WHAT IS CLAIMED IS:

1. A method for labeling a region of a tissue or tissue sample, comprising:
   a) providing a three-dimensional tissue or tissue sample;
   b) clearing the sample;
   c) contacting the tissue or tissue sample with a photo-activatable label; and
   d) subjecting a region of the tissue or tissue sample to a multi-photon laser, thereby labeling the region.

~~2. The method of claim 1, wherein the multi-photon laser is a two-photon laser.~~

~~3. The method of claim 1, wherein the multi-photon laser is a three-photon laser.~~

~~4.~~2. The method of ~~any one of~~ claim~~s~~ 1 ~~to 3~~, wherein the region comprises a cell, a subcellular compartment, an aggregate, or a secreted aggregate.

~~5. The method of claim 4, wherein the subcellular compartment is a nucleus.~~

~~6.~~3. The method of ~~any one of~~ claim~~s~~ 1 or 2 ~~5~~, further comprising imaging the tissue or tissue sample.

~~7. The method of any of claims 1-6, wherein the tissue or tissue sample is a fixed tissue or fixed tissue sample.~~

~~8.~~4. The method of any one of the above claims, wherein the photo-activatable label comprises a detectable moiety or a tag.

~~9. The method of claim 8, wherein the detectable moiety comprises a light emitting moiety.~~

~~10. The method of claim 9, wherein the light emitting moiety is a fluorescent moiety, a chemiluminescent moiety, a bioluminescent moiety, or an electrochemiluminescent moiety.~~

~~11. The method of claim 10, wherein the fluorescent moiety comprises a fluorophore.~~

~~12. The method of claim 8, wherein one of the detectable moiety comprises an antibody or a functional derivative thereof.~~

~~13. The method of any of claims 1-7, wherein the photo-activatable label comprises a tag.~~

~~14. The method of claim 13, wherein the tag is chosen from the group comprising an affinity tag, an epitope tag, a fluorescent tag, an oligonucleotide tag, or a biotin tag.~~

~~15.~~5. The method of any one of claims 1-~~4~~14, wherein the sample clearing process comprises dehydrating the sample and transferring the sample into a medium with a refraction index similar to or matching the tissue.

~~16. The method of claim 15, wherein the refractive index is between about 1.3 and about 1.6.~~

~~17. The method of claim 15, wherein the medium comprises a solution of Benzyl Alcohol, Benzyl Benzoate (BABB) or derivative thereof, with or without one or more of triethylamine, diphenyl ether, dibenzyl ether, α-tocopherol, and/or Quadrol.~~

~~18. The method of claim 17, wherein the medium comprises a BABB solution.~~

~~19. The method of any one of claims 1-17, wherein the sample is dehydrated by a tert-butanol solution.~~

~~20. The method of claim 19, wherein the tert-butanol solution comprises trimethylamine, tetrahydrofuran, ethanol, or methanol.~~

~~21.~~6. The method of any one of claims 1-~~19~~5, wherein the photo-activatable label is hydrophobic.

~~22. The method of any one of claims 1-21, wherein the photo-activatable label comprises a phenyl azide group, an ortho-hydroxyphenyl azide group, a meta-hydroxyphenyl azide group, a tertrafluorophenyl azide group, an ortho-nitrophenyl azide group, a meta-nitrophenyl azide group, a diazirine group, an azido-methylcoumarin group, or a psoralen group.~~

~~23. The method of claim 22, wherein the photo-activatable label comprises an aryl azide group.~~

~~24.~~7. The method of any one of claims 1-~~6~~23, further comprising isolating the labeled region or a portion of the labeled region from the tissue or tissue sample.

~~25. The method of claim 24, wherein the labeled region or portion is isolated by FACS sorting for the label.~~

~~26.~~8. The method of claim ~~24 or 25~~7, further comprising analyzing a composition of the isolated labeled region to create analysis data,

wherein analyzing comprises determining a DNA, RNA, and/or protein composition of the isolated labeled region; and

optionally wherein the RNA is analyzed by sequencing or SPLITseq, the protein is analyzed by mass spectrometry, and/or the DNA is analyzed by DNA sequencing.

