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WHAT IS CLAIMED IS:

1. A method for identifying a presence of one or more target nucleotide sequences in a sample comprising:

5 providing a sample potentially containing the one or more target nucleotide sequences;

providing one or more oligonucleotide probe sets, each set comprising (a) a first oligonucleotide probe having a target-specific portion, and (b) a second oligonucleotide probe having a target specific portion, wherein the first and second oligonucleotide probes of a probe set are configured to hybridize adjacent to one another on the target nucleotide sequence with a junction between the first and second oligonucleotide probes, and wherein, in a probe set, the target specific portion of the second oligonucleotide probe has an overlapping identical nucleotide at the junction with the first oligonucleotide probe;

15 contacting the sample and the one or more oligonucleotide probe sets under conditions effective for first and second oligonucleotide probes of a probe set to hybridize at adjacent positions in a base specific manner to their corresponding target nucleotide sequences, if present in the sample, wherein upon hybridization the overlapping identical nucleotide of the second oligonucleotide probe forms a flap at the junction comprising the overlapping identical nucleotide;

20 cleaving the overlapping identical nucleotide of the second oligonucleotide probe with an enzyme having 5' nuclease activity, thereby liberating a phosphate at the second oligonucleotide probe's 5' end;

ligating first and second oligonucleotide probes of the one or more oligonucleotide probe sets together at the junction to form ligated product sequences; detecting the ligated product sequences in the sample; and identifying the presence of one or more target nucleotide sequences in the sample based on said detecting.

30 2. The method of claim 1 further comprising:
amplifying the target nucleotide sequences in the sample prior to said contacting.

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3. The method of claim 1, wherein said detecting comprises:
sequencing the ligated product sequences in the sample.
4. The method of claim 1, wherein said detecting comprises:
5 separating the ligated product sequences by size.
5. The method of claim 1, wherein one of the oligonucleotide
probes in a probe set further comprises a zip-code portion, wherein the zip-code
portions hybridize to their complementary capture oligonucleotides under uniform
10 hybridization conditions, said method further comprising:
providing a collection of the capture oligonucleotides and
contacting the ligation product sequence with the collection of capture
oligonucleotides under conditions effective to hybridize the zip-code portion of each
ligated product sequence to its complementary capture oligonucleotide in the collection
15 with minimal non-specific hybridization and under uniform hybridization conditions,
whereby said detecting takes place after hybridization of the ligated product sequences
to their complementary capture oligonucleotides.
6. The method of claim 5, wherein each type of capture
20 oligonucleotide in the collection comprises a nucleotide sequence that is greater than
sixteen nucleotides and differs from nucleotide sequences of other types of capture
oligonucleotides in the collection, when aligned to each other, by at least 25%.
7. The method of claim 5, wherein the collection of capture
25 oligonucleotides is immobilized on a solid support.
8. The method of claim 7, wherein the solid support is in a form
selected from the group consisting of beads, slides, discs, membranes, films,
microtiter plates, and composites thereof.
9. The method of claim 7, wherein the solid support comprises an
30 array of positions, with the collection of capture oligonucleotides being immobilized
at the array of positions.

10. The method of claim 1, wherein the first oligonucleotide probe of the probe set further comprises a 5' primer-specific portion and the second oligonucleotide probe in a probe set further comprises a 3' primer-specific portion,
5 wherein each ligated product sequence comprises the 5' primer-specific portion, the target-specific portions, and the 3' primer-specific portion.

11. The method of claim 10 further comprising:
providing one or more oligonucleotide primer sets, each set comprising
10 (a) a first oligonucleotide primer comprising the same nucleotide sequence as the 5' primer-specific portion of the ligated product sequence and (b) a second oligonucleotide primer comprising a nucleotide sequence that is complementary to the 3' primer-specific portion of the ligated product sequence;
blending the ligated product sequences, the one or more
15 oligonucleotide primer sets, and a DNA polymerase to form a polymerase chain reaction mixture; and
subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles comprising a denaturation treatment, a hybridization treatment, and an extension treatment thereby forming primary extension products,
20 whereby said detecting involves detection of the primary extension products.

12. The method of claim 11, wherein one of the first or second oligonucleotide primers of a primer set comprises a detectable label, whereby said detecting involves detection of labeled primary extension products.
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13. The method of claim 11, wherein said detecting comprising:
sequencing said extension products after said subjecting.

14. The method of claim 11, wherein said detecting comprises:
30 separating the ligated product sequences by size.

15. The method of claim 11, wherein either or both of the first and second oligonucleotide probes in a probe set further comprises a zip-code or a portion

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thereof, where the zip-codes hybridize to complementary capture oligonucleotides under uniform hybridization conditions.

16. The method of claim 15 further comprising:
5 providing a collection of capture oligonucleotides, wherein each capture oligonucleotide hybridizes to complementary zip code portions, and comprises a quencher molecule and a detectable label that are separated from each other;
adding the collection of capture oligonucleotides to the polymerase chain reaction mixture; and
10 hybridizing capture oligonucleotides of the collection to their complementary zip-code portions of the ligated product sequences or complement thereof during said subjecting, whereby the quencher molecule and/or the detectable label are cleaved from the hybridized capture oligonucleotide during said extension treatment whereby said detecting involves the detection of the cleaved detectable
15 label.

17. The method of claim 15 further comprising:
providing a collection of capture oligonucleotides, wherein each capture oligonucleotide hybridizes to complementary zip code portions, and comprises a
20 quencher molecule and a detectable label that are separated from each other;
providing one or more secondary oligonucleotide primer sets capable of hybridizing to the primary extension products;
blending the collection of capture oligonucleotides, the one or more secondary oligonucleotide primer sets, the primary extension products, and a
25 polymerase to form a secondary polymerase chain reaction mixture;
subjecting the secondary polymerase chain reaction mixture to one or more polymerase chain reaction cycles comprising a denaturation treatment, a hybridization treatment, wherein capture oligonucleotides of the collection hybridize to their complementary zip-code portions of the primary extension products and the
30 secondary oligonucleotide primers hybridize to the primary extension products, and an extension treatment, wherein the hybridized primers are extended thereby forming secondary extension products; and

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cleaving the quencher molecule and/or the detectable label from the hybridized capture oligonucleotides during said extension treatment, whereby said detecting involves the detection of the cleaved detectable label.

5 18. The method of claim 16 or 17, wherein each type of capture oligonucleotide in the collection comprises a nucleotide sequence that differs from nucleotide sequences of other types of capture oligonucleotides in the collection, when aligned to each other, by at least 25%.

10 19. The method of claim 18 further comprising:
 providing a collection of the capture oligonucleotides, wherein each capture oligonucleotide of the collection hybridizes to complementary zip-code portions and

 contacting the primary extension products, after said subjecting, with
15 the collection of capture oligonucleotides under conditions effective to hybridize the zip-code portion of each primary extension product to its complementary capture oligonucleotide in the collection with minimal non-specific hybridization and under uniform hybridization conditions, whereby said detecting takes place after hybridization of the primary extension products to their complementary capture
20 oligonucleotides.

