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Review Article

Impact the Influence of Immunotherapy on Cancer

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Abstract:

Immunotherapy is a treatment that uses certain parts of a person's immune system to fight diseases such as cancer, when the immune response is not strong enough to recognize cancer cells or signals are produced by cancer cells that make the immune system unable to attack them or the cancer cells escape from the immune system. Immunotherapy helps the immune system to destroy cancer. Immunotherapy can be useful for a few types of cancer, but it is not suitable for all types of cancers. Immunotherapy can be used on its own(alone), or in combination with other treatments such as chemotherapy, surgery, or radiotherapy. This review article emphasizes the pivotal role that advancements in cancer immunotherapy's history have played in establishing treatments that are now considered standard of care and delineates several primary strategies employed in the field of cancer immunotherapy (cancer vaccines, adoptive cellular immunotherapy, immune checkpoint blockade, and oncolytic viruses, Immunomodulators).

keywords: immune system and immunotherapy; necessity of immunotherapy; testing; typing of immunotherapy; side effects

Introduction

In contrast to prior benchmarks of treatment (such as radiotherapy, chemotherapy, and surgery), cancer immunotherapy has yielded substantial advancements in both survival rates and overall well-being for cancer patients. Immunotherapy has emerged as an innovative cornerstone in cancer treatment (Esfahani et al., 2020). Agents are utilized in cancer immunotherapy to stimulate or enhance the immune system's activation to combat cancer cells via intrinsic mechanisms, many of which are circumvented as the disease advances (Riley et al., 2019). The goal of cancer immunotherapy is to activate a patient's T-cells so that they can attack and kill malignancies. Amazing recovery stories abound, with individuals remaining cancer-free for years after receiving the treatment. Although using immune cells to combat cancer is not new, scientists have recently accumulated enough clinical evidence to show how transformative cancer immunotherapy can be. Because this field is not without its challenges, the future seems bright (Meiliana, Dewi, and Wijaya, 2016). "immunotherapy" refers to the application of substances that suppress or restore the immune system's capacity to defend against and prevent illness. A balance is maintained in the immune system so that cancer cells can be eliminated without unchecked autoimmune inflammatory responses, which are detrimental to the efficacy of immunotherapies and represent one of their therapeutic limitations. Innate immunity is restricted to the activation of non-specific immune responses by releasing cytokines that recruit immune cells to begin the non-specific immune response (Abbott and Ustoyev, 2019). For cancer immune therapy, these are exciting times. After years of poor results, the tide has finally turned, and immunotherapy has been clinically approved for various malignancies. Cancer vaccines, oncolytic viruses, adoptive transfer of ex vivo activated T and natural killer cells, and administration of antibodies or recombinant proteins that either co-stimulate cells or block so-called immune checkpoint pathways are all examples of immunotherapeutic techniques. The recent success of certain immunotherapeutic regimens, such as monoclonal antibody blocking of cytotoxic T lymphocyte-associated protein 4 (CTLA-4) and programmed cell death protein 1 (PD1), has accelerated the development of this therapy modality, resulting in the rapid creation of novel therapy targets and schemes that combine multiple immunological agents(Farkona, Diamandis and Blasutig, 2016). Controlled modulation of the immune system continues to be a significant obstacle in the widespread application of immunotherapies for cancer, given that these treatments induce severe adverse effects such as autoimmunity and nonspecific inflammation. Gaining insight into methods to enhance response rates for different categories of immunotherapy is crucial for optimizing effectiveness and managing these detrimental effects (Riley et al., 2019).

The Immune System and Immunotherapy

The immune system has created a range of intricate processes to identify and eliminate cancer cells(Kennedy and Salama, 2020). By distinguishing between self and non-self, the human immune system safeguards the body

against both exogenous and endogenous pathogens. The immune system, which is comprised of white blood cells and lymphatic system organs and tissues (thymus, spleen, tonsils, lymph nodes, lymph vessels, and bone marrow), recognizes and eliminates numerous threats to maintain homeostasis. To comprehend how immunotherapy has become a cornerstone of cancer treatment, one must know the interaction between cancer cells and the immune system An objective of immunotherapy is to maintain immune system equilibrium so that cancer cells can be eliminated without unchecked autoimmune inflammatory responses, which are detrimental to the efficacy of immunotherapies (Abbott and Ustoyev, 2019).