~~27. The method of claim 26, wherein analyzing comprises determining a DNA, RNA, and/or protein composition of the isolated labeled region.~~

~~28. The method of claim 27, wherein the RNA is analyzed by sequencing.~~

~~29. The method of claim 27, wherein the RNA is analyzed by SPLITseq.~~

~~30. The method of claim 27, wherein the protein is analyzed by mass spectrometry.~~

~~31. The method of claim 27, wherein the DNA is analyzed by DNA sequencing.~~

~~32.~~9. The method of ~~any one of claims 26 to 31~~claim 7, wherein the tissue or tissue sample was imaged to create an image prior to isolating the labeled region, further comprising combining the image with the analysis data to create a 3-dimensional composition map of the region.

~~33.~~10. A method for 3-dimensional expression profiling of an intact tissue or tissue sample, comprising:

a) providing a three-dimensional intact tissue or tissue sample;

b) clearing the sample;

c) contacting the tissue or tissue sample with photo-activatable label;

d) subjecting a region of the tissue or tissue sample to a multi-photon laser, thereby labeling the region;

e) imaging the labeled region to create an image;

f) isolating the labeled region from the tissue or tissue sample;

g) determining a DNA, RNA, and/or protein composition of the isolated labeled region;

h) combining the image with the DNA, RNA, and/or protein composition of the isolated labeled region to create a 3-dimensional expression profile of the intact tissue or tissue sample.

~~34. The method of claim 33, wherein the multi-photon laser is a two-photon laser.~~

~~35. The method of claim 33, wherein the multi-photon laser is a three-photon laser.~~

~~36.~~11. The method of ~~any one of claims 33 to 35~~claim 10, wherein the region is a cell, a subcellular compartment, an aggregate, or a secreted aggregate.

~~37. The method of any one of claims 33 to 36, wherein the isolated labeled region is a single nuclei.~~

~~38.~~12. The method of ~~any one of claims 33 to 37~~claim 9, wherein an RNA composition, a protein composition, and/or a DNA composition of the isolated labeled region is determined, and

optionally wherein the RNA composition is determined by sequencing or SPLITseq, the protein composition is determined by mass spectrometry, and/or the DNA composition is determined by DNA sequencing.

~~39. The method of claim 38, wherein the RNA composition is determined by sequencing.~~

~~40. The method of claim 38, wherein the RNA composition is determined by SPLITseq.~~

~~41. The method of any one of claims 33 to 40, wherein a protein composition of the isolated labeled region is determined.~~

~~42. The method of claim 41, wherein the protein composition is determined by mass spectrometry.~~

~~43. The method of any one of claims 33 to 40, wherein a DNA composition of the isolated labeled region is determined.~~

~~44. The method of claim 43, wherein the DNA composition is determined by DNA sequencing.~~

~~45.~~13. A method for isolating a single cell or a nucleus, in a tissue or tissue sample, comprising:

a) providing a three-dimensional tissue or tissue sample;
b) clearing the sample;
c) contacting the tissue or tissue sample with photo-activatable label;
d) subjecting a cell to a multi-photon laser, thereby labeling the cell;
e) dissociating the labeled cell from the tissue or tissue sample; and
f) isolating the labeled cell or nucleus.

~~46. The method of claim 45, wherein the multi-photon laser is a two-photon laser.~~

~~47. The method of claim 45, wherein the multi-photon laser is a three-photon laser.~~

~~48.~~14. The method of claim 13 ~~any one of claims 45 to 47~~, further comprising imaging the tissue or tissue sample.

~~49. The method of claim any one of claims 33 to 48, wherein the tissue or tissue sample is a fixed tissue or fixed tissue sample.~~

~~50.~~15. The method of any one of claims ~~33~~10 to ~~49~~14, wherein the photo-activatable label comprises a detectable moiety or a tag.

~~51. The method of claim 50, wherein the detectable moiety comprises a light emitting moiety.~~

~~52. The method of claim 51, wherein the light emitting moiety is a fluorescent moiety, a chemiluminescent moiety, a bioluminescent moiety, or an electrochemiluminescent moiety.~~

~~53. The method of claim 52, wherein the fluorescent moiety comprises a fluorophore.~~

~~54. The method of claim 50, wherein the detectable moiety comprises an antibody or a functional derivative thereof.~~

~~55. The method of any one of claims 33 to 49, wherein the photo-activatable label comprises a tag.~~

~~56. The method of claim 55, wherein the tag is chosen from the group comprising an affinity tag, an epitope tag, a fluorescent tag, or a biotin tag.~~

~~57.~~16. The method of any one of claims 10~~33~~ to ~~56~~15, wherein the sample clearing process comprises dehydrating the sample and transferring the sample into medium with a refraction index similar to or matching the tissue.

