## WHAT IS CLAIMED IS:

1. A recombinant microorganism comprising a DHAD-requiring biosynthetic pathway, wherein said microorganism is engineered to overexpress one or more polynucleotides encoding one or more Aft proteins or homologs thereof.

2. The recombinant microorganism of claim 1, wherein said one or more polynucleotides is a native polynucleotide.

3. The recombinant microorganism of claim 1, wherein said one or more polynucleotides is a heterologous polynucleotide.

4. The recombinant microorganism of claim 1, wherein said DHAD-requiring biosynthetic pathway comprises a cytosolically-localized DHAD.

5. The recombinant microorganism of claim 1, wherein said DHAD-requiring biosynthetic pathway comprises a mitochondrially-localized DHAD.

6. The recombinant microorganism of claim 1, wherein said DHAD-requiring biosynthetic pathway is a pathway for the production of a metabolite selected from isobutanol, 3-methyl-1-butanol, 2-methyl-1-butanol, valine, isoleucine, leucine, and pantothenic acid.

7. The recombinant microorganism of any of claims 1-6, wherein said Aft protein is selected from SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 209, SEQ ID NO: 211, SEQ ID NO: 213, SEQ ID NO: 215, SEQ ID NO: 217, SEQ ID NO: 219, SEQ ID NO: 221, SEQ ID NO: 223, and SEQ ID NO: 225.

8. The recombinant microorganism of claim 7, wherein said Aft protein is a constitutively active Aft protein.

9. The recombinant microorganism of claim 8, wherein said constitutively active Aft protein comprises a mutation at a position corresponding to the cysteine 291 residue of the native *S. cerevisiae* Aft1 protein (SEQ ID NO: 2).

10. The recombinant microorganism of claim 8, wherein said constitutively active Aft protein comprises a mutation at a position corresponding to the cysteine 187 residue of the native *S. cerevisiae* Aft2 protein (SEQ ID NO: 4).

11. A recombinant microorganism comprising a DHAD-requiring biosynthetic pathway, wherein said microorganism is engineered to overexpress one or more polynucleotides encoding one or more proteins or homologs thereof regulated by an Aft protein.

12. The recombinant microorganism of claim 11, wherein said one or more proteins regulated by an Aft protein is selected from *FET3, FET4, FET5, FTR1, FTH1, SMF3, MRS4, CCC2, COT1, ATX1, FRE1, FRE2, FRE3, FRE4, FRE5, FRE6, FIT1, FIT2, FIT3, ARN1, ARN2, ARN3, ARN4, ISU1, ISU2, TIS11, HMX1, AKR1, PCL5, YOR387C, YHL035C, YMR034C, ICY2, PRY1, YDL124W, BNA2, ECM4, LAP4, YOL083W, YGR146C, BIO5, YDR271C, OYE3, CTH1, CTH2, MRS3, MRS4, HSP26, YAP2, VMR1, ECL1, OSW1, NFT1, ARA2, TAF1/TAF130/TAF145, YOR225W, YKR104W, YBR012C,* and *YMR041C* or a homolog thereof.

13. The recombinant microorganism of claim 11, wherein said one or more polynucleotides is a native polynucleotide.

14. The recombinant microorganism of claim 11, wherein said one or more polynucleotides is a heterologous polynucleotide.

15. The recombinant microorganism of claim 11, wherein said DHAD-requiring biosynthetic pathway comprises a cytosolically-localized DHAD.

16. The recombinant microorganism of claim 11, wherein said DHAD-requiring biosynthetic pathway comprises a mitochondrially-localized DHAD.

17. The recombinant microorganism of claim 11, wherein said DHAD-requiring biosynthetic pathway is a pathway for the production of a metabolite selected from isobutanol, 3-methyl-1-butanol, 2-methyl-1-butanol, valine, isoleucine, leucine, and pantothenic acid.

18. A recombinant microorganism comprising a DHAD-requiring biosynthetic pathway, wherein said recombinant microorganism further comprises a nucleic acid encoding a chaperone protein, wherein said chaperone protein assists the folding of a protein exhibiting cytosolic activity.

19. The recombinant microorganism of claim 18, wherein said chaperone protein is a native protein.

20. The recombinant microorganism of claim 18, wherein said chaperone protein is a heterologous protein.

21. The recombinant microorganism of claim 18, wherein said chaperone protein is selected from the group consisting of: endoplasmic reticulum oxidoreductin 1 (Ero1), including variants of Ero1 that have been suitably altered to reduce or prevent its localization to the endoplasmic reticulum; thioredoxin (Trx1 and Trx2), thioredoxin reductase (Trr1), glutaredoxin (Grx1, Grx2, Grx3, Grx4, Grx5, Grx6, Grx7, and Grx8,); glutathione reductase (Glr1), and Jac1, including variants of Jac1 that have been suitably altered to reduce or prevent its mitochondrial localization; Hsp10, Hsp60, GroEL, and GroES and homologs or variants thereof.

