CLAIMS

1. An altered archaeal Family B DNA polymerase, wherein the altered archaeal Family B DNA polymerase comprises at least one amino acid substitution mutation at a position functionally equivalent to an amino acid in a reference archaeal Family B DNA polymerase of SEQ ID NO:1, and the altered archaeal Family B DNA polymerase is capable of incorporating a modified nucleotide comprising a 3'-OH acetal blocking group or a 3'-OH thiocarbamate blocking group at (i) a lower error rate, (ii) a lower phasing rate, or both (i) and (ii), compared to SEQ ID NO:1;

wherein the amino acid is at position Glu580, and a second amino acid is at position Phe405;

wherein the amino acid is at position Glu580, and a second amino acid is at position Val485;

wherein the amino acid is at position Glu580, and a second amino acid is at position Trp516;

wherein the amino acid is at position Glu580, and a second amino acid is at position Leu571;

wherein the amino acid is at position Glu580, and a second amino acid is at position Leu571;

wherein the amino acid is at position Glu580, a second amino acid is at position Ala408, and a third mutation is at position Ile410;

wherein the amino acid is at position Glu580, and a second amino acid is at position Ala408**;**

wherein the amino acid is at position Glu580, and a second amino acid is at position Phe405**;**

wherein the amino acid is at position Glu580, and a second amino acid is at position Ile410;

wherein the amino acid is at position Phe405, and a second amino acid is at position Val485**;**

wherein the amino acid is at position Phe405, a second amino acid is at position Val485, and a third mutation is at position Ala408;

wherein the amino acid is at position Phe405, and a second amino acid is at position Ile410;

wherein the amino acid is at position Phe140, and a second amino acid is at position Ser407;

wherein the amino acid is at position Leu403, a second amino acid is at position Ala408, a third amino acid is at position Ile410, and a fourth amino acid is at position Gly497;

wherein the amino acid is at position Phe405, a second amino acid is at position Ile410, a third amino acid is at position Ile412, a fourth amino acid is at position Thr514, and a fifth amino acid is at position Ile521; or

wherein the amino acid is at position Phe405, a second amino acid is at position Ala408, a third amino acid is at position Ile410, a fourth amino acid is at position Ile412, a fifth amino acid is at position Thr514, and a sixth amino acid is at position Ile521.

2. An altered archaeal Family B DNA polymerase comprising the amino acid sequence of any one of SEQ ID NOs:2-8 or any one of SEQ ID NOs:16-32.

3. The altered archaeal Family B DNA polymerase of claim 1, wherein the polymerase comprises reduced exonuclease activity as compared to SEQ ID NO:9.

4. A nucleic acid molecule encoding a DNA polymerase as defined in claim 1.

5. An expression vector comprising the nucleic acid molecule of claim 4.

6. A host cell comprising the vector of claim 5.

7. A method for incorporating modified nucleotides into a polynucleotide complementary to a target nucleic acid comprising allowing the following components to interact: (i) the altered archaeal Family B DNA polymerase of claim 1, (ii) a DNA template; and (iii) a nucleotide solution.

8. The method of claim 7, wherein the DNA template comprises a clustered array.

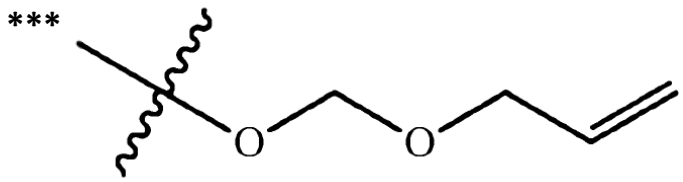
9. A kit for performing a nucleotide incorporation reaction comprising: the altered archaeal Family B DNA polymerase of claim 1, and a solution comprising second generation fully functional nucleotides.

10. The kit of claim 9, wherein the second generation fully functional nucleotides comprise a detectable label.

11. The kit of claim 9, wherein the second generation fully functional nucleotides have been modified at the 3' sugar hydroxyl such that the substituent is larger in size than the naturally occurring 3' hydroxyl group.

12. The kit of claim 11, wherein the second generation fully functional nucleotides comprise a modified nucleotide molecule comprising a purine or pyrimidine base and a deoxyribose sugar moiety comprising a removable 3'-OH acetal blocking group or a 3'-OH thiocarbamate blocking group attached to the 3' carbon of the deoxyribose sugar moiety.

13. The kit of claim 12, wherein the 3'-OH acetal blocking group has the structure



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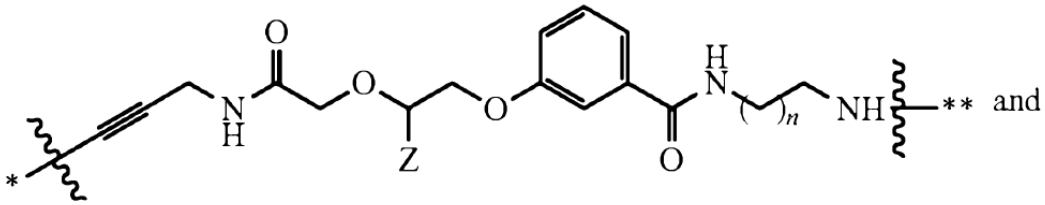
wherein the *** indicates the attachment point of the 3'-OH acetal blocking group to the 3' carbon of the modified nucleotide sugar.

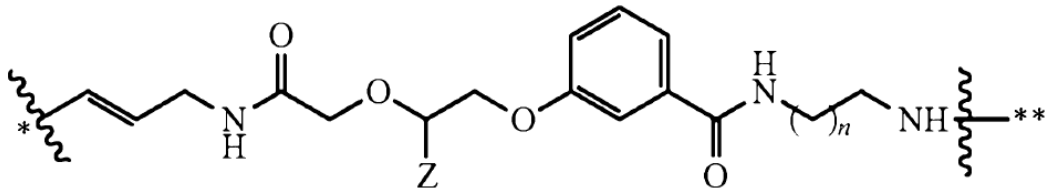
14. The kit of claim 9, wherein the second generation fully functional nucleotides comprise a nucleotide molecule comprising a purine or pyrimidine base attached to a detectable label via a cleavable linker.

15. The kit of claim 14, wherein the detectable label comprises a fluorescent label.

16. The kit of claim 14, wherein the cleavable linker is selected from the group consisting of



and



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wherein Z is —O—CH_2—CH=CH_2; n is an integer of 1, 2, 3, 4 or 5; * indicates the attachment point of the cleavable linker to the purine or pyrimidine base; and ** indicates the attachment point of the cleavable linker to the detectable label.

17. The kit of claim 9, further comprising one or more DNA template molecules and/or primers.