~~58. The method of claim 57, wherein the medium comprises a solution of Benzyl Alcohol, Benzyl Benzoate (BABB) or derivatives thereof, with or without one or more of triethylamine, diphenyl ether, dibenzyl ether, α-tocopherol, and/or Quadrol.~~

~~59. The method of claim 58, wherein the medium comprises a BABB solution.~~

~~60. The method of any one of claims 33 to 59, wherein the sample is dehydrated by a tert-butanol solution.~~

~~61. The method of claim 60, wherein the tert-butanol solution comprises trimethylamine, tetrahydrofuran, ethanol, or methanol.~~

~~62.~~17. The method of any one of claims 10~~33~~ to 16~~61~~, wherein the photo-activatable label is hydrophobic.

~~63. The method of any one of claims 33 to 62, wherein the photo-activatable label comprises a phenyl azide group, a ortho-hydroxyphenyl azide group, a meta-hydroxyphenyl azide group, a tertrafluorophenyl azide group, a ortho-nitrophenyl azide group, a meta-nitrophenyl azide group, a diazirine group, an azido-methylcoumarin group, or a psoralen group.~~

~~64. The method of claim 63, wherein the photo-activatable label comprises an aryl azide group.~~

~~65.~~18. The method of any one of claims ~~45~~13 to ~~64~~17, further comprising isolating the labeled cell or nucleus.

~~66. The method of any one of claims 33 to 44 or 65, wherein the labeled cell or nucleus is isolated by FACS sorting for the label.~~

~~67.~~19. The method of claim ~~65 or 66~~18, further comprising analyzing the isolated labeled cell or nucleus.

wherein analyzing comprises determining a DNA composition , RNA composition, and/or protein composition of the isolated labeled cell or nucleus;

wherein the RNA composition is determined by sequencing , the protein composition is determined by mass spectrometry, and/or the DNA composition is determined by DNA sequencing.

~~68. The method of claim 67, wherein analyzing comprises determining a DNA, RNA, and/or protein composition of the isolated labeled cell or nucleus.~~

~~69. The method of claim 38 or 68, wherein the RNA is analyzed by single-cell RNA sequencing (scRNAseq).~~

~~70. The method of claim 68, wherein the RNA composition is determined by sequencing.~~

~~71. The method of claim 68, wherein a protein composition of the isolated labeled region is determined.~~

~~72. The method of claim 71, wherein the protein composition is determined by mass spectrometry.~~

~~73. The method of claim 68, wherein a DNA composition of the isolated labeled region is determined.~~

~~74. The method of claim 73, wherein the DNA composition is determined by DNA sequencing.~~

~~75. The method of claim 68, wherein the RNA is analyzed by SPLITseq.~~

~~76.~~20. The method of any one of claims 1-~~75~~19, further comprising contacting the tissue or tissue sample with a second photo-activatable label and subjecting a second cell or nucleus in the tissue or tissue sample to a multi-photon laser, thereby labeling the second cell or nucleus.

~~77. The method of claim 76, wherein the multi-photon laser is a two-photon laser.~~

~~78. The method of claim 76, wherein the multi-photon laser is a three-photon laser.~~

~~79. The method of any one of claims 1-78, wherein the tissue or tissue sample is a whole organ, tumor, or animal.~~

~~80. The method of any one of claims 1-79, wherein the wavelength of each photon in the two photon laser is between about 175 nm and about 350 nm.~~

~~81. The method of any one of claims 1-80, wherein the tissue or tissue sample is from a tumor.~~

~~82.~~21. A composition comprising a tissue sample, a medium having a refraction index similar to or matching the tissue, and a photo-activatable label,

wherein the tissue comprises a labeled region comprising a cell, subcellular compartment, an aggregate, or a secreted aggregate,

wherein the cell was labeled by a multi-photon method.

