

WHAT IS CLAIMED:

1. A method of detecting, in solution, water-immiscible compound (WIC) recombinantly produced from a plurality of cells, the method comprising:
 - (a) contacting a solution with a fluorescent dye that directly binds the WIC, wherein the solution comprises a plurality of cells recombinantly producing the WIC; and
 - (b) detecting the fluorescent dye under spectral conditions suitable for the selective detection of the fluorescent dye bound to the recombinantly produced WIC.
2. The method of claim 1, wherein the WIC is secreted from said cells recombinantly producing said WIC.
3. The method of claim 1 or 2, wherein the fluorescent dye is Nile Red.
4. The method of claim 1 or 2, wherein the fluorescent dye is BODIPY 493/503 or BODIPY 505/515.
5. The method of any one of claims 1 to 4, wherein the solution comprising the plurality of cells is contained in a well of a multi-well cell culture plate.
6. The method of any one of claims 1 to 5, wherein the cells are cultured for a period of at least 12 hours prior to said detecting.
7. The method of any one of claims 1 to 6, further comprising the step of determining a WIC:cell biomass ratio.
8. The method of claim 7, wherein the cell biomass is determined by a method comprising detecting the autofluorescence of said plurality of cells.
9. The method of claim 8, wherein detecting the autofluorescence of said plurality of cells comprises detecting the autofluorescence under spectral conditions that do not detect fluorescence from the fluorescent dye bound to the WIC.

10. The method of claim 9, wherein said autofluorescence is detected at an excitation wavelength of 330 to 350 nm, and an emission wavelength of 470 to 510 nm.

11. The method of claim 7, wherein the fluorescent dye is Nile Red, and determining a WIC:cell biomass ratio comprises determining the ratio of green to red fluorescence.

12. The method of any one of claims 1 to 11, wherein said spectral conditions comprise detecting the fluorescent dye at an excitation wavelength that is selected by:

- (a) contacting the fluorescent dye with a first plurality of cell populations and a second plurality of cell populations, wherein cells of the first and second plurality are of the same cell type as the cells of claim 1, wherein each plurality comprises a cell population having a cell density of x and a cell population having a cell density of $5x$, wherein each of the cell populations of the first plurality comprise WIC, and the cell populations of the second plurality do not comprise WIC;
- (b) determining an excitation spectrum for the first plurality and the second plurality, respectively; and
- (c) selecting an excitation wavelength wherein:
 - (i) the difference in fluorescence between a cell population from the first plurality and a cell population from the second plurality having the same cell density is at least 80%; and
 - (ii) the difference in fluorescence between cell populations of cell density x and cell density $5x$ from the second plurality is no greater than 250%.

13. The method of claim 12, wherein the emission wavelength for said excitation spectrum of step (b) is fixed at 550 nm.

14. The method of any one of claims 1 to 13, wherein the said spectral conditions comprise detecting the fluorescent dye at an emission wavelength that is selected by:

- (a) contacting the fluorescent dye with a first plurality of cell populations and a second plurality of cell populations, wherein cells of the first and second plurality are of the same cell type as the cells of claim 1, wherein each plurality comprises a cell population having a cell density of x and a cell population having a cell density of $5x$,

wherein each of the cell populations of the first plurality comprise WIC, and the cell populations of the second plurality do not comprise WIC;

(b) determining an emission spectrum for the first plurality and the second plurality, respectively; and

(c) selecting an emission wavelength wherein:

(i) the difference in fluorescence between a cell population from the first plurality and a cell population from the second plurality having the same cell density is at least 80%; and

(ii) the difference in fluorescence between cell populations having cell density x and cell density $5x$ from the second plurality is no greater than 250%.

15. The method of claim 14, wherein the excitation wavelength for said emission spectrum of step (b) is fixed at 290 nm.

16. The method of any one of claims 12 to 14, wherein the cell populations of the first plurality comprise at least 2 g/L WIC.

17. The method of any one of claims 1 to 16, wherein the recombinantly produced water-immiscible compound is an isoprenoid.

18. The method of any one of claims 1 to 17, wherein the recombinantly produced water-immiscible compound is a terpene, C5 isoprenoid, C10 isoprenoid or C15 isoprenoid.

