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Oncological Applications of Next Generation Sequencing

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Introduction

Over the last decade, as new sequencing technology has been developed and improved, next-generation sequencing (NGS) has become more widely used in cancer genomics research. NGS has recently been used in clinical oncology to advance individualised cancer treatment. NGS is used to find new and unusual cancer mutations, as well as to locate cancer mutation carriers in families and to offer molecular basis for targeted therapy. NGS has several advantages over traditional sequencing, including the capacity to thoroughly sequence all types of mutations for many genes (hundreds to thousands) in a single test at a cheap cost. Whole-genome sequencing, whole-exome sequencing, transcriptome sequencing, targeted area sequencing, epigenetic sequencing, and other sequencing have all benefited from next-generation sequencing (NGS). With the development of this technology, NGS applications in disease management and therapy, genetic counselling, and risk assessment have a lot of potential. In terms of clinical applications, the technique can be utilized for molecular diagnosis of genetic and infectious diseases, prenatal diagnostics, carrier detection, medical genetics and pharmacogenomics, and cancer molecular diagnosis and prognosis, among others. However, considerable obstacles must be overcome in order to bring NGS to the bedside of cancer patients, including the need for simpler assays, more flexible throughput, faster turnaround time, and, most significantly, easier data analysis and interpretation. Overall, we will be one step closer to customised therapy if we continue to employ NGS in clinical oncology practice [1-2].

Description

Cancer is a complex illness caused by the accumulation of DNA mutations. The influence of new sequencing technologies on cancer diagnosis, management, and treatment will be enormous. NGS sequencing of human genomes and hundreds of cancer genomes provides a road map of the normal human genome and a landscape of mutations in cancer genomes across a wide range of cancer types. This advances our understanding of oncogenesis' molecular mechanisms and the justification for molecule-guided therapy. In the not-too-distant future, every patient's normal and malignant genomes will be sequenced. Sanger invented a DNA sequencing method based on electrophoresis over 30 years ago. However, due to its low throughput and relatively high costs, sequencing a huge number of genes and samples was never viable. New sequencing technologies were developed to solve this challenge. Thousands of DNA molecules are sequenced in parallel using NGS methods. It allows for great throughput and rapidity. In two weeks, it can yield quantitative and qualitative sequence data that is comparable to the Human Genome Project's data. Several commercial NGS platforms are currently available.

NGS is also used to improve rationally planned customised therapy, in addition to finding genetic and new somatic mutations. Many research have used NGS for customised cancer treatment to date. NGS has been employed in the treatment of pancreatic cancer. It has also been utilised to detect epidermal growth factor receptor (EGFR) deletions in non-small cell lung cancer patients, which has substantial pathogenetic and clinical consequences for these patients. Rare mutations in circulating DNA have long been used to diagnose and manage somatic alterations in cancer. Peptide nucleic acid and primer extension, as well as bead-based digital PCR in emulsions ("BEAMing"), are all options for detecting these alterations. Nonetheless, uncommon mutations in tumour suppressor genes like TP53, which is substantially altered throughout the gene, are difficult to detect. NGS could be the most cost-effective way to detect and quantify the allele frequency of TP53 and other tumour gene mutations in plasma. For single-nucleotide variations and modest insertions/deletions, Sanger sequencing is the gold standard, but it is ineffective for gross insertions/deletions and big rearrangements. NGS can detect all forms of target gene mutations as well as chromosomal abnormalities.

Conclusion

It's not always possible to obtain a large amount of DNA for genetic testing, particularly from small amounts of tumour tissue. For BRCA1 and BRCA2, traditional Sanger sequencing requires about 3 g of DNA, but chip-captured NGS sequencing only requires 500 ng. NGS is expected to produce hundreds of gigabytes of data. Filtering duplicate and massive amounts of data is a difficult and complex task for bioinformatics personnel. There are a few open source-tools available, however they are only for simple and routine situations [3-5].

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