Necessities of Immunotherapy

Immunotherapy for the treatment of cancer is a critically important and validated method. In light of the substantial research and clinical investigation endeavors devoted to the advancement of endogenous and synthetic immunotherapy strategies, it is imperative to concentrate on fundamental inquiries and delineate obstacles impeding both fundamental comprehension and clinical advancement. From identifying the most effective combinations of immune-based therapies for a given patient to overcoming a lack of confidence in the translation of preclinical findings, here we identify ten of the most significant obstacles that cancer immunotherapy must overcome (Hegde and Chen, 2020).

Ten Key Challenges of Immunotherapy

- Establishment of pre-clinical models applicable to the study of human immunity
- 2. Identifying the primary determinants of cancer immunity
- Recognizing the immune context specific to organ-specific tumors
- 4. Comprehension of the cellular and molecular mechanisms underlying primary as opposed to secondary immune evasion
- Comparing the advantages of endogenous and synthetic immunity.
- Evaluation of cancer immunotherapy combinations in earlyphase clinical studies in an effective and efficient manner.
- Comprehensive analysis of the effects of immune suppression and steroid use on cancer immunotherapy and autoimmune toxicities.
- 8. Optimizing individualized strategies via composite biomarkers.
- Establishing enhanced regulatory endpoints for immunotherapy against cancer.

 Maximizing long-term survival through combination regimens of multiagent cancer immunotherapy (Hegde and Chen, 2020).

Testing

Numerous studies provide empirical evidence in favor of the hypothesis that immunotherapy exhibits heightened efficacy when applied to tumors that are highly mutagenized. Immunotherapy has significantly transformed the landscape of cancer treatment with immune checkpoint-based therapy experiencing especially rapid advancements. However, the efficacy of these immunotherapies is limited to a fraction of patients. As a result, patient selection is critical to prevent treatment-associated toxicity and expense for patients who are likely to gain any benefit. The establishment and verification of dependable surrogate biomarkers that can forecast clinical benefit or offer an early indication of response will be necessary for this purpose. Numerous ongoing initiatives are focused on the identification of predictive biomarkers for immune checkpoint therapy (Farkona, Diamandis and Blasutig, 2016).

Types of Cancer Immunotherapy

- 1-Immune checkpoint therapy
- 2-T-cell transfer therapy
- 3-Monoclonal antibodies
- 4-Oncolytic virus immunotherapy
- 5-Immunomodulators
- 6-Cancer vaccines

1.Immune checkpoint therapy

The recent success of immune checkpoint therapy, which uses antibodies to block the CTLA-4 and PD-1 pathways to treat cancer patients, is due to the elucidation of mechanisms underlying cancer immune regulation (Yang, 2015). CTLA-4 isn't the only checkpoint being studied by scientists and drug makers. Drugs that block a particular checkpoint, PD-1, seem to be more successful and have fewer side effects than Ipilimumab (anti-CTLA4 drug), according to early trials (Meiliana, Dewi and Wijaya, 2016). The accumulation of evidence about immune checkpoint inhibitors indicates that their efficacy is not universal, but rather restricted to certain subpopulations of cancer (Igarashi and Sasada, 2020).

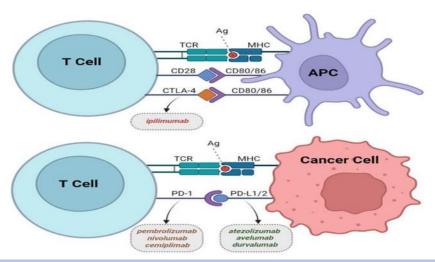


Figure 1: Blockade of immune checkpoints to enhance T cell responses. After T cell activation, T cells express immune checkpoints (Basudan, 2022).

