group operatively associates with said first tag via a first linkage wherein said first linkage is a cross-linking oligonucleotide comprising a cyanovinylcarbazole that spans the junction between two adjacent tags and that operatively associates with said two adjacent tags via one or more reversible co-reactive groups.

In another aspect, there is provided a complex comprising: (i) a chemical entity comprising one or more scaffolds or one or more building blocks; (ii) *n* number of oligonucleotide tags having *n-1* linkages, wherein *n* is an integer between 1 and 10, and wherein each of said linkages is between two adjacent tags and each tag encodes the identity of at least one of said one or more scaffolds or building blocks; and (iii) a headpiece having a first functional group operatively associated with said chemical entity and a second functional group operatively associated with at least one of said *n* number of tags via a first linkage, wherein at least one of said first linkage and *n-1* linkages is a cross-linking oligonucleotide comprising a cyanovinylcarbazole that spans the junction between two adjacent tags and that operatively associates with said two adjacent tags via one or more reversible co-reactive groups.

In some embodiments, *n* is between 1 and 2, 1 and 3, 1 and 4, 1 and 5, 1 and 6, 1 and 7, 1 and 8, 1 and 9, 1 and 10, 1 and 12, 1 and 15, 1 and 18, 1 and 20, 2 and 3, 2 and 4, 2 and 5, 2 and 6, 2 and 7, 2 and 8, 2 and 9, 2 and 10, 2 and 12, 2 and 15, 2 and 18, 2 and 20, 3 and 4, 3 and 5, 3 and 6, 3 and 7, 3 and 8, 3 and 9, 3 and 10, 3 and 12, 3 and 15, 3 and 18, 3 and 20, 4 and 5, 4 and 6, 4 and 7, 4 and 8, 4 and 9, 4 and 10, 4 and 12, 4 and 15, 4 and 18, or 4 and 20.

In some embodiments, the polymerase has reduced ability to read or translocate through at least about 10% (e.g., about 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or even 100%, as compared to control) of the first linkage and *n-1* linkages. In particular embodiments, the polymerase has reduced ability to read or translocate through about 10% to about 100% of the first linkage and *n-1* linkages (e.g., 20% to 100%, 25% to 100%, 50% to 100%, 75% to 100%, 90% to 100%, 95% to 100%, 10% to 95%, 20% to 95%, 25% to 95%, 50% to 95%, 75% to 95%, 90% to 95%, 10% to 90%, 20% to 90%, 25% to 90%, 50% to 90%, or 75% to 90%, as compared to control (e.g., as compared to a control oligonucleotide lacking the linkage)).

In some embodiments, one or more tags include a 5'-connector at the 5'-terminus of the one or more tags and a 3'-connector at the 3'-terminus of the one or more tags. In particular embodiments, each 5'-connector and/or each 3'-connector includes the same sequence. In other embodiments, each 5'-connector and/or each 3'-connector include a different sequence.

In some embodiments, the first linkage and/or *n-1* linkages are at least about 3 angstroms in length (e.g., at least about 5, 8, 10, 15, 20, 30, 35, 40, 50, 60, 65 or 70 angstroms). In some embodiments, the first linkage and/or *n-1* linkages are less than about 30 angstroms in length (e.g., less than about 25, 20, 15, or 10 angstroms).

In some embodiments, a DNA polymerase and/or an RNA polymerase (e.g., as described herein) has reduced ability to read or translocate through the first linkage and/or *n-1* linkages.

(b) binding said first functional group of said headpiece to a first component of said chemical entity, wherein said headpiece is directly connected to said first component or said headpiece is indirectly connected to said first component by a bifunctional spacer; and

(c) binding said second functional group of said headpiece to a first oligonucleotide tag via a first linkage to form a complex, wherein said first linkage is a cross-linking oligonucleotide comprising a cyanovinylcarbazole that spans the junction between two adjacent tags and that operatively associates with said two adjacent tags via one or more reversible co-reactive groupswherein said steps (b) and (c) can be performed in any order and wherein said first tag encodes for the binding reaction of said step (b), thereby providing a tagged library.

In another embodiment, the disclosure features a method of tagging a first library including an encoded chemical entity, the method including: (a) providing a headpiece having a first functional group and a second functional group (e.g., where the headpiece optionally encodes information); (b) binding the first functional group of the headpiece to a first component of the chemical entity, where the headpiece is directly connected to the first component or the headpiece is indirectly connected to the first component by a bifunctional spacer; and (c) binding the second functional group of the headpiece to a first oligonucleotide tag via a first linkage to form a complex, where a polymerase has reduced ability to read or translocate through the first linkage; where the steps (b) and (c) can be

performed in any order and where the first tag encodes for the binding reaction of the step (b), thereby providing a tagged library.

