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Review

Emerging Immunotherapeutic Approaches for Managing Metastasis

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ABSTRACT

Metastatic cancer is a stage where cancer cells from the primary site have spread to other parts of the body, and treatment options may be limited. However, immunotherapy is a promising treatment approach for this condition. Immunotherapy is a treatment modality that stimulates the immune system to fight against cancer cells, thereby aiming to inhibit the growth of cancer cells. In recent years, new immunotherapies used in the treatment of metastatic cancer have been developed. These new immunotherapies are performed using drugs that target the checkpoints on the immune system and aim to prevent the mechanisms by which cancer cells disable the immune system. In this way, the immune system attacks cancer cells and tries to eliminate them. It has been observed that new immunotherapies have shown positive results in patients with metastatic cancer. However, the efficacy and side effects may vary for each patient. Immunotherapy can sometimes lead to excessive immune reactions and cause side effects such as inflammation. However, the potential benefits of immunotherapy justify overcoming these side effects. New immunotherapy treatments hold promise for patients with metastatic cancer. However, it is important to make treatment choices based on individual cases and to closely collaborate with healthcare professionals. The development and optimization of new immunotherapies can support advancements in the treatment of metastatic cancer and enhance patients' quality of life. In this review, cancer and metastasis followed by cancer types and cancer treatments are explained. New methods of immunotherapy, one of the types of cancer treatment, are also explained.

Keywords: Cancer, immunotherapy, metastasis, treatment

Potential treatments for advanced breast cancer, colorectal cancer, gastric cancer, non-small cell lung cancer, ovarian cancer, and pancreatic cancer are being studied.[1] It reports a 2.4% decrease in cancer deaths from 2017 to 2018.[2] Cancer concerns and cancer screening among men and different racial/ethnic groups are suggested as future research strategies.[3] Countless scientists are working to develop a cure for cancer, a serious disease that affects people's lives.[4] Breast cancer that occurs during pregnancy or within one year after delivery is considered pregnancy-associated breast cancer.[5] In the United States, there are more than 14 million cancer survivors.[6] Breast cancer has become the most common cancer in the world, accounting for 11.72% of all cancers, and is one of the cancers with the highest mortality rate.[7] Cancer has not yet been defeated.[8] Making informed research choices is critical to increase the likelihood that research will help inform a community-wide discourse about the extent, origins, and remedies for social injustices in cancer, and thereby aid efforts to eliminate social inequalities in health.[9]

Cancer is a complex disease that can affect any part of the body. It occurs when cells in the body grow and divide uncontrollably, leading to the formation of a mass of abnormal cells called a tumor. Tumors can be benign (non-cancerous) or malignant (cancerous). Malignant tumors can invade nearby tissues and organs, and can also spread to other parts of the body through the bloodstream or lymphatic system, a process known as metastasis.[10-18]

Metastasis is the process by which cancer cells spread from the primary tumor to other parts of the body through the bloodstream or lymphatic

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system. It is the most dangerous stage of cancer progression, causing more than 90% of cancer deaths.[19] The mechanisms of metastasis are complex and involve cellular transformation, promotion, genomic instability, resistance to apoptosis, survival, proliferation, invasion, angiogenesis, and metastasis.[20] Recent studies have demonstrated the importance of non-protein-coding parts of the human genome in carcinogenesis and metastasis.[21]

Metastasis can occur in various organs, including the liver, lungs, bones, and brain, among others.[22] The genes involved in the pathogenesis of metastasis are numerous and include the Ras and EF-hand domain containing (RASEF) gene, RAB31, hTERT, embryonal Fyn-associated substrate, and deleted in split-hand/split-foot 1.[23] Other genes, such as multiple tumor suppressor 1, p120 catenin, and CT45A1, increase the possibility of hepatic metastasis in lung cancer, whereas Tip30/CC3, CUL5, and SOCS3 expression in lung tumors inhibit tumor metastasis.[22]

The occurrence of muscle metastasis is rare, and it correlates with clinical experience.[24] Similarly, reports on intramedullary spinal cord metastasis from renal cell carcinoma are limited, and more studies are needed to explore the mechanisms of metastasis and the optimal forms of therapy. In conclusion, metastasis is a complex process that involves numerous genes and cellular mechanisms. Understanding the mechanisms of metastasis is crucial for developing effective treatments and improving outcomes for cancer patients.[25]