2.T-cell transfer therapy

Particularly during the equilibrium phase, T cells play a crucial role in regulating tumor development throughout the immunoediting process(O'Donnell, Teng and Smyth, 2019). Regarding the treatment of cancer, immunotherapy represents an extraordinary clinical development. Current immunotherapies for cancer, such as immune checkpoint inhibitors and adoptive cell therapies, rely heavily on T cells for their effectiveness. T cell exhaustion, a hypofunctional state distinguished by

a gradual decline in the ability of T cells to renew themselves and execute effector functions, is, nevertheless, a correlation with cancer. Considered a pathway of resistance for cellular immunotherapies, the "un-exhaustion" of T cells in the microenvironment of the tumor is widely recognized as a crucial mechanism by which immune checkpoint inhibitors function. Insights into the transcriptional and epigenetic mechanisms that regulate T-cell exhaustion have been illuminated by several elegant studies (Chow et al., 2022).

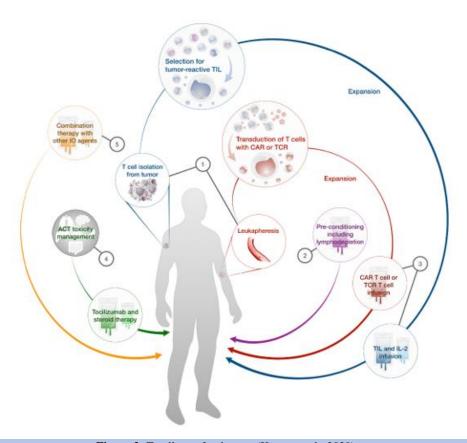


Figure 2: T-cell transfer therapy (Kruger et al., 2020).

There are two types of T-cell transfer therapy

A-Chimeric Antigen Receptors

Therapeutic applications of chimeric antigen receptor (CAR)-T cells are revolutionary due to the remarkable efficacy and durability of the results. CARs are synthetic receptors that have been engineered to redirect lymphocytes, predominantly T cells, to identify and eradicate cells that express a particular target antigen. The binding of CARs to target antigens that are expressed on the cell surface occurs in a manner that is not reliant on the MHC receptor. This leads to robust T-cell activation and potent anti-tumor responses. In 2017 the Food and Drug Administration (FDA) of the United States approved anti-CD19 CAR-T cell therapy in response to its extraordinary efficacy against B cell malignancies. Life-threatening CAR-T cell-associated toxicities, limited efficacy against solid tumors, inhibition and resistance in B cell malignancies, antigen escape, limited

persistence, poor trafficking, and tumor infiltration, and an immunosuppressive microenvironment are significant limitations of CAR-T cell therapy that remain to be addressed. Furthermore, to accommodate the demands of this expanding and dynamic industry, it is imperative to establish educational initiatives that provide workforce training. To increase antitumor efficacy, expand clinical efficacy, and reduce toxicities, numerous strategies have been suggested, such as combining CAR-T cell therapy with other anticancer therapies or employing novel CAR engineering techniques. This review examines recent advancements in CAR-T cell engineering that aim to enhance clinical effectiveness against solid and hematological tumors. It also addresses approaches to surmount existing obstacles, such as CAR-T cell-associated toxicities, antigen evasion, tumor infiltration, the immunosuppressive microenvironment, and tumor infiltration (Sterner and Sterner, 2021).

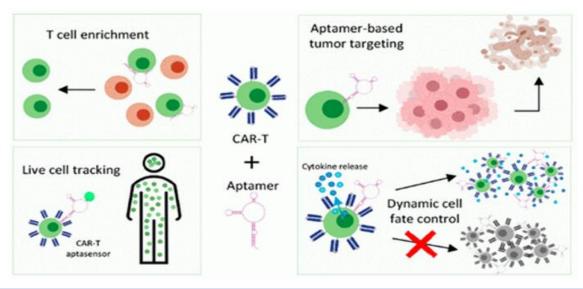


Figure 3: Chimeric antigen receptors therapy (Maru, Nadeau and McKeague, 2021).

