Methods and Systems for Direct Sequencing of Single DNA Molecules

Tech ID: 19181 / UC Case 2009-127-0

TECHNOLOGY DESCRIPTION

Scientists at UC San Diego have discovered a method for the direct sequencing of single DNA molecules by monitoring the dynamic conformational changes of the DNA or RNA polymerase when each base is incorporated into the extending primer hybridized to the DNA template in the DNA synthesis or RNA transcription process. The method enables direct real-time sequencing of single DNA molecules from genomic DNA at the speed and accuracy of the natural DNA polymerases using native nucleotides. The method is called READS Genome Technology (READS: REAl-time DNA Sequencing from Single Molecules Using Chemo-Mechanical Nanosensor) and enables high-speed and accurate sequencing of single DNA molecules of up to tens of thousands of bases in a matter of minutes. A platform combining the sequencing method with a high-speed imaging system quickly enables the sequencing of a whole human genome. The method is inexpensive and does not require the cyclic addition of reagents.

ADVANTAGES

▶ Inexpensive natural nucleotides are used.
▶ No cyclic addition of reagents is required during the sequencing process.
▶ Very long read (up to tens of thousands of bases) is feasible.
▶ Rapid sequencing of a whole genome is feasible (within minutes).
▶ Epigenome sequencing (decode the chemical modifications on the DNA in addition to the base sequence).

OTHER INFORMATION

A provisional patent application has been filed.

BACKGROUND

Knowledge of DNA gene sequences and other parts of the genome of organisms has become indispensable when studying biological processes, diagnostic research, and forensic research. Following the development of dye-based sequencing methods with automated analysis, DNA sequencing has become easier and faster by a magnitude of orders. The prominent rapid high-throughput DNA sequencing methods include Genome Sequencer using pyrosequencing by Roche/454, SOLID technology by Applied Biosystems, and the sequencing by synthesis technology employed by Illumina/Solexa. Methods for real-time direct sequencing from single DNA molecules are also emerging. These include the SMART technology being developed by Pacific Biosciences and the FRET-based sequencing method by VisiGen Biotechnologies (a part of Life Technologies Incorporated). The use of fluorescent-labeled nucleotides in almost all current single molecule-sequencing methods with optical imaging presents numerous problems, including background fluorescence and the requirement for a polymerase capable of incorporating labeled nucleotides.

PATENT STATUS

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<td>United States Of America</td>
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ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

▶ A Novel Technique for Fabricating Biomolecular Nano-Arrays Enabling High-DNA Amplification and Sequencing
▶ Methods And Apparatuses For Duplicating Genomic Dna With Contiguity Barcodes For De Novo Genome And Epigenome Sequencing