

rearrangement. In some embodiments, the chromosomal rearrangement is at least one of a deletion, duplication, inversion, and translocation. In some embodiments, the combined length of sequence portions of the target polynucleotide corresponding to, from 5' to 3' along the target polynucleotide, (i) sequence complementary to the first 3' end, (ii) sequence identical to the second 3' end, and (iii) intervening sequence between (i) and (ii), is 75 nucleotides or less. In some embodiments, at least 50% of concatemers comprise a target polynucleotide of at least 75 nucleotides in length. In some embodiments, the circular target polynucleotide is single-stranded. In some embodiments, the method further comprises sequencing the plurality of amplicons produced in step (c). In some embodiments, the sequencing is performed without selectively purifying amplicons comprising two or more copies of the target polynucleotide from amplicons comprising only one copy of the target polynucleotide. In some embodiments, the method further comprises purifying amplicons in the plurality of amplicons produced in step (c) that comprise two or more copies of the target polynucleotide. In some embodiments, the method further comprises sequencing the purified amplicons. In some embodiments, a plurality of different target polynucleotides is amplified in the same reaction mixture.

[0007a] In another aspect, a reaction mixture for enriching amplicons comprising a concatemer of at least two or more copies of a target polynucleotide, the reaction mixture comprising: (a) a circular target polynucleotide; (b) a first primer comprising a first 3' end that specifically hybridizes to the target polynucleotide via sequence complementarity and a first 5' end comprising a first common sequence that does not specifically hybridize to the target polynucleotide via sequence complementarity; and (c) a second primer comprising a second 3' end that specifically hybridizes to the concatemer via sequence complementarity and a second 5' end comprising a second common sequence that does not specifically hybridize to the concatemer via sequence complementarity, wherein the first common sequence and the second common sequence each comprise at least 10 contiguous nucleotides at a 5' end and are at least 90% identical when optimally aligned.

[0008] In another aspect, a reaction mixture for enriching amplicons comprising a concatemer of at least two or more copies of a target polynucleotide is disclosed. In one embodiment, the reaction mixture comprises (a) a circular target polynucleotide, (b) a first primer comprising a first 3' end that specifically hybridizes to the target polynucleotide via sequence complementarity and a first 5' end comprising a first common sequence that does not specifically hybridize to the target polynucleotide via sequence complementarity, and (c) a second primer comprising a second 3' end that specifically hybridizes to the concatemer via

sequence complementarity and a second 5' end comprising a second common sequence that does not specifically hybridize to the concatemer via sequence complementarity, wherein the first common sequence and the second common sequence each comprise at least 10 contiguous nucleotides at a 5' end and are at least 90% identical when optimally aligned, and the concatemer is an extension product of the first primer. In some embodiments, the first common sequence and the second common sequence are identical. In some embodiments, the reaction mixture is contained in a container. In some embodiments, the container is a well, a plate, a tube, a chamber, a flow cell, or a chip. In some embodiments, the reaction mixture further comprises a third primer having a sequence that specifically hybridizes to the first common sequence or the second common sequence via sequence complementarity. In some embodiments, the first common sequence, the second common sequence, and the hybridizing

CLAIMS

WHAT IS CLAIMED IS:

1. A method for enriching amplicons comprising a concatemer of at least two or more copies of a target polynucleotide, the method comprising:
 - (a) generating a concatemer comprising a single-stranded polynucleotide from a circular target polynucleotide by extension of a first primer, the first primer comprising a first 3' end that specifically hybridizes to the target polynucleotide via sequence complementarity and a first 5' end comprising a first common sequence that does not specifically hybridize to the target polynucleotide via sequence complementarity;
 - (b) generating a plurality of extension products containing one or more copies of the target polynucleotide by extension of a second primer comprising a second 3' end that specifically hybridizes to the concatemer via sequence complementarity and a second 5' end comprising a second common sequence that does not specifically hybridize to the concatemer via sequence complementarity, wherein the first common sequence and the second common sequence each comprise at least 10 contiguous nucleotides at a 5' end and are at least 90% identical when optimally aligned; and
 - (c) amplifying the plurality of extension products of step (b) under conditions to generate a plurality of amplicons, wherein amplicons comprising at least 2 or more copies of the target polynucleotide are enriched.
2. The method of claim 1, wherein the first common sequence and the second common sequence are identical.
3. The method of claim 1, wherein in the amplifying of step (c) comprises primer extension of a third primer, wherein the third primer comprises a sequence that specifically hybridizes to the first common sequence or the second common sequence via sequence complementarity.
4. The method of claim 1, wherein the amplifying step of (c) yields a percentage of amplicons having two or more copies of the target polynucleotide that is greater than a percentage of amplicons having fewer than two copies of the target polynucleotide.
5. The method of claim 4, wherein the percentage of amplicons having two or more copies of the target polynucleotide is at least 60%.
6. The method of claim 1, wherein the extension products form stem loop structures comprising intramolecular hybridization between (i) the first common sequence and a complement of the second common sequence, or (ii) the second common sequence and a complement of the first common sequence.

7. The method of claim 1, wherein the circular target polynucleotide is a circularized cell free DNA.
8. The method of claim 1, wherein the circular target polynucleotide is a circularized fragment of genomic DNA.
9. The method of claim 1, wherein the circular target polynucleotide is single-stranded.
10. The method of claim 1, further comprising sequencing the plurality of amplicons produced in step (c).
11. The method of claim 1, wherein a plurality of different target polynucleotides are amplified in the same reaction mixture.
12. A reaction mixture for enriching amplicons comprising a concatemer of at least two or more copies of a target polynucleotide, the reaction mixture comprising:
 - (a) a circular target polynucleotide;
 - (b) a first primer comprising a first 3' end that specifically hybridizes to the target polynucleotide via sequence complementarity and a first 5' end comprising a first common sequence that does not specifically hybridize to the target polynucleotide via sequence complementarity; and
 - (c) a second primer comprising a second 3' end that specifically hybridizes to the concatemer via sequence complementarity and a second 5' end comprising a second common sequence that does not specifically hybridize to the concatemer via sequence complementarity, wherein the first common sequence and the second common sequence each comprise at least 10 contiguous nucleotides at a 5' end and are at least 90% identical when optimally aligned.
13. The reaction mixture of claim 12, wherein the first common sequence and the second common sequence are identical.
14. The reaction mixture of claim 12, further comprising a third primer having a sequence that specifically hybridizes to the first common sequence or the second common sequence via sequence complementarity.
15. The reaction mixture of claim 14, wherein the first common sequence, the second common sequence, and the hybridizing sequence of the third primer all have melting temperatures (T_m 's) within $\pm 5^\circ\text{C}$ of one another.
16. The reaction mixture of claim 12, wherein the first common sequence and the second common sequence each comprise at least 15 nucleotides.

17. The reaction mixture of claim 12, wherein the circular target polynucleotide is a circularized cell free DNA.

18. The reaction mixture of claim 12, wherein the circular target polynucleotide is a circularized fragment of genomic DNA.

19. The reaction mixture of claim 12, wherein the combined length of sequence portions of the target polynucleotide corresponding to, from 5' to 3' along the target polynucleotide, (i) sequence complementary to the first 3' end, (ii) sequence identical to the second 3' end, and (iii) intervening sequence between (i) and (ii), is 75 nucleotides or less.