RISK FACTORS FOR CANCER

Cancer is a disease caused by the uncontrolled growth and division of cells in the body. Normally, the growth and division of cells are strictly regulated. Cancer, however, occurs when this order is disrupted. There are many different types of cancer and each can start in different organs or tissues. Some common types of cancer include breast cancer, lung cancer, colon cancer, prostate cancer, and skin cancer. The symptoms of cancer can vary depending on the type and stage of spread. There are many causes of cancer formation. Genetic factors, age, smoking, alcohol consumption, eating habits, environmental factors, infections, and certain hormones can increase the risk of cancer. However, exactly how cancer develops and why it occurs in some people is still not fully understood. Diagnosing and treating cancer involves a range of methods. Diagnosis is usually done using medical imaging tests, biopsies, and laboratory tests. Treatment options vary depending on the type of cancer, the extent of spread, and the patient's general health. These include surgery, chemotherapy, radiotherapy, immunotherapy, and targeted therapies. Early detection is crucial in cancer treatment, as cancers diagnosed at an early stage can often be better treated. Cancer prevention includes measures such as healthy lifestyle choices, regular screenings, vaccinations (e.g. the human papillomavirus vaccine), avoiding exposure to harmful substances, and controlling environmental factors. Cancer research and treatment methods have made significant advances in recent years, but cancer is still a major health problem worldwide. It is possible to reduce the risk of cancer through early detection, informed lifestyle choices, and regular attendance at health check-ups.[26-30]

Environmental and Genetic Factors

Cancer is a multifactorial disease caused by a combination of genetic and environmental factors. Genetic predisposition, environmental factors, and their interaction are the main causes of cancer.[31-33] Environmental factors that contribute to cancer include lifestyle factors such as tobacco and alcohol consumption, dietary habits, and exposure to radiation.[34-36] Inherited genetic factors, such as alterations in breast cancer susceptibility gene 1 (BRCA1) and BRCA2, also contribute to the risk of developing certain types of cancer.[37] Other factors that can cause cancer include gut microbiota dysbiosis, which is caused by the interaction between host and environmental factors,[38] and low-penetrance genes that interact with environmental risk factors.[39]

The accumulation of cell divisions in stem cells is the main biological cause of cancer, which drives the accumulation of deoxyribonucleic acid alterations required for carcinogenesis and the formation and growth of abnormal cell populations. The mechanisms of carcinogenesis are complex and involve cellular transformation, promotion, genomic instability, resistance to apoptosis, survival, proliferation, invasion, angiogenesis, and metastasis. In conclusion, cancer is a complex disease caused by a combination of genetic and environmental factors. Understanding the mechanisms of carcinogenesis and the risk factors associated with cancer is crucial for developing effective prevention and treatment strategies.[31]

TYPES OF CANCERS

These are just some examples, but there are many different types of cancer. Each type of cancer

comes with different symptoms, treatment options, and prognoses. It is important to seek support from health professionals and trusted medical sources for more information.

Lung Cancer

Lung cancer is a type of cancer that starts in cells in the lungs. Smoking, exposure to passive smoke, air pollution, and genetic factors can increase the risk of lung cancer. Lung cancer is generally associated with smoking, but it can also occur in rare cases in non-smokers. The risk of developing lung cancer is much higher in smokers compared to non-smokers. Additionally, passive smoking can also increase the risk of lung cancer. The treatment of lung cancer is determined based on the stage, type of cancer, and the overall health condition of the patient. Treatment options include surgical intervention, chemotherapy, radiotherapy, and targeted therapies (immunotherapy, targeted drugs). In cases of lung cancer detected and treated at an early stage, the treatment outcomes are generally better. Preventive measures include not smoking, avoiding exposure to secondhand smoke, reducing indoor air pollution sources such as radon, and avoiding occupational exposure. Additionally, regular health check-ups and lung cancer screening tests are important for early diagnosis and treatment.[40]

Breast Cancer

Breast cancer is a type of cancer that starts in the breast tissue. It usually occurs in women, but can also occur rarely in men. Genetic factors, hormonal changes, obesity, and aging can affect the risk of breast cancer. Breast cancer is a type of cancer where cancer cells form in the breast tissue of women. Breast cancer typically starts in the milk ducts or glands of the breast but can spread to other tissues and organs. Breast cancer is generally seen in women but can rarely develop in men as well. Risk factors include age, genetic factors, hormonal imbalances, obesity, alcohol consumption, smoking, and factors such as estrogen therapy. Various methods are used for the diagnosis of breast cancer, including mammography, ultrasound, magnetic resonance imaging (MRI), biopsy, and blood tests. Once the diagnosis is made, the stage of cancer is determined, and an appropriate treatment plan is developed. The treatment of breast cancer varies depending on the stage, type of cancer, and the overall health condition of the patient. Treatment options include surgery, radiation therapy, chemotherapy, hormone therapy, and targeted therapy. In some cases, these treatments are used in combination. Early detection and treatment are important in the treatment of breast cancer. It is important to perform self-breast exams, undergo regular mammographic screening tests, and monitor breast cancer symptoms. Awareness campaigns for breast cancer emphasize the importance of early detection and encourage women to undergo regular screenings.[41]

