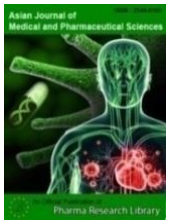

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New Immunotherapy Approaches for Preventing Cancer

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A B S T R A C T

Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body. Cancer can start almost anywhere in the human body, which is made up of trillions of cells. Normally, human cells grow and multiply to form new cells as the body needs them. When cells grow old or become damaged, they die, and new cells take their place. Sometimes this orderly process breaks down, and abnormal or damaged cells grow and multiply faster compared to other cells. These cells may form tumors, which are lumps of tissue. Tumors can be cancerous or not cancerous. Cancerous tumors spread into, or invade, nearby tissues and can travel to distant places in the body to form new tumors. Immunotherapy is a pivotal intervention in managing a spectrum of immunological disorders, from immune deficiencies to malignancies. The diverse modalities of immunotherapy, their mechanisms of action, potential adverse events, and crucial considerations such as dosing and monitoring. Cancer immunotherapy, encompassing both experimental and standard-of-care therapies, has emerged as a promising approach to harnessing the immune system for tumor suppression. Experimental strategies, including novel immunotherapies and preclinical models, are actively being explored, while established treatments, such as immune checkpoint inhibitors. Cancer immunotherapy has introduced novel possibilities for cancer treatment. The development of advanced animal models is essential to better replicate human tumor-immune system interactions, facilitating more accurate preclinical assessments and optimizing therapeutic strategies can lower the cancer progression in the community. Deploying immune-based interventions in the early stage of cancer is likely most effective, and application of immune-based interventions to intercept and even prevent the future occurrence of cancer.

Keywords: Cancer, Immunotherapy, Animal models, Immune-based interventions, Tumor suppression.

A R T I C L E I N F O

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C O N T E N T S

1. Introduction

Cancer is a condition characterized by the abnormal behavior of certain cells within the body. In a healthy person, cells follow a specific pattern of growth, division, and eventually, natural death, which is essential to maintain proper bodily function. However, in the case of cancer, these cells deviate from this normal behaviour, undergoing uncontrollable and abnormal growth.

Types of Cancer

Cancers are named after the organs or tissues in which they originate. The specific type of cell that gives rise to cancer, such as epithelial or squamous cells, is also used in the classification.

1. Carcinoma: The Most Common Type Carcinoma is the most prevalent type of cancer. It primarily consists of epithelial cells that line both the inner and outer surfaces of

the body. A variant known as basal cell carcinoma is also noteworthy.

2. Sarcoma: Affecting Bone and Soft Tissues

Sarcomas are cancers that develop in bone and soft tissues, encompassing muscle, fat, blood vessels, lymphatics, as well as fibrous tissues like tendons and ligaments.

3. Leukaemia: Blood-Related Cancer

Leukaemia is a form of cancer that originates in the blood-forming tissues of the bone marrow. Unlike other cancers, leukaemia does not form solid tumours. Instead, it results in the accumulation of abnormal white blood cells (leukaemia cells and leukemic blast cells) in the blood and bone marrow, displacing normal blood cells[1-3].

4. Lymphoma: Involving Lymphocytes

Lymphoma is characterized by the malignancy of lymphocytes, a type of white blood cell crucial for the immune system. In this type of cancer, abnormal cells accumulate in the body's lymph nodes, lymphatic vessels, and other organs.

5. Multiple Myeloma: Affecting Plasma Cells

Multiple myeloma originates in plasma cells, another type of immune cell. The abnormal plasma cells, referred to as myeloma cells, accumulate in the bone marrow, forming tumours throughout the skeletal system.

6. Melanoma: Skin and Beyond:

Melanoma is a cancer that begins in specialized melanocytes, cells responsible for producing melanin. While most melanomas develop in the skin, they can also occur in other pigmented tissues, including the eye.

7. Brain and Spinal Cord Tumours: Diverse Forms

Tumours originating in the brain and spinal cord manifest in various forms. They are classified based on the cell type of origin and the location within the central nervous system where they first appear.