In one aspect, there is provided a method of tagging a first library comprising an encoded chemical entity, said method comprising:

(a) providing a headpiece having a first functional group and a second functional group;

(b) binding said first functional group of said headpiece to a first component of said chemical entity, wherein said headpiece is directly connected to said first component or said headpiece is indirectly connected to said first component by a bifunctional spacer;

(c) binding said second functional group of said headpiece to a first oligonucleotide tag via a first linkage;

(d) binding n_c number of additional components of said chemical entity, wherein n_c is an integer between 1 and 10; and

(e) binding n_t number of additional oligonucleotide tags having n_t linkages to form a complex, wherein n_t is an integer between 1 and 10 and wherein each of said linkages is between two adjacent tags and each tag encodes the identity of at least one of said components;

wherein at least one of said first linkage and n_t linkages is a cross-linking oligonucleotide comprising a cyanovinylcarbazole that spans the junction between two adjacent tags and that operatively associates with said two adjacent tags via one or more reversible co-reactive groups; and

wherein said steps (b) and (c) can be performed in any order and wherein said first tag encodes for the binding reaction of said step (b); wherein said steps (d) and (e) can be performed in any order and wherein each additional tag encodes for the binding reaction of each additional component of said step (d), thereby providing a tagged library.

In yet another embodiment, the disclosure features a method of tagging a first library including an encoded chemical entity, the method including: (a) providing a headpiece having a first functional group and a second functional group (e.g., where the headpiece optionally encodes information); (b) binding the first functional group of the headpiece to a first component of the chemical entity, where the headpiece is directly connected to the first component or the headpiece is indirectly connected to the first component by a bifunctional spacer; (c) binding the second functional group of the headpiece to a first oligonucleotide tag via a first linkage; (d) binding n_c number of additional components of the chemical entity, where n_c is an integer between 1 and 10; and (e) binding n_t number of additional oligonucleotide tags having n_t linkages to form a complex, where n_t is an integer between 1 and 10, where each of the linkages is between two adjacent tags and where each tag encodes the identity of at least one of the components; where a polymerase has reduced ability to read or translocate through at least one of the first linkage and n_t linkages; and where the steps (b) and (c) can be performed in any order and where the first tag encodes for the binding reaction of the step (b); where the steps (d) and (e) can be performed in any order and where each additional tag encodes for the binding reaction of each additional component of the step (d), thereby providing a tagged library.

In some embodiments, n_c and n_t are each independently an integer between 1 and 2, 1 and 3, 1 and 4, 1 and 5, 1 and 6, 1 and 7, 1 and 8, 1 and 9, 1 and 10, 1 and 12, 1 and 15, 1 and 18, 1 and 20, 2 and 3, 2 and 4, 2 and 5, 2 and 6, 2 and 7, 2 and 8, 2 and 9, 2 and 10, 2 and 12, 2 and 15, 2 and 18, 2 and 20, 3 and 4, 3 and 5, 3 and 6, 3 and 7,

Claims

1. A complex comprising:

(i) a chemical entity comprising one or more scaffolds or one or more building blocks;

(ii) a first oligonucleotide tag encoding the identity of at least one of said one or more scaffolds or building blocks; and

(iii) a headpiece having a first functional group and a second functional group, wherein said first functional group operatively associates with said chemical entity and said second functional group operatively associates with said first tag via a first linkage wherein said first linkage is a cross-linking oligonucleotide comprising a cyanovinylcarbazole that spans the junction between two adjacent tags and that operatively associates with said two adjacent tags via one or more reversible co-reactive groups.

2. A complex comprising:

(i) a chemical entity comprising one or more scaffolds or one or more building blocks;

(ii) *n* number of oligonucleotide tags having *n-1* linkages, wherein *n* is an integer between 1 and 10, and wherein each of said linkages is between two adjacent tags and each tag encodes the identity of at least one of said one or more scaffolds or building blocks; and

(iii) a headpiece having a first functional group operatively associated with said chemical entity and a second functional group operatively associated with at least one of said *n* number of tags via a first linkage,

wherein at least one of said first linkage and *n-1* linkages is a cross-linking oligonucleotide comprising a cyanovinylcarbazole that spans the junction between two adjacent tags and that operatively associates with said two adjacent tags via one or more reversible co-reactive groups.

3. The complex of claim 1 or 2, wherein one or more tags comprise a 5'-connector at the 5'-terminus of said one or more tags and a 3'-connector at the 3'-terminus of said one or more tags.

4. The complex of claim 3, wherein each 5'-connector comprises the same sequence.

5. The complex of claim 3 or 4, wherein each 3'-connector comprises the same sequence.

6. The complex of claim 3, wherein each 5'-connector and/or each 3'-connector comprise a different sequence.

7. The complex of any one of claims 1 to 6, wherein said first linkage and/or *n-1* linkages are at least about 3 angstroms in length.