Prostate Cancer

Prostate cancer is a type of cancer that starts in the prostate gland. It is one of the most common types of cancer in men. Aging, family history, and racial factors can affect the risk of prostate cancer. Prostate cancer is a type of cancer where cancer cells form in the prostate gland. The prostate is a gland located just below the urinary bladder and is associated with the male reproductive system. Prostate cancer is generally a slow-growing tumor and often does not cause symptoms in the early stages. The exact cause of prostate cancer is unknown, but there are certain risk factors. The risk of prostate cancer increases with age. Additionally, individuals with a family history of prostate cancer have a higher risk. Other risk factors include racial factors, obesity, high-fat diet, lack of physical activity, and smoking. Various methods are used for the diagnosis of prostate cancer. These include digital rectal examination, prostate-specific antigen blood test, and prostate biopsy. These tests provide information about the presence, size, and stage of the cancer. The treatment of prostate cancer varies depending on the stage, size, and overall health condition of the patient. Treatment options include active surveillance, surgery, radiation therapy, hormone therapy, chemotherapy, and targeted therapy. The treatment plan should be discussed in detail with your doctor and tailored to the individual. Early diagnosis is important, therefore it is crucial to regularly visit doctors for check-ups and participate in prostate cancer screenings. Adopting a healthy lifestyle, engaging in regular exercise, maintaining a balanced diet, and avoiding smoking are important to minimize risk factors.[42]

Colorectal Cancer

Colorectal cancer is a type of cancer that starts in the large intestine (colon) or rectum (the area between the anus and the colon). Aging, genetic factors, poor eating habits, inflammatory bowel diseases, and the presence of polyps can increase the risk of colorectal cancer. Colorectal cancer is a type of cancer where cancer cells form in the inner wall of the colon or rectum. The colon serves

as a part of the body's digestive system and is also known as the large intestine. The rectum is the final section of the colon and connects to the anus. Colorectal cancer typically arises from small, early-stage tumors called polyps. These polyps can eventually develop into cancer cells. In the early stages, colorectal cancer is often asymptomatic, so regular screenings are important. The risk factors for colorectal cancer include age, genetic predisposition, family history, inflammatory bowel disease (such as ulcerative colitis or Crohn's disease), obesity, smoking, alcohol consumption, and low-fiber diet. Various methods are used for the diagnosis of colorectal cancer. These include fecal occult blood tests, colonoscopy, sigmoidoscopy, bowel imaging tests (such as colonography), biopsy, and blood tests. These tests provide information about the presence, size, and extent of the spread of the cancer. The treatment of colorectal cancer varies depending on the stage, size, extent of spread, and overall health condition of the patient. Treatment options include surgery, radiation therapy, chemotherapy, targeted therapy, and immunotherapy. In some cases, these treatments are used in combination. Early diagnosis and regular screenings are important in the treatment of colorectal cancer. Adopting a healthy lifestyle, engaging in regular exercise, maintaining a healthy diet, avoiding smoking, and limiting alcohol intake can also help reduce the risk.[43]

Gastric Cancer

Gastric cancer is a type of cancer that starts in the stomach tissue. Factors such as *Helicobacter pylori* infection, smoking, excessive salt consumption, stomach polyps, and a family history of stomach cancer can affect the risk of stomach cancer. Gastric cancer is a type of cancer that originates from cancer cells forming in the inner lining of the stomach. The stomach serves as part of the digestive system and aids in the digestion of food. Gastric cancer can be classified into various types, but the most common type is called adenocarcinoma. Gastric cancer usually does not show symptoms in the early stages and may go unnoticed until it reaches advanced stages. Various methods are used for the diagnosis of gastric cancer. These include endoscopy, gastric biopsy, MRI, computed tomography (CT), blood tests, and screening methods. These tests provide information about the presence of cancer, the degree of spread, and the stage of the disease. Gastric cancer treatment varies depending on the stage, size, extent of spread, and the patient's overall health condition. Treatment options include surgery, chemotherapy, radiation therapy, and targeted therapy. In some cases, these treatments are used in combination. Early diagnosis and treatment are important in the fight against gastric cancer. Regular screenings and measures such as adopting a healthy lifestyle, balanced nutrition, not smoking, and limiting alcohol can also help reduce the risk.[44]

