POLYNUCLEOTIDES, REAGENTS, AND METHODS FOR NUCLEIC ACID HYBRIDIZATION

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. provisional patent application number 62/673,704 filed on May 18, 2018, U.S. provisional patent application number 62/810,343 filed on February 25, 2019, U.S. provisional patent application number 62/814,749 filed on March 6, 2019, U.S. provisional patent application number 62/675,647 filed May 23, 2018, U.S. provisional patent application number 62/810,293 filed February 25, 2019, U.S. provisional patent application number 62/814,753 filed March 6, 2019, U.S. provisional patent application number 62/833,440 filed April 12, 2019, each of which is incorporated herein by reference in its entirety.

BACKGROUND

[0002] Highly efficient chemical gene synthesis with high fidelity and low cost has a central role in biotechnology and medicine, and in basic biomedical research. De novo gene synthesis is a powerful tool for basic biological research and biotechnology applications. While various methods are known for the synthesis of relatively short fragments in a small scale, these techniques often suffer from scalability, automation, speed, accuracy, and cost.

INCORPORATION BY REFERENCE

[0003] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF SUMMARY

[0003a] In one aspect, disclosed herein is a composition for nucleic acid hybridization comprising: a first polynucleotide library; a second polynucleotide library, wherein at least one polynucleotide in the first library is at least partially complimentary to at least one polynucleotide of the second library; and an additive, wherein the additive comprises an oil that reduces off-target hybridization of the at least one polynucleotide of the first library with the at least one polynucleotide of the second library by decreasing a local concentration of the first polynucleotide library or the second polynucleotide library at an air-liquid interface.

[0004] Provided herein are methods for sequencing genomic DNA, comprising: contacting a composition comprising a first polynucleotide library comprising at least 30,000 polynucleotides, wherein each of the at least 30,000 polynucleotides is present in an amount such that, following hybridization with genomic fragments and sequencing of the hybridized genomic fragments, the polynucleotide library provides a read depth of at least 80 percent of the bases of the genomic fragments corresponding to the polynucleotides; and a total number of sequencing reads, wherein the total number of sequencing reads are capable of covering 100 percent of each of the bases of the genomic fragments corresponding to the polynucleotides at a theoretical read depth, wherein the ratio of the read depth of at least 80 percent of the bases of the genomic fragments corresponding to the polynucleotides to the theoretical read depth is at least 0.5 with a plurality of genomic

CLAIMS

1. A composition for nucleic acid hybridization comprising:

   a first polynucleotide library;

   a second polynucleotide library, wherein at least one polynucleotide in the first library is at least partially complimentary to at least one polynucleotide of the second library; and

   an additive, wherein the additive comprises an oil that reduces off-target hybridization of the at least one polynucleotide of the first library with the at least one polynucleotide of the second library by decreasing a local concentration of the first polynucleotide library or the second polynucleotide library at an air-liquid interface.

2. The composition of claim 1, wherein the additive is mineral oil, a nucleotide triphosphate, polyether, or urea.
3. The composition of any one of claims 1-2, wherein the additive is a hydrocarbon comprising at least six carbon atoms.
4. The composition of any one of claims 1-3, wherein the additive is silicon oil.
5. The composition of claim 1, wherein the oil is derived from plant sources.
6. The composition of any one of claims 1-4, wherein the composition further comprises dimethyl sulfoxide.
7. The composition of any one of claims 1-5, wherein the composition does not comprise a formamide.
8. The composition of any one of claims 1-6, wherein the size of the first polynucleotide library is less than 10 million bases.
9. The composition of any one of claims 1-6, wherein the size of the first polynucleotide library is less than 1 million bases.
10. The composition of any one of claims 1-6, wherein the size of the first polynucleotide library is less than 0.5 million bases.
11. The composition of any one of claims 1-10, wherein the first polynucleotide library comprises as least one exon sequence.
12. The composition of any one of claims 1-11, wherein the first polynucleotide library comprises polynucleotides encoding for at least 10 genes.
13. The composition of any one of claims 1-11, wherein the first polynucleotide library comprises polynucleotides encoding for at least 100 genes.

14. The composition of any one of claims 1-13, wherein the first polynucleotide library comprises at least one genomic fragment.
15. The composition of any one of claims 1-13, wherein the first polynucleotide library comprises RNA, DNA, cDNA, or genomic DNA.
16. The composition of any one of claims 1-15, wherein the first polynucleotide library comprises genomic DNA.
17. The composition of any one of claims 1-16, wherein the additive decreases off-target binding by at least 10%.
18. The composition of any one of claims 1-16, wherein the additive decreases off-target binding by at least 20%.
19. The composition of any one of claims 1-16, wherein the additive decreases off-target binding by at least 30%.
20. The composition of any one of claims 1-19, wherein the off-target binding is random off-target binding.