CLAIMS:

1. A method for making an oxygenated product of a sesquiterpene, comprising, contacting the sesquiterpene with *Stevia rebaudiana* Kaurene Oxidase (*Sr*KO) or derivative thereof having sesquiterpene oxidizing activity, and recovering the oxygenated product.

2. The method of claim 1, wherein the *Sr*KO derivative comprises an amino acid sequence having from 1 to 50 mutations independently selected from substitutions, deletions, or insertions relative to *Sr*KO (SEQ ID NO: 37, 38, or 55).

3. The method of claim 2, wherein the *Sr*KO derivative comprises an amino acid sequence having from 1 to 40 mutations relative to *Sr*KO (SEQ ID NO:37, 38, or 55).

4. The method of any one of claims 1 to 3, wherein the *Sr*KO derivative comprises an amino acid sequence having at least 70% sequence identity to *Sr*KO (SEQ ID NO: 37, 38, or 55), and has valencene oxidase activity.

5. The method of any one of claims 2 to 4, wherein one or more mutations relative to *Sr*KO (SEQ ID NO: 37, 38, or 55) are selected from Table 2 or Table 6.

6. The method of claim 5, where at least 2 mutations are selected from Table 2 and/or Table 6.

7. The method of claim 2, wherein the *Sr*KO is a derivative having a deletion of at least a portion of its N-terminal transmembrane region, and the addition of an inner membrane transmembrane domain from *E. coli* yhcB or derivative thereof.

8. The method of claim 7, wherein the SrKO is a derivative having a deletion of from 15 to 35 amino acids of its N-terminal transmembrane domain, and the addition of from 15 to 25 amino acids of the transmembrane domain from *E. coli* yhcB or derivative thereof.

9. The method of claim 8, wherein the N-terminal transmembrane domain from yhcB comprises the amino acid sequence of SEQ ID NO: 118, or an amino acid sequence having from 1 to 5 amino acid mutations with respect to SEQ ID NO: 118.

10. The method of any one of claims 1 to 9, wherein the SrKO is a derivative having one or more mutations at positions selected from 46, 76, 94, 131, 231, 284, 383, 390, 400, 444, 468, 488 and 499 relative to SEQ ID NO:37.

11. The method of claim 10, wherein the SrKO is a derivative having one or more mutations selected from R76K, M94V, T131Q, F231L, H284Q, R383K, I390L, T468I, and T499N relative to SEQ ID NO:37.

12. The method of claim 1, wherein the SrKO is a derivative comprising an amino acid sequence selected from SEQ ID NOS:55-61, 104, and 105 or an amino acid sequence having from one to twenty mutations relative to a sequence selected from SEQ ID NOS: 55-61, 104 and 105.

13. The method of any one of claims 1 to 12, wherein the sesquiterpene is valencene, germacrene (A, B, C, D, or E), farnesene, farnesol, nootkatol, patchoulol, cadinene, cedrol, humulene, longifolene, and/or bergamotene, β-Ylangene, β-santalol, β-santalene, α-santalene, α-santalol, ß-vetivone, a-vetivone, khusimol, bisabolene, β-aryophyllene, Longifolene; α-sinensal; α-bisabolol, (-)-β-Copaene, (-)-α-Copaene, 4(Z),7(Z)-ecadienal, cedrol, cedrene, cedrol, guaiol, (-)-6,9-guaiadiene, bulnesol, guaiol, ledene, ledol, lindestrene, and alpha-bergamotene.

14. The method of claim 1 to 13, wherein the predominant sesquiterpene is valencene, germacrene (A, B, C, D, or E), farnesene, farnesol, nootkatol, patchoulol, cadinene, cedrol, humulene, longifolene, and/or bergamotene, β-Ylangene, β-santalol, β-santalene, α-santalene, α-santalol, ß-vetivone, a-vetivone, khusimol, bisabolene, β-aryophyllene, Longifolene; α-sinensal; α-bisabolol, (-)-β-Copaene, (-)-α-Copaene,

4(Z),7(Z)-ecadienal, cedrol, cedrene, cedrol, guaiol, (-)-6,9-guaiadiene, bulnesol, guaiol, ledene, ledol, lindestrene, and alpha-bergamotene.

