Chapter 18
Implementation of Nanoparticles in Cancer Therapy

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ABSTRACT
Cancer is a wide group of diseases and generally characterized by uncontrolled proliferation of cells whose metabolic activities are disrupted. Conventionally, chemotherapy, radiotherapy, and surgery are used in the treatment of cancer. However, in theory, even a single cancer cell may trigger recurrence. Therefore, these treatments cannot provide high survival rate for deadly types. Identification of alternative methods in treatment of cancers is inevitable because of adverse effects of conventional methods. In the last few decades, nanotechnology developed by scientists working in different disciplines—physics, chemistry, and biology—offers great opportunities. It is providing elimination of both circulating tumor cells and solid cancer cells by targeting cancer cells. In this chapter, inadequate parts of conventional treatment methods, nanoparticle types used in new treatment methods of cancer, and targeting methods of nanoparticles are summarized; furthermore, recommendations of future are provided.

1. CANCER BIOLOGY
Cancer, although one of the world’s most widely studied medical conditions, remains as the leading cause of death after the heart failure, accounted for 7.6 million deaths (around 13% of all deaths) in 2008. According to comprehensive, 184 country survey of WHO’s International Agency for Research on Cancer (IARC), about 70% of all cancer deaths occur in low- and middle-income countries. Worldwide cancer mortalities are envisioned to continue to rise to over 13.1 million in 2030 (http://globocan.iarc.fr).
Normal eukaryotic cells tend to increase their number by mitosis and meiosis, and the cell division process is triggered by activation of the metabolic pathways when the cell size and the environmental conditions are favorable. The metabolic pathways that are necessary for cell division include the specific signaling pathways, the transmitting signal molecules, enzymes and proteins (Cooper & Hausmann, 2013). After completion of division process, the cell enters into a new cycle again and the cycle is repeated approximately 50 times before the cell goes to apoptosis. Apoptosis is the death of a cell programmed by specific genes. The reason for the limited number of cell divisions is telomeres, regions of repetitive nucleotide sequences at each end of a chromatid, which protect the ends of the chromosomes from deterioration or from fusion with neighboring chromosomes. Telomeres shorten with each cell division and eventually the cell cannot be divided further, progresses into senescence or dies (Counter et al., 1992).

Some cells, due to hereditary and environmental factors, continue to grow and proliferate even in the presence of cell growth and division inhibitory factors. Thereby, cells start division without special signals. Cell growth is disrupted, cells begin to divide too quickly and telomere shortening stops due to telomerase activity (Yoshida et al., 1997). When unnatural telomerase activity is observed, cell structure changes, adhesion property increases, abnormal signal transduction occurs, tumor suppressor genes are silenced and growth factors and their receptors are generated irregularly. These are typical characteristics of cancer cells. Therefore, the researchers specify that cancer originates in fast-growing and immortal cells. Abnormal cells affect the cells around them and they also lead to deterioration of their functions. The other most important feature of these cells is that they may maintain their lives regardless of the specific microenvironment. Thereby, they can easily spread to the surrounding tissues, blood and entire body (metastasis). These abnormal cells generate new blood vessels around them by secreting vascularization factors, and they can make the metastasis process more quickly and efficiently (Sooriakumaran & Kaba, 2005) (Figure 1).

Formation of such a cell abnormality is caused by mutations due to environmental factors and/or heredity. X-rays, UV light, tobacco products, diet and obesity, environmental pollutants and viruses are considered the most common environmental carcinogens.

Although many methods have been developed in the treatment of cancer, the WHO figures suggest that a highly effective treatment technique is yet to be found. Surgery, radiotherapy, chemotherapy, immunotherapy and hormone therapy, which are the most commonly used conventional methods have specific advantages and disadvantages. The chosen treatment type depends on the location, the progress status and the type of cancer. The limitations of status quo treatments are commonly due to nonspecific bio-distribution and insufficient targeting of the therapeutic agents, poor oral bio-availability, low therapeutic indices, dose-limiting toxicity to healthy tissues, and almost invariably emerging drug resistance and subsequent challenge of providing remissive therapy. Multimodal therapy methods are under investigation, and researchers are looking into developing alternative therapies. Oncology is one of the disciplines that will potentially benefit the most from nanotechnology. The nanoparticle based targeted delivery vehicles can effectively overcome the major challenges in successful clinical translation, including specificity, proper dosage, overcoming various biological barriers and demonstrating better therapeutic efficacy than that of the current clinical standards.
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