BTumor Infiltrating Lymphocytes Immunotherapy

In contrast to other types of cancer, the clinical success of immune checkpoint blockade (ICB) for cancer has redirected interest toward tumor-infiltrating lymphocytes (TILs). In cancer patients, the efficacy of immune checkpoint inhibitor therapy has been associated with the magnitude and quality of T cell, NK cell, and, more recently, B cell responses in the tumor microenvironment. The examination of TIL gene expression profiles and clonality using cutting-edge single-cell analysis has unveiled an exceptional level of cellular heterogeneity, as well as discernible patterns of immune activation and exhaustion. Consistent with the broad clinical responses, a number of these states are standardized across tumor types. Notwithstanding this similarity, how various cancer types with comparable TIL landscapes react to immunotherapy differs, underscoring the intricate nature of the tumor-immune interactions that

lie beneath. Additionally, this observation is complicated by the substantial prognostic advantage of TILs observed in tumor types that have exhibited inadequate response to immunotherapy thus far. Thus, although there is a growing recognition of the importance of unifying single-cell-level lymphocyte infiltration and dysfunction, the investigation into biomarkers that predict response and prognosis is still in its early stages. It is now indisputable that the presence, activation, and stimulation of all lymphoid components of the immune system—CD8+ T cells, CD4+ T cells, B cells, and innate lymphoid cells—are essential for a successful antitumor immune response. This is demonstrated in particular by the identification of tertiary lymphoid structures (TLSs), which are clusters of TILs that are exceptionally well-organized and generate an advanced immune response (Paijens et al., 2021).

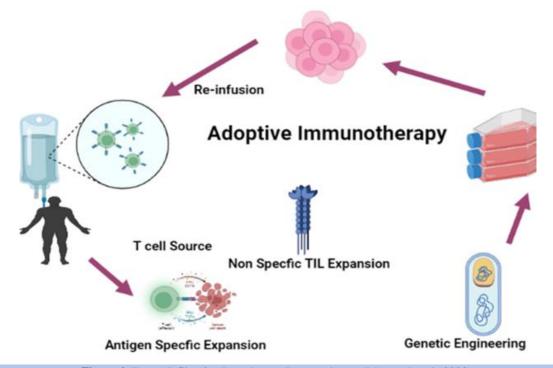


Figure 4: Tumor Infiltrating Lymphocyte Immunotherapy(Maqsood et al., 2023).

3.monoclonal antibodies

As an alternate treatment, monoclonal antibodies can be administered to cancer patients whose regular chemotherapy has failed or

progressed(Bayer, 2019). B-lymphocytes become active as a result of a foreign substance entering the body, and antibodies are produced in response to this foreign substance (antigen). Antibodies recognize the antigen's epitope regions. Monoclonal antibodies are antibodies that are generated against a single epitope rather than a complete epitope (mAb). The efficacy of mAbs in cancer immunotherapy is dependent on three basic mechanisms:

- 1-Antibody binding inhibits the factors and receptors that activate the signal pathways employed by cancer cells in division and angiogenesis, which is one of these processes.
- 2- Antibody-dependent cellular cytotoxicity (ADCC), which is made up of target monoclonal antibodies made up of chimeric or fully human antibody components that bind to specific antigens found in tumors.
- 3- Complement-dependent cytotoxicity (CDC) is a type of cytotoxicity caused by the activation of the complement system (Kimiz-Gebologlu, Gulce-Iz and Biray-Avci, 2018).

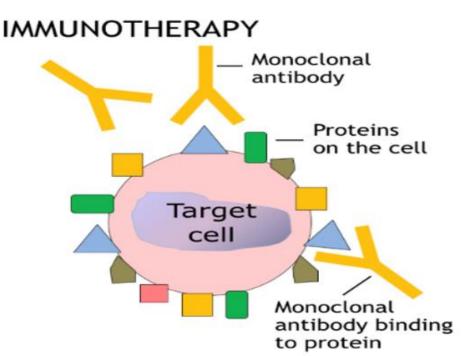


Figure 5: Monoclonal antibody immunotherapy in cancer(Xu, 2021).