15. The method of claim 14, wherein the predominant sesquiterpene is valencene.

16. The method of claim 15, wherein the predominant oxygenated products are nootkatone, and optionally nootkatol.

17. The method of any one of claims 1 to 16, wherein the contacting takes place in a host cell, which is a bacterium.

18. The method of claim 17, wherein the host cell is *E. coli*, *Bacillus subtillus*, or *Pseudomonas putida*.

19. The method of any one of claims 1 to 16, wherein the contacting takes place in a host cell which is a yeast.

20. The method of claim 19, wherein the host cell is a species of *Saccharomyces*, *Pichia*, or *Yarrowia*, including *Saccharomyces cerevisiae*, *Pichia pastoris*, and *Yarrowia lipolytica*.

21. The method of any one of claims 17 to 20, wherein the host cell produces isopentyl pyrophosphate (IPP).

22. The method of claim 21, wherein the IPP is produced by metabolic flux through an endogenous or heterologous MEP or MVA pathway.

23. The method of claim 22, wherein the sesquiterpene is produced at least in part by metabolic flux through an MEP pathway, and wherein the host cell has at least one additional copy of a dxs, ispD, ispF, and/or idi gene.

24. The method of any one of claims 17 to 23, wherein the host cell further expresses a farnesyl pyrophosphate synthase.

25. The method of any one of claims 17 to 24, wherein the host cell further expresses a heterologous sesquiterpene synthase.

26. The method of claim 25, wherein the sesquiterpene synthase is a valencene synthase.

27. The method of claim 26, wherein the valencene synthase is *Citrus sinensis* or *Vitis vinfera* valencene synthase or derivative thereof.

28. The method of claim 21, wherein the VvVS comprises an amino acid sequence having from 1 to 40 mutations independently selected from substitutions, deletions, or insertions with respect to VvVS (SEQ ID NO:1).

29. The method of claim 27, wherein the CsVS comprises an amino acid sequence having from 1 to 40 mutations independently selected from substitutions, deletions, or insertions with respect to CsVS (SEQ ID NO:12).

30. The method of claim 28, wherein one or more mutations are selected from Table 3.

31. The method of any one of claims 1 to 30, wherein the SrKO is expressed in a host cell that co-expresses a cytochrome P450 reductase.

32. The method of claim 31, wherein the P450 reductase is a CPR from *Stevia sp.*

33. The method of claim 31, wherein the P450 reductase comprises an amino acid sequence selected from SEQ ID NOS: 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, and 82, or a derivative thereof.

34. The method of any one of claims 1 to 33, wherein the *Sr*KO is expressed as a fusion with a cytochrome P450 reductase partner.

35. The method of any one of claims 1 to 34, wherein the host cell further expresses an alcohol dehydrogenase producing nootkatone from nootkatol.

36. The method of any one of claims 1 to 35, wherein oxidized oil is extracted from aqueous reaction medium followed by fractional distillation.

37. The method of claim 36, wherein the oxidized oil is extracted from aqueous reaction medium using an organic solvent.

38. The method of claim 36, wherein sesquiterpene and sesquiterpenoid components of fractions are measured quantitatively by GC/MS, followed by blending of the fractions to generate a desired nootkatone-containing ingredient.

39. The method of claim 38, wherein the nootkatone component is measured quantitatively.

40. The method of claim 36 or 37, wherein the nootkatone fraction is recovered.

41. A method for making a product containing an oxygenated sesquiterpene, comprising: incorporating the oxygenated sesquiterpene prepared by the method of any one of claims 1 to 40 into said product.

42. The method of claim 41, wherein the product is a flavor product, a fragrance product, a cosmetic, a cleaning product, a detergent or soap, or a pest control product.

43. The method of claim 42, wherein the product is a flavor product selected from a beverage, a chewing gum, a candy, or an artificial flavor.

44. The method of claim 42, wherein the product is an insect repellant.

45. An *Sr*KO derivative comprising at least one mutation with respect to SEQ ID NO: 37, 38, or 55 that increases valencene oxidase activity.

46. The SrKO derivative of claim 45, wherein the *Sr*KO derivative has a deletion of at least a portion of its N-terminal transmembrane region, and the addition of an inner membrane transmembrane domain from *E. coli* yhcB or derivative thereof.

47. The *Sr*KO derivative of claim 46, wherein the *Sr*KO derivative has a deletion of from 15 to 35 amino acids of its N-terminal transmembrane domain, and the addition of from 15 to 25 amino acids of the transmembrane domain from *E. coli* yhcB or derivative thereof.

48. The *Sr*KO derivative of claim 46, wherein the N-terminal transmembrane domain comprises the amino acid sequence of SEQ ID NO: 118, or an amino acid sequence having from 1 to 5 amino acid mutations with respect to SEQ ID NO: 118.