Other Types of Cancer

Germ Cell Tumours: These tumours initiate in the cells responsible for sperm or ovum production and can appear in various body locations, potentially being benign or malignant.

Neuroendocrine Tumours: These tumours arise from cells that secrete hormones into the bloodstream in response to nervous system signals. They may lead to a wide range of symptoms due to the excessive hormone production.

Carcinoid Tumours: Carcinoid tumours, a subset of neuroendocrine tumours, typically grow slowly and are commonly found in the gastrointestinal system. In some cases, they can metastasize to the liver or other body parts.

Symptoms of Cancer

Cancer can present with a variety of signs and symptoms, which may vary depending on the specific area of the body that is affected. To help better recognize potential warning signs, here is a list of common indicators that are not exclusive to cancer but should prompt you to seek medical attention:

Changes in Bowel or Bladder Habits:

Look out for unexplained changes like persistent diarrhoea or constipation, frequent urgency when urinating, or any other unusual bowel or bladder irregularities.

- **Non-Healing Sores:** It's important to pay attention to any sore on the body that doesn't seem to heal as expected.
- **Unusual Bleeding or Discharge:**
- Any unexplained bleeding or discharge, such as blood in urine, stool, between menstrual periods, vomit, or cough, should be investigated.
- **Thickening or Lump:** If you notice any unexplained lump or thickening in any part of the body, you should consult a medical professional promptly.
- **Wart or Mole Changes:** Any noticeable changes in the size, shape, or colour of warts or moles should be examined by a doctor.
- **Nagging Cough, Breathlessness, or Hoarseness:** Medical advice should be sought if one has a cough or experiences breathlessness for more than two weeks, or if you notice blood in the phlegm.
- **Fatigue or Unexplained Swelling:** Keep an eye out for fatigue that doesn't improve with rest, or areas of swelling that can be felt under the skin.
- **Weight Fluctuations:** Significant unintentional weight loss or gain should be investigated.
- **Skin Changes:** Changes in the skin, including yellowing, darkening, redness, non-healing wounds, or alterations in existing birthmarks, require medical attention.
- **Persistent Indigestion after Eating:** If one experiences ongoing discomfort or indigestion after eating, they should consult a healthcare professional.
- **Unexplained Persistent Fever/ Night Sweats:** Prolonged, unexplained fever or night sweats should not be ignored.
- **Unexplained Persistent Muscle or Joint Pain:** One should seek medical evaluation for persistent, unexplained muscle or joint pain[4-9].
- **Common Causes of Cancer**:
- The primary cause of cancer is mutations, or alterations in the DNA within an individual's cells. These genetic mutations may either be inherited or acquired after birth due to exposure to certain substances and environmental factors. Carcinogens, which are substances known to increase the risk of cancer, can be categorized into three main groups:
- **Physical Carcinogens**: These encompass exposure to radiation and ultraviolet (UV) light, like that from the sun, which can be harmful to the skin.
- **Chemical Carcinogens**: Examples include cigarette smoke, asbestos, alcohol, air pollution, and certain chemicals found in contaminated food and drinking water. These are substances that, when encountered, can potentially lead to cancer.
- **Biological Carcinogens**: This category involves viruses, bacteria, and parasites that are linked to an increased risk of cancer development.
- **Risk Factors of Cancer**
- The risk of developing cancer is influenced by various factors, and understanding these risk factors is crucial. Some common risk factors that can increase the likelihood of developing cancer include:
- **Tobacco Use:** Smoking and the use of tobacco products significantly elevate the risk of various types of cancer.

High Alcohol Consumption: Excessive alcohol intake is associated with an increased risk of certain cancers, including those of the mouth, throat, and liver.

Lack of Physical Activity: A sedentary lifestyle can be a risk factor, as regular physical activity has been shown to reduce the risk of certain cancers.

Exposure to Air Pollution: Prolonged exposure to polluted air, especially in urban areas, may contribute to cancer risk, particularly lung cancer.

