Cancer Genomics: Chapter 2. Second-Generation Sequencing for Cancer Genome Analysis

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Cancer results from accumulated mutations in the genome. Sequencing is an accurate method to detect mutations. Second-generation sequencing technology, commonly referred to as next-generation sequencing technology, enables rapid, efficient and affordable DNA sequencing, and is transforming the scale and scope of cancer research. The technology is sufficiently flexible and affordable to allow sequencing of many cancer genomes, and thus facilitates both sequencing of samples from large patient cohorts and during disease progression in individual cancer patients. The high depths of redundant sequence coverage that can be obtained using some second-generation sequencing technologies, along with sequencing reads amplified from single DNA molecules, facilitate detection of subclones of cells in tumors. Large-scale genome sequencing of hundreds or even thousands of cancer samples is being conducted by several groups that aim to identify and characterize cancer driver mutations. Goals of such work, previously infeasible with Sanger sequencing instruments, are to use this information to improve cancer prognosis, diagnosis and therapeutic decision-making. The speed of data analysis is rate limiting, and investigators are struggling to accommodate and interpret the data deluge produced by second-generation technologies. In this chapter, we discuss cancer properties that are revealed by sequencing and the implication of such properties in experimental design and data interpretation. We describe past, current and upcoming sequencing technologies and the application of second-generation sequencing technologies in cancer genomics. Finally, we discuss the impact of second-generation sequencing technology in shaping personalized medicine.

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