Chapter 32
Gene Editing and Gene Therapies in Cancer Treatment

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ABSTRACT

In past years, several novel treatments have been given by gene therapies for the treatment of cancer. Gene-based therapeutic approaches include gene transfer, oncolytic virotherapy, and immunotherapy. Gene Transfer or gene editing is the most recent treatment method that allows the insertion of new genes into the cancer cell to mediate the slow growth or death of the cancerous cell. Gene transfer is a very flexible technique, and a wide range of genes and vectors are being used in clinical trials with positive results. CRISPR/Cas9 is found to be a promising technology in cancer research. It helps to dissect the mechanism of tumorigenesis, identify the target for drug development, and helps in the cell-based therapies. Oncology virotherapy uses viral particles that are capable of replicating within the cancer cell and results in cell death. Oncology virotherapy has shown great efficiency in metastatic cancer. In immunotherapy, cells and viral particles are genetically modified before being introduced within the patient's body to trigger the host immune response to destroy cancer cells.

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INTRODUCTION

World Health Organisation (WHO) defines cancer as a large group of diseases characterized by the uncontrollable growth of abnormal cells in the body. Such cells gain the ability to go beyond their usual boundaries and invade neighbouring cells/tissues/parts of the body. When the cancerous cell becomes malignant, the process called metastasizing starts which are considered as the major reason for death from cancer. Neoplasm and malignant tumours are other names to refer to cancer. Globally, in 2018, cancer accounts for an estimated death of about 9.6 million i.e., one in every 6th person dies off due to cancer. Men are found more prone to lung, prostate, and colorectal cancer being the top 3, apart from stomach and liver cancer while in women breast, colorectal, lung, cervical, and thyroid cancer is found more prevalent (Bray et al., 2018). Considered as an important barrier to increasing life expectancy, researchers, scientists, and biotechnologists are trying hard to make early detection accessible, provisions for quality treatment, and survivorship care to the sufferer (Lagergren, 2019). Amongst other highly successful and reliable methods/processes to overcome this global burden, gene editing, and gene therapy are gaining high importance. Gene therapy uses gene(s) as pharmaceutical agents to treat genetic disorders. It promises to prevent the mortality rate by providing innovative treatment options (Cross & Burmester, 2006). On the other hand, Gene editing offers a way to rewrite the genome of the species wherein the mutated genes are revised, spliced, or substituted with the functional and healthy gene at the DNA level. This nullifies the effect of the existing mutated gene by giving its healthy version. Owing to its importance in treating diseases, science personnel approach this by identifying the precise location of mutated genes and exchange them with the functional one (Ormond et al., 2017). With no permanent and clear-cut cure for cancer, gene editing is thought of as a cutting-edge tool to restore the effectiveness of treatments and gene therapy as one of the most recent and best approaches to reduce the mortality rate by targeting gene expression of the genome (Das et al., 2015). Gene editing and gene therapy have revolutionized the world of biotechnology by giving and understanding an insight into cancer born as a result of the genetic defect. Cancer cell genome exhibits multiple genetic and epigenetic variations such as the ineffective working of enzymes during DNA methylation, histone acetylation, methylation of histone proteins amongst many other factors which are responsible for the pathogenesis of the disease (Cheng et al., 2019). Further development of such variation introduces disturbance in cell signalling, cell division, and growth, cell motility, etc. that transforms normal cell to tumour resulting in malignancy at later stages (Sever & Brugge, 2015). Considered as one of the most serious diseases, cancer offers challenges to both human lives as well as public health. The majority of the on-going clinical trials based on gene therapy are focused to come up with a solution that has a cure for cancer (Wirth & Yla-Herttuala, 2014). Finding novel ways to treat cancer has become important because the present therapies are not sufficient because of the toxicity they offer. RNAi strategies, prodrug activating suicide gene therapy, oncolytic virotherapy, immunomodulation based on gene therapy, anti-angiogenic gene therapy, gene defect correction/compensation, manipulation of the genes involved in the pathways leading to apoptosis and invasion by tumorigenic factors, and antisense therapies are a few gene modulation methods that are reported to be employed for cancer treatment. Gene therapy has been used to target various types of cancer such as the brain, breast, lung, pancreatic, liver, skin, ovarian, colorectal, bladder, prostate, head and neck, and renal cancer (Roma-Rodrigues et al., 2020). Treating cancer with therapeutic approaches has gained much importance because of its ability to activate the host's immune response against cancer cells by killing it. Currently, recombinant vaccines for cancer are being developed that unlike other vaccines works by boosting the patient's immune system to identify