Exposure to Radiation: Occupational or medical exposure to radiation, such as X-rays and certain treatments, can increase the risk of cancer.

Unprotected Exposure to UV Light: Excessive and unprotected exposure to UV light, like sunlight and tanning beds, is linked to skin cancer.

Cancer Stages:

Cancer staging systems play a pivotal role in guiding healthcare providers as they chart a course of treatment and offer patients a prognosis, or an anticipated outcome. Among the various staging systems, the TNM classification is the most widely employed. It simplifies the complex reality of cancer progression into three key factors:

T represents the primary tumour.

N indicates lymph nodes and signals whether the cancer has extended to these vital components of the immune system.

M is for metastasis, indicating the spread of cancer to distant parts of the body.

Most cancer types are categorised into four primary stages. The specific stage assigned to a patient depends on several factors, including the tumour's size and its location within the body:

Stage I: At this stage, cancer is confined to a small, localised area, without any evidence of spreading to nearby lymph nodes or other tissues.

Stage II: Cancer has experienced some growth, but it still remains localised and hasn't extended to other areas of the body.

Stage III:

Cancer has grown larger, possibly involving nearby lymph nodes or adjacent tissues.

Stage IV: This advanced stage indicates that cancer has spread to other organs or distant areas of the body, a condition often termed metastatic cancer.

Introduction to Cancer Therapies

Immunotherapy is a pivotal intervention in managing a spectrum of immunological disorders, from immune deficiencies to malignancies. This activity discusses the diverse modalities of immunotherapy, their mechanisms of action, potential adverse events, and crucial considerations such as dosing and monitoring. Participants will explore the conditions amenable to immunotherapeutic interventions to better comprehend immunotherapy's role in enhancing the quality of life, longevity of afflicted individuals. Attendees will gain additional insights into immunotherapeutic agents by discussing their pharmacodynamics, pharmacokinetics, and pertinent interactions. By fostering a comprehensive understanding of immunotherapeutic principles, this program empowers healthcare teams to deliver personalized, efficacious care to patients navigating immunological challenges, thereby advancing the frontier of modern medicine.

Cancer immunotherapy is emerging as a beneficial tool for cancer treatment by activating the immune system to produce antitumor effects. In 1891, Dr. William Coley, the father of immunotherapy, made the first attempt to stimulate the immune system for improving a cancer patient's condition by intratumoral injections of inactivated bacterial toxin[10-15].

All cancers arise as a result of somatic genomic alterations. These alterations arise sequentially and give rise to the progressively more aggressive and invasive phenotypes during tumorigenesis. Such genomic variations could give rise to tumor antigens, which could be recognized by the immune system as nonself and elicit cellular immunwponses. However, avoiding immune destruction is one of the hallmarks of cancer. HNSCCs are highly immunosuppressive malignancy with high mutational burden. Cancer cells have evolved multiple mechanisms, such as defects in antigen presentation machinery, the upregulation of negative regulatory pathways and the recruitment of immunosuppressive cell populations to escape immune surveillance. There has been extensive research on the complex and dynamic interaction between tumor cells and host immune cells which has led to the development of currently approved immunotherapies. Immunotherapy is designed to either actively target a specific antigen on the tumor or enhance the host's immune system.

Cancer immunotherapy was voted “breakthrough of the year” by Science in 2013 and has revolutionized the field of oncology. The cancer immunotherapy aims at harnessing the specificity and killing mechanisms of the immune system to target and eradicate malignant cells. The Society for Immunotherapy of Cancer established the Cancer Immunotherapy Guideline-Head and Neck Cancer subcommittee to provide evidence-based recommendations on how best to incorporate immunotherapies into practice for the treatment of patients with HNSCC.

2. Tumor Immunology

Immune system

The immune system is comprised of the innate and adaptive immune system. The innate immune system includes dendritic cells (DCs), natural killer cells (NK), macrophages, neutrophils, eosinophils, basophils and mast cells. Innate immune cells do not require prior stimulation by antigens and act as a first line of defense against foreign antigens. The adaptive immune system includes B lymphocytes, CD4+ helper T lymphocytes and CD8+ cytotoxic T lymphocytes, and requires formal presentation by antigen-presenting cells (APCs) for its activation. The adaptive immune system generates antigen-specific T- and B-cell lymphocytes.