 20. The method of claim 19, wherein each type of capture oligonucleotide in the collection comprises a nucleotide sequence that is greater than sixteen nucleotides and differs from nucleotide sequences of other types of capture
25 oligonucleotides in the collection, when aligned to each other, by at least 25%.

 21. The method of claim 19, wherein one of the oligonucleotide primers of the one or more oligonucleotide primer sets further comprises a detectable label thereby forming labeled primary extension products.

30 22. The method of claim 19, wherein the collection of capture oligonucleotides is immobilized on a solid support.

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23. The method of claim 23, wherein the solid support is in a form selected from the group consisting of beads, slides, discs, membranes, films, microtiter plates, and composites thereof.

5 24. The method of claim 23, wherein the solid support comprises an array of positions, wherein the collection of capture oligonucleotides is immobilized at the array of positions.

10 25. The method of claim 15, wherein the first oligonucleotide probe further comprises a first portion of the zip-code and a first tag portion that is 3' to the first zip-code portion, and the second oligonucleotide probe further comprises a second portion of the zip-code and a second tag portion that is 5' to the second zip-code portion, wherein the first and second zip-code portions of an oligonucleotide probe set, when adjacently positioned, form a full-length zip-code, and wherein the
15 first and second tag portions of an oligonucleotide probe set are complementary to each other, said method further comprising:

providing a collection of capture oligonucleotides complementary to a portion of the first zip-code portion and a portion of the second zip-code portion, wherein each capture oligonucleotide of the collection comprises a quencher molecule
20 and a detectable label that are separated from each other;

subjecting the primary extension products and the collection of capture oligonucleotides to conditions effective for (i) the first and second tag portions of a particular primary extension product to hybridize to each other to form hairpinned extension products with adjacently positioned first and second zip-code portions and
25 (ii) the capture oligonucleotides of the collection to hybridize to complementary adjacently positioned first and second zip-code portions of the hairpinned extension products; and

30 cleaving the quencher molecule or the detectable label from hybridized capture oligonucleotides, whereby said detecting involves detection of the detectable label separated from the quencher molecule.

26. The method of claim 15, wherein (i) the first oligonucleotide probe further comprises a second primer-specific portion that differs for each different

oligonucleotide probe set, a first portion of the zip-code, and a first tag portion that is 3' to the first zip-code portion, and (ii) the second oligonucleotide probe further comprises a second portion of the zip-code and a second tag portion that is 5' to the second zip-code portion, wherein the first and second zip-code portions of an
5 oligonucleotide probe set, when adjacently positioned, form a full-length zip-code, and wherein the first and second tag portions of an oligonucleotide probe set are complementary to each other, said method further comprising:

providing one or more secondary primer sets comprising (i) a first secondary oligonucleotide primer having (a) a nucleotide sequence that is the same as
10 the second primer-specific portion of the first oligonucleotide probe, (b) a capture oligonucleotide portion that is complementary to adjacently positioned first and second zip-code portions of an oligonucleotide probe set, (c) a quencher molecule and a detectable label separated by said capture oligonucleotide portion, and (ii) a second secondary oligonucleotide primer having the same nucleotide sequence as the second
15 primary oligonucleotide primer;

blending the primary extension products, the one or more secondary oligonucleotide primer sets, and a polymerase to form a second polymerase chain reaction mixture;

subjecting the second polymerase chain reaction mixture to one or
20 more polymerase chain reaction cycles thereby forming secondary extension products;

subjecting the secondary extension products to conditions effective for the first and second tag portions of a particular secondary extension product to hybridize to each other to form hairpinned secondary extension products with
25 adjacently positioned first and second zip-code portions and (ii) the capture oligonucleotide portion of a particular hairpinned secondary extension product to hybridize to complementary adjacently positioned first and second zip-code portions of the hairpinned extension product; and

cleaving the quencher molecule or the detectable label from the capture
30 oligonucleotide portion of the hairpinned secondary extension products whereby said detecting involves detection of the detectable label separated from the quencher molecule.

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27. The method of claim 11, wherein the second oligonucleotides probe further comprises a unitaq detection portion, thereby forming ligated product sequences comprising the 5' primer-specific portion, the target-specific portions, the unitaq detection portion, and the 3' primer-specific portion, said method further comprising

5 providing one or more unitaq detection probes, wherein each unitaq detection probe hybridizes to a complementary unitaq detection portion and comprises a quencher molecule and a detectable label that are separated from each other;

adding the one or more unitaq detection probes to the polymerase

10 chain reaction mixture; and

hybridizing the one or more unitaq detection probes to complementary unitaq detection portions on the ligated product sequence or complement thereof during said subjecting, whereby the quencher molecule and the detectable label are cleaved from the one or more unitaq detection probes during said extension treatment,

15 whereby said detecting involves the detection of the cleaved detectable label.

28. The method of claim 11, wherein the second oligonucleotides probe further comprises a unitaq detection portion, whereby the primary extension product sequences formed comprise the 5' primer-specific portion, the target-specific

20 portions, the unitaq detection portion, and the 3' primer-specific portion, said method further comprising

providing one or more unitaq detection probes, wherein each unitaq detection probe hybridizes to a complementary unitaq detection portion and comprises a quencher molecule and a detectable label that are separated from each other;

25 providing one or more secondary oligonucleotide primer sets capable of hybridizing to the primary extension products;

blending the one or more unitaq detection probes, the one or more secondary oligonucleotide primer sets, the primary extension products, and a polymerase to form a secondary polymerase chain reaction mixture;

30 subjecting the secondary polymerase chain reaction mixture to one or more polymerase chain reaction cycles comprising a denaturation treatment, a hybridization treatment, wherein the one or more unitaq detection probes hybridize to their complementary unitaq detection portions of the extension products and the

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secondary oligonucleotide primers hybridize to the primary extension products, and an extension treatment, wherein the hybridized primers are extended thereby forming secondary extension products;

5 cleaving the quencher molecule and/or the detectable label from the one or more hybridized unitaq detection probes during said extension treatment, whereby said detecting involves the detection of the cleaved detectable label.

10 29. The method of claim 27 or 28, wherein the unitaq detection probe is coupled via a further portion to the 5' end of the secondary oligonucleotide primer.

