CLAIMS

1. A method of modifying a nucleic acid, the method comprising:

(a) providing a single stranded deoxyribonucleic acid (ssDNA) and a nucleoside triphosphate comprising a modified base; and

(b) contacting the ssDNA and the nucleoside triphosphate comprising the modified base with a recombinant terminal deoxynucleotidyl transferase (TdT) to generate a ssDNA scaffold, wherein the ssDNA scaffold comprises the ssDNA incorporated with one or more nucleotides comprising the modified base from the nucleoside triphosphate,

wherein the recombinant TdT comprises an amino acid sequence that is at least 80% identical to SEQ ID NO: 1, and wherein the recombinant TdT comprises one or more amino acid substitution mutations at one or more positions functionally equivalent to Glu191, Lys193, Glu194, Asp242, Lys287, Phe296, Met299, Thr342, and His420 in the *Bos taurus* TdT of SEQ ID NO: 12.

2. The method of claim 1, further comprising:

(c) contacting the ssDNA scaffold with a first adapter oligonucleotide comprising a first adapter sequence and a second adapter oligonucleotide comprising a second adapter sequence to generate a nucleic acid carrier comprising the ssDNA scaffold attached to the first adapter oligonucleotide and the second adapter oligonucleotide.

3. The method of claim 1, wherein contacting the ssDNA scaffold with the first adapter oligonucleotide comprises contacting the ssDNA scaffold with a first adapter comprising the first adapter oligonucleotide and a first polymer.

4. The method of claim 1, wherein contacting the ssDNA scaffold with the second adapter oligonucleotide comprises contacting the ssDNA scaffold with a second adapter comprising the second adapter oligonucleotide and a second polymer.

5. The method of claim 2, wherein the ssDNA scaffold comprises a third polymer.

6. The method of claim 2, further comprising:

(d) providing a nucleic acid template comprising the first adapter sequence, or a reverse complement thereof, the second adapter sequence, or a reverse complement thereof, and a nucleic acid hybridization sequence;

(e) contacting the nucleic acid carrier with the nucleic acid template to generate the

nucleic acid carrier having the nucleic acid template hybridized to a template capture site of the nucleic acid carrier via the nucleic acid hybridization sequence of the nucleic acid template;

(f) performing amplification on the nucleic acid carrier hybridized with the nucleic acid template to generate a plurality of amplified nucleic acids each comprising the first adapter oligonucleotides and the second adapter oligonucleotides extended to comprise a sequence of the nucleic acid template, or a reverse complement thereof; and

(g) determining the sequence of the nucleic acid template using the plurality of amplified nucleic acids.

7. A method of modifying a nucleic acid, the method comprising:

(a) providing a first nucleic acid and a first nucleoside triphosphate comprising a first modified base; and

(b) contacting the first nucleic acid and the first nucleoside triphosphate comprising the first modified base with a recombinant terminal deoxynucleotidyl transferase (TdT) for a first reaction time at a first temperature in a first reaction to generate a second nucleic acid, wherein the second nucleic acid comprises the first nucleic acid incorporated with one or more first nucleotides comprising the first modified base from the first nucleoside triphosphate,

wherein the recombinant TdT comprises an amino acid sequence that is at least 80% identical to SEQ ID NO: 1, and wherein the recombinant TdT comprises one or more amino acid substitution mutations at one or more positions functionally equivalent to Glu191, Lys193, Glu194, Asp242, Lys287, Phe296, Met299, Thr342, and His420 in the *Bos taurus* TdT of SEQ ID NO: 12.

8. The method of claim 7, wherein one or more of the first nucleic acid and the second nucleic acid comprise a single stranded nucleic acid, a double stranded nucleic acid with a 3’ overhang, a double stranded nucleic acid with a 3’ recess, or a combination thereof.

9. The method of claim 7, wherein the first modified base of the first nucleoside triphosphate comprises a modified adenine, a modified guanine, a modified cytosine, a modified thymine, or a modified uracil.

10. The method of claim 7, wherein the first nucleoside triphosphate comprises the first modified base and a first accessory oligonucleotide covalently linked.

11. The method of claim 7,

wherein providing the first nucleic acid and the first nucleoside triphosphate comprising the first modified base comprises: providing the first nucleic acid, the first nucleoside triphosphate comprising the first modified base, and a second nucleoside triphosphate,

wherein contacting the first nucleic acid and the first nucleoside triphosphate comprising the first modified base with the recombinant TdT comprises: contacting the first nucleic acid, the first nucleoside triphosphate comprising the first modified base, and the second nucleoside triphosphate with the recombinant TdT for the first reaction time at the first temperature in the first reaction to generate the second nucleic acid, and

wherein the second nucleic acid comprises the first nucleic acid incorporated with (i) one or more of the first nucleotides comprising the first modified base from the first nucleoside triphosphate and (ii) one or more second nucleotides.

12. The method of claim 7,

wherein providing the first nucleic acid and the first nucleoside triphosphate comprising the first modified base comprises: providing the first nucleic acid, the first nucleoside triphosphate comprising the first modified base, and a plurality of second nucleoside triphosphates,

wherein contacting the first nucleic acid and the first nucleoside triphosphate comprising the first modified base with the recombinant TdT comprises: contacting the first nucleic acid, the first nucleoside triphosphate comprising the first modified base, and the plurality of second nucleoside triphosphates with the recombinant TdT for the first reaction time at the first temperature in the first reaction to generate the second nucleic acid, and

wherein the second nucleic acid comprises the first nucleic acid incorporated with one or more of the first nucleotides comprising the first modified base and one or more second nucleotides from the plurality of second nucleoside triphosphates.

13. The method of claim 7, wherein modified bases and unmodified bases of nucleotides are incorporated into the second nucleic acid at a ratio that ranges from about 1:100 to about 100:1.

14. The method of claim 7, wherein the modified bases are distributed randomly throughout the second nucleic acid.

15. The method of claim 7, wherein the first nucleic acid comprises a template capture site capable of binding a nucleic acid template.

16. The method of claim 7, wherein one or more of the first modified base of the first nucleoside triphosphate and the first nucleotide in the second nucleic acid comprise a functional moiety.

17. The method of claim 16, wherein the functional moiety of the first modified base is capable of participating in a click chemistry reaction.

18. The method of claim 7, further comprising:

providing a first accessory oligonucleotide; and

contacting the second nucleic acid with the first accessory oligonucleotide for a second reaction time at a second temperature in a second reaction to generate a third nucleic acid comprising the second nucleic acid attached to one or more of the first accessory oligonucleotides.

19. The method of claim 18, wherein the first accessory oligonucleotide comprises a first adapter sequence, or a reverse complement thereof.

20. The method of claim 19, further comprising:

(c) providing the nucleic acid template comprising the first adapter sequence, or a reverse complement thereof, the second adapter sequence, or a reverse complement thereof, and a nucleic acid hybridization sequence capable of hybridizing to the template capture site on the third nucleic acid;

(d) contacting the third nucleic acid with the nucleic acid template to generate the third nucleic acid with the nucleic acid template hybridized to the template capture site on the third nucleic acid via the nucleic acid hybridization sequence of the nucleic acid template;

(e) performing amplification on the third nucleic acid hybridized with the nucleic acid template to generate a fourth nucleic acid comprising the third nucleic acid attached to one or more of the first accessory oligonucleotides and one or more of the second accessory oligonucleotides extended to comprise a sequence of the nucleic acid template, or a reverse complement thereof; and

(f) determining the sequence of the nucleic acid template using the fourth nucleic acid.