Liver Cancer

Liver cancer is a type of cancer that starts in liver cells.. Chronic hepatitis B or hepatitis C infections, cirrhosis, alcohol abuse, and obesity can increase the risk of liver cancer. Liver cancer is a type of cancer that occurs due to abnormal growth and multiplication of liver cells. The liver is a large organ in our body that performs many important functions, including metabolism, detoxification, digestion, and immune regulation. Liver cancer generally develops as a result of other conditions such as liver disease (e.g., cirrhosis) or risk factors like hepatitis B or C virus infection. Liver cancer is classified into two main types: primary liver cancer and metastatic liver cancer. Primary liver cancer originates directly from liver cells, while metastatic liver cancer is a cancer caused by cancer cells that have spread to the liver from other organs. Various methods are used for the diagnosis of liver cancer. These include blood tests, imaging tests (such as ultrasound, MRI, CT), biopsy, and a detailed evaluation of the liver. Treatment for liver cancer varies depending on the stage, size, extent of spread, and overall health condition of the patient. Treatment options include surgical intervention, radiation therapy, chemotherapy, ablation (destruction of the tumor using heat or cryogenic energy), embolization (cutting off the tumor's blood supply), and targeted therapies. The treatment plan is determined by a specialist physician based on the individual's situation. When liver cancer is not diagnosed early, the prognosis is generally worse. To minimize risk factors, it is important to adopt a healthy lifestyle, protect against infections such as hepatitis B and C, and limit alcohol consumption.[45]

Skin Cancer

Skin cancer is a type of cancer that starts in cells in the skin. The most common types are basal cell carcinoma, squamous cell carcinoma, and melanoma. Sunlight exposure, ultraviolet rays, skin burns, and familial predisposition can affect the risk of skin cancer. Skin cancer is a type of cancer that occurs due to abnormal cell growth or proliferation on the skin. The skin is the largest organ of our body and provides protection against external factors. Skin cancer

typically develops as a result of exposure to sunlight. However, genetic factors, skin type, age, immune system status, and other environmental factors can also influence the risk. Types of skin cancer include basal cell carcinoma, squamous cell carcinoma, and melanoma. The treatment of skin cancer varies depending on the type, stage, size, and extent of spread of the cancer. Treatment options include surgical removal, radiation therapy, chemotherapy, immunotherapy, and targeted therapies. Early diagnosis and treatment are important for successful treatment of skin cancer.[46]

DIAGNOSIS OF CANCER

Cancer diagnosis is a crucial step in the management of cancer. Diagnostic delay is a significant factor that affects cancer outcomes, especially in gynaecological cancers.[47] Health literacy is also an essential factor that affects cancer diagnosis and outcomes, especially in ethnic minorities.[48] Various techniques are used for cancer diagnosis, including machine learning and deep learning-based computational techniques.[49] The coronavirus disease 2019 pandemic has also impacted cancer diagnosis worldwide, leading to a decrease in cancer diagnostic tests and diagnoses.[50] The triple diagnostic method, consisting of clinical evaluation, mammography, and fine needle aspiration cytology, is an effective technique for breast cancer diagnosis.[51] Mass spectrometry-based "omics" approaches are also used for molecular diagnosis of human cancers.[52] Endoscopic ultrasound is an effective technique for the diagnosis and staging of pancreatic cancer.[53] Superficial head and neck cancer is a new field of diagnosis and therapy, and diagnostic and treatment strategies are yet to be established.[54] Limitations in health literacy are a significant issue among patients facing a cancer diagnosis, and there is a need for simple communication in patient education materials.[55]

CANCER TREATMENTS

Cancer treatments include chemotherapy, radiation therapy, surgery, hormone therapy, targeted drugs, immunotherapy, and gene therapy.[56] However, these treatments have limitations such as severe side effects, drug resistance, and unsatisfactory effectiveness.[57-59] Therefore, researchers are exploring new treatment options such as high-intensity focused ultrasound for targeted drug delivery,[60] biodegradable nanoparticles for drug delivery,[61] and magnetic field therapy.[59] Additionally, chemopreventive and therapeutic properties of natural compounds such as ginger extracts are being studied.[62] Aspirin and non-steroidal anti-inflammatory drugs are also being investigated for cancer prevention.[63] Immunotherapeutic agents such as checkpoint inhibitors have revolutionized the treatment of some cancer types, but there is still an unmet need for tolerable and effective treatments for many patients with metastatic solid tumors.[64] Patients with gastrointestinal cancer have numerous treatment options, but many participants are not healthy enough for surgery, experience harsh side effects from chemotherapy, or pass away before receiving an organ for transplantation.[65]

