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Short Commentary

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African Americans, Cancer, Gene Therapy and Gene Editing

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Abstract

African Americans suffer the greatest burden for the most common types of cancer. Although the overall difference in cancer death rates among racial groups is decreasing, the death rates for all cancers combined continued to be higher in African Americans. Due to the toxicity and side effects of the use of traditional chemotherapy to treat cancer, scientists are working on the development of alternative therapeutic technologies. An example of this is gene therapy, the use of genetic material to treat genetic diseases. This may involve adding a wild type copy of the gene (gene addition) or altering a gene with mutation to the wild type gene (gene editing). Cell therapy is the use of cells that are taken either from the patient themselves or a donor to treat diseases. Cells used for cell therapy are often stem cells, cells that can mature into different types of specialized cells. Cells used for cell therapy may or may not be genetically altered. It is sometimes easier to remove cells from the body, treat them with gene therapy and then place them back than treating the cells inside the body. Gene and cell therapy have become a realistic choice for the treatment of diseases caused by genetic deficits.

Keywords: African Americans; Cancer; Cell Therapy; Cancer Therapy; Gene Therapy; Gene Editing

Introduction

African Americans experience higher cancer death rates than any other racial and ethnic groups. The common misconception is that racial disparities among cancer patients are caused by genetic differences. Though genetic abnormalities certainly play a role, they are not the only contributing factor. The role of socioeconomic status (SES), low education and literacy levels, obesity, environmental toxins and lifestyle factors that could explain higher mortality rates in African Americans[1]. The recent proliferation of knowledge of cancer has led to the development of novel therapeutic approaches in cancer management, particularly gene and cell therapy. Targeted cancer therapies are drugs or other substances that block the growth and spread of cancer by interfering with specific molecules. Gene and cell therapy are the use of genes and cells to treat disease. Gene therapy and cell therapy are overlapping fields of biomedical research with similar therapeutic goals. Gene therapy can be defined as the use of genetic material to manipulate a patient's cells for the treatment of an inherited or acquired disease. Cell therapy can be defined as the infusion or transplantation of whole cells into a patient for the treatment of an inherited or acquired disease.Genetic diseases are caused by errors, or mutations, in genes that result in a loss or change of function of RNA or protein molecules.

A classic example of gene therapy is the efforts to correct hemophilia, and the most common Cell therapy (other than blood transfusions) is bone marrow transplantation. Gene therapy and cell therapy overlap in the treatment of Severe Combined Immuno-Deficiency(SCID). Another example of cell and gene therapy overlapping is in the use of T-lymphocytes to treat cancer. Gene and cell therapy technology is gaining momentum and we are now closer than ever to gene and cell therapies as promising early success for many different diseases. However, gene and cell therapies remain experimental medicines and much more research is needed before many of these therapies are available to all patients everywhere. Apoptosis (programmed cell death) is a hot topic both in biological research and medicine. Targeting cell death process is the common way in cancer treatment. Ferro ptosis, a newly coined non-apoptotic programmed) represents a new way of non-apoptotic cell death process.

