

Next-Generation Sequencers: What Can We Learn?

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The epigenome is defined as DNA methylation of all genes that influences expression without alteration of the DNA sequence itself [1]. Epigenetic mechanisms include DNA methylation and histone modification [2], as well as nucleosome repositioning [3-5]. The next-generation sequencers (NGS) provide an attractive opportunity for studying DNA methylation patterns.

The NGS were released several years ago, but the high cost limited their popularity in those days. More recently, extensive sequence analysis performed by the NGS has provided rapid and low-cost DNA sequencing. These machines are becoming increasingly available and are currently used at many laboratories. NGS will ultimately contribute to elucidation of the genomic mechanisms responsible for various diseases.

What we can learn from the NGS? The technology provides an efficient method for epigenome-wide analysis, allowing easy detection of disease-related genes and genetic variations. This new approach can be applied to obtain high-quality sequence data by using the genomic DNA isolated from a single cell. For example, NGS provided the substantial breakthrough that led to the first practical applications in analysis of cancer genomics. Scientists are currently sequencing genomic DNA extracted from various cancers and comparing the whole cancer genome with the normal genome. We can identify functionally important cancer-related gene, which act to transform normal cells into tumor cells, by comprehensive comparison of various cancer genomes with the normal genome. Furthermore, recent advances in cancer research based on NGS technology have allowed scientists to identify cancer-specific alleles that are responsible for malignant behavior and can be used to predict the responsiveness to treatment and prognosis of cancer. The second impact of this evolving technology is identification of individual susceptibility genes for complex diseases. Analysis of single nucleotide polymorphisms (SNPs) has previously been used in genome-wide association studies (GWAS) to identify genetic variants that influence susceptibility to common diseases or

complex diseases. However, analysis of SNPs takes a long time. Exon sequencing with NGS seems to be the most effective strategy to reduce costs and save time, while improving both quality and productivity. The third important advance is that NGS protocols have recently been extended to analyze DNA methylation. Analysis of DNA methylation relies on bisulfite conversion of DNA. We can analyze the genome-wide DNA methylation profile of people with age-related diseases and can compare the methylation profile between cells from diseased organ and cells from the unaffected organs of healthy people.

However, use of NGS has some problems. One of the important issues raised by NGS technology is how to analyze enormous amounts of sequence data correctly within a limited period. The second issue is how to select specific genes from the huge number of candidate signals identified by NGS. The third issue is the ethical, legal, and social consequences of mapping and sequencing the human genome. Handling genomic data requires careful attention to the protection of personal information. If these issues can be solved, NGS technology could become a valuable tool for use in the identification of susceptibility genes for complex diseases.

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