15 30. The method of claim 11, wherein (i) the second oligonucleotide probe further comprises a unitaq detection portion, thereby forming ligated product sequences comprising the 5' primer-specific portion, the target-specific portions, the unitaq detection portion, and the 3' primer-specific portion, (ii) the first oligonucleotide primer further comprises a unitaq detection probe that is complementary to the unitaq detection portion of the ligated product sequence, and a quencher molecule and a detectable label separated by said unitaq detection probe, and (iii) the primary extension products formed during said subjecting comprise the
20 detectable label, the unitaq detection probe, the quencher molecule, the 5' primer-specific portion, the target specific portions, the unitaq detection portion, and the 3' primer-specific portion, said method further comprising:

25 subjecting primary extension products to conditions effective for the unitaq detection probe of a particular extension product to hybridize to its complementary unitaq detection portion, thereby forming hairpinned extension products; and

30 cleaving the quencher molecule or the detectable label from the unitaq detection probe of the hairpinned extension product, whereby said detecting involves detection of the labeled hairpinned extension product or the cleaved detectable label.

31. The method of claim 1, wherein the first and second oligonucleotide probes of the one or more oligonucleotide probe sets further comprise a first and second tag portion, respectively, wherein the first and second tag portions

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of an oligonucleotide probe set are complementary to each other, and wherein the first and second tag portions for each different oligonucleotide probe set have different nucleotide sequences, said method further comprising:

- 5 subjecting the sample, after said ligating, to conditions effective for the first and second tag portions of a particular ligated product sequence to hybridize, thereby forming hairpinned ligated product sequences; and
- removing unligated oligonucleotide probes from the sample after said subjecting.

- 10 32. The method of claim 31, wherein the first oligonucleotide probe of the probe set further comprises a 5' primer-specific portion and the second oligonucleotide probe in a probe set further comprises a 3' primer-specific portion, said method further comprising:

- providing one or more oligonucleotide primer sets, each set comprising
- 15 (a) a first oligonucleotide primer comprising the same nucleotide sequence as the 5' primer-specific portion of the ligated product sequence and (b) a second oligonucleotide primer comprising a nucleotide sequence that is complementary to the 3' primer-specific portion of the ligated product sequence;

- blending, after said digesting, the ligated product sequences, the one or
- 20 more oligonucleotide primer sets, and a DNA polymerase to form a polymerase chain reaction mixture; and

- subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles thereby forming primary extension products, whereby said detecting involves detection of the primary extension products.

- 25 33. The method of claim 32, wherein one of the first or second oligonucleotide primers of a primer set comprises a detectable label, whereby said detecting involves detection of labeled primary extension products

- 30 34. The method of claim 11 further comprising:
- occluding unligated oligonucleotide probes from the sample comprising ligated product sequences prior to said subjecting to prevent unligated oligonucleotide probe extension or amplification.

35. The method of claim 34, wherein the second oligonucleotide probe further comprises a nucleotide flap that is 5' to the overlapping identical nucleotide at the junction, wherein at least a portion of the nucleotide flap is complementary to at least a portion of the 3' primer-specific portion of the second oligonucleotide probe, and wherein, in the absence of ligation, complementary regions of the nucleotide flap and the 3' primer-specific portion of unligated second oligonucleotide probes hybridize to each other to form hairpinned second oligonucleotide probes.

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36. The method of claim 35 further comprising:
extending the 3' primer-specific portion of the hairpinned second oligonucleotide probe during said subjecting to form an extended hairpinned second oligonucleotide probe that cannot hybridize to the second oligonucleotide primer.

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37. The method of claim 11, wherein the 5' end of the first oligonucleotide probe is coupled to the 3' end of the second oligonucleotide probe, thereby forming a coupled oligonucleotide probe, said coupled oligonucleotide probe forming a circular ligated product sequence comprising the 5' primer-specific portion, the target specific portions, and the 3' primer-specific portion.

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38. The method of claim 37, wherein the coupled probe further comprises a polymerase blocker within the portion where the 5' end of the first oligonucleotide probe is coupled to the 3' end of the second oligonucleotide probe, and wherein during said subjecting non-circularized extension products are formed.

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39. The method of claim 37, wherein the coupled probe further comprises a cleavable nucleotide or nucleotide analogue within the portion where the 5' end of the first oligonucleotide probe is coupled to the 3' end of the second oligonucleotide probe, and wherein during said subjecting non-circularized extension products are formed.

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40. The method of claim 37, wherein the coupled oligonucleotide probe further comprises a segment that is complementary to the 3' target specific portion, wherein, in the absence of ligation, the 3' target specific portion of the coupled probe hybridizes to the complementary segment to form a hairpinned coupled oligonucleotide probe.

41. The method of claim 40, further comprising:
extending the 3' target-specific portion of the coupled hairpinned oligonucleotide probe during said subjecting to form an extended coupled hairpinned oligonucleotide probe that occludes binding of the second oligonucleotide primer to its complementary sequence.

42. The method of claim 1, wherein the one or more oligonucleotide probe sets further comprise a third oligonucleotide probe having a target-specific target portion, wherein the second and third oligonucleotide probes of a probe set are configured to hybridize adjacent to one another on the target nucleotide sequence with a junction between the second and third oligonucleotide probes during said contacting, and wherein, in a probe set, the target specific portion of the third oligonucleotide probe has an overlapping identical nucleotide at the junction with the second oligonucleotide probe in a probe set that is removed during said cleaving to allow ligation between the second and third oligonucleotide probes at the junction to form a ligated product sequence comprising the first, second, and third oligonucleotide probes of a probe set.

43. The method of claim 1, wherein the sample is selected from the group consisting of tissue, cells, serum, blood, plasma, amniotic fluid, sputum, urine, bodily fluids, bodily secretions, bodily excretions, cell-free circulating nucleic acids, cell-free circulating fetal nucleic acids in pregnant woman, circulating tumor cells, tumor, tumor biopsy, and exosomes.

44. The method of claim 1, wherein the one or more target nucleotide sequences are low abundance nucleic acid molecules comprising one or

more nucleotide base insertions, deletions, translocations, mutations, and/or damaged nucleotide bases.

45. The method of claim 44, wherein the low abundance nucleic acid molecules with one or more nucleotide base insertions, deletions, translocations, mutations and/or damaged nucleotide bases are identified and distinguished from an excess of nucleic acid molecules in the sample having a similar nucleotide sequence as the low abundance nucleic acid molecules but without the one or more nucleotide base insertions, deletions, translocations, mutations, and/or damaged bases.

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46. The method of claim 45, wherein the wherein the first oligonucleotide probe comprises a mismatch nucleotide or nucleotide analog at a base position that is two or three bases from the junction between the second and first oligonucleotide probes.

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47. The method of claim 45, wherein the second oligonucleotide probe comprises one or more thiophosphate-modified nucleotide bases that is 3' to the overlapping identical nucleotide at the junction between the second and first oligonucleotide probes.

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48. The method of claim 45, wherein the second oligonucleotide probe comprises one or more thiophosphate-modified nucleotide bases that are 5' to the overlapping nucleotide at the junction between the second and first oligonucleotide probes.

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49. The method of claim 45, wherein the copy number of one or more low abundance target nucleotide sequences are quantified relative to the copy number from an excess of nucleic acid molecules in the sample having a similar nucleotide sequence as the low abundance nucleic acid molecules.