~~83. The composition of claim 82, wherein the tissue comprises a labeled region.~~

~~84. The composition of claim 83, wherein the region comprises a cell, a subcellular compartment, an aggregate, or a secreted aggregate~~

~~85. The composition of claim 83 or 84, wherein the cell was labeled by a multi-photon method.~~

~~86. The composition of claim 85, wherein the cell was labeled by a two-photon method.~~

~~87. The composition of claim 85, wherein the cell was labeled by a three-photon method.~~

~~88. The composition of any one of claims 82-87, wherein the photo-activatable label comprises a detectable moiety.~~

~~89. The composition of claim 88, wherein the detectable moiety comprises a light emitting moiety.~~

~~90. The composition of claim 89, wherein the light emitting moiety is a fluorescent moiety, a chemiluminescent moiety, a bioluminescent moiety, or an electrochemiluminescent moiety.~~

~~91. The composition of claim 90, wherein the fluorescent moiety comprises a fluorophore.~~

~~92. The composition of any one of claims 82-87, wherein the photo-activatable label comprises a tag.~~

93. The composition of claim 92, wherein the tag is chosen from the group comprising an affinity tag, an epitope tag, a fluorescent tag, or a biotin tag.

94. The composition of claim 88, wherein the detectable moiety is an antibody or a functional derivative thereof.

95. The composition of any one of claims 82-94, wherein the photo-activatable label is hydrophobic.

96. The composition of any one of claims 82-95, wherein the photo-activatable label comprises a phenyl azide group, an ortho-hydroxyphenyl azide group, a meta-hydroxyphenyl azide group, a tertrafluorophenyl azide group, an ortho-nitrophenyl azide group, a meta-nitrophenyl azide group, a diazirine group, an azido-methylcoumarin group, or a psoralen group.

97. The composition of any one of claims 82-96, wherein the medium comprises a solution of Benzyl Alcohol, Benzyl Benzoate (BABB) or derivatives thereof, with or without one or more of triethylamine, diphenyl ether, dibenzyl ether, α-tocopherol, and/or Quadrol.

98. The composition of claim 97, wherein the medium comprises a BABB solution.

99. A cleared tissue sample comprising a photo-activatable label and a medium having a refraction index substantially matching the index of the tissue.

100. The cleared tissue of claim 99, wherein the medium comprises a solution of Benzyl Alcohol, Benzyl Benzoate (BABB) or derivatives thereof, with or without one or more of triethylamine, diphenyl ether, dibenzyl ether, α-tocopherol, and/or Quadrol.

101. The cleared tissue of claim 100, wherein the medium comprises a BABB solution.

102. The cleared tissue of any one of claims 99-101, comprising a labeled cell.

103. The cleared tissue of claim 102, wherein the cell was labeled by a multi-photon method.

104. The cleared tissue of any one of claims 99-103, wherein the photo-activatable label comprises a detectable moiety.

105. The cleared tissue of claim 104, wherein the detectable moiety comprises a light emitting moiety.

106. The cleared tissue of claim 105, wherein the light emitting moiety is a fluorescent moiety, a chemiluminescent moiety, a bioluminescent moiety, or an electrochemiluminescent moiety.

~~107. The cleared tissue of claim 106, wherein the fluorescent moiety comprises a fluorophore.~~

~~108. The cleared tissue of any one of claims 99-107, wherein the photo-activatable label comprises a tag.~~

~~109. The cleared tissue of claim 108, wherein the tag is chosen from the group comprising an affinity tag, an epitope tag, a fluorescent tag, or a biotin tag.~~

~~110. The cleared tissue of claim 104, wherein the detectable moiety is an antibody or a functional derivative thereof.~~

~~111. The cleared tissue of any one of claims 99-110, wherein the photo-activatable label is hydrophobic.~~

~~112. The cleared tissue of any one of claims 99-111, wherein the photo-activatable label comprises a phenyl azide group, an ortho-hydroxyphenyl azide group, a meta-hydroxyphenyl azide group, a tertrafluorophenyl azide group, an ortho-nitrophenyl azide group, a meta-nitrophenyl azide group, a diazirine group, an azido-methylcoumarin group, or a psoralen group.~~

~~113. The composition or cleared tissue of any one of claims 82-112, wherein the tissue or tissue sample is from a tumor.~~