19. The method of any one of claims 1 to 18, wherein the recombinantly produced water-immiscible compound is farnesene.

20. The method of any one of claims 1 to 19, wherein the cell is a recombinant yeast cell comprising one or more heterologous nucleotide sequences encoding one or more enzymes of the mevalonate (MEV) pathway.

21. The method of claim 20, wherein the recombinant yeast cell comprises a nucleic acid encoding farnesene synthase.

22. The method of claim 20, wherein the recombinant yeast cell comprises a heterologous nucleotide sequence that encodes an enzyme that can convert HMG-CoA into mevalonate.

23. The method of claim 20, wherein the recombinant yeast cell comprises a heterologous nucleotide sequence that encodes an enzyme that can convert mevalonate into mevalonate 5-phosphate.

24. The method of claim 20, wherein the one or more heterologous nucleotide sequences encodes more than one enzyme of the mevalonate pathway.

25. The method of claim 20, wherein the cell further comprises a heterologous nucleotide sequence encoding an enzyme that can convert isopentenyl pyrophosphate (IPP) into dimethylallyl pyrophosphate (DMAPP).

26. The method of claim 25, wherein the cell further comprises a heterologous nucleotide sequence encoding an enzyme that can modify IPP or a polyprenyl to form an isoprenoid compound.

27. The method of claim 26, wherein the enzyme is selected from the group consisting of carene synthase, geraniol synthase, linalool synthase, limonene synthase, myrcene synthase, ocimene synthase, α -pinene synthase, β -pinene synthase, γ -terpinene synthase, terpinolene synthase, amorphadiene synthase, α -farnesene synthase, β -farnesene synthase, farnesol synthase, nerolidol synthase, patchouliol synthase, nootkatone synthase, and abietadiene synthase.

28. The method of claim 26, wherein the isoprenoid is a C5-C20 isoprenoid.

29. The method of claim 28, wherein the isoprenoid is selected from the group consisting of abietadiene, amorphadiene, carene, α -farnesene, β -farnesene, farnesol, geraniol, geranylgeraniol, isoprene, linalool, limonene, myrcene, nerolidol, ocimene, patchoulol, β -pinene, sabinene, γ -terpinene, terpinolene, and valencene.

30. A method of detecting, in solution, farnesene produced and secreted from a cell, the method comprising:

(a) contacting a solution with Nile Red, wherein the solution comprises a cell recombinantly producing and secreting farnesene; and

(b) detecting Nile Red at an excitation wavelength of about 260 to 290 nm and an emission wavelength of about 530 to 570 nm.

31. The method of claim 30, wherein the solution comprising the plurality of cells is contained in a well of a multi-well cell culture plate.

32. The method of claim 31, wherein the multi-well cell culture plate is coated with Teflon.

33. The method of any one of claims 30 to 32, wherein the cells are cultured for a period of at least 12 hours prior to said detecting.

34. The method of any one of claims 30 to 33, further comprising the step of shaking the multi-well cell culture plate prior to said detecting.

35. The method of any one of claims 30 to 34, wherein the cell is selected from the group consisting of a yeast cell, a bacterial cell, a mammalian cell, a fungal cell, an insect cell, and a plant cell.

36. The method of claim 35, wherein the cell is a yeast cell.

37. The method of claim 36, wherein the yeast is *Saccharomyces cerevisiae*.

38. A liquid composition comprising:

- (a) a cell recombinantly producing and secreting a water-immiscible compound;
- (b) water immiscible-compound secreted from said cell;
- (c) a fluorescent dye that directly binds to the secreted water-immiscible compound; and
- (d) cell culture medium.

39. The composition of claim 38, wherein the cell is selected from the group consisting of a yeast cell, a bacterial cell, a mammalian cell, a fungal cell, an insect cell, and a plant cell.
40. The composition of claim 38, wherein the cell is a yeast cell.
41. The composition of claim 39, wherein the yeast is *Saccharomyces cerevisiae*.
42. The composition of any one of claims 38 to 41, wherein the recombinantly produced water-immiscible compound is an isoprenoid.
43. The composition of any one of claims 38 to 42, wherein the fluorescent dye is Nile Red.
44. The composition of any one of claims 38 to 42, wherein the fluorescent dye is BODIPY 493/503 or BODIPY 505/515.
45. The composition of any one of claims 38 to 44, wherein the recombinantly produced water-immiscible compound is a terpene, C5 isoprenoid, C10 isoprenoid or C15 isoprenoid.
46. The composition of any one of claims 38 to 45, wherein the recombinantly produced water-immiscible compound is farnesene.
47. The composition of any one of claims 38 to 46, wherein the cell is a recombinant yeast cell comprising one or more heterologous nucleotide sequences encoding one or more enzymes of the mevalonate (MEV) pathway.
48. The composition of claim 47, wherein the recombinant yeast cell comprises a nucleic acid encoding farnesene synthase.
49. The composition of claim 47, wherein the recombinant yeast cell comprises a heterologous nucleotide sequence that encodes an enzyme that can convert HMG-CoA into mevalonate.