22. A recombinant microorganism comprising a DHAD-requiring biosynthetic pathway, wherein said recombinant microorganism further comprises one or more genes encoding an iron-sulfur cluster assembly protein.

23. The recombinant microorganism of claim 22, wherein said one or more genes encoding an iron-sulfur cluster assembly protein are selected from the group consisting of *cyaY, iscS, iscU, iscA, hscB, hscA, fdx, isuX, sufA, sufB, sufC, sufD, sufS, sufE, apbC*, and homologs or variants thereof.

24. The recombinant microorganism of claim 23, wherein said genes encoding an iron-sulfur cluster assembly are derived from an organism selected from the group consisting of *Escherichia coli* and *Lactococcus lactis.*

25. The recombinant microorganism of claim 22, wherein said one or more genes encoding an iron-sulfur cluster assembly are selected from the group consisting of *nifS*, *nifU*, and homologs or variants thereof.

26. The recombinant microorganism of claim 25, wherein said genes encoding an iron-sulfur cluster assembly are derived from an organism selected from the group consisting of *Helicobacter pylori* and *Entamoeba histolytica*.

27. The recombinant microorganism of claim 22, wherein said one or more genes encoding an iron-sulfur cluster assembly are selected from the group consisting of CFD1, NBP35, NAR1, CIA1, and homologs or variants thereof.

28. The recombinant microorganism of claim 27, wherein said genes encoding an iron-sulfur cluster assembly are derived from yeast.

29. The recombinant microorganism of any of claims 22-28, wherein said one or more genes encoding an iron-sulfur cluster assembly is mutated or modified to remove a signal peptide, whereby localization of the product of said one or more genes to the mitochondria is prevented.

30. The recombinant microorganism of claim 29, wherein the genes encoding an iron-sulfur cluster assembly are overexpressed.

31. A recombinant microorganism comprising a DHAD-requiring biosynthetic pathway, wherein said recombinant microorganism is engineered to reduce or eliminate the activity of one or more iron-sulfur cluster containing cytosolic proteins.

32. The recombinant microorganism of claim 31, wherein said iron-sulfur cluster containing cytosolic protein is 3-isopropylmalate dehydratase (*LEU1*).

33. A recombinant microorganism comprising a DHAD-requiring biosynthetic pathway, wherein said recombinant microorganism is engineered to express one or more proteins in the cytosol that reduce the concentration of reactive oxygen species (ROS) in said cytosol.

34. The recombinant microorganism of claim 33, wherein said one or more proteins are selected from the group consisting of catalases, superoxide dismutases, metallothioneins, and methionine sulphoxide reductases.

35. The recombinant microorganism of claim 34, wherein said catalase is encoded by one of more of the genes selected from the group consisting of the *E. coli* genes *katG* and *katE*, the *S. cerevisiae* genes *CTT1* and *CTA1*, or homologs thereof.

36. The recombinant microorganism of claim 34, wherein said superoxide dismutase is encoded by one of more of the genes selected from the group consisting of the *E. coli* genes *sodA*, *sodB*, *sodC*, the *S. cerevisiae* genes *SOD1* and *SOD2*, or homologs thereof.

37. The recombinant microorganism of claim 34, wherein said metallothionein is encoded by one of more of the genes selected from the group consisting of the *S. cerevisiae CUP1-1* and *CUP1-2* genes or homologs thereof.

38. The recombinant microorganism of claim 34, wherein said metallothionein is encoded by one or more genes selected from the group consisting of the Mycobacterium tuberculosis *MymT* gene and the Synechococcus PCC 7942 *SmtA* gene or homologs thereof.

39. The recombinant microorganism of claim 34, wherein said methionine sulphoxide reductase is encoded by one or more genes selected from the group consisting of the *S. cerevisiae* genes *MXR1* and *MXR2*, or homologs thereof.

40. A recombinant microorganism comprising a DHAD-requiring biosynthetic pathway, wherein said recombinant microorganism has further been engineered to

express one or more enzymes that increase the level of available glutathione in the cytosol.

41. The recombinant microorganism of claim 40, wherein said one or more enzymes are selected from the group consisting of glutaredoxin, glutathione reductase, and glutathione synthase.

42. The recombinant microorganism of claim 41, wherein said glutaredoxin is encoded by one of more of the genes selected from the group the *S. cerevisiae* genes *GRX2, GRX4, GRX6,* and *GRX7*, or homologs thereof.

43. The recombinant microorganism of claim 41, wherein said glutathione reductase is encoded by the *S. cerevisiae* genes *GLR1* or homologs thereof.