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50. The method of claim 1, wherein the one or more target nucleotide sequences are quantified.

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51. The method of claim 50, wherein the one or more target nucleotide sequences are quantified relative to other nucleotide sequences in the sample.

5 52. The method of claim 50, wherein the relative copy number of one or more target nucleotide sequences are quantified.

10 53. The method of claim 1, further comprising:
diagnosing or prognosing a disease state based on said identifying.

54. The method of claim 1, further comprising:
distinguishing a genotype or disease predisposition based on said
identifying.

15 55. A method for identifying a presence of one or more target nucleotide sequences in a sample, said method comprising:
providing a sample potentially containing the target nucleotide
sequence;

20 providing one or more oligonucleotide probe sets, each set comprising
(a) a first oligonucleotide probe having a target-specific portion, and (b) a second
oligonucleotide probe having 5' non-target specific flap portion and a target-specific
portion containing one or more thiophosphate-modified nucleotide bases, wherein the
first and second oligonucleotide probes of a probe set are configured to hybridize on
25 the target nucleotide sequence;

contacting the sample and the one or more oligonucleotide probe sets
under conditions effective for first and second oligonucleotide probes of a probe set to
hybridize in a base specific manner to their corresponding target nucleotide
sequences, if present in the sample;

30 cleaving the 5' non-target specific flap portion of the second
oligonucleotide probe with an enzyme having 5' nuclease activity, thereby liberating a
5' phosphate at a first nucleotide base of the target-specific portion of the second
oligonucleotide;

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ligating first and second oligonucleotide probes of the one or more oligonucleotide probe sets together to form ligated product sequences containing the target-specific portions with the one or more thiophosphate-modified nucleotide bases;

5 detecting ligated product sequences in the sample; and
identifying the presence of the one or more target nucleotide sequences in the sample based on said detecting.

10 56. The method of claim 55 further comprising:
extending the first oligonucleotide probe with a polymerase prior to said cleaving to form a junction with the second oligonucleotide probe, wherein the target specific portion of the second oligonucleotide probe has an overlapping identical nucleotide at the junction with the extended first oligonucleotide probe.

15 57. The method of claim 55, wherein at least one of the first or second oligonucleotide probes further comprises a detectable label wherein said detecting involves detection of the labeled ligated product sequences.

20 58. The method of claim 55, wherein said detecting comprises:
sequencing the ligated product sequences in the sample.

59. The method of claim 55, wherein said detecting comprises:
separating the ligated product sequences by size.

25 60. The method of claim 55, wherein at least one of the one or more thiophosphate-modified nucleotide bases of the second oligonucleotide probe is 3' to the first target-specific nucleotide base.

30 61. The method of claim 55, wherein the first oligonucleotide probe of a probe set further comprises a 5' primer-specific portion and the second oligonucleotide probe in a probe set further comprises a 3' primer-specific portion, wherein each ligated product sequence comprises the 5' primer-specific portion, the

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target-specific portions with one or more thiophosphates, and the 3' primer-specific portion.

62. The method of claim 61 further comprising:
5 providing one or more oligonucleotide primer sets, each set comprising
(a) a first oligonucleotide primer comprising the same nucleotide sequence as the 5' primer-specific portion of the ligated product sequence and (b) a second oligonucleotide primer comprising a nucleotide sequence that is complementary to the 3' primer-specific portion of the ligated product sequence;
10 blending the ligated product sequences, the one or more oligonucleotide primer sets, and a polymerase to form a polymerase chain reaction mixture; and
subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles thereby forming extension products; whereby said
15 detecting involved detection of said extension products.

63. The method of claim 62 further comprising:
occluding unligated oligonucleotide probes from the sample comprising ligated product sequences prior to said subjecting to prevent unligated
20 probe extension or amplification.

64. The method of claim 62, wherein at least a portion of said 5' nucleotide flap of the second oligonucleotide probe is complementary to at least a portion of the 3' primer-specific portion of the second oligonucleotide probe, and
25 wherein, in the absence of ligation, complementary regions of the 5' nucleotide flap and the 3' primer-specific portion of an unligated second oligonucleotide probe hybridize to each other to form a hairpinned second oligonucleotide probe.

65. The method of claim 64, further comprising:
30 extending the 3' primer-specific portion of the hairpinned second oligonucleotide probe during said subjecting to form an extended hairpinned second oligonucleotide probe that occludes binding of the second oligonucleotide primer to its complementary sequence.

66. The method of claim 62, wherein said detecting comprising: sequencing said extension products after said subjecting.

5 67. The method of claim 55, wherein the sample is selected from the group consisting of tissue, cells, serum, blood, plasma, amniotic fluid, sputum, urine, bodily fluids, bodily secretions, bodily excretions, cell-free circulating nucleic acids, cell-free circulating fetal nucleic acids in pregnant woman, circulating tumor cells, tumor, tumor biopsy, and exosomes.

10 68. The method of claim 55, wherein the one or more target nucleotide sequences are low abundance nucleic acid molecules comprising one or more nucleotide base insertions, deletions, translocations, mutations, and/or damaged nucleotide bases.

15 69. The method of claim 68, wherein the low abundance nucleic acid molecules with one or more nucleotide base insertions, deletions, translocations, mutations and/or damaged nucleotide bases are identified and distinguished from an excess of nucleic acid molecules in the sample having a similar nucleotide sequence
20 as the low abundance nucleic acid molecules but without the one or more nucleotide base insertions, deletions, translocations, mutations, and/or damaged bases.

 70. The method of claim 55, wherein the one or more target nucleotide sequences are quantified.

25 71. The method of claim 70, wherein the one or more target nucleotide sequences are quantified relative to other nucleotide sequences in the sample.

30 72. The method of claim 70, wherein the relative copy number of one or more target nucleotide sequences are quantified.

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73. The method of claim 69, wherein the copy number of one or more low abundance target nucleotide sequences are quantified relative to the copy number from an excess of nucleic acid molecules in the sample having a similar nucleotide sequence as the low abundance nucleic acid molecules.

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74. The method of claim 55, further comprising:
diagnosing or prognosing a disease state based on said identifying.

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75. The method of claim 55, further comprising:
distinguishing a genotype or disease predisposition based on said identifying.