50. The composition of claim 47, wherein the recombinant yeast cell comprises a heterologous nucleotide sequence that encodes an enzyme that can convert mevalonate into mevalonate 5-phosphate.

51. The composition of claim 47, wherein the one or more heterologous nucleotide sequences encodes more than one enzyme of the mevalonate pathway.

52. The composition of claim 47, wherein the cell further comprises a heterologous nucleotide sequence encoding an enzyme that can convert isopentenyl pyrophosphate (IPP) into dimethylallyl pyrophosphate (DMAPP).

53. The composition of claim 52, wherein the cell further comprises a heterologous nucleotide sequence encoding an enzyme that can modify IPP or a polyprenyl to form an isoprenoid compound.

54. The composition of claim 53, wherein the enzyme is selected from the group consisting of carene synthase, geraniol synthase, linalool synthase, limonene synthase, myrcene synthase, ocimene synthase, α -pinene synthase, β -pinene synthase, γ -terpinene synthase, terpinolene synthase, amorphadiene synthase, α -farnesene synthase, β -farnesene synthase, farnesol synthase, nerolidol synthase, patchouliol synthase, nootkatone synthase, and abietadiene synthase.

55. The composition of claim 53, wherein the isoprenoid is a C5-C20 isoprenoid.

56. The composition of claim 55, wherein the isoprenoid is selected from the group consisting of abietadiene, amorphadiene, carene, α -farnesene, β -farnesene, farnesol, geraniol, geranylgeraniol, isoprene, linalool, limonene, myrcene, nerolidol, ocimene, patchoulol, β -pinene, sabinene, γ -terpinene, terpinolene, and valencene.

57. A method of determining spectral conditions for the selective detection of a fluorescent dye directly bound to water-immiscible compound (WIC) recombinantly produced from a cell, the method comprising the steps of:

(a) contacting the fluorescent dye with a first plurality of cell populations and a second plurality of cell populations, wherein cells of the first and second plurality are

of the same cell type, wherein each plurality comprises a cell population having a cell density of x and a cell population having a cell density of $5x$, wherein each of the cell populations of the first plurality comprise WIC, and the cell populations of the second plurality do not comprise WIC;

(b) determining an excitation spectrum for the first plurality and the second plurality, respectively; and

(c) selecting an excitation wavelength wherein:

(i) the difference in fluorescence between a cell population from the first plurality and a cell population from the second plurality having the same cell density is at least 80%; and

(ii) the difference in fluorescence between cell populations having cell density x and cell density $5x$ from the second plurality is no greater than 250%.

58. The method of claim 56, wherein the emission wavelength for said excitation spectrum of step (b) is fixed at 550 nm.

59. A method of determining spectral conditions for the selective detection of a fluorescent dye directly bound to water-immiscible compound recombinantly produced from a cell, the method comprising the steps of:

(a) contacting the fluorescent dye with a first plurality of cell populations and a second plurality of cell populations, wherein cells of the first and second plurality are of the same cell type, wherein each plurality comprises a cell population having a cell density of x and a cell population having a cell density of $5x$, wherein each of the cell populations of the first plurality comprise WIC, and the cell populations of the second plurality do not comprise WIC;

(b) determining an emission spectrum for the first plurality and the second plurality, respectively; and

(c) selecting an emission wavelength wherein:

(i) the difference in fluorescence between a cell population from the first plurality and a cell population from the second plurality having the same cell density is at least 80%; and

(ii) the difference in fluorescence between cell populations having cell density x and cell density $5x$ from the second plurality is no greater than 250%.