44. The recombinant microorganism of claim 41, wherein said glutathione synthase is encoded by one of more of the genes selected from the group the *S. cerevisiae* genes *GSH1* and *GSH2*, or homologs thereof.

45. The recombinant microorganism of claim 40, wherein two enzymes are expressed in and targeted to the cytosol of yeast to increase the level of available glutathione in the cytosol.

46. The recombinant microorganism of claim 45, wherein said enzymes are γ-glutamyl cysteine synthase and glutathione synthase.

47. The recombinant microorganism of claim 46, wherein said glutathione synthase is encoded by one of more of the genes selected from the group the *S. cerevisiae* genes *GSH1* and *GSH2*, or homologs thereof.

48. The recombinant microorganism of claim 47, wherein said glutathione synthase is encoded by one of more of the genes selected from the group the *S. cerevisiae* genes *GSH1* and *GSH2*, or homologs thereof.

49. A recombinant microorganism comprising a DHAD-requiring biosynthetic pathway, wherein said recombinant microorganism has further been engineered to overexpress one or more cytosolic functional components of the thioredoxin system.

50. The recombinant microorganism of claim 49, wherein said one or more cytosolic functional components of the thioredoxin system are selected from a thioredoxin and a thioredoxin reductase.

51. The recombinant microorganism of claim 50, wherein said thioredoxin is encoded by the *S. cerevisiae TRX1* and *TRX2* genes or homologs thereof.

52. The recombinant microorganism of claim 50, wherein said thioredoxin reductase is encoded by S. cerevisiae *TRR1* gene or homologs thereof.

53. The recombinant microorganism of claim 50, wherein said recombinant microorganism further overexpresses the mitochondrial thioredoxin system.

54. The recombinant microorganism of claim 53, wherein said mitochondrial thioredoxin system is comprised of the mitochondrial thioredoxin and mitochondrial thioredoxin reductase.

55. The recombinant microorganism of claim 54, wherein said mitochondrial thioredoxin is encoded by the *S. cerevisiae TRX3* gene or homologs thereof.

56. The recombinant microorganism of claim 54, wherein said mitochondrial thioredoxin reductase is encoded by the *S. cerevisiae TRR2* gene or homologs thereof.

57. A recombinant microorganism comprising a DHAD-requiring biosynthetic pathway, wherein said recombinant microorganism is further engineered to increase inner mitochondrial membrane electrical potential, $\Delta\Psi_M$.

58. The recombinant microorganism of claim 57, wherein said recombinant microorganism comprises a mutation in the mitochondrial ATP synthase complex that increases ATP hydrolysis activity.

59. The recombinant microorganism of claim 58, wherein said mutation is an ATP1-111 suppressor mutation or a corresponding mutation in a homologous protein.

60. The recombinant microorganism of claim 57, wherein said recombinant microorganism has been engineered to overexpress an ATP/ADP carrier protein, wherein said overexpression increases $ATP^{4-}$ import into the mitochondrial matrix in exchange for $ADP^{3-}$.

61. The recombinant microorganism of claim 60, wherein said ATP/ADP carrier protein is encoded by the *S. cerevisiae AAC1*, *AAC2*, and/or *AAC3* genes or homologs thereof.

62. A recombinant microorganism comprising a DHAD-requiring biosynthetic pathway, wherein said recombinant microorganism has further been engineered to express one or more enzymes in the cytosol that reduce the concentration of reactive nitrogen species (RNS) and/or nitric oxide (NO) in said cytosol.

63. The recombinant microorganism of claim 62, wherein said one or more enzymes are selected from the group consisting of nitric oxide reductases and glutathione-S-nitrosothiol reductase.

64. The recombinant microorganism of claim 63, wherein said nitric oxide reductase is encoded by one of more of the genes selected from the group consisting of the *E. coli* gene *norV* and the *Fusarium oxysporum* gene *P-450dNIR*, or homologs thereof.

65. The recombinant microorganism of claim 63, wherein said glutathione-S-nitrosothiol reductase is encoded by the *S. cerevisiae* gene *SFA1* or homologs thereof.

66. The recombinant microorganism of claim 66, wherein said glutathione-S-nitrosothiol reductase gene *SFA1* is overexpressed.

67. The recombinant microorganism of claim 62, wherein said one or more enzymes is encoded by a gene selected from the group consisting of the *E. coli* gene *ytfE*, the *Staphylococcus aureus* gene *scdA*, and *Neisseria gonorrhoeae* gene *dnrN*, or homologs thereof.

68. A recombinant microorganism comprising a DHAD-requiring biosynthetic pathway, wherein said recombinant microorganism is engineered to overexpress one or more of the genes selected from the *S. cerevisiae* genes *MET1, MET2, MET3, MET5, MET8, MET10, MET14, MET16, MET17, HOM2, HOM3, HOM6, CYS3, CYS4, SUL1*, and *SUL2*, or homologs thereof.