Immunoediting

Each cell is estimated to experience over 20,000 DNA damaging events each day which are normally repaired. Cells which are not repaired and which acquire malignant or potentially malignant changes are then usually recognized and killed by the tumor immunosurveillance system. However, tumor cells develop mechanisms to thwart immune recognition and response, a dynamic process termed immunoediting that leads to immune escape.

There is now an improved understanding of the complex interaction between immune system and tumor cells. The theory of Immune Editing was put forth by Schreiber et al. where they hypothesize that the body's immune system interacts with the tumor in three distinct phases namely elimination, equilibrium and escape.The cancer immunosurveillance hypothesis developed by Burnet and Thomas is now considered a component of cancer immunoediting.

The elimination phase refers to the initial damage and possible destruction of tumor cells by the innate immune system, followed by presentation of the tumor antigens in the cellular debris to DCs which then present them to T-cells and thereby create tumor-specific CD4+ and CD8+ T-cells. These help destroy the remaining tumor cells if elimination is complete. The equilibrium phase occurs when any tumor cells survive the initial elimination attempt but are not able to progress, being maintained in a state of equilibrium with the immune cells. In the escape phase, cancer cells grow and metastasize due to loss of control by the immune system.

Escape mechanisms of HNSCC

HNSCC is one of the most immunosuppressive human tumors. Tumor is able to evade immune destruction not only by modulating its own cellular characteristics but also by creating its own "tumor microenvironment (TME)." Many signaling molecules and cell types play a role in tumor-driven immune tolerance, from cytokines to both the innate and adaptive arms of the cellular immune system[16-20].

Molecular Escape Mechanisms

Tumor-derived factors

The production of immunosuppressive cytokines, including transforming growth factor (TGF)-b, interleukin (IL)-6 and IL-10 inhibit T cell proliferation and effector functions. Tumor cells also deplete local micronutrients and overexpress indoleamine 2,3-dioxygenase, an enzyme responsible for depletion of tryptophan, which hinders T cell proliferation and activation. It has also been shown that exosomes secreted by HNSCC are enriched for suppressive compounds (including cyclooxygenase-2, TGF-b, programmed death 1 [Programmed cell death receptor 1] and cytotoxic T lymphocyte antigen 4 [Cytotoxic T lymphocyte associated molecule 4]) that promote CD8+ T cell apoptosis, inhibit CD4+ T cell proliferation, upregulate (regulatory T cells) Tregs and impair NK cell function. Beyond secreted cytokines and metabolites, HNSCCs have developed mechanisms of human leukocyte antigen (HLA) modulation for immune escape. HNSCC provoke genetic alterations in key genes associated with processing and presentation of neoantigens, including signal transducer and activator of signal 1 deficiency and downregulated transporter for antigen processing, without significantly affecting HLA expression itself.

Suppressive cellular tumor infiltrate

HNSCC regulate and recruit immune populations capable of modulating T and NK cell responses, including Tregs, myeloid-derived suppressor cells, tumor-associated macrophages and cancer-associated fibroblasts. Immunomodulation enacted by these various cell populations contributes tumor-promoted microenvironment.

The cancer–immunity cycle is a schematic representation of the principles of cancer immunotherapy. This cycle begins with the release of tumor antigens, which are taken up, processed, and presented to naive T cells (APCs). As a result, cytotoxic T cells are produced that can specifically recognize and kill cancer cells. Lysed cancer cells then release antigens and costimulatory signals, triggering another round of the immune response cascade.