Surgical Treatment

Surgical treatment is a crucial component of cancer management, and it remains the most important treatment modality for curative intent in many cases.[66] Surgical interventions for cancer management include transurethral resections, cystectomy, and systemic chemotherapy and radiotherapy for muscle-invasive and metastatic bladder cancer.[67] For non-muscle-invasive bladder cancer, surgical intervention with transurethral resection and intravesical therapy using chemotherapy and immunotherapy agents are common.[68] Surgical resection is the first effective treatment for breast cancer and remains the most important treatment modality for curative intent.[66] Subcutaneous breast demolition surgery, also known as oncoplasty, is a multimodal treatment that involves contemporary demolition and reconstructive surgery to ensure a good quality of life for women after surgery.[69]

Surgical intervention is also required for the management of colon cancer, with chemotherapy administration as adjuvant therapy for stages II to III to minimize recurrence or as a palliative modality for patients with stage IV disease.[70] Surgical interventions are also required for the management of peripheral clinical T1a (≤2 cm) N0 non-small cell lung cancer, with some surgeons advocating for surgical intervention by lobectomy or sublobar resection, whereas others advocate for nonsurgical treatments such as stereotactic body radiation therapy.[71]

Most children with tumors will require one or more surgical interventions as part of the care and treatment, including making a diagnosis, obtaining adequate venous access, performing a surgical resection for solid tumors, performing procedures for cancer prevention and its late effects, and managing complications of treatment.[72] Advances in endoscopic

tumor resection, such as transoral laser microsurgery and transoral robotic surgery, have demonstrated improved functional outcomes in the treatment of primary glottic cancer.[73] Surgical management of colorectal cancer has been subject to pivotal changes regarding the surgical approach by means of laparoscopic and conventional open surgery, with laparoscopic surgery for colon cancer being proven to be equal to the open approach in terms of overall and disease-free survival.[74] Advancements in surgical techniques of resection and spinal reconstruction have led to increasingly aggressive interventions for patients with metastatic spine disease.[75]

Chemotherapy

Chemotherapy is a widely used treatment modality for cancer patients, particularly those with metastatic cancers.[76] It is often used in combination with other treatments such as surgery and radiation therapy to achieve the best possible outcomes.[77] However, chemotherapy has several side effects, and there is a continuous demand for developing novel and specific targets for cancer therapy.[78] In prostate cancer, chemotherapy is used in combination with other treatments, and there is ongoing research to compare the effectiveness of different chemotherapy agents.[79]

Cytotoxic luteinizing hormone-releasing hormone analogs have been proposed as targeted chemotherapy for breast, ovarian, and endometrial cancers.[80] Hyperthermia is also being studied as an adjunct treatment to chemotherapy and radiation therapy for various cancer types.[81] Trifluridine/tipiracil has shown efficacy benefits in chemotherapy-refractory metastatic colorectal cancer.[82] Megakaryocytopoiesis is being studied as a potential therapeutic target for patients with life-threatening thrombocytopenia, such as those undergoing bone marrow transplantation or high-dose chemotherapy.[83] Kahalalide F and its analogs are being studied as effective antileishmanial agents, and non-traditional antitumor drugs are being investigated for their tumoricidal activity.[84,85] Overall, chemotherapy remains an important treatment modality for cancer patients, but ongoing research is needed to improve its effectiveness and minimize its side effects.[84]

Radiotherapy

Radiotherapy is a common treatment modality for cancer patients, and it can be used alone or in combination with other treatments such as surgery and chemotherapy. Hypofractionated external beam radiotherapy has gained popularity for prostate cancer treatment due to the low alpha/beta (α/β) ratio of prostate cancer.[86] Stereotactic body radiotherapy has also shown clinical benefit for patients with metastatic and/or unresectable cancer.[87] Brachytherapy treatment involves the insertion of radioactive sources into tissue to deliver radiotherapy directly to the tumor.[88] Proton beam therapy has emerged as an exciting radiotherapy modality for breast cancer due to its ability to minimize exposure to surrounding organs.[89]

Short-term endocrine therapy prior to and during radiotherapy has been shown to increase disease-free survival and reduce the incidence of distant metastases in prostate cancer patients.[90] However, the side effects of radiotherapy can be significant, and there is ongoing research to improve its effectiveness and minimize its side effects. For example, hyperbaric oxygen therapy has been studied as a potential method to improve the side effects of radiotherapy, but its effectiveness is not yet satisfactory. Overall, radiotherapy remains an important treatment modality for cancer patients, and ongoing research is needed to improve its effectiveness and minimize its side effects.[91]

