Claims

1. A method of tagging DNA-encoded chemical libraries, said method comprising binding a first functional group of a bifunctional linker to an initiator oligonucleotide at the 5' end of said initiator oligonucleotide, wherein said initiator oligonucleotide bound to said bifunctional linker forms a hairpin structure, and binding a second functional group of said bifunctional linker to a component of said chemical library.

2. The method of claim 1, wherein said initiator oligonucleotide comprises a first identifier region.

3. The method of claim 2, wherein said initiator oligonucleotide comprises a second identifier region hybridizes to said first identifier region of the initiator oligonucleotide.

4. The method of claim 3, wherein the second identifier region comprises a fluorescent tag or biotin label.

5. The method of claim 4, wherein said second identifier region is not amplified prior to analysis following a selection step.

6. The method of any one of claims 1-5, wherein said bifunctional linker, initiator oligonucleotide, first identifier region, or second identifier region is modified to increase solubility of a member of said DNA-encoded chemical library in organic conditions.

7. A method of creating DNA-encoded libraries, said method comprising:

(a) creating a first diversity node;

(b) encoding said first diversity node in separate vessels;

(c) pooling said first diversity node; and

(d) splitting said pooled first diversity node into a second set of separate vessels, wherein said first diversity node reacts to form a second diversity node.

8. The method of claim 7, wherein the second diversity node is not encoded and pooled.

Claims

1. A method of tagging DNA-encoded chemical libraries, said method comprising:

(a) binding a first functional group of a bifunctional linker to an initiator oligonucleotide at the 5' end of said initiator oligonucleotide, wherein said initiator oligonucleotide bound to said bifunctional linker forms a hairpin structure;

(b) binding a second functional group of said bifunctional linker to a component of said chemical library; and

(c) ligating an identifier region at the 3' end of said initiator oligonucleotide,

wherein said bifunctional linker or initiator oligonucleotide is modified to increase solubility of a member of said DNA-encoded chemical library in organic conditions.

2. The method of claim 1, wherein said initiator oligonucleotide comprises an identifier region.

3. The method of claim 1, wherein said bifunctional linker is modified to increase solubility of a member of said DNA-encoded chemical library in organic conditions.

4. The method of claim 3, wherein the modified bifunctional linker comprises one or more of an alkyl chain, a polyethylene glycol unit, or a branched species with positive charges.

5. The method of claim 1, wherein said initiator oligonucleotide is modified to increase solubility of a member of said DNA-encoded chemical library in organic conditions.

6. The method of claim 5, wherein said initiator oligonucleotide comprises an identifier region, and wherein said identifier region is modified to increase solubility of a member of said DNA-encoded chemical library in organic conditions.

7. The method of claim 5, wherein the modified initiator oligonucleotide comprises one or more of a modified nucleotide.

8. The method of claim 7, wherein said modified nucleotide comprises a modified nucleoside, wherein said modified nucleoside is modified at the C5 position of a Thymine or Cytidine base.

9. The method of claim 7, wherein said modified initiator oligonucleotide comprises one or more of a modified sugar and/or a modified phosphate group.

10. The method of claim 1, wherein the combination of said initiator oligonucleotide and linker has an octanol:water coefficient from 1.0 to 2.5.

11. A method of creating DNA-encoded libraries, said method comprising:

(a) binding a first functional group of a bifunctional linker to an initiator oligonucleotide at the 5' end of said initiator oligonucleotide, wherein said bifunctional linker or initiator oligonucleotide is modified to increase solubility of a member of said DNA-encoded chemical library in organic conditions;

(b) creating a first diversity node, wherein said creating comprises binding a second functional group of said bifunctional linker to a scaffold;

(c) encoding said first diversity node in separate vessels, wherein said encoding comprises ligating an identifier region at the 3' end of said initiator oligonucleotide;

(d) pooling said first diversity node; and

(e) splitting said pooled first diversity node into a second set of separate vessels, wherein said first diversity node reacts to form a second diversity node.

12. The method of claim 11, wherein the second diversity node is not encoded and pooled.