4. Oncolytic virus immunotherapy

Oncolytic viruses, like other immunotherapies, operate by a multimodal mechanism that imparts direct and indirect toxicity to tumor cells. These effects include autolysis, immune cell honing, vascular supply disruption, and enhancement of other complementary anti-cancer treatments(Raja et al., 2018). At the outset, oncolytic viruses may be administered intratumorally, subcutaneously, intraperitoneally, or intraarterially, among others. The preferred entry of oncolytic viruses into tumor cells is facilitated by natural tropism and genetic targeting. Following this, oncolytic viruses begin to identify abnormal cells via substances expressed in the tumor environment and can connect with and infect the host cell via various receptors. At this juncture, the virus initiates its utilization of the cellular apparatus to facilitate its replication process. This results in the production of viral proteins, impairment of cellular functionality, induction of oxidative stress states, and activation of certain pathways associated with autophagic processes. Simultaneously, certain viral organisms are encapsulated within the antigen-presenting cells,

which initiates the formation of an endosomal vesicle that subsequently fuses with a lysosomal vesicle, resulting in the virus being digested and reduced to smaller particles that can be processed within the cell. Subsequently, the viral proteins and major histocompatibility complex class 2 are expressed on the cell surface, fostering an environment conducive to antigenic presentation and subsequent activation and stimulation of CD4+ and CD8+ T cells. The latter are involved in the direct destruction of the pathogen and the former in the synthesis of cytokines that aid in the maturation and migration of inflammatory cells. Ultimately, the eradication of tumor cells is facilitated by both the viral action and the immune response, which release viral progeny into the host organism. This allows the virus to infect additional aberrant cells and recommence its fight against the tumor. In addition, cell death facilitates the release of tumor antigens that can be recognized by the immune system, thereby promoting the development of novel inflammatory responses that can operate not only within the tumor microenvironment but also at metastatic sites (Apolonio et al., 2021).

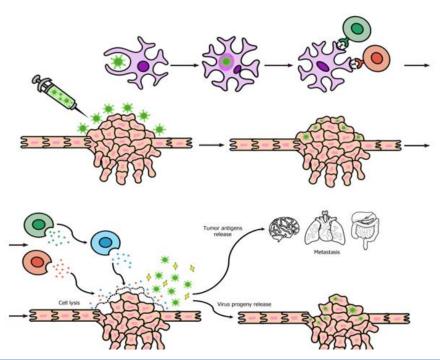


Figure 6: Oncolytic Virus therapy(Apolonio et al., 2021).

5.Immunomodulators

Small molecule immunomodulators targeting the adaptive immune system. Programmed cell death protein 1 (PD-1), also known as CD279, is a surface protein that can regulate the immune system by inhibiting Tcell activity. PD-1 is an important immunosuppressive molecule that plays a key role in the inhibition of antigen-specific T-cell response in diseases such as cancer. PD-1 is constitutively expressed in various immune cells like T lymphocytes, natural killer T cells, activated monocytes, and B lymphocytes. Nevertheless, PD-1 is only expressed on the cell surface of activated T lymphocytes rather than resting T cells. Thus, PD-1 can function as an intrinsic negative feedback loop for preventing T cell activation, thus reducing autoimmunity and promoting self-tolerance. PD-1 can be activated by two ligands including PD-L1 and PD-L2, which are also type I transmembrane proteins belonging to the B7/CD28 family. PD-L1 is widely expressed in lymphoid as well as tumor cells. Unlike PD-L1, the expression of PD-L2 is more restricted and barely found in tumor tissues. the infiltrated T cells overexpress PD-1, while tumor cells overexpress PD-L1 and PD-L2, which are induced by the tumor microenvironment (TME) in the body. The binding between

PD-1 and PD-L1 causes a down-regulation of T cell effector functions in cancer patients, thereby promoting immune escape and leading to the survival of tumor cells. Inhibitors that inhibit the interaction between PD-1/PD-L1 reinstate the functionality of T cells, thereby restoring their immune function in the fight against cancer. Inhibitors of PD-1/PD-L1, also referred to as ICIs (immune checkpoint inhibitors), have exhibited remarkable effectiveness against a wide range of tumor types. As of now, the FDA has approved a multitude of ICIs, all of which are monoclonal antibodies (mAbs). Notable examples include Pembrolizumab (BMS), which is anti-PD-1; Avelumab, which is anti-PD-L1; Ipilimumab (BMS), which is anti-CTLA-4; Duvalumab, which is anti-PD-L1; Nivolumab, which is anti-PD-1; atezolizumab (Roche, anti-PD-L1). Despite the promising anti-tumor activities demonstrated by these mAbs in patients with specific tumor types, the clinical implementation of these antibodybased ICIs was impeded by obstacles including oral bioavailability and immune-related adverse effects. Consequently, there has been a heightened focus on the advancement of small molecule-based ICIs due to their potential to surmount the aforementioned constraints associated with therapeutic antibodies (Wu et al., 2022).