Hormone Treatment

Hormone therapy is a common treatment modality for various types of cancer, including breast, ovarian, and prostate cancer. Adjuvant hormonal treatment has been shown to reduce the relative breast cancer recurrence risk by up to 50% in women with hormone-responsive early breast cancer.[92] However, doctors have been reluctant to give patients with ovarian cancer hormone replacement therapy due to fears that it would decrease survival by increasing the chance of relapse.[93]

Hormone therapy for prostate cancer is positioned as a standard treatment for metastatic prostate cancer, but the proportion of hormone therapy for localized prostate cancer has tended to increase rapidly in recent years.[94] Hormonal therapy is the first-line treatment for HR+ metastatic breast cancer, even in cases of visceral metastases, if hormone therapy resistance is not suspected or disease progression is not too fast.[95] Hormone treatment for gynecological cancers involves the use of medications that reduce the level of hormones or inhibit their biological activity, thereby stopping or slowing cancer growth.[96] Hormone therapy reduces levels of hormones in the body to prevent them from allowing cancer cells to grow further.[97] However,

there are concerns about the side effects of hormone therapy, and ongoing research is needed to improve its effectiveness and minimize its side effects.[98] Additionally, socioeconomic status can impact the incidence of breast cancer, which may be explained by reproductive factors, mammography screening, hormone replacement therapy, and lifestyle factors. Overall, hormone therapy remains an important treatment modality for cancer patients, and ongoing research is needed to improve its effectiveness and minimize its side effects.[99]

Targeted Drug Treatment

Targeted drug therapy is a promising approach to cancer treatment that aims to selectively target cancer cells while sparing normal cells. This approach involves the use of drugs that target specific molecules or pathways that are critical for cancer cell growth and survival.[100] Molecularly targeted therapies, including monoclonal antibodies, small molecule receptor tyrosine kinase inhibitors, and drugs that block downstream signaling pathways, have been developed for various types of cancer, such as breast cancer,[101] osteosarcoma,[102] and gastric cancer.[103] The success of molecularly targeted therapies has revolutionized cancer treatment and paved the way for modern precision medicine.[104]

Combination therapies involving molecularly targeted agents have also attracted significant attention in the development of cancer treatment.[105] Moreover, the development and application of new anticancer drugs, including chemotherapy drugs, molecularly targeted drugs, and immunotherapy drugs, have been reported for advanced cancer treatment.[103] Targeted drug therapy is expected to play a significant role in precision medicine for cancer patients. Overall, targeted drug therapy is a promising approach for cancer treatment, and ongoing research is needed to improve its effectiveness and minimize its side effects.[106]

Gene Therapy

Gene therapy is a promising approach to cancer treatment that involves the introduction of genetic material into cancer cells to correct genetic abnormalities or enhance the immune response against cancer cells. Different approaches to gene therapy for cancer treatment include gene addition therapy, immunotherapy, gene therapy using oncolytic viruses, antisense ribonucleic acid (RNA), and RNA interference-based gene therapy.[107] Gene therapy has been studied for various types of cancer, including breast cancer, lung cancer, pancreatic cancer, liver cancer, bladder cancer, head and neck cancer, skin cancer, and ovarian cancer.[108] The use of tumor-specific promoters in gene therapy has also been explored as a way to target cancer cells specifically.[109] Adenovirus-mediated gene transfer is one of the most commonly used methods for cancer gene therapy.[110] However, the clinical efficacy of gene therapy for cancer treatment is still limited, and ongoing research is needed to improve its effectiveness and minimize its side effects. Overall, gene therapy remains a promising approach for cancer treatment, and ongoing research is needed to improve its effectiveness and safety.[111]

Immunotherapy

Immunotherapy is a promising approach to cancer treatment that involves the use of the immune system to target and destroy cancer cells, as shown in Figure 1. This approach includes the use of immune checkpoint inhibitors, chimeric antigen receptor (CAR) T-cell therapy, cancer vaccines, and adoptive cell transfer therapy.[112] Immunotherapy has been successfully used to treat various types of cancer, including melanoma, lung cancer, breast cancer, and gastric cancer.[113-116]

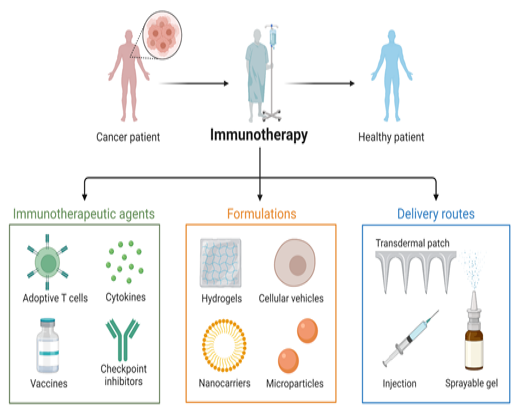

Figure 1: Immunotherapy, a cancer treatment method, aims to halt or decelerate cancer progression by harnessing immune system cells or agents. These components are directed toward tumor tissues or cells to intervene in their activities.