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76. A method for identifying a presence of one or more target nucleotide sequences in a sample comprising:

providing a sample potentially containing the one or more target nucleotide sequences;

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providing one or more oligonucleotide probe sets, each set comprising
(i) a first oligonucleotide probe comprising a 5' primer-specific portion, a first portion of a zip-code portion, a first tag portion that is 3' to the first zip-code portion, and a target-specific portion, and (ii) a second oligonucleotide probe comprising a 3' primer-specific portion, a second portion of the zip-code portion, a second tag portion that is 5' to the second zip-code portion, and a target-specific portion, wherein the first and second zip-code portions of an oligonucleotide probe set, when adjacently positioned, form a full-length zip-code, and wherein the first and second tag portions of an oligonucleotide probe set are complementary to each other;

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contacting the sample and the one or more oligonucleotide probe sets under conditions effective for first and second oligonucleotide probes of a probe set to hybridize in a base specific manner to their corresponding target nucleotide sequences, if present in the sample;

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ligating first and second oligonucleotide probes of the one or more probe sets together to form ligated product sequences;

providing one or more oligonucleotide primer sets, each set comprising
(a) a first oligonucleotide primer comprising the same nucleotide sequence as the 5'

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primer-specific portion of the ligated product sequence and (b) a second oligonucleotide primer comprising a nucleotide sequence that is complementary to the 3' primer-specific portion of the ligated product sequence;

blending the ligated product sequences, the one or more
5 oligonucleotide primer sets, and a DNA polymerase to form a polymerase chain reaction mixture;

subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles thereby forming primary extension products;

providing a collection of capture oligonucleotides complementary to a
10 portion of the first zip-code portion and a portion of the second zip-code portion, wherein each capture oligonucleotide of the collection comprises a quencher molecule and a detectable label separated from each other;

subjecting the primary extension products and the collection of capture oligonucleotides to conditions effective for (i) the first and second tag portions of a
15 particular primary extension product to hybridize to each other to form hairpinned extension products with adjacently positioned first and second zip-code portions and (ii) the capture oligonucleotides of the collection to hybridize to complementary adjacently positioned first and second zip-code portions of the hairpinned extension products;

20 cleaving the quencher molecule or the detectable label from the hybridized capture oligonucleotides;

detecting the detectable label separated from the quencher molecule;

and

identifying the presence of the one or more target nucleotide sequences
25 in the sample based on said detecting

77. A method for identifying a presence of one or more target nucleotide sequences in a sample comprising:

providing a sample potentially containing the one or more target
30 nucleotide sequences;

providing one or more oligonucleotide probe sets, each set comprising (i) a first oligonucleotide probe comprising a 5' primer-specific portion, a first portion of a zip-code portion, a first tag portion that is 3' to the first zip-code portion, and a

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target-specific portion, and (ii) a second oligonucleotide probe comprising a 3' primer-specific portion, a second portion of the zip-code portion, a second tag portion that is 5' to the second zip-code portion and a target-specific portion, wherein the first and second zip-code portions of an oligonucleotide probe set, when adjacently positioned, form a full-length zip-code, and wherein the first and second tag portions of an oligonucleotide probe set are complementary to each other;

contacting the sample and the one or more oligonucleotide probe sets under conditions effective for first and second oligonucleotide probes of a probe set to hybridize in a base specific manner to their corresponding target nucleotide

sequences, if present in the sample;

ligating first and second oligonucleotide probes of the one or more probe sets together to form ligated product sequences;

providing one or more oligonucleotide primer sets, each set comprising (i) a first oligonucleotide primer having (a) a nucleotide sequence that is the same as the second primer-specific portion of the first oligonucleotide probe, (b) a capture oligonucleotide portion that is complementary to adjacently positioned first and second zip-code portions of an oligonucleotide probe set, (c) a quencher molecule and a detectable label separated by said capture oligonucleotide portion, (ii) a second oligonucleotide primer comprising a nucleotide sequence that is complementary to the 3' primer-specific portion of the ligated product sequence;

blending the ligated product sequences, the one or more oligonucleotide primer sets, and a DNA polymerase to form a polymerase chain reaction mixture;

subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles thereby forming primary extension products;

subjecting the primary extension products to conditions effective for the first and second tag portions of a particular primary extension product to hybridize to each other to form hairpinned primary extension products with adjacently positioned first and second zip-code portions and (ii) the capture oligonucleotide portion of a particular hairpinned primary extension product to hybridize to complementary adjacently positioned first and second zip-code portions of the hairpinned extension product;

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cleaving the quencher molecule or the detectable label from capture
oligonucleotide portion of the hairpinned primary extension products;

detecting the detectable label separated from the quencher molecule;

and

5 identifying the presence of the one or more target nucleotide sequences
in the sample based on said detecting

78. A kit for identifying a presence of one or more target
nucleotide sequences in a sample comprising:

10 an enzyme having 5' nuclease activity;

a ligase; and

one or more oligonucleotide probe sets, each set comprising (a) a first
oligonucleotide probe having a target-specific portion, and (b) a second
oligonucleotide probe having a target specific portion, wherein the first and second
15 oligonucleotide probes of a probe set are configured to hybridize adjacent to one
another on the target nucleotide sequence with a junction between the first and second
oligonucleotide probes, and wherein, in a probe set, the target specific portion of the
second oligonucleotide probe has an overlapping identical nucleotide at the junction
with the first oligonucleotide probe.

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79. A kit for identifying a presence of one or more target
nucleotide sequences in a sample comprising:

an enzyme having 5' nuclease activity;

a ligase; and

25 one or more oligonucleotide probe sets, each set comprising (a) a first
oligonucleotide probe having a target-specific portion, and (b) a second
oligonucleotide probe having 5' non-target specific flap portion and a target-specific
portion containing one or more thiophosphate-modified nucleotide bases, wherein the
first and second oligonucleotide probes of a probe set are configured to hybridize on
30 the target nucleotide sequence.

WHAT IS CLAIMED IS

1. A method for identifying a presence of one or more target nucleotide sequences in a sample comprising:

providing a sample potentially containing the one or more target nucleotide sequences;

providing one or more oligonucleotide probe sets, each set comprising (a) a first oligonucleotide probe having a 5' primer-specific portion and a target-specific portion, and (b) a second oligonucleotide probe having a 3' primer-specific portion, a target specific portion, and a 5' nucleotide sequence, wherein said 5' nucleotide sequence is complementary to at least a portion of the 3' primer-specific portion and hybridizes to said complementary portion of the 3' primer-specific portion to form a hairpinned second oligonucleotide probe when said second probe is not hybridized to a target nucleotide sequence, wherein the first and second oligonucleotide probes of a probe set are configured to hybridize adjacent to one another on the target nucleotide sequence with a junction between the first and second oligonucleotide probes, and wherein, in a probe set, the target specific portion of the second oligonucleotide probe has an overlapping identical nucleotide at the junction with the first oligonucleotide probe;

contacting the sample and the one or more oligonucleotide probe sets under conditions effective for first and second oligonucleotide probes of a probe set to hybridize at adjacent positions in a base specific manner to their corresponding target nucleotide sequences, if present in the sample, wherein upon hybridization the overlapping identical nucleotide and the 5' nucleotide sequence of the second oligonucleotide probe forms a flap at the junction comprising the overlapping identical nucleotide;

cleaving the overlapping identical nucleotide of the second oligonucleotide probe with an enzyme having 5' nuclease activity, thereby liberating a phosphate at the second oligonucleotide probe's 5' end;

ligating first and second oligonucleotide probes of the one or more oligonucleotide probe sets together at the junction to form ligated product sequences, wherein each ligated product sequence comprises the 5' primer-specific portion, the target-specific portions, and the 3' primer-specific portion;

detecting the ligated product sequences in the sample; and

identifying the presence of one or more target nucleotide sequences in the sample based on said detecting.