8. The complex of any one of claims 1 to 7, wherein said first linkage and/or *n-1* linkages are less than about 30 angstroms in length.

9. The complex of any one of claims 1 to 8, wherein less than about 50% of said first linkage and *n-1* linkages comprise an enzymatic linkage.

10. The complex of any one of claims 1 to 9, wherein said first linkage and/or *n-1* linkages comprise a chemical linkage.

11. The complex of any one of claims 1 to 10, wherein at least one photo-reactive group, or intercalating moiety is present in a 5'-connector at or in proximity to the 5'-terminus of said tag and/or in a 3'-connector at or in proximity to the 3'-terminus of said tag.

12. The complex of claim 11, wherein the sequence of at least one of said 5'-connector is complementary to the sequence of the adjacent 3'-connector or is identical or is sufficiently similar to allow for hybridization to the same complementary oligonucleotide on either side of the junction in separate hybridization events.

13. The complex of any one of claims 1 to 12, wherein said chemical entity is operatively associated to said headpiece via a bifunctional spacer.

14. The complex of any one of claims 1 to 13, wherein said chemical entity is covalently attached to said headpiece.

15. The complex of any one of claims 1 to 14, wherein said headpiece comprises an oligonucleotide selected from the group consisting of a double-stranded oligonucleotide, a single-stranded oligonucleotide, or a hairpin oligonucleotide.

16. The complex of claim 15, wherein said headpiece comprises a primer-binding region.

17. The complex of any one of claims 1 to 16, further comprising one or more first library-identifying tag(s), use tag(s), and/or origin tag(s).

18. The complex of any one of claims 1 to 17, wherein said complex comprises between 2 to 20 tags.

19. The complex of any one of claims 1 to 18, wherein each of said tags comprises from 5 to 75 nucleotides.

20. The complex of any one of claims 1 to 19, wherein each of said tags within an individual tag set comprises about the same mass.

21. The complex of any one of claims 1 to 20, wherein said complex comprises RNA, DNA, modified DNA, and/or modified RNA.

22. The complex of claim 21, wherein said modified DNA or modified RNA is PNA, LNA, GNA, TNA, or a mixture thereof within the same oligonucleotide.

23. The complex of any one of claims 1 to 22, further comprising a tailpiece.

24. A library comprising one or more complexes of any one of claims 1 to 23.

25. The library of claims 1 to 24, wherein said library comprises a plurality of headpieces.

26. The library of claim 25, wherein each headpiece of said plurality of headpieces comprises an identical sequence region and a different encoding region.

27. The library of claim 26, wherein said identical sequence region is a primer-binding region.

28. The library of claim 26 or 27, wherein said different encoding region is a first tag that encodes for use of the library, origin of the library, identity of the library, history of the library, a linkage, a spacer, or addition of a first component; or an oligonucleotide sequence that facilitates hybridization, amplification, cloning, or sequencing technologies.

29. The library of any one of claims 24 to 28, comprising between about 10^2 to 10^{20} complexes.

30. The library of any one of claims 24 to 29, wherein each complex is different.

31. A method of tagging a first library comprising an encoded chemical entity, said method comprising:

(a) providing a headpiece having a first functional group and a second functional group;

(b) binding said first functional group of said headpiece to a first component of said chemical entity, wherein said headpiece is directly connected to said first component or said headpiece is indirectly connected to said first component by a bifunctional spacer; and

(c) binding said second functional group of said headpiece to a first oligonucleotide tag via a first linkage to form a complex, wherein said first linkage is a cross-linking oligonucleotide comprising a cyanovinylcarbazole that spans the junction between two adjacent tags and that operatively associates with said two adjacent tags via one or more reversible co-reactive groups

wherein said steps (b) and (c) can be performed in any order and wherein said first tag encodes for the binding reaction of said step (b), thereby providing a tagged library.

32. A method of tagging a first library comprising an encoded chemical entity, said method comprising:

(a) providing a headpiece having a first functional group and a second functional group;

(b) binding said first functional group of said headpiece to a first component of said chemical entity, wherein said headpiece is directly connected to said first component or said headpiece is indirectly connected to said first component by a bifunctional spacer;

(c) binding said second functional group of said headpiece to a first oligonucleotide tag via a first linkage;

(d) binding n_c number of additional components of said chemical entity, wherein n_c is an integer between 1 and 10; and

(e) binding n_t number of additional oligonucleotide tags having n_t linkages to form a complex, wherein n_t is an integer between 1 and 10 and wherein each of said linkages is between two adjacent tags and each tag encodes the identity of at least one of said components;

wherein at least one of said first linkage and nt linkages is a cross-linking oligonucleotide comprising a cyanovinylcarbazole that spans the junction between two adjacent tags and that operatively associates with said two adjacent tags via one or more reversible co-reactive groups;

and

wherein said steps (b) and (c) can be performed in any order and wherein said first tag encodes for the binding reaction of said step (b); wherein said steps (d) and (e) can be performed in any order and wherein each additional tag encodes for the binding reaction of each additional component of said step (d), thereby providing a tagged library.

