THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. Use of adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) for sequencing a nucleic acid molecule.

2. The use of claim 1 further comprising ADP-glucose, a substrate of the adenosine diphosphate (ADP)-glucose pyrophosphorylase.

3. The use of claim 1 or 2 wherein the sequencing comprises converting PPi to ATP in a DNA sequencing based on a detection of base incorporation by a release of PPi.

4. The use of any one of claims 1 to 3 wherein the DNA sequencing based on the detection of base incorporation by the release of PPi is pyrosequencing.

5. The use of any one of claims 1 to 4 wherein a low background signal and a high sample signal is achieved in a presence of a large amount of luciferease.

6. The use of claim 5 wherein the large amount of luciferase is an amount used in pyrosequencing.

7. The use of claim 5 or 6 wherein the large amount of luciferase ranges from about 0.3 μg to about 3 μg.

8. The use of any one of claims 1 to 7 wherein a DNA sample in the DNA sequencing based on the detection of base incorporation by the release of PPi ranges in concentration of about 0.025 pmol or less to about 2 pmol, from about 2 pmol to about 15 pmol, or from about 0.025 pmol or less to about 15 pmol of DNA.

9. The use of any one of claims 1 to 8 wherein a distinguishable signal for homopolymeric DNA region is achieved.

10. The use of any one of claims 1 to 8 wherein a high throughput allele frequency is developed on a large-scale pooled DNA sample.

11. The use of any one of claims 1 to 10 wherein the DNA sequencing based on the detection of base incorporation by the release of PPi comprises sequencing a monopolymeric region, a homopolymeric region or a combination thereof.

12. The use of claim 11 wherein the homopolymeric region comprises up to 10 consecutive nucleotides.

13. The use of any one of claims 1 to 12 wherein the DNA sequencing based on the detection of base incorporation by a release of PPi comprises sequencing a DNA having more than about 70 bases.

14. The use of any one of claims 1 to 13 wherein the DNA sequencing based on the detection of base incorporation by a release of PPi comprises sequencing a DNA having about 5% allele frequencies.

15. The use of any one of claims 1 to 14 wherein the use yields a read-length of about 400 to about 1000 base pairs.

16. The use of claim 15 wherein the use yields a read-length of about 800 to about 1000 base pairs.

17. The use of any one of claims 1 to 16 further comprising luciferase.

18. The use of any one of claims 1 to 17 further comprising a nucleotide degrading enzyme.

19. The use of claim 18 wherein the nucleotide degrading enzyme is apyrase.

20. The use of any one of claims 1 to 19 wherein the DNA sequencing based on the detection of base incorporation by a release of PPi is step-wise sequencing.

21. The use of any one of claims 1 to 20 wherein the DNA sequencing based on the detection of base incorporation by a release of PPi is continuous sequencing.

22. The use of claim 21 wherein the continuous sequencing is monitored in real time.

23. The use of any one of claims 1 to 22 wherein the DNA sequencing based on the detection of base incorporation by a release of PPi comprises sequencing a single-stranded DNA.

24. The use of any one of claims 1 to 23 wherein the DNA sequencing based on the detection of base incorporation by a release of PPi comprises sequencing DNA in solution.

25. The use of any one of claims 1 to 23 wherein the DNA sequencing based on the detection of base incorporation by a release of PPi comprises sequencing DNA immobilized on a solid support.

26. The use of claim 25 wherein the solid support is chemically modified to comprise a functional group, a moiety or a combination thereof.

27. The use of claim 25 or 26 wherein the solid support comprises a particle, a fiber, a capillary, an array or a combination thereof.

28. The use of any one of claims 25 to 27 wherein the solid support may be washed following a reaction, an addition of a reagent, or a combination thereof.

29. The use of any one of claims 1 to 28 wherein the DNA sequencing based on the detection of base incorporation by the release of PPi comprises unamplified DNA, amplified DNA or a combination thereof.

30. The use of claim 29 wherein the amplified DNA comprises DNA obtained from PCR, an insert in a vector, an insert in a plasmid, or a combination thereof.

31. Adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) for use in sequencing a nucleic acid molecule.

32. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of claim 31 further comprising a substrate ADP-glucose.

33. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of claim 31 or 32 wherein the sequencing comprises converting PPi to ATP in a DNA sequencing based on a detection of base incorporation by a release of PPi.

34. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of any one of claims 31 to 33 wherein the sequencing is pyrosequencing.

35. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of any one of claims 31 to 34 wherein a low background signal and a high sample signal is achieved in a presence of a large amount of luciferease.

36. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of claim 35 wherein the large amount of luciferase is an amount used in pyrosequencing.

37. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of claim 35 wherein the large amount of luciferase ranges from about 0.3 μg to about 3 μg.

38. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of any one of claims 31 to 37 wherein a DNA sample in the DNA sequencing based on the detection of base incorporation by the release of PPi ranges in concentration of about 0.025 pmol or less to about 2 pmol, from about 2 pmol to about 15 pmol, or from about 0.025 pmol or less to about 15 pmol.

39. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of any one of claims 31 to 38 wherein a distinguishable signal for homopolymeric DNA region is achieved.

40. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of any one of claims 31 to 38 wherein a high throughput allele frequency is developed on a large-scale pooled DNA sample.

41. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of any one of claims 31 to 40 wherein the DNA sequencing based on the detection of base incorporation by the release of PPi comprises sequencing a monopolymeric region, a homopolymeric region or a combination thereof.

42. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of claim 41 wherein the homopolymeric region comprises up to 10 consecutive nucleotides.

43. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of any one of claims 31 to 42 wherein the DNA sequencing based on the detection of base incorporation by a release of PPi comprises sequencing a DNA having more than about 70 bases.

44. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of any one of claims 31 to 43 wherein the DNA sequencing based on the detection of base incorporation by a release of PPi comprises sequencing a DNA having about 5% allele frequencies.

45. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of any one of claims 31 to 44 wherein the use yields a read-length of about 400 to about 1000 base pairs.

46. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of claim 45 wherein the use yields a read-length of about 800 to about 1000 base pairs.

47. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of any one of claims 31 to 46 further comprising luciferase.

48. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of any one of claims 31 to 47 further comprising a nucleotide degrading enzyme.

49. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of claim 48 wherein the nucleotide degrading enzyme is apyrase.

50. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of any one of claims 31 to 49 wherein the DNA sequencing based on the detection of base incorporation by a release of PPi is step-wise sequencing.

51. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of any one of claims 31 to 50 wherein the DNA sequencing based on the

detection of base incorporation by a release of PPi is continuous sequencing.

52. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of claim 51 wherein the continuous sequencing is monitored in real time.

53. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of any one of claims 31 to 52 wherein the DNA sequencing based on the detection of base incorporation by a release of PPi comprises sequencing a single-stranded DNA.

54. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of any one of claims 31 to 53 wherein the DNA sequencing based on the detection of base incorporation by a release of PPi comprises sequencing DNA in solution.

55. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of any one of claims 31 to 53 wherein the DNA sequencing based on the detection of base incorporation by a release of PPi comprises sequencing DNA immobilized on a solid support.

56. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of claim 55 wherein the solid support is chemically modified to comprise a functional group, a moiety or a combination thereof.

57. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of claim 55 or 56 wherein the solid support comprises a particle, a fiber, a capillary, an array or a combination thereof.

58. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of any one of claims 55 to 57 wherein the solid support may be washed following an addition of a reagent, a reaction or a combination thereof.

59. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of any one of claims 31 to 58 wherein the DNA sequencing based on the detection of base incorporation by the release of PPi comprises unamplified DNA, amplified DNA or a combination thereof.

60. The adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) of claim 59 wherein the amplified DNA comprises DNA obtained from PCR, an insert in a vector, an insert in a plasmid, or a combination thereof.

61. An apparatus for simultaneous analysis of multiple nucleic acid molecules, the apparatus comprising:

(a) a reaction platform comprising a plurality of wells, each of the plurality of wells entrapping a sample solid support having an immobilized sample nucleic acid molecule;

(b) a reagent source in fluid communication with each of the plurality of wells for flowing a reagent to each of the plurality of wells and for transporting a product away from each of the

plurality of wells while the sample solid support remains entrapped in the respective well; and

(c) an imaging sensor mounted on the reaction platform for acquisition of chemiluminescence intensity from each of the plurality of wells.