2. The method of claim 1 further comprising:
amplifying the target nucleotide sequences in the sample prior to said contacting.
3. The method of claim 1, wherein said detecting comprises:
sequencing the ligated product sequences in the sample.
4. The method of claim 1, wherein said detecting comprises:
separating the ligated product sequences by size.
5. The method of claim 1, wherein one of the oligonucleotide probes in a probe set further comprises a zip-code portion, wherein the zip-code portions hybridize to their complementary capture oligonucleotides under uniform hybridization conditions, said method further comprising:
providing a collection of the capture oligonucleotides and
contacting the ligation product sequence with the collection of capture oligonucleotides under conditions effective to hybridize the zip-code portion of each ligated product sequence to its complementary capture oligonucleotide in the collection with minimal non-specific hybridization and under uniform hybridization conditions, whereby said detecting takes place after hybridization of the ligated product sequences to their complementary capture oligonucleotides.
6. The method of claim 5, wherein each type of capture oligonucleotide in the collection comprises a nucleotide sequence that is greater than sixteen nucleotides and differs from nucleotide sequences of other types of capture oligonucleotides in the collection, when aligned to each other, by at least 25%.

7. The method of claim 5, wherein the collection of capture oligonucleotides is immobilized on a solid support.

8. The method of claim 7, wherein the solid support is in a form selected from the group consisting of beads, slides, discs, membranes, films, microtiter plates, and composites thereof.

9. The method of claim 7, wherein the solid support comprises an array of positions, with the collection of capture oligonucleotides being immobilized at the array of positions.

10. The method of claim 1 further comprising:
providing one or more oligonucleotide primer sets, each set comprising (a) a first oligonucleotide primer comprising the same nucleotide sequence as the 5' primer-specific portion of the ligated product sequence and (b) a second oligonucleotide primer comprising a nucleotide sequence that is complementary to the 3' primer-specific portion of the ligated product sequence;

blending the ligated product sequences, the one or more oligonucleotide primer sets, and a DNA polymerase to form a polymerase chain reaction mixture; and

subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles comprising a denaturation treatment, a hybridization treatment, and an extension treatment thereby forming primary extension products, whereby said detecting involves detection of the primary extension products.

11. The method of claim 10 wherein one of the first or second oligonucleotide primers of a primer set comprises a detectable label, whereby said detecting involves detection of labeled primary extension products.

12. The method of claim 10, wherein said detecting comprising:
sequencing said extension products after said subjecting.

13. The method of claim 10, wherein said detecting comprises:
separating the ligated product sequences by size.

14. The method of claim 10, wherein either or both of the first and second oligonucleotide probes in a probe set further comprises a zip-code or a portion thereof, where the zip-codes hybridize to complementary capture oligonucleotides under uniform hybridization conditions.

15. The method of claim 14 further comprising:
providing a collection of capture oligonucleotides, wherein each capture oligonucleotide hybridizes to complementary zip code portions, and comprises a quencher molecule and a detectable label that are separated from each other;
adding the collection of capture oligonucleotides to the polymerase chain reaction mixture; and
hybridizing capture oligonucleotides of the collection to their complementary zip-code portions of the ligated product sequences or complement thereof during said subjecting, whereby the quencher molecule and/or the detectable label are cleaved from the hybridized capture oligonucleotide during said extension treatment whereby said detecting involves the detection of the cleaved detectable label.

16. The method of claim 14 further comprising:
providing a collection of capture oligonucleotides, wherein each capture oligonucleotide hybridizes to complementary zip code portions, and comprises a quencher molecule and a detectable label that are separated from each other;
providing one or more secondary oligonucleotide primer sets capable of hybridizing to the primary extension products;
blending the collection of capture oligonucleotides, the one or more secondary oligonucleotide primer sets, the primary extension products, and a polymerase to form a secondary polymerase chain reaction mixture;
subjecting the secondary polymerase chain reaction mixture to one or more polymerase chain reaction cycles comprising a denaturation treatment, a hybridization

treatment, wherein capture oligonucleotides of the collection hybridize to their complementary zip-code portions of the primary extension products and the secondary oligonucleotide primers hybridize to the primary extension products, and an extension treatment, wherein the hybridized primers are extended thereby forming secondary extension products; and

cleaving the quencher molecule and/or the detectable label from the hybridized capture oligonucleotides during said extension treatment, whereby said detecting involves the detection of the cleaved detectable label.

17. The method of claim 15 or 16, wherein each type of capture oligonucleotide in the collection comprises a nucleotide sequence that differs from nucleotide sequences of other types of capture oligonucleotides in the collection, when aligned to each other, by at least 25%.

18. The method of claim 14 further comprising:
providing a collection of the capture oligonucleotides, wherein each capture oligonucleotide of the collection hybridizes to complementary zip-code portions and
contacting the primary extension products, after said subjecting, with the collection of capture oligonucleotides under conditions effective to hybridize the zip-code portion of each primary extension product to its complementary capture oligonucleotide in the collection with minimal non-specific hybridization and under uniform hybridization conditions, whereby said detecting takes place after hybridization of the primary extension products to their complementary capture oligonucleotides.

19. The method of claim 18, wherein each type of capture oligonucleotide in the collection comprises a nucleotide sequence that is greater than sixteen nucleotides and differs from nucleotide sequences of other types of capture oligonucleotides in the collection, when aligned to each other, by at least 25%.

20. The method of claim 18, wherein one of the oligonucleotide primers of the one or more oligonucleotide primer sets further comprises a detectable label thereby forming labeled primary extension products.

21. The method of claim 18, wherein the collection of capture oligonucleotides is immobilized on a solid support.

22. The method of claim 21 wherein the solid support is in a form selected from the group consisting of beads, slides, discs, membranes, films, microtiter plates, and composites thereof.

23. The method of claim 22, wherein the solid support comprises an array of positions, wherein the collection of capture oligonucleotides is immobilized at the array of positions.

24. The method of claim 14, wherein the first oligonucleotide probe further comprises a first portion of the zip-code and a first tag portion that is 3' to the first zip-code portion, and the second oligonucleotide probe further comprises a second portion of the zip-code and a second tag portion that is 5' to the second zip-code portion, wherein the first and second zip-code portions of an oligonucleotide probe set, when adjacently positioned, form a full-length zip-code, and wherein the first and second tag portions of an oligonucleotide probe set are complementary to each other, said method further comprising:

providing a collection of capture oligonucleotides complementary to a portion of the first zip-code portion and a portion of the second zip-code portion, wherein each capture oligonucleotide of the collection comprises a quencher molecule and a detectable label that are separated from each other;

subjecting the primary extension products and the collection of capture oligonucleotides to conditions effective for (i) the first and second tag portions of a particular primary extension product to hybridize to each other to form hairpinned extension products with adjacently positioned first and second zip-code portions and (ii) the capture oligonucleotides of the collection to hybridize to complementary adjacently positioned first and second zip-code portions of the hairpinned extension products; and

cleaving the quencher molecule or the detectable label from hybridized capture oligonucleotides, whereby said detecting involves detection of the detectable label separated from the quencher molecule.