Tumors can disrupt critical elements of the cancer–immunity cycle via a variety of negative feedback immune regulatory pathways, which are increasingly becoming cancer immunotherapy targets. These treatments aim to boost antitumor immune responses while having fewer side effects than chemotherapies and other drugs that directly destroy cancer cells. Therapeutic agents aiming to stimulate or increase the naturally ability of immune system to kill cancer cells, which often diminishes as the disease progresses, are used in cancer immunotherapy. Immunotherapy, which attempts to use the host's adaptive and innate immune responses to achieve long-term eradication of diseased cells, can be broadly classified as passive or active[21-25].

Immunotherapy is a pivotal intervention in managing a spectrum of immunological disorders, from immunodeficiencies to malignancies. This activity discusses the diverse modalities of immunotherapy, their mechanisms of action, potential adverse events, and crucial considerations such as dosing and monitoring. Participants will explore the conditions amenable to immunotherapeutic interventions to better comprehend immunotherapy's role in enhancing the quality of life and longevity of afflicted individuals. Attendees will gain additional insights into immunotherapeutic agents by discussing their pharmacodynamics, pharmacokinetics, and pertinent interactions. By fostering a comprehensive understanding of immunotherapeutic principles, this program empowers healthcare teams to deliver personalized, efficacious care to patients navigating immunological challenges, thereby advancing the frontier of modern medicine.

3. Indications

Immunotherapy is the use of drugs, biologicals (eg, cytokines, monoclonal antibodies, and antisera), vitamins and minerals (eg, zinc, vitamin C, and vitamin B6), transplantation (eg, bone marrow), and immunizations (eg, prophylactic and therapeutic vaccines) to control immune responses. For example, immunotherapy works to upregulate or down regulate the immune system to achieve a therapeutic effect in immunologically mediated disorders, including immunodeficiencies, hypersensitivity reactions, autoimmune diseases, tissue and organ transplantations, malignancies, inflammatory disorders, infectious diseases, and any other disease, where immunotherapy can improve the quality and life expectancy.

Immunoglobulin Therapy

- X-linked agammaglobulinemia
- Transient hypogammaglobulinemia of infancy
- Variable common immunodeficiency
- Selective immunoglobulin deficiencies (except for IgA)
- Hyper-IgM syndrome
- Lupus-like syndromes

Use of Transfer Factor (Dialysable Leukocyte Extract)

- Interstitial pneumonia in acquired immunodeficient states
- Recurrent viral infections in immunodeficiency syndromes
- Chronic mucocutaneous candidiasis
- Primary tuberculosis with immunodeficiency
- Wiskott-Aldrich syndrome
- Severe combined immunodeficiency disease (SCID)
- Chronic active hepatitis
- Coccidioidomycosis
- Behçet disease
- Aphthous stomatitis
- Familial keratoacanthoma
- Malignancy

Use of Immunosuppressors

- Systemic lupus erythematosus (SLE)
- Wiskott-Aldrich syndrome
- Autoimmune polyendocrinopathy candidiasis ectodermal dystrophy
- Autoimmune lymphoproliferative syndrome
- Idiopathic CD4+ lymphocytopenia
- Complement system deficiencies
- Various malignancies

Transplantation

- Bone marrow transplant
- RAG-1/RAG-2 SCID
- ADA-SCID
- Artemis SCID
- Wiskott-Aldrich syndrome
- X-linked agammaglobulinemia
- Acute leukemia
- Thymus transplant
- DiGeorge syndrome

Immunizations

- Diphtheria, tetanus, and pertussis (DTP)
- Inactivated Polio vaccine
- Measles, Mumps, and Rubella
- Pneumococcal conjugate
- Hemophilus B conjugate
- Hepatitis B
- Varicella
- BacilleCalmette-Guérin (BCG)
- Human Papillomavirus (HPV)
- Meningococcal vaccine
- Cholera vaccine
- Rotavirus vaccine
- Yellow fever vaccine
- Dengue vaccine

Use of Cytokines in the Immunotherapy of Advanced Malignancies

- Interleukin-2
- Interleukin-7
- Interleukin-12
- Interleukin-18
- Interleukin-21

Use of Nutritional Supplements (Vitamins A, C, E, and B6, Iron, Zinc, Selenium, and Copper)