The use of immunotherapy in cancer treatment has profoundly changed the mode of cancer treatment and is on the rise.[117,118] Combination therapies involving immunotherapy and other treatment modalities, such as chemotherapy and radiation therapy, have also been explored as a way to improve the effectiveness of cancer treatment.[119] However, there are still challenges in cancer immunotherapy,

including the development of resistance to immunotherapy and the identification of biomarkers to predict patient response to immunotherapy. Overall, immunotherapy is a promising approach to cancer treatment, and ongoing research is needed to improve its effectiveness and minimize its side effects.[112]

INNOVATIVE APPROACHES

Metastasis is a major challenge in cancer treatment, and novel immunotherapies have been developed to address this issue. Several studies have reported the effectiveness of immunotherapy in treating metastatic cancer, including nasopharyngeal carcinoma, melanoma, intrahepatic cholangiocarcinoma, colon cancer, and non-small-cell lung cancer.[120-124]

The use of immunotherapy in combination with other treatment modalities, such as stereotactic radiosurgery and targeted therapy, has also been explored as a way to improve the effectiveness of cancer treatment.[125,126] However, there are still challenges in cancer immunotherapy, including the development of resistance to immunotherapy and the identification of biomarkers to predict patient response to immunotherapy. Overall, immunotherapy is a promising approach for the treatment of metastatic cancer, and ongoing research is needed to improve its effectiveness and minimize its side effects.[127,128]

CART-T Cell Therapy

CAR-T cell therapy is a promising immunotherapy approach for cancer treatment, as shown in Figure 2. It involves genetically modifying a patient's T cells to express CARs that can recognize and target cancer cells.[129,130]

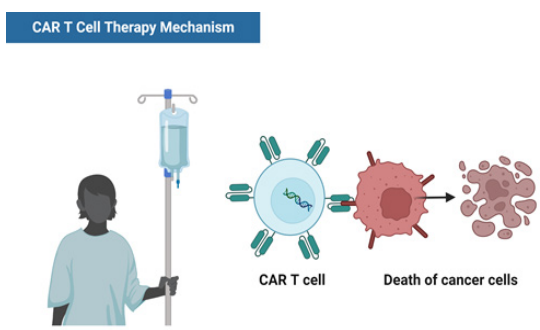

Figure 2: CAR-T cell therapy has revolutionized cancer treatment and has the potential to provide a curative option for patients who are refractory to standard treatments.

The CAR-T cell therapy has shown significant clinical success in treating hematological malignancies, such as acute lymphoblastic leukemia and multiple myeloma.[131-133] However, there are still challenges in optimizing CAR target design, enhancing CAR-T cell efficacy and persistence, and reducing toxicity.[134,135]

Additionally, emerging resistance to CAR-T cell therapy associated with antigen escape and poor CAR-T cell persistence has been identified, highlighting the need for ongoing research to address these issues.[131]

Despite these challenges, CAR-T cell therapy has revolutionized cancer treatment and has the potential to provide a curative option for patients who are refractory to standard treatments.[131,136]

Checkpoint Inhibitor Therapy

Checkpoint inhibitors are a class of immunotherapy drugs that have revolutionized cancer treatment, as shown in Figure 3. They work by blocking the immune checkpoint proteins that cancer cells use to evade the immune system, allowing the immune system to recognize and attack cancer cells.[137,138]

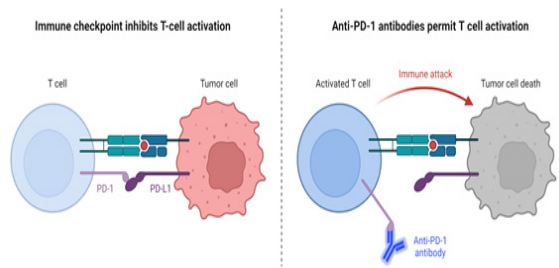

Figure 3: Checkpoint inhibitors are a type of immunotherapy that has revolutionized the treatment of various types of cancer. They work by targeting specific proteins called immune checkpoints, which regulate the immune system's response to prevent it from attacking healthy cells. These immune checkpoints, such as programmed cell death protein 1 (PD-1) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), are often exploited by cancer cells to evade immune detection.