25. The method of claim 14, wherein (i) the first oligonucleotide probe further comprises a second primer-specific portion that differs for each different oligonucleotide probe set, a first portion of the zip-code, and a first tag portion that is 3' to the first zip-code portion, and (ii) the second oligonucleotide probe further comprises a second portion of the zip-code and a second tag portion that is 5' to the second zip-code portion, wherein the first and second zip-code portions of an oligonucleotide probe set, when adjacently positioned, form a full-length zip-code, and wherein the first and second tag portions of an oligonucleotide probe set are complementary to each other, said method further comprising:

providing one or more secondary primer sets comprising (i) a first secondary oligonucleotide primer having (a) a nucleotide sequence that is the same as the second primer-specific portion of the first oligonucleotide probe, (b) a capture oligonucleotide portion that is complementary to adjacently positioned first and second zip-code portions of an oligonucleotide probe set, (c) a quencher molecule and a detectable label separated by said capture oligonucleotide portion, and (ii) a second secondary oligonucleotide primer having the same nucleotide sequence as the second primary oligonucleotide primer;

blending the primary extension products, the one or more secondary oligonucleotide primer sets, and a polymerase to form a second polymerase chain reaction mixture;

subjecting the second polymerase chain reaction mixture to one or more polymerase chain reaction cycles thereby forming secondary extension products;

subjecting the secondary extension products to conditions effective for the first and second tag portions of a particular secondary extension product to hybridize to each other to form hairpinned secondary extension products with adjacently positioned first and second zip-code portions and (ii) the capture oligonucleotide portion of a particular hairpinned secondary extension product to hybridize to complementary adjacently positioned first and second zip-code portions of the hairpinned extension product; and

cleaving the quencher molecule or the detectable label from the capture oligonucleotide portion of the hairpinned secondary extension products whereby said detecting involves detection of the detectable label separated from the quencher molecule.

26. The method of claim 10, wherein the second oligonucleotides probe further comprises a unitaq detection portion, thereby forming ligated product sequences comprising the 5' primer-specific portion, the target-specific portions, the unitaq detection portion, and the 3' primer-specific portion, said method further comprising

providing one or more unitaq detection probes, wherein each unitaq detection probe hybridizes to a complementary unitaq detection portion and comprises a quencher molecule and a detectable label that are separated from each other;

adding the one or more unitaq detection probes to the polymerase chain reaction mixture; and

hybridizing the one or more unitaq detection probes to complementary unitaq detection portions on the ligated product sequence or complement thereof during said subjecting, whereby the quencher molecule and the detectable label are cleaved from the one or more unitaq detection probes during said extension treatment, whereby said detecting involves the detection of the cleaved detectable label.

27. The method of claim 10, wherein the second oligonucleotides probe further comprises a unitaq detection portion, whereby the primary extension product sequences formed comprise the 5' primer-specific portion, the target-specific portions, the unitaq detection portion, and the 3' primer-specific portion, said method further comprising

providing one or more unitaq detection probes, wherein each unitaq detection probe hybridizes to a complementary unitaq detection portion and comprises a quencher molecule and a detectable label that are separated from each other;

providing one or more secondary oligonucleotide primer sets capable of hybridizing to the primary extension products;

blending the one or more unitaq detection probes, the one or more secondary oligonucleotide primer sets, the primary extension products, and a polymerase to form a secondary polymerase chain reaction mixture;

subjecting the secondary polymerase chain reaction mixture to one or more polymerase chain reaction cycles comprising a denaturation treatment, a hybridization treatment, wherein the one or more unitaq detection probes hybridize to their complementary unitaq detection portions of the extension products and the secondary oligonucleotide primers hybridize to the primary extension products, and an extension treatment, wherein the hybridized primers are extended thereby forming secondary extension products;

cleaving the quencher molecule and/or the detectable label from the one or more hybridized unitaq detection probes during said extension treatment, whereby said detecting involves the detection of the cleaved detectable label.

28. The method of claim 26 or 27, wherein the unitaq detection probe is coupled via a further portion to the 5' end of the secondary oligonucleotide primer.

29. The method of claim 10, wherein (i) the second oligonucleotide probe further comprises a unitaq detection portion, thereby forming ligated product sequences comprising the 5' primer-specific portion, the target-specific portions, the unitaq detection portion, and the 3' primer-specific portion, (ii) the first oligonucleotide primer further comprises a unitaq detection probe that is complementary to the unitaq detection portion of the ligated product sequence, and a quencher molecule and a detectable label separated by said unitaq detection probe, and (iii) the primary extension products formed during said subjecting comprise the detectable label, the unitaq detection probe, the quencher molecule, the 5' primer-specific portion, the target specific portions, the unitaq detection portion, and the 3' primer-specific portion, said method further comprising:

subjecting primary extension products to conditions effective for the unitaq detection probe of a particular extension product to hybridize to its complementary unitaq detection portion, thereby forming hairpinned extension products; and

cleaving the quencher molecule or the detectable label from the unitaq detection probe of the hairpinned extension product, whereby said detecting involves detection of the labeled hairpinned extension product or the cleaved detectable label.

30. The method of claim 1, wherein the first and second oligonucleotide probes of the one or more oligonucleotide probe sets further comprise a first and second tag portion, respectively, wherein the first and second tag portions of an oligonucleotide probe set are complementary to each other, and wherein the first and second tag portions for each different oligonucleotide probe set have different nucleotide sequences, said method further comprising:

subjecting the sample, after said ligating, to conditions effective for the first and second tag portions of a particular ligated product sequence to hybridize, thereby forming hairpinned ligated product sequences; and

removing unligated oligonucleotide probes from the sample after said subjecting.

31. The method of claim 30 further comprising:

providing one or more oligonucleotide primer sets, each set comprising (a) a first oligonucleotide primer comprising the same nucleotide sequence as the 5' primer-specific portion of the ligated product sequence and (b) a second oligonucleotide primer comprising a nucleotide sequence that is complementary to the 3' primer-specific portion of the ligated product sequence;

blending, after said removing, the ligated product sequences, the one or more oligonucleotide primer sets, and a DNA polymerase to form a polymerase chain reaction mixture; and

subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles thereby forming primary extension products, whereby said detecting involves detection of the primary extension products.