69. A recombinant microorganism comprising a DHAD-requiring biosynthetic pathway, wherein said recombinant microorganism is engineered to overexpress one or more of the genes selected from the *S. cerevisiae* genes *YCT1, MUP1, GAP1, AGP1, GNP1, BAP1, BAP2, TAT1*, and *TAT2*.

70. The recombinant microorganism of any of claims 1-69, wherein said recombinant microorganism is a yeast microorganism.

71. A method of producing a metabolite, said method comprising:

(a) providing a recombinant microorganism comprising a DHAD-requiring biosynthetic pathway according to any of claims 1-70; and

(b) cultivating said recombinant microorganism in a culture medium containing a feedstock providing a carbon source, until a recoverable quantity of said metabolite is produced.

72. The method of claim 71, wherein said metabolite is selected from isobutanol, 3-methyl-1-butanol, 2-methyl-1-butanol, valine, isoleucine, leucine, and pantothenic acid.

Claims

1. A recombinant yeast microorganism comprising:

(a) a recombinantly overexpressed polynucleotide encoding a dihydroxy acid dehydratase (DHAD), wherein said DHAD is localized to the cytosol, and

(b) one or more recombinantly overexpressed polynucleotide encoding one or more activator of ferrous transport (Aft) proteins which increase the dehydratase activity of DHAD.

2. The recombinant yeast microorganism of claim 1, wherein said recombinant microorganism comprises an isobutanol producing metabolic pathway, said isobutanol producing metabolic pathway comprising the following substrate to product conversions: (a) pyruvate to acetolactate; (b) acetolactate to 2,3-dihydroxyisovalerate; (c) 2,3-dihydroxyisovalerate to α-ketoisovalerate; (d) α-ketoisovalerate to isobutyraldehyde; and (e) isobutyraldehyde to isobutanol; and wherein said DHAD catalyzes the conversion of 2,3-dihydroxyisovalerate to α-ketoisovalerate.

3. The recombinant yeast microorganism of claim 2, wherein the enzyme that catalyzes the conversion of pyruvate to acetolactate is an acetolactate synthase (ALS).

4. The recombinant yeast microorganism of claim 2, wherein the enzyme that catalyzes the conversion of acetolactate to 2,3-dihydroxyisovalerate is a ketol-acid reductoisomerase (KARI).

5. The recombinant yeast microorganism of claim 4, wherein said ketol-acid reductoisomerase is an NADH-dependent ketol-acid reductoisomerase.

6. The recombinant yeast microorganism of claim 2, wherein the enzyme that catalyzes the conversion of α-ketoisovalerate to isobutyraldehyde is a 2-keto acid decarboxylase (KIVD).

7. The recombinant yeast microorganism of claim 2, wherein the enzyme that catalyzes the conversion of isobutyraldehyde to isobutanol is an alcohol dehydrogenase (ADH).

8. The recombinant yeast microorganism of claim 7, wherein said alcohol dehydrogenase is an NADH-dependent alcohol dehydrogenase.

9. The recombinant yeast microorganism of claim 2, wherein said recombinant yeast microorganism has reduced or no pyruvate decarboxylase (PDC) activity.

10. The recombinant yeast microorganism of claim 2 or claim 9, wherein said recombinant yeast microorganism has reduced or no glycerol-3-phosphate dehydrogenase (GPD) activity.

11. The recombinant yeast microorganism of claim 1, wherein said one or more polynucleotides encoding said one or more Aft proteins is a native polynucleotide.

12. The recombinant yeast microorganism of claim 1, wherein said one or more polynucleotides encoding said one or more Aft proteins is a heterologous polynucleotide.

13. The recombinant yeast microorganism of claim 1, wherein said Aft protein is a constitutively active Aft protein.

14. The recombinant yeast microorganism of claim 1, wherein said Aft protein is encoded by *AFT1*.

15. The recombinant yeast microorganism of claim 1, wherein said Aft protein is encoded by *AFT2*.

16. The recombinant yeast microorganism of claim 1, wherein said DHAD is derived from a yeast organism.

17. The recombinant yeast microorganism of claim 1, wherein said recombinant yeast microorganism is a yeast microorganism selected from one of the following genera: *Saccharomyces, Kluyveromyces, Pichia, Candida, Zygosaccharomyces,* Debaromyces, *Schizosaccharomyces.*

18. The recombinant yeast microorganism of claim 1, wherein said recombinant yeast microorganism is a yeast microorganism selected from one of the following genera: *Saccharomyces, Kluyveromyces, Candida, Pichia, Issatchenkia, Debaryomyces, Hansenula, Pachysolen, Yarrowia and Schizosaccharomyces.*