Checkpoint inhibitors have shown significant clinical success in treating various types of cancer, including metastatic colorectal cancer, lung adenocarcinoma, and triple-negative breast cancer.[139-1441] However, they can also cause immune-related adverse effects (irAEs), such as autoimmune disorders and fulminant diabetic ketoacidosis.[137]

To improve the efficacy of checkpoint inhibitors,

combination therapy strategies have been explored, including combinations with radiation therapy, chemotherapy, and other existing cancer treatments.[142]

Additionally, the identification and validation of predictive biomarkers for checkpoint inhibitor response are crucial for personalized cancer treatment. Overall, checkpoint inhibitors have provided a new direction in cancer treatment, and ongoing research is needed to optimize their effectiveness and minimize their side effects.[143]

Therapeutic Cancer Vaccines

Cancer vaccines are a promising approach to cancer treatment that aims to activate the patient's immune system to specifically target cancer cells, as shown in Figure 4. Several types of cancer vaccines have been developed, including peptide vaccines, dendritic cell vaccines, and adoptive cell transfer therapies.[144]

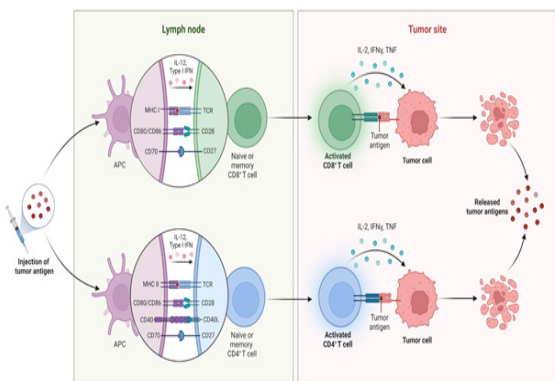

Figure 4: Cancer vaccines are designed to stimulate the body's immune system to recognize and destroy cancer cells. The principle behind cancer vaccines is to activate and strengthen the immune response against cancer-specific antigens, substances found in cancer cells but not in normal cells. By targeting these antigens, cancer vaccines aim to elicit a specific immune response against cancer cells while protecting normal cells.

Clinical trials have shown promising results for cancer vaccines in combination with other active therapies, such as immune checkpoint inhibitors, chemotherapy, and radiotherapy.[145,146] However, the selection of suitable peptide antigens and treatment conditions is crucial for the success of cancer vaccine therapy.[147]

Future perspectives for cancer vaccines include the identification of biomarkers for response prediction and patient selection, as well as the optimization of clinical trial design and combination therapies. Overall, cancer vaccines have the potential to provide a personalized and effective treatment option for cancer patients, and ongoing research is needed to optimize their effectiveness and minimize their side effects.[148,149]

Adoptive Cell Transfer Therapy

Adoptive cell transfer therapy is a promising approach to cancer treatment that involves the extraction and manipulation of a patient's immune cells to target cancer cells. This therapy has shown significant clinical success in treating various types of cancer, including lung and liver cancer, hematologic malignancies, and pancreatic cancer.[150-153]

Adoptive cell transfer therapy can involve the transfer of various immune cells, including T cells, natural killer cells, and regulatory immune cells.[154,155] Genetic engineering can also be employed to enhance the effectiveness of adoptively transferred immune cells.[156,157] Despite the promising results, there are still challenges in optimizing the efficacy and safety of adoptive cell transfer therapy, including the selection of suitable immune cells and the identification of predictive biomarkers for response. Overall, adoptive cell transfer therapy has the potential to provide a personalized and effective treatment option for cancer patients, and ongoing research is needed to optimize its effectiveness and minimize its side effects.[158-160]

In conclusion, metastatic cancer signifies the spreading of cancer to distant organs, imposing limitations on treatment options. While conventional therapies like chemotherapy and radiotherapy are frequently employed for metastatic cancer, a fresh perspective emerges through immunotherapy. This approach leverages the immune system's potential to combat cancer cells, aiming to arrest their growth. Immunotherapy employs drugs targeting immune system checkpoints, thwarting cancer cells' mechanisms that hinder immunity. Consequently, the immune system launches an assault, eradicating cancer cells. Encouraging outcomes have manifested in metastatic cancer patients through these innovative immunotherapies. Notably, certain immunotherapy drugs have exhibited efficacy in treating resilient cases of melanoma, lung cancer, kidney cancer, and bladder cancer. Nevertheless, immunotherapy's impact may vary, accompanied by potential side effects. Immune responses can occasionally escalate, causing inflammation and organ susceptibility. Yet, the benefits frequently outweigh these drawbacks. In essence, immunotherapy presents newfound

optimism for those with metastatic cancer. Nonetheless, individual responses differ, underscoring the need for close collaboration with healthcare professionals to comprehend the potential and risks of immunotherapy.

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