wherein the AKG is a salt of α -ketoglutaric acid.

30. The method of any one of claims 1 to 29 wherein the AKG is a calcium salt of AKG (Ca-AKG).

31. The method of claim 30 wherein the therapeutically effective amount of Ca-AKG is at least 350 mg and no greater than 2000 mg.

32. The method of any one of claim 1 to 31 wherein the composition further comprises vitamin A.

33. The method of any one of claim 1 to 32 wherein the composition further comprises vitamin D3.

34. The method of any one of claim 1 to 33 wherein the composition further comprises a sweetener.

35. The composition of claim 34 wherein the sweetener is isomalt.

36. The method of any one of claim 1 to 35 wherein the composition further comprises wax.

37. The composition of claim 36 wherein the wax is carnauba wax and/or rice bran wax.

38. The method of any one of claim 1 to 37 wherein the composition further comprises a first lubricant.

39. The composition of claim 38 wherein the first lubricant is stearic acid.

40. The method of any one of claim 1 to 39 wherein the composition comprises a second lubricant.

41. The composition of claim 40 wherein the second lubricant is magnesium stearate.

42. The method of any one of claim 1 to 41 wherein the composition comprises a glidant.

43. The composition of claim 42 wherein the glidant is silica.

44. The method of any one of claim 1 to 43 wherein the calcium alpha-ketoglutarate is calcium alpha-ketoglutarate monohydrate.

45. The method of any one of claim 1 to 44 wherein the composition comprises 500 mg of calcium alpha-ketoglutarate monohydrate; 450 mcg of retinyl palmitate; and further comprising isomalt, vegetable wax (carnauba and/or rice bran), stearic acid, magnesium stearate, and silica.

46. The method of any one of claim 1 to 44 wherein the composition comprises 500 mg of calcium alpha-ketoglutarate monohydrate; 12.5 mcg (500 IU) of cholecalciferol; and further comprising isomalt, vegetable wax (carnauba and/or rice bran), stearic acid, magnesium stearate, and silica.

WHAT IS CLAIMED IS:

1. Use of a composition in the manufacture of a medicament for increasing mobility in a subject, wherein the composition comprises a therapeutically effect amount of an AKG.

2. The use of claim 1 wherein increasing mobility includes increasing exercise endurance in the subject.

3. The use of claim 1 wherein increasing mobility includes increasing exercise efficiency, metabolism, or both exercise efficiency and metabolism in the subject.

4. The use of claim 1 wherein increasing mobility includes improving gait in the subject.

5. The use of claim 1 wherein increasing mobility includes improving locomotion in the subject.

6. The use of claim 1 wherein increasing mobility includes improving balance in the subject.

7. Use of a composition in the manufacture of a medicament for altering senescence-associated secretory phenotype (SASP) of a senescent cell in a subject, wherein the composition comprises a therapeutically effect amount of an alpha-ketoglutarate (AKG) to delay SASP.

8. Use of a composition in the manufacture of a medicament for altering senescence-associated secretory phenotype (SASP) of a senescent cell in a subject, wherein the composition comprises a therapeutically effect amount of an alpha-ketoglutarate (AKG) to reduce SASP.

9. Use of a composition in the manufacture of a medicament for re-growing hair on a subject, wherein the composition comprises a therapeutically effect amount of an AKG.

10. Use of a composition in the manufacture of a medicament for treating sarcopenia in a subject, wherein the composition comprises a therapeutically effect amount of an AKG.

11. Use of a composition in the manufacture of a medicament for increasing collagen synthesis in a subject, wherein the composition comprises a therapeutically effect amount of an AKG.

12. The use of any one of claims 1 to 11 wherein the therapeutically effect amount alters secretion of at least one SASP factor.

13. The use of any one of claims 1 to 11 wherein the therapeutically effect amount reduces secretion of at least one SASP factor.

14. The use of any one of claims 12 or 13 wherein the SASP factors comprise an interleukin (IL), a chemokine, an inflammatory factor, a growth factor, a protease, an extracellular matrix component, or a combination thereof.

15. The use of any one of claims 12 or 13 wherein the SASP factors comprise IL-1β, IL-3, IL-6, IL-7, MIP-1β, TNF-α, CCL2, MMP3, or a combination thereof.

16. The use of any one of claims 12 or 13 wherein at least one senescent marker comprises $p16^{INK4a}$.

17. The use of any one of claims 12 or 13 wherein at least one senescent marker comprises $p21^{WAF1}$.

18. The method of any one of claims 1 to 17 wherein the therapeutically effect amount does not clinically affect formation of senescent cells.

19. The method of any one of claims 1 to 17 wherein the therapeutically effect amount does not clinically affect the number of senescent cells.

20. The use of any one of claims 1 to 19 wherein the medicament is configured to be administered twice daily.

21. The use of any one of claims 1 to 20 wherein the medicament is formulated into an orally administered form.

22. The use of any one of claims 1 to 21 wherein the subject has at least a 6 fold lower level of plasma AKG level compared to a control subject, where the control subject is at least 2 years younger than the subject.

23. The use of any one of claims 1 to 22 wherein the therapeutically effective amount is in the range from about 350 mg to about 2000 mg, and where the AKG is calcium alpha-ketoglutarate or calcium alpha-ketoglutarate monohydrate, or a combination thereof.

24. The use of any one of claim 1 to 23 wherein the composition further comprises vitamin A.

25. The use of any one of claim 1 to 23 wherein the composition further comprises vitamin D3.

26. The use of any one of claims 1 to 22 wherein the composition comprises 500 mg of calcium alpha-ketoglutarate monohydrate, 450 mcg of retinyl palmitate, isomalt, vegetable wax, stearic acid, magnesium stearate, and silica.

27. The use of any one of claim 1 to 22 wherein the composition comprises 500 mg of calcium alpha-ketoglutarate monohydrate, 12.5 mcg (500 IU) of cholecalciferol, isomalt, vegetable wax, stearic acid, magnesium stearate, and silica.