49. The *Sr*KO derivative of claims 45 to 48, wherein the *Sr*KO derivative has one or more mutations at positions selected from 46, 76, 94, 131, 231, 284, 383, 390, 400, 444, 468, 488 and 499 relative to SEQ ID NO:37.

50. The *Sr*KO derivative of claim 49, wherein the *Sr*KO derivative has one or more mutations selected from R76K, M94V, L107M, T131Q, F231L, H284Q, R383K, I390L, T468I, and T499N relative to SEQ ID NO:37.

51. The *Sr*KO derivative of claim 50, wherein the *Sr*KO derivative comprises an amino acid sequence selected from SEQ ID NOS:55-61, 104, and 105.

52. The SrKO derivative of claim 50, wherein the *Sr*KO derivative comprises an amino acid sequence having from 1 to 20 mutations with respect to an amino acid sequence selected from SEQ ID NOS:55-61, 104 or 105, with the proviso that the amino acid sequence has one or more mutations at positions selected from 46, 76, 94,

131, 231, 284, 383, 390, 400, 444, 468, 488 and 499 relative to SEQ ID NO:37, or the proviso that the amino acid sequence has one or more of the mutations selected from R76K, M94V, T131Q, F231L, H284Q, R383K, I390L, T468I, and T499N relative to SEQ ID NO:37.

53. The *Sr*KO derivative of any one of claims 45 to 52, wherein the derivative is isolated or partially purified, or is heterologously expressed in a host cell.

54. A host cell producing an oxygenated sesquiterpene: wherein the host cell produces isopentyl pyrophosphate (IPP); and the host cell expresses a farnesyl pyrophosphate synthase, a sesquiterpene synthase, and *Sr*KO or derivative thereof having valencene oxidase activity.

55. The host cell of claim 54, wherein the *Sr*KO derivative comprises at least one mutation with respect to SEQ ID NO: 37, 38, or 55 that increases valencene oxidase activity

56. The host cell of claim 54 or 55, wherein the host cell expresses an MVA or MEP pathway.

57. The host cell of claim 56, wherein the host cell is a bacterium or yeast.

58. The host cell of claim 57, wherein the host cell is *E. coli*, *Bacillus subtillus*, or *Pseudomonas putida*.

59. The host cell of claim 57, wherein the host cell is a species of Saccharomyces, Pichia, or Yarrowia, including Saccharomyces cerevisiae, Pichia pastoris, and Yarrowia lipolytica.

60. The host cell of any one of claims 54 to 59, wherein the *Sr*KO derivative has from 1 to 50 mutations independently selected from substitutions, deletions, or insertions relative to *Sr*KO (SEQ ID NO: 37, 38, or 55).

61. The host cell of claim 60, wherein the *Sr*KO derivative has from 1 to 40 mutations relative to *Sr*KO (SEQ ID NO: 37, 38, or 55).

62. The host cell of claim 60 or 61, wherein the *Sr*KO derivative comprises an amino acid sequence having at least 70% sequence identity to *Sr*KO (SEQ ID NO: 37, 38, or 55), and has valencene oxidase activity.

63. The host cell of any one of claims 54 to 62, wherein one or more mutations relative to *Sr*KO (SEQ ID NO:37 or 38) are selected from Table 2 or Table 6.

64. The host cell of claim 63, where at least 2 mutations are selected from Table 2 and/or Table 6.

65. The host cell of claim 54, wherein the *Sr*KO derivative has a deletion of at least a portion of its N-terminal transmembrane region, and the addition of an inner membrane transmembrane domain from *E. coli* yhcB or derivative thereof.

66. The host cell of claim 65, wherein the SrKO derivative has a deletion of from 15 to 35 amino acids of its N-terminal transmembrane domain, and the addition of from 15 to 25 amino acids of the transmembrane domain from E. coli yhcB or derivative thereof.

67. The host cell of claim 66, wherein the N-terminal transmembrane domain comprises the amino acid sequence of SEQ ID NO: 118, or an amino acid sequence having from 1 to 5 amino acid mutations with respect to SEQ ID NO: 118.

68. The host cell of any one of claims 54 to 67, wherein the *Sr*KO derivative has one or more mutations at positions selected from 46, 76, 94, 131, 231, 284, 383, 390, 400, 444, 468, 488 and 499 relative to SEQ ID NO:37.

69. The host cell of claim 68, wherein the *Sr*KO derivative has one or more mutations selected from R76K, M94V, L107M, T131Q, F231L, H284Q, R383K, I390L, T468I, and T499N relative to SEQ ID NO:37.