62. The apparatus of claim 61 further comprising a thermal system for modulating a temperature of the reagent source, the reaction platform, the imaging sensor, or a combination thereof.

63. The apparatus of claim 61 or 62 wherein the plurality of reaction wells comprises an array of microwells.

64. The apparatus of claim 63 wherein each of the array of microwells has a depth of about 45 μm.

65. The apparatus of claim 63 wherein the array of microwells is photolithographically fabricated.

66. The apparatus of claim 65 wherein the reaction platform is a fiberoptic plate.

67. The apparatus of any one of claims 61 to 66 wherein the sample solid support comprises a bead, a particle, a fiber, or a capillary.

68. The apparatus of any one claims 61 to 67 wherein the sample solid support is a bead.

69. The apparatus of any one of claims 61 to 67 further comprising a reagent solid support comprising the reagent, the reagent solid support disposed in each of the plurality of reaction wells.

70. The apparatus of claim 69 wherein the reagent comprises polymerase, adenosine diphosphate (ADP)-glucose pyrophosphorylase, PPDK, luciferase, apyrase, or a combination thereof.

71. The apparatus of claim 70 further comprising ADP-glucose.

72. The apparatus of any one of claims 61 to 71 further comprising a packing support disposed in each of the plurality of wells for providing packing within each of the wells, reducing delamination, loss or a combination thereof of the sample solid support, the reagent solid support or both.

73. The apparatus of claim 72 wherein the packing support is a bead.

74. The apparatus of any one of claims 61 to 73 wherein the reagent source comprises a nucleotide, a buffer, an enzyme or a combination thereof.

75. The apparatus of any one of claims 61 to 74 wherein the acquisition of chemiluminescence intensity from each of the plurality of reaction wells is

synchronized with a reagent flow from the reagent source to the reaction platform.

76. The apparatus of any one of claims 61 to 75 wherein the temperature of the reagent is about 5°C.

77. The apparatus of any one of the claims 67 to 76 wherein the temperature of the reaction platform, the imaging sensor, or a combination thereof is about 0°C.

78. The apparatus of any one of claims 61 to 77 wherein the reaction platform is silicon-based, polymer-based or a combination thereof.

79. The apparatus of any one of claims 61 to 78 wherein the reaction platform is chemically modified.

80. The apparatus of any one of claims 61 to 79 wherein the nucleic acid sample comprises unamplified DNA, amplified DNA, or a combination thereof.

81. The apparatus of any one of claims 61 to 80 wherein the imaging sensor is a CMOS image sensor or a CCD image sensor.

82. The apparatus of any one of claims 61 to 81 wherein the analysis of multiple nucleic acid molecules comprises pyrosequencing.

83. The apparatus of claim 82 wherein the pyrosequencing comprises *de novo* genome sequencing or ultra-high throughput pyrosequencing.

84. The apparatus of claim 82 wherein the pyrosequencing comprises paired-end ditagging.

85. The apparatus of any one of claims 82 to 84 wherein the pyrosequencing is real-time pyrosequencing.

86. The apparatus of any one of claims 82 to 85 wherein the pyrosequencing comprises sequencing a few genomes per day.

87. The apparatus of any one of claims 82 to 86 wherein the pyrosequencing comprises sequencing ranging from a few kilobases to a few hundred megabases.

88. The apparatus of any one of claims 61 to 87 wherein the reagent source, the reaction platform and the imaging sensor form an integrated system, an automated system, or both an integrated and an automated system for pyrosequencing the nucleic acid sample.

89. The apparatus of any one of claims 61 to 88 wherein the nucleic acid sample comprises about 0.025 pmol DNA or less.

90. The apparatus of any one of claims 61 to 89 wherein the apparatus is re-usable.

91. A method for sequencing a target nucleic acid molecule, the method comprising:

(a) contacting the target nucleic acid molecule with a pyrophosphate sequencing reagent, the pyrophosphate sequencing reagent comprising:

(i) a nucleotide triphosphate,

(ii) a polymerase,

(iii) a pyrophosphate to ATP converting enzyme comprising adenosine diphosphate (ADP)-glucose pyrophosphorylase and a substrate ADP-glucose; and

(iv) an ATP detecting enzyme; and

(b) detecting a resulting optical signal wherein the optical signal is indicative of a reaction of the pyrophosphate sequencing reagent with the target nucleic acid molecule, thereby sequencing the nucleic acid molecule.