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Gene Therapy

Gene therapy has historically been defined as the addition of new genes to human cells. Gene therapy implies any procedure intended to treat or alleviate a disease by genetically modifying the cell of a patient. Gene modification, gene transfer method, gene transfer to specific cell line, and the adoption of the most appropriate genetic engineering viz., gene injection, gene targeting, and the elimination of specific genes through nuclease engineering are some of the approaches used in gene therapy.Retroviruses, Adenoviruses, Adeno-Associated viruses, Herpes Simplex Viruses are the common vectors used in gene therapy. Electroporation, gene gun, sonoporation, and magnetofection are the physical methods for improving DNA transfer. Oligonucleotides, lipoplex, polyplex, dendrimers, hybrid methods are the chemical methods for improving DNA transfer[2]. Gene therapy is expected to play an important role as part of a multi-faceted treatment for cancer. The type and state of gene therapy are determined based on individual genome components, tumor characteristics, genetics and host immune status in order to design a multifaceted treatment that is unique to the individual need. Gene therapy has been widely studied as a new method for the treatment of pancreatic cancer; it is considered a new and promising way of treating pancreatic cancer patients in the future. Several methods of gene therapy have been developed for breast cancer, the most common cancer among women. Among them are neutralization of the mutation, molecular chemotherapy, proapoptotic gene therapy, anti-angiogenesis gene therapy, immunopotentiation, and genetic modulation of resistancesensitivity[3]. Gene therapy, as an advanced technology, goes beyond the modification of genetic disorders and has spread to a wide range of applications. In fact, promising progress made in the treatment of leukemia using modified chimeric antigen receptors (CAR) of T-cells encouraged Science magazine to select cancer immunotherapy as the most important scientific achievement of 2013[4]. Gene therapy, which involves replacement of a defective gene with a functional, healthy copy of that gene, is a potentially beneficial cancer treatment approach particularly over chemotherapy [5].

Gene Editing

Gene editing is the discovery that targeted DNA double-strand breaks (DSBs) could be used to stimulate the endogenous cellular repair machinery. Breaks in the DNA are typically repaired through one of two major pathways- homology directed repair (HDR) or nonhomologous end-joining (NHEJ)[6]. The greatest promise of gene editing lies in precise correction of disease variants. Specific tools and knowledge are needed to advance gene editing into therapeutic use. Most importantly, improved editors are needed. The advent of Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)/Cas(CRISPR-associated protein) technology promises to revolutionize the field of gene therapy. CRISPR/Cas is one of the fastest-growing areas of gene therapy research[7]. A reasonable path toward somatic gene editing for the treatment of cystic fibrosis have been presented by Hodges and Conlon (2019). After an introduction of single target genome editing tools, current focus is on the spectacular development of multiplexed genome editing by Cas9 (type II) and Cas12a (type V)[8-10].

Discussion

Hormone therapies, signal transduction inhibitors, gene expression modulators, apoptosis inducers, angiogenesis inhibitors, immunotherapies, and monoclonal antibodies that deliver toxic molecules are some of the targeted therapies available for cancer treatment. The FDA has approved targeted therapies for the treatment of some patients with adenocarcinoma of the stomach or gastroesophageal junction, bladder cancer, brain cancer, breast cancer, cervical cancer, colorectal cancer, endocrine tumors, head and neck cancer, kidney cancer, leukemia, liver cancer, lung cancer, lymphoma, multiple myeloma, neuroblastoma, ovarian cancer, pancreatic cancer, prostate cancer, skin cancer, soft tissue sarcoma, solid tumors, stomach cancer, and thyroid cancer. Gene therapy is an exciting new technology and potential way to treat AIDS and cancer.One of the most widespread and well-established methods of gene therapy is the insertion of foreign genes into target cells through number of different transfer methods. Some developments that have been crucial for gene and cell therapies are gene editing particularly Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR), which is more efficient and more precise than zinc finger nucleases and Transcription Activator-Like Effector Nucleases (TALENs), induced pluripotent (iPS) cells and safer viral vectors for gene delivery. Gene therapy has been effectively used to treat Parkinson's disease, Alzheimer's disease, Cystic Fibrosis and Diabetic Neuropathy.Death-induced gene therapy consists of the killing of tumor cells via transfection with plasmid DNA (pDNA) that contains a gene which produces a protein that results in the apoptosis of cancerous cells.

When gene therapy is combined with cell therapy, cells become smart vectors for gene therapy purposes. Gene therapy can also be used to modify a patient's immune system in order to strengthen the response against cancer cells. Number of promising genetically modified cancer vaccines are currently being tested in clinical trials. CRISPR-Cas9 technology has drastically revolutionized DNA engineering and biomedical research. Application of CRISPR is gaining momentum and is seen in sickle cell disease gene modification of hematopoietic stem cells, embryonic stem cells, gene-based therapy. As a new coined programmed cell death process, Ferro ptosis shows great potentials in the cancer therapy.

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