70. The host cell of claim 68 or 69, wherein the *Sr*KO derivative comprises an amino acid sequence selected from SEQ ID NOS:55-61, 104, or 105; or an amino acid sequence having from one to twenty mutations relative to a sequence selected from SEQ ID NOS:55-61, 104, or 105 with the proviso that the amino acid sequence has one or more mutations at positions selected from 46, 76, 94, 131, 231, 284, 383, 390, 400, 444, 468, 488 and 499 relative to SEQ ID NO:37, or the proviso that the amino acid sequence has one or more of the mutations selected from R76K, M94V, T131Q, F231L, H284Q, R383K, I390L, T468I, and T499N relative to SEQ ID NO:37.

71. The host cell of any one of claims 54 to 70, wherein the host cell produces nootkatone.

72. The host cell of claim 71, wherein the host cell is an *E. coli* having at least one additional copy of a dxs, ispD, ispF, and/or idi gene.

73. The host cell of any one of claims 54 to 72, wherein the sesquiterpene synthase is a valencene synthase.

74. The host cell of claim 73, wherein the valencene synthase is *Citrus sinensis* or *Vitis vinfera* valencene synthase, or derivative thereof having increased expression and/or activity in E. coli.

75. The host cell of claim 74, wherein the VvVS derivative has from 1 to 40 mutations independently selected from substitutions, deletions, or insertions with respect to VvVS (SEQ ID NO:1).

76. The host cell of claim 74, wherein the CsVS has from 1 to 40 mutations independently selected from substitutions, deletions, or insertions with respect to CsVS (SEQ ID NO:12).

77. The host cell of claim 75, wherein one or more mutations are selected from Table 3.

78. The host cell of any one of claims 54 to 77, wherein the *Sr*KO or derivative thereof is expressed in a host cell that co-expresses a cytochrome P450 reductase.

79. The host cell of claim 78, wherein the *Sr*KO is expressed as a fusion with a cytochrome P450 reductase partner.

80. The host cell of any one of claims 54 to 79, wherein the P450 reductase is a CPR from *Stevia sp.*

81. The host cell of any one of claims 54 to 79, wherein the P450 reductase comprises an amino acid sequence selected from SEQ ID NOS: 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, and 82, or a derivative thereof.

82. The host cell of any one of claims 54 to 79, wherein the host cell further expresses an alcohol dehydrogenase enzyme that converts nootkatol to nootkatone.

83. An Oxygenated sesquiterpene product obtainable by the method of any one of claims 1 to 40.

84. A Flavour or a Fragrance product comprising the oxygenated sesquiterpene product as defined in claim 83.

85. An insect rellant product comprising the oxygenated sesquiterpene product as defined in claim 83.

86. A valencene synthase enzyme comprising an amino acid sequence selected from SEQ ID NO: 3 (Vv1MI), SEQ ID NO: 5(Vv2MI), SEQ ID NO: 7 (Vv1M5), SEQ ID NO: 9 (Vv2M5), and SEQ ID NO:11 (VS2), or derivative thereof having increased activity in *E. coli*.

87. A recombinant nucleic acid molecule comprising a nucleotide sequence encoding an *Sr*KO derivative having at least one mutation that increases valencene oxidase activity, a leader sequence that supports expression and activity in *E. coli*, a linker sequence, and an *Sr*CPR or derivative thereof sufficient to regenerate the SrKO derivative.

88. A recombinant nucleic acid molecule, comprising a nucleotide sequence that encodes the *Sr*KO derivative of any one of claims 45 to 52.

89. An isolated nucleotide sequence, recombinant vector, or host cell comprising a nucleotide sequence encoding a modified *Sr*KO polypeptide according to claim 88.

90. An isolated nucleotide sequence of claim 88, wherein the nucleotide sequence is expressed in a host cell, and wherein the host cell is an *E. coli* cell.

91. A method of preparing a modified *Sr*KO polypeptide according to claim 45 to 52 wherein the method comprises the steps of: (i) culturing a host cell expressing the modified polypeptide under conditions which permit expression of the polypeptide; and (ii) optionally recovering the polypeptide.

92. A method of producing an oxygenated sesquiterpene comprising the steps of:

(i) providing a modified *Sr*KO polypeptide according to claim 45 or 52

(ii) contacting a sesquiterpene with the modified *Sr*KO polypeptide in the presence of a cytochrome P450 reductase, and

(iii) recovering the produced oxygenated sesquiterpene.

93. The method according to claim 92, wherein the oxygenated sesquiterpene is recovered as an oil.

94. The method according to claims 91 to 93, wherein the sesquiterpene is valencene.