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The Role of CD8+ T Cell in Lung Cancer

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Abstract

English:

Background and Objective: *Lung cancer is a common and difficult-to-diagnose form of cancer. CD8+ T cells, a type of white blood cell, play a crucial role in the immune system's ability to recognize and eliminate cancerous cells. The presence of CD8+ T cells in lung cancer patients is associated with a better prognosis. Immunotherapy utilizing CD8+ T cells has shown promise in treating lung cancer and improving patient survival rates. However, there are challenges to using CD8+ T cells as a therapy. This article aims to explore the role of CD8+ cell in lung cancer.*

Methods: *Literature searches were conducted using four databases, namely PubMed, Scopus, Central, and EBSCOhost. We used mesh terms and Boolean operators for optimal results.*

Key Content and Findings: *T cells and B cells are important components of the immune system in fighting cancer. T cells, specifically CD8+ T cells, can identify and kill cancer cells, but they can also be inhibited by cancer cells. B cells recognize cancer cells and produce antibodies to fight them, but their effectiveness can be limited. CD8+ T cells play a role in lung cancer prognosis, and their activity is influenced by the tumor microenvironment. Understanding these immune system mechanisms can help develop more effective cancer treatments.*

Conclusions: *CD8+ T cells play an important role in the body's immune system to fight lung cancer cells, through antigen recognition, effector mechanisms (granzyme and perforin), cytokine production, and activation of natural killer (NK) cells.*

Keywords

CD8+ T cells • immuno-oncology • lung cancer

Rolul celulelor T CD8+ în cancerul pulmonar

Rezumat

Romanian:

Context și Obiectiv: *Cancerul pulmonar este o formă comună și dificil de diagnosticat a cancerului. Celulele T CD8+, un tip de globule albe, joacă un rol crucial în capacitatea sistemului imunitar de a recunoaște și elimina celulele canceroase. Prezența celulelor T CD8+ la pacienții cu cancer pulmonar este asociată cu un prognostic mai bun. Imunoterapia utilizând celulele T CD8+ a arătat promisiuni în tratarea cancerului pulmonar și îmbunătățirea ratei de supraviețuire a pacienților. Cu toate acestea, există provocări în utilizarea celulelor T CD8+ ca terapie. Acest articol își propune să exploreze rolul celulelor CD8+ în cancerul pulmonar.*

Metode: *S-au efectuat căutări în literatură folosind patru baze de date, respectiv PubMed, Scopus, Central și EBSCOhost. Am folosit termeni mesh și operatori booleani pentru rezultate optime. Conținut cheie și Descoperiri: Celulele T și celulele B sunt componente importante ale sistemului imunitar în lupta împotriva cancerului. Celulele T, în special celulele T CD8+, pot identifica și ucide celulele canceroase, dar pot fi, de asemenea, inhibită de celulele canceroase. Celulele B recunosc celulele canceroase și produc anticorpi pentru a le combate, dar eficacitatea lor poate fi limitată. Celulele T CD8+ joacă un rol în prognosticul cancerului pulmonar, iar activitatea lor este influențată de micromediul tumoral. Înțelegerea acestor mecanisme ale sistemului imunitar poate contribui la dezvoltarea unor tratamente mai eficiente împotriva cancerului.*

Concluzii: *Celulele T CD8+ joacă un rol important în sistemul imunitar al organismului în lupta împotriva celulelor canceroase pulmonare, prin recunoașterea antigenului, mecanismele efector (granzimă și perforină), producția de citokine și activarea celulelor ucigașe naturale (NK).*

Cuvinte-cheie

Celule T CD8+ • imuno-oncologie • cancer pulmonar

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Introduction

One of the most prevalent cancers worldwide is lung cancer. Changes in lung cells that cause unchecked cell development are typically the cause of this malignancy. Effective lung cancer treatment is still a problem for medical professionals since lung cancer is frequently challenging to diagnose in its early stages. White blood cells called CD8+ T cells are a crucial component of the human immune system. CD8+ T cells have the ability to identify and eliminate virus-infected or cancerous cell-mutated cells [1].

The immune system's role in inhibiting cancer cell proliferation and preventing cancer cells from spreading to other human tissues is crucial. CD8+ T cells play this job. Recent research has demonstrated that CD8+ T lymphocytes are crucial in regulating lung cancer cell proliferation. The amount of CD8+ T cell infiltration and the prognosis of lung cancer are related, according to one of the research done by Zhang et al. (2020). Compared to patients with low levels of CD8+ T-cell infiltration, patients with high levels of CD8+ T-cell infiltration have a better prognosis, according to the study's findings [1, 2] .

Additionally, a number of studies indicate that immunotherapy using CD8+ T cells may be a successful therapy for the treatment of lung cancer. The use of immunotherapy therapy in patients with advanced lung cancer can markedly improve the patient survival rate, according to a study by Hellmann et al. (2018) [2]. In order to eliminate lung cancer cells, immunotherapy activates CD8+ T lymphocytes. There are still some difficulties in employing CD8+ T cells as a lung cancer therapy, despite the fact that their involvement in regulating lung cancer cell proliferation has been established. The success of immunotherapy therapy utilizing CD8+ T cells in patients with lung cancer may be hampered by a number of reasons, including the low level of infiltration of CD8+ T cells in tumors and tumor resistance to CD8+ T cells [1] .This article aims to explore the role of CD8+ cell in lung cancer, especially its role in lung cancer treatment. We present this article in accordance with the narrative review reporting checklist.

Methods

We conducted literature searches using four public databases: PubMed, Scopus, Central, and EBSCO. Our search strategy is summarized in Table 1.

Results

Immunity system

The immune system is a complex and coordinated system that protects the body from pathogens, microbes, mutated cells, and other foreign substances. The immune system is made up of many types of cells and molecules that interact in complex ways to provide effective protection. In addition, the immune system is also involved in many other biological processes such as tissue formation and maintenance, homeostasis, and immune tolerance. Therefore, a better understanding of the structure, function, and regulation of the immune system can aid in the diagnosis, treatment, and prevention of disease [3]. The immune system consists of two types of immune responses, namely the innate immune response and the adaptive immune response [3].

The innate immune response is an immune response that occurs quickly and generally is not specific to a particular pathogen. The innate immune response involves various types of immune cells such as macrophages, neutrophils, dendritic cells, and natural killer (NK) cells. In addition, the innate immune response also involves various immune molecules such as complement proteins, cytokines, and

Table 1. Search Strategy

Items	Specification	
Date of search	**March 27, 2023**	
Databases and search terms used	PubMed	("Immune System"[Mesh]) OR "CD8-Positive T-Lymphocytes"[Majr] AND (("Lung Neoplasms"[Mesh]) AND "Therapeutics"[Mesh])
	Scopus	(("immune system") OR ("CD8")) AND (("lung cancer") OR ("lung neoplasm"))
	Central	((MeSH descriptor: [Immune System] explode all trees) OR (MeSH descriptor: [CD8-Positive T-Lymphocytes] explode all trees)) AND (MeSH descriptor: [Lung Neoplasms] explode all trees)
	EBSCO	(MM"immune system") AllFields AND (MM"lung cancer")
Inclusion criteria	Study designs: meta-analysis, systematic review, randomized controlled trial, prospective or retrospective cohort, cross-sectional Relevance to the topic Articles reported in English	
Exclusion criteria	