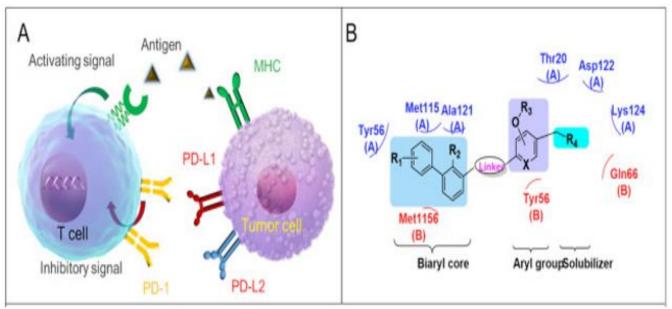


Figure 7: (A) PD-1/PD-L1 interaction between T cell and tumor cells. (B) Pharmacophore model of PD-1/PD-L1 immunomodulators (Wu et al., 2022).

6.Cancer Vaccines

In the past decade, therapeutic vaccinations against cancer have witnessed a revival. Advancements in understanding the magnitude of tumorassociated antigens, the mechanisms behind the host immune response, and the development of novel antigen delivery methods have collectively facilitated the enhancement of vaccine design(Song, Zhang and Wu, 2018). Therapeutic cancer vaccines can be incorporated into the treatment regimen for a wide array of cancer subtypes and stages(Schlom et al., 2014). Analyses of many tumor antigens have uncovered target characteristics that result in a high degree of selectivity towards tumor cells as opposed to normal cells and sufficient immunogenicity to impact therapeutic effectiveness. A limited number of tumor-associated antigens (TAIs), which are host proteins that are normally expressed but abnormally expressed in cancer cells, have exhibited promise as immunotherapeutic targets(Hollingsworth and Jansen, Therapeutic cancer vaccines aim to achieve the following objectives: promote tumor regression, eliminate minimal residual disease, establish durable antitumor memory, and prevent non-specific or adverse reactions. However, monoresistance and tumor-induced immunosuppression present formidable obstacles to achieving this objective. Vaccines against cancer commonly comprise exogenous delivery of specific tumor antigens in conjunction with adjuvants that stimulate dendritic cells

(DCs), or DCs themselves. Boosting the patient's adaptive immune system against particular tumor antigens is the objective of therapeutic cancer vaccines to restore tumor growth control, induce regression of established tumors, and eliminate minimal residual disease. Successful therapeutic vaccination against tumors requires the following fundamentals: delivery of large quantities of a high-quality antigen to dendritic cells (DCs), optimal activation of DCs, induction of robust and sustained CD4+ T helper cell and cytotoxic T lymphocyte (CTL) responses, infiltration of the tumor microenvironment (TME), and maintenance and durability of the immune response. There are multiple approaches to achieve this goal, including the use of immune checkpoint inhibitors to reverse the immune exhaustion induced by the tumor, the administration of adjuvants containing tumor-associated antigens to stimulate DCs and effector T cells, or vaccination with autologous DCs loaded with specific tumor antigens. Conversely, the local immune environment of the tumor can be extensively stimulated to promote apoptosis of tumor cells. Furthermore, the availability of tumor antigens can be enhanced through the application of in situ vaccines (ISVs). In contrast to conventional vaccine methods, which involve the meticulous selection, purification, or preparation of antigens before injection into patients, the in-situ approach produces the vaccine within the tumor microenvironment (TME) through the utilization of antigens derived from deceased or dying tumor cells (Saxena et al., 2021).