- Primary immunodeficiency with malnutrition
- Lymphoma
- Malignancies in general
- Graft-versus-host reaction
- Diseases with impaired cell-mediated immunity
- Recurrent and chronic bacterial infections
- SCID
- HIV/AIDS
- Burns

Phase III Clinical Trials of the Bruton's Tyrosine Kinase (BTK) Inhibitor Ibrutinib

- Relapsed or refractory chronic lymphocytic leukemia
- Small lymphocytic lymphoma
- Relapsed or refractory Mantle cell lymphoma
- Newly diagnosed non-germinal center B-cell subtype of diffuse large B-cell lymphoma

Use of Interferon Gamma

- Chronic granulomatous disease
- Bladder carcinoma
- Melanoma
- Chagas disease
- Lepromatous leprosy
- HIV/AIDS
- Cryptococcal meningitis

Immune Checkpoint Inhibitors

- Ipilimumab
- Nivolumab
- Pembrolizumab
- Atezolizumab
- Avelumab
- Durvalumab

Cytokine Antagonists (IL-1RA)

- Septic shock
- Inflammatory bowel disease
- Ischemia-reperfusion injury
- Adult respiratory distress syndrome
- Osteoporosis
- Polyarteritisnodosa
- Glomerulonephritis

Granulocyte-macrophage Colony-stimulating Factor (GM-CSF)

- Accelerate marrow recovery after autologous bone marrow transplantation
- Primary neutropenia
- Myelodysplasia
- Myeloproliferative disorders
- AIDS
- Aplastic anemia

- Neutropenia associated with Felty syndrome

Immunosuppressors

Steroids inhibit cytokine synthesis, affect cell migration, and inhibit the production of leukocytes. Together with chlorambucil, cyclophosphamide acts by covalent alkylation to exert an immunomodulatory effect. This combination inhibits the separation of DNA strands during replication. Methotrexate is an analog of folic acid and blocks pathways essential for DNA synthesis. Azathioprine is a drug that can convert to 6-mercaptopurine to be incorporated into DNA as a fraudulent base.

Transplantation

Transplantation is a promising solution for many rare diseases that can manifest as primary immunodeficiencies, including severe-combined immunodeficiency disorder (SCID), DiGeorge syndrome, Wiskott-Aldrich syndrome, and X-linked agammaglobulinemia.

Several Immunotherapy Modalities Used in Cancer Treatment:

The use of monoclonal antibodies can be used in cancer immunotherapy (eg, immune checkpoint inhibitors (ICIs). These drugs include pembrolizumab and atezolizumab. These ICIs unlock the immune system, which is then able to recognize tumors and kill them.

Cytokines have successfully treated certain malignancies. For example, IL-2 combined with interferon-γ for renal carcinoma, interferon-α and β for hairy leukemia, and TNF-α used in various tumors caused a notable reduction of the mass. These cytokines upregulated the immune system by stimulating T-cell and NK cell activation and increased MHC class I expression. CAR T-cell therapy, or Chimeric Antigen Receptor T-cell therapy, is a groundbreaking immunotherapy approach used to treat certain types of cancer.

Here are the key principles:

CAR Structure:

CARs are synthetic receptors that redirect T-cells to recognize and attack cancer cells. They consist of an extracellular antigen-binding domain, a transmembrane domain, and intracellular signaling domains.

Antigen Recognition: The extracellular domain of the CAR is engineered to recognize a specific antigen present on the surface of cancer cells. This antigen is often a tumor-associated antigen (TAA) or a cancer-specific antigen.

T-Cell Activation: Upon binding to the target antigen, the CAR activates the T-cell, leading to its proliferation, cytokine release, and cytotoxic activity against the cancer cell. Persistence and Memory: CAR T-cells are designed to persist in the body and form memory cells, providing long-term surveillance against cancer recurrence.

Treatment Process:

The CAR T-cell therapy process involves collecting a patient's T-cells through leukapheresis, genetically engineering them to express the CAR, expanding them in the laboratory, and then reinfusing them into the patient.