33. The method of claim 31 or 32, wherein said first component and/or additional components comprise a scaffold or a building block.

34. The method of any one of claims 31 to 33, wherein step (b) comprises binding said headpiece indirectly to said first component via a bifunctional spacer.

35. The method of any one of claims 31 to 34, further comprising binding a use tag and/or an origin tag to said complex.

36. The method of any one of claims 31 to 35, further comprising binding a first library-identifying tag to said complex.

37. The method of claim 36, further comprising providing a second library and combining said first library with said second library.

38. The method of any one of claims 31 to 37, further comprising binding a tailpiece to said complex.

39. The method of any one of claims 31 to 38, further comprising performing split-and-pool synthesis in one or more steps, separating one or more complexes, and/or purifying one or more complexes.

40. The method of any one of claims 31 to 38, further comprising a complex of any one of claims 1 to 23 and/or a library of any one of claims 24 to 30.

41. A method of screening a plurality of chemical entities, said method comprising:

(a) contacting a target with a complex of any one of claims 1 to 23 and/or a library of any one of claims 24 to 30; and

(b) selecting one or more complexes having a predetermined characteristic for said target, as compared to a control, thereby screening said chemical entity.

42. The method of claim 41, where said predetermined characteristic comprises increased binding for said target, as compared to a control.

43. The method of claim 41 or 42, wherein, prior to step (a), one or more operations are performed, said operations being selected from the list consisting of: annealing one or more relay primers with said complex, wherein said one or more relay primers span said first linkage and/or *n-1* linkages; extending said relay primers using a polymerase to produce oligonucleotide fragments; and ligating said oligonucleotide fragments to produce a template.

44. A method of determining the nucleotide sequence of a complex of any one of claims 1 to 23, said method comprising:

(a) annealing one or more relay primers with said complex, wherein said one or more relay primers span said first linkage and/or *n-1* linkages;

(b) extending said relay primers using a polymerase to produce oligonucleotide fragments;

(c) ligating said oligonucleotide fragments to produce a template;

(d) amplifying said template by polymerase chain reaction to produce an amplified mix; and

(e) sequencing said amplified mix to determine the sequence of said complex.

45. The method of claim 44, wherein said complex comprises a 5'-connector at the 5'-terminus of one or more tags and a 3'-connector at the 3'-terminus of one or more tags, and wherein each of said one or more relay primers hybridizes to adjacent 5'- and 3'-connectors.

46. The method of claim 45, wherein each 5'-connector comprises the same sequence.

47. The method of claim 46, wherein each 3'-connector comprises the same sequence.

48. The method of any one of claims 45 to 47, wherein the sequence of at least one of said 5'-connector is complementary to the sequence of the adjacent 3'-connector or is identical

or is sufficiently similar to allow hybridization to the same complementary oligonucleotide on either side of the junction in separate hybridization events.

49. The method of claim 48, further comprising hybridizing said 5'-connecter to said adjacent 3'-connector.

50. The method of any one of claims 45 to 49, wherein each relay primer for a specific junction between the 5'- and 3'-connectors comprises the same sequence.

51. A method of determining the nucleotide sequence of a complex of any one of claims 1 to 23, said method comprising:

(a) providing said complex;

(b) releasing said cross-linking oligonucleotide to produce a template;

(c) amplifying said template by polymerase chain reaction to produce an amplified mix; and

(d) sequencing said amplified mix to determine the sequence of said complex.

52. The method of claim 51, wherein a portion of said cross-linking oligonucleotide hybridizes to the termini of two adjacent tags, thereby producing a nick or a gap between said two adjacent tags.

53. The method of claim 52, further comprising ligating said tags using a chemical process or an enzymatic process prior to step (b).

54. The method of claim 53, wherein said chemical process or enzymatic process comprises 5'-phosphorylation.

55. The method of any one of claims 44 to 54, further comprising repairing said template prior to said optional amplifying step or said sequencing step.

56. The method of claim 55, wherein said repairing step comprises modifying at least one of said first linkage and/or *n-1* linkages to be a repaired linkage capable of being read or translocated through by a polymerase.

57. The method of claim 56, wherein said polymerase can read or translocate through at least 90% of said repaired linkages.

58. The method of any one of claims 55 to 57, wherein said repairing step comprises providing said template with a repair enzyme.

59. The method of claim 58, wherein said repair enzyme is a photolyase, a glycosylase, an endonuclease, a Flap endonuclease, an apurinic/apyrimidinic (AP) endonuclease, a poly ADP ribose polymerase, or a methyltransferase.