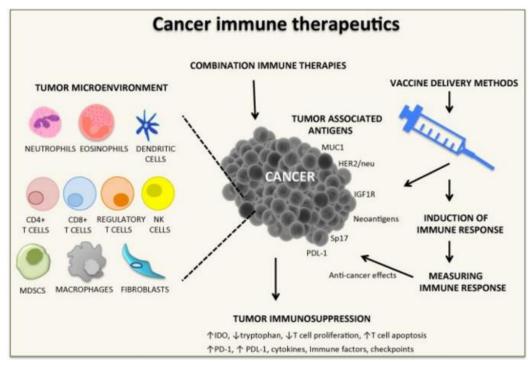


Figure 8: Mechanism of Cancer Vaccine (Apostolopoulos, 2019).

Side Effects of Cancer Immunotherapy

Immunotherapies cause adverse effects through immune-mediated tissue damage to healthy tissues as shown in the(table1) below. This is because these therapies operate by modulating the interactions that occur between cancer cells and the immune system. Skin and mucosal surfaces, the luminal gastrointestinal tract, the liver, and the endocrine system are the most frequently affected organs. Mucositis may manifest as a dry mouth, whereas erythematous, reticular, or maculopapular skin rashes are typically the initial adverse effects. A prevalent adverse effect of anti-CTLA-4 antibodies is diarrhea. Similar characteristics to graft-versushost disease are observed in luminal gastrointestinal tract biopsies, including villous blunting (small intestine), increased crypt epithelial cell apoptosis, lymphoplasmacytic lamina propria expansion, neutrophilic

infiltration of epithelium, cryptitis, and crypt abscess formation. Although elevated levels of lymphocytes within the epithelial lining are uncommon, ipilimumab treatment may be linked to symptoms in the duodenal mucosa that resemble coeliac disease. It is noteworthy that immunotherapy-associated colitis may exhibit a favorable response to antitumor necrosis factor- α therapy, such as in the case of infliximab. Histolytic symptoms typically manifest as increased levels of transaminase in the bloodstream, although elevated bilirubin levels may also be detected. Lobular inflammation accompanied by perivenular accentuation or inflammation of the portal tract encompassing the bile ducts may be observed in liver biopsies. Involvement of the endocrine system generally leads to generalized symptoms including fatigue, nausea, and headache. (Bateman, 2019).

Sites of potential side effects for immune checkpoint inhibitor therapies	
Sites	Examples
Kidney	Granulomatous interstitial nephritis. Membranous glomerulopathy
Pancreas	Acute pancreatitis
Neurological system	Encephalitis. Aseptic meningitis. Enteric neuropathy. Transverse myelitis.
Hematological system	Red cell aplasia. Neutropenia. Thrombocytopenia.
Lungs	Sarcoidosis. Organizing pneumonia. Pneumonitis.
Endocrine system	Hypophysitis Hypothyroidism. Adrenal crisis.
Liver	Hepatitis
Luminal gastrointestinal tract	Gastritis. Enteritis. Colitis.
Skin and mucosae	Rash. Oral mucositis.

Table 1: Sites of potential side effects for immune checkpoint inhibitor therapies (Bateman, 2019).

The mechanism of drug resistance in immunotherapy

Immunity against cancer comprises immune surveillance, equilibrium, and evasion. By recruiting immune regulatory cells, downregulating tumor antigen expression, releasing immune inhibitory factors, and employing other immune evasion mechanisms within the host, tumor

cells can elude immune system recognition and attack. This enables the cells to progress to metastasize and ultimately develop into visible tumor lesions. Additionally, it is possible to induce tumor proliferation through the targeted amplification of proteins that evade immune detection, such as PD-L1, arachidonic acid lipoxygenase, and IDO1/IDO-2. Mechanisms underlying resistance(Tan, Li and Zhu, 2020).

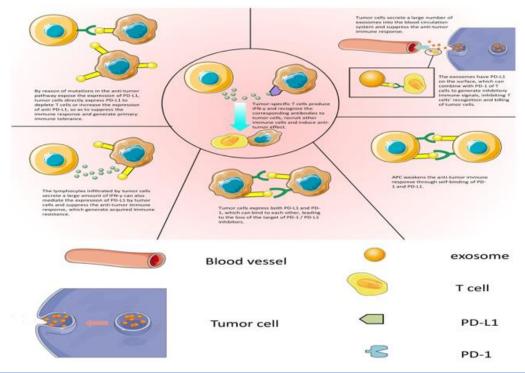


Figure 9: The mechanism by which immunotherapy induces drug resistance (Tan, Li and Zhu, 2020).