32. The method of claim 31, wherein one of the first or second oligonucleotide primers of a primer set comprises a detectable label, whereby said detecting involves detection of labeled primary extension products

33. The method of claim 10 further comprising:

extending the 3' primer-specific portion of the hairpinned second oligonucleotide probe during said subjecting to form an extended hairpinned second oligonucleotide probe that cannot hybridize to the second oligonucleotide primer to prevent second oligonucleotide probe extension or amplification.

34. The method of claim 1, wherein the sample is selected from the group consisting of tissue, cells, serum, blood, plasma, amniotic fluid, sputum, urine, bodily fluids, bodily secretions, bodily excretions, cell-free circulating nucleic acids, cell-free circulating fetal nucleic acids in pregnant woman, circulating tumor cells, tumor, tumor biopsy, and exosomes.

35. The method of claim 1, wherein the one or more target nucleotide sequences are low abundance nucleic acid molecules comprising one or more nucleotide base insertions, deletions, translocations, mutations, and/or damaged nucleotide bases.

36. The method of claim 35, wherein the low abundance nucleic acid molecules with one or more nucleotide base insertions, deletions, translocations, mutations and/or damaged nucleotide bases are identified and distinguished from an excess of nucleic acid molecules in the sample having a similar nucleotide sequence as the low abundance nucleic acid molecules but without the one or more nucleotide base insertions, deletions, translocations, mutations, and/or damaged bases.

37. The method of claim 36, wherein the wherein the first oligonucleotide probe comprises a mismatch nucleotide or nucleotide analog at a base position that is two or three bases from the junction between the second and first oligonucleotide probes.

38. The method of claim 36 wherein the second oligonucleotide probe comprises one or more thiophosphate-modified nucleotide bases that is 3' to the overlapping identical nucleotide at the junction between the second and first oligonucleotide probes.

39. The method of claim 36, wherein the second oligonucleotide probe comprises one or more thiophosphate-modified nucleotide bases that are 5' to the overlapping nucleotide at the junction between the second and first oligonucleotide probes.

40. The method of claim 36, wherein the copy number of one or more low abundance target nucleotide sequences are quantified relative to the copy number from an excess of nucleic acid molecules in the sample having a similar nucleotide sequence as the low abundance nucleic acid molecules.

41. The method of claim 1, wherein the one or more target nucleotide sequences are quantified.

42. The method of claim 41, wherein the one or more target nucleotide sequences are quantified relative to other nucleotide sequences in the sample.

43. The method of claim 41, wherein the relative copy number of one or more target nucleotide sequences are quantified.

44. The method of claim 1, further comprising:
diagnosing or prognosing a disease state based on said identifying.

45. The method of claim 1, further comprising:
distinguishing a genotype or disease predisposition based on said identifying.

46. A kit for identifying a presence of one or more target nucleotide sequences in a sample comprising:
an enzyme having 5' nuclease activity;
a ligase; and
one or more oligonucleotide probe sets, each set comprising (a) a first oligonucleotide probe having a 5' primer-specific portion and a target-specific portion, and (b)

a second oligonucleotide probe having a 3' primer-specific portion, a target specific portion, and a 5' nucleotide sequence, wherein said 5' nucleotide sequence is complementary to at least a portion of the 3' primer-specific portion, wherein the first and second oligonucleotide probes of a probe set are configured to hybridize adjacent to one another on the target nucleotide sequence with a junction between the first and second oligonucleotide probes, and wherein, in a probe set, the target specific portion of the second oligonucleotide probe has an overlapping identical nucleotide at the junction with the first oligonucleotide probe.

47. A method for identifying a presence of one or more target nucleotide sequences in a sample comprising:

providing a sample potentially containing the one or more target nucleotide sequences;

providing one or more coupled oligonucleotide probe sets, each coupled probe set comprising (a) a first oligonucleotide probe having a 5' primer-specific portion and a 3' target-specific portion and, and (b) a second oligonucleotide probe having a 5' target-specific portion and a 3' primer-specific portion, wherein said 5' end of the first oligonucleotide probe is coupled to the 3' end of the second oligonucleotide probe, wherein the coupled oligonucleotide probe further comprises a nucleotide sequence that is complementary to the 3' target specific portion and that hybridizes to said complementary 3' target specific portion to form a hairpinned coupled oligonucleotide probe when said coupled oligonucleotide probe is not hybridized to a target nucleotide sequence, wherein the target-specific portions of the coupled oligonucleotide probe set are configured to hybridize adjacent to one another on the target nucleotide sequence with a junction between them, and wherein the target specific portion of the second oligonucleotide probe has an overlapping identical nucleotide at the junction with the first oligonucleotide probe;

contacting the sample and the one or more coupled oligonucleotide probe sets under conditions effective for the target-specific portions of the first and second oligonucleotide probes to hybridize at adjacent positions in a base specific manner to their corresponding target nucleotide sequences, if present in the sample, wherein upon

hybridization the overlapping identical nucleotide of the second oligonucleotide probe forms a flap at the junction comprising the overlapping identical nucleotide;

cleaving the overlapping identical nucleotide of the second oligonucleotide probe with an enzyme having 5' nuclease activity, thereby liberating a phosphate at the second oligonucleotide probe's 5' end;

ligating first and second oligonucleotide probes of the one or more coupled oligonucleotide probe sets together at the junction to form circular ligated product sequences, wherein each circular ligated product sequence comprises the 5' primer-specific portion, the target specific portions, and the 3' primer-specific portion;

detecting the circular ligated product sequences in the sample; and

identifying the presence of one or more target nucleotide sequences in the sample based on said detecting.

48. The method of claim 47 further comprising:

providing one or more oligonucleotide primer sets, each set comprising (a) a first oligonucleotide primer comprising the same nucleotide sequence as the 5' primer-specific portion of the circular ligated product sequence and (b) a second oligonucleotide primer comprising a nucleotide sequence that is complementary to the 3' primer-specific portion of the circular ligated product sequence;

blending the circular ligated product sequences, the one or more oligonucleotide primer sets, and a DNA polymerase to form a polymerase chain reaction mixture; and

subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles comprising a denaturation treatment, a hybridization treatment, and an extension treatment thereby forming primary extension products, whereby said detecting involves detection of the primary extension products.

49. The method of claim 48, wherein the coupled probe further comprises a polymerase blocker within the portion where the 5' end of the first oligonucleotide probe is coupled to the 3' end of the second oligonucleotide probe, and wherein, during said subjecting, non-circularized primary extension products are formed by said extension treatment.

50. The method of claim 48, wherein the coupled probe further comprises a cleavable nucleotide or nucleotide analogue within the portion where the 5' end of the first oligonucleotide probe is coupled to the 3' end of the second oligonucleotide probe, and wherein, during said subjecting, non-circularized primary extension products are formed by said extension treatment.

51. The method of claim 48, further comprising:
extending the 3' target-specific portion of coupled hairpinned oligonucleotide probes during said subjecting to form an extended coupled hairpinned oligonucleotide probe that occludes binding of the second oligonucleotide primer to its complementary sequence.