60. The method of claim 59, wherein the excitation wavelength for said emission spectrum of step (b) is fixed at 290 nm.

WHAT IS CLAIMED:

1. A liquid composition comprising:
 - (a) a cell recombinantly producing and secreting a water-immiscible compound;
 - (b) water immiscible-compound secreted from said cell;
 - (c) a fluorescent dye that directly binds to the secreted water-immiscible compound; and
 - (d) cell culture medium.
2. The composition of claim 1, wherein the cell is selected from the group consisting of a yeast cell, a bacterial cell, a mammalian cell, a fungal cell, an insect cell, and a plant cell.
3. The composition of claim 2, wherein the yeast is *Saccharomyces cerevisiae*.
4. The composition of any one of claims 1 to 3, wherein the recombinantly produced water-immiscible compound is an isoprenoid.
5. The composition of any one of claims 1 to 4, wherein the fluorescent dye is Nile Red.
6. The composition of any one of claims 1 to 4, wherein the fluorescent dye is BODIPY 493/503 or BODIPY 505/515.
7. The composition of any one of claims 1 to 6, wherein the recombinantly produced water-immiscible compound is a terpene, C5 isoprenoid, C10 isoprenoid or C15 isoprenoid.
8. The composition of any one of claims 1 to 7, wherein the recombinantly produced water-immiscible compound is farnesene.
9. The composition of any one of claims 1 to 8, wherein the cell is a recombinant yeast cell comprising one or more heterologous nucleotide sequences encoding one or more enzymes of the mevalonate (MEV) pathway.
10. The composition of claim 9, wherein the recombinant yeast cell comprises a nucleic acid encoding farnesene synthase.

11. The composition of claim 9, wherein the recombinant yeast cell comprises a heterologous nucleotide sequence that encodes an enzyme that can convert HMG-CoA into mevalonate.

12. The composition of claim 9, wherein the recombinant yeast cell comprises a heterologous nucleotide sequence that encodes an enzyme that can convert mevalonate into mevalonate 5-phosphate.

13. The composition of claim 9, wherein the one or more heterologous nucleotide sequences encodes more than one enzyme of the mevalonate pathway.

14. The composition of claim 9, wherein the cell further comprises a heterologous nucleotide sequence encoding an enzyme that can convert isopentenyl pyrophosphate (IPP) into dimethylallyl pyrophosphate (DMAPP).

15. The composition of claim 14, wherein the cell further comprises a heterologous nucleotide sequence encoding an enzyme that can modify IPP or a polyprenyl to form an isoprenoid compound.

16. The composition of claim 15, wherein the enzyme is selected from the group consisting of carene synthase, geraniol synthase, linalool synthase, limonene synthase, myrcene synthase, ocimene synthase, α -pinene synthase, β -pinene synthase, γ -terpinene synthase, terpinolene synthase, amorphadiene synthase, α -farnesene synthase, β -farnesene synthase, farnesol synthase, nerolidol synthase, patchouliol synthase, nootkatone synthase, and abietadiene synthase.

17. The composition of claim 15, wherein the isoprenoid is a C5-C20 isoprenoid.

18. The composition of claim 17, wherein the isoprenoid is selected from the group consisting of abietadiene, amorphadiene, carene, α -farnesene, β -farnesene, farnesol, geraniol, geranylgeraniol, isoprene, linalool, limonene, myrcene, nerolidol, ocimene, patchoulol, β -pinene, sabinene, γ -terpinene, terpinolene, and valencene.

19. A method of detecting, in solution, farnesene produced and secreted from a cell, the method comprising:

(a) contacting a solution with Nile Red, wherein the solution comprises a cell recombinantly producing and secreting farnesene; and

(b) detecting Nile Red at an excitation wavelength of about 260 to 290 nm and an emission wavelength of about 530 to 570 nm.

20. The method of claim 19, wherein the solution comprising the plurality of cells is contained in a well of a multi-well cell culture plate.

21. The method of claim 20, wherein the multi-well cell culture plate is coated with Teflon.

22. The method of any one of claims 19 to 21, wherein the cells are cultured for a period of at least 12 hours prior to said detecting.

23. The method of any one of claims 19 to 22, further comprising the step of shaking the multi-well cell culture plate prior to said detecting.

24. The method of any one of claims 19 to 23, wherein the cell is selected from the group consisting of a yeast cell, a bacterial cell, a mammalian cell, a fungal cell, an insect cell, and a plant cell.

25. The method of claim 24, wherein the cell is a yeast cell.

26. The method of claim 25, wherein the yeast is *Saccharomyces cerevisiae*.