The pros and cos of Cancer Immunotherapy

Anti-tumor immunotherapy is presently assuming a role of growing significance within the domain of tumor therapy. Positive outcomes have been observed in treatment trials about a range of malignant tumors. By identifying novel targets and approaches, including combination therapy, the effectiveness of immunotherapy is enhanced, and adverse reactions are diminished. However, immunotherapy remains a subject of controversy due to several factors, including empirical and practical limitations, treatments that result in blindness, individual cases of severe and potentially fatal adverse reactions, the unpredictable nature of the therapeutic effect, and the exorbitant cost of treatment. Below the benefits and drawbacks of immunotherapy are detailed. Recognizing that tumor

development is a dynamic and intricate process, it would be possible to conduct targeted immunotherapy under the immune status of patients and the characteristics of the tumor to achieve the most effective therapeutic effect and restore the health of patients afflicted with tumors (Tan, Li and Zhu, 2020).

The Advantages of Cancer Immunotherapy

- The prognosis for patients with "immunoinflammatory" tumors is considerably improved over the long term.
- Exceptional precision, targeting, and specificity of immunotherapy.
- 3. Immunotherapy exhibits sustained efficacy.
- 4. Extensive flexibility. The therapy is effective against and fatal to numerous types of tumors.
- 5. Maintain your persistence. The treatment stimulates the immune system to restore immune function and permanently eliminate tumor cells.
- Strive for comprehensiveness. It can enhance and reinstate
 the immune system, precisely detect, locate, and eliminate
 malignant cells, as well as efficiently thwart tumor
 regrowth and metastasis.

- 7. With meticulousness. It can eliminate microscopic lesions and residual tumor cells from the body.
- 8. There are fewer adverse effects compared to the conventional treatment (Tan, Li and Zhu, 2020).

The disadvantages of cancer immunotherapy

- 1. The treatment objects have limitations, and the users are subject to a high degree of selectivity. When "immune suppression type" and "immune exclusion type" tumors are present, immunotherapy has a diminished effect.
- 2. Employing immune checkpoint inhibitors may result in adverse regulatory responses, which may escalate to the point of fatal autoimmune diseases.
- Certain patients may experience a range of non-specific toxic and side effects following treatment, including hyper progressive disease that has the potential to hasten their demise.
- The efficacy of immunotherapy is contingent upon a multitude of factors. Patients' prognoses and rates of survival are uncertain.
- 5. The cost of treatment is substantial(Tan, Li and Zhu, 2020).

Conclusion

Cancer immunotherapy, a therapeutic approach that harnesses the patient's immune system to combat the disease, is currently experiencing a surge in popularity. Vaccines, CAR-T cell therapy, and immune checkpoint therapy have collectively transformed the landscape of cancer treatment. Using CRISPR/Cas9 technology, specific genes or receptors can be silenced in allogenic T cells, potentially stimulating an immune response against these genetically modified cells when introduced intravenously into a patient. Furthermore, inaccessible to a surgeon, the activated and tumor-specific T cells are capable of efficiently penetrating those regions. The genetically modified tumor-specific T cells can therefore target even the most minute components of the disease. As

opposed to alternative anti-cancer therapies, cancer immunotherapy does not induce significant cellular damage in healthy cells that are near the cancerous cells. In contrast to alternative treatments, it elicits prolonged clinical benefits and induces fewer adverse effects. Despite being regarded as a safer alternative to chemotherapy, immunotherapy is not without its limitations and adverse effects. Generally, dramatic and diverse treatments are administered, depending on the type, location, and patient of the cancer. As a result of the progress made in the field of cancer immunotherapy, the current emphasis is on treating the biological characteristics of tumors. In particular, for cancer immunotherapy to be effective, methods must be developed to regulate acquired resistance and ensure that tumors exhibit almost no resistant response. Therefore, the immunotherapy patient must be treated with caution and under appropriate monitoring.

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