Clinical Applications:

CAR T-cell therapy has shown remarkable success in treating certain hematological malignancies, such as B-cell acute lymphoblastic leukemia (B-ALL) and certain types of non-Hodgkin lymphoma (NHL). It is also being investigated for solid tumors[26-30].

Challenges and Side Effects: Despite its efficacy, CAR T-cell therapy can be associated with side effects such as cytokine release syndrome (CRS) and neurotoxicity. Managing these side effects and improving the therapy's safety profile are ongoing research areas[31-39].

Administration

IVIG can be administered intravenously with a dosage of 0.4 g/kg for 5 days to treat Guillain–Barré syndrome, but the dose varies depending on the pathology. Low-dose cyclophosphamide has had a more significant impact on cell-mediated immunity. In humans, a low-dose bolus of 600 mg/m B-cells decreases more than T-cells, and among T-cells, the CD8 subset diminishes more than CD4 cells.

Adverse Effects

Adverse effects of immunotherapy include:

Cyclophosphamide and chlorambucil include bone marrow toxicity; therefore, leukopenia requires monitoring. Azathioprine produces reductions of both T and B-lymphocytes. Interleukins must be given in a low dose to prevent side effects and decrease morbidity. Glucocorticoid therapy causes negative calcium balance, leading to osteoporosis, increased appetite, central obesity, impaired wound healing, increased risk of infection, suppression of the hypothalamic-pituitary-adrenal axis, and growth arrest in children. Other side effects include myopathy, avascular necrosis, hypertension, plethora, hyperlipidemia, and edema[40-46].

Contraindications

Patients with T-cell deficiencies should not be vaccinated with the live-attenuated vaccine because there is a danger that the antigen will reverse its pathogenicity and cause illness. Patients with IgA deficiency should not receive IgG preparations that are not highly purified because there is a danger of a hypersensitivity reaction. If the immune system does not recognize the IgA in the preparation, this can be life-threatening. Patients with DiGeorge syndrome should not be transplanted with a thymus older than 14 weeks because a graft-versus-host reaction may occur. The donor can be a sibling or a parent if genetic compatibility exists. Blood group compatibility for major antigens (such as the ABO system and Rh system) must match.

Challenges and Future Progress

New developments in understanding the cancer prognosis and novel therapeutic approaches have called for innovative delivery methods in administering anticancer drugs. Immunotherapy-based drugs are currently studied in various types of cancers; their effect on solid tumors is meager because the low infiltration of immune cells makes lower tumor immunogenicity, leading to an immunosuppressive tumor environment. Developing unique and novel drug delivery systems in combination with multiple cancer therapies would allow the treatment of solid tumors. The key issues such as the controlled release of drugs at the specific site, techniques to assess these delivery mechanisms and their effect on the cellular or molecular level are some of the constraints in developing a robust delivery system[47-49]. In the past thirty years, cancer nanomedicines-based approaches have achieved progress in tackling the tumor microenvironment by understanding the

enhanced permeability and retention, but still certain hurdles in clinically driven transition in developing and approving are needed to be addressed.

4. Conclusion

Cancer is a diverse group of diseases characterized by the uncontrolled growth and division of abnormal cells that can invade surrounding tissues and spread to other parts of the body (metastasis). This breakdown of the normal cellular process, where cells should grow, divide, and die in an orderly manner, is caused by genetic changes (mutations) in a cell's DNA. While most cancers involve solid tumors, blood cancers like leukemia do not. Cancer is a leading cause of death worldwide, placing significant strain on individuals, communities, and health systems. Immunotherapy is a diverse medical treatment that harnesses the body's own immune system to prevent, control, or eliminate disease, including certain cancers, autoimmune disorders, and allergies. It works by either stimulating the immune system to be more active, suppressing it to reduce inflammation, or by altering specific immune cells to target diseased cells[50]. To lower the cancer the novel strategies and therapy regimens tested in preclinical and clinical research.

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