92. The method of claim 91 wherein the pyrophosphate sequencing reagent further comprises a nucleotide degrading enzyme.

93. The method of claim 92 wherein the nucleotide degrading enzyme is apyrase.

94. The method of any one of claims 91 to 93 wherein the target nucleic acid molecule comprises a concentration of DNA of about 0.025 pmol or less to about 2 pmol, from about 2 pmol to about 15 pmol, or from about 0.025 pmol or less to about 15 pmol.

95. The method of any one of claims 91 to 94 wherein the target nucleic acid molecule is immobilized on a solid support.

96. The method of any one of claims 91 to 95 wherein the solid support is a bead.

97. The method of any one of claims 91 to 96 wherein the ATP detecting enzyme is luciferase.

98. The method of any one of claims 91 to 97 wherein the contacting and detecting steps are performed in the apparatus of claims 61 to 90.

99. A kit for identifying a base at a target position in a sample DNA sequence, the kit comprising:

(a) a polymerase;

(b) a nucleotide triphosphate;

(c) a pyrophosphate to ATP converting enzyme comprising adenosine diphosphate (ADP)-glucose pyrophosphorylase (AGPase) and a substrate ADP-glucose; and

(d) an ATP detecting enzyme.

100. The kit of claim 99 further comprising a nucleotide degrading enzyme.

101. The kit of claim 100 wherein the nucleotide degrading enzyme is apyrase.

102. The kit of any one of claims 99 to 101 wherein the sample DNA sequence comprises a concentration of DNA of about 0.025 pmol or less to about 2 pmol, from about 2 pmol to about 15 pmol, or from about 0.025 pmol or less to about 15 pmol.

103. The kit of any one of claims 99 to 102 wherein the identifying step is performed using the apparatus of claims 61 to 90.

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OF PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. A method for sequencing a target nucleic acid molecule, the method comprising:

(a) contacting the target nucleic acid molecule with a pyrophosphate sequencing reagent comprising:

(i) a nucleotide triphosphate,

(ii) a polymerase,

(iii) a pyrophosphate to ATP converting enzyme comprising adenosine diphosphate (ADP)-glucose pyrophosphorylase and a substrate ADP-glucose; and

(iV) an ATP detecting enzyme; and

(b) detecting a resulting optical signal wherein the optical signal is indicative of a reaction of the pyrophosphate sequencing reagent with the target nucleic acid molecule, thereby sequencing the nucleic acid molecule.

2. The method of claim 1 wherein the pyrophosphate sequencing reagent further comprises a nucleotide degrading enzyme.

3. The method of claim 2 wherein the nucleotide degrading enzyme is apyrase.

4. The method of claim 1 wherein the target nucleic acid molecule comprises an amount of DNA of 0.025 pmol or less.

5. The method of claim 1 wherein the target nucleic acid molecule is immobilized on a solid support.

6. The method of claim 1 wherein the ATP detecting enzyme is luciferase.

7. The method of claim 1 wherein the contacting and detecting steps are performed in an apparatus comprising:

(a) a reaction platform comprising a plurality of wells, each of the plurality of wells entrapping a sample solid support having an immobilized sample nucleic acid molecule;

(b) a reagent source in fluid communication with each of the plurality of wells for flowing a reagent to each of the plurality of wells and for transporting a product away from each of the plurality of wells while the sample solid support remains entrapped in the respective well;

and

(c) an imaging sensor mounted on the reaction platform for acquisition of chemiluminescence intensity from each of the plurality of wells.

8. The method of claim 6 wherein the luciferase is present in an amount ranging from 0.3μg to 3 μg.

9. The method of claim 1 wherein a homopolymeric region of the target nucleic acid molecule is sequenced.

10. The method of claim 1 wherein the target nucleic acid molecule comprises an amount of DNA of 0.025 pmol or less, wherein the ATP detecting enzyme is luciferase, and wherein the luciferase is present in an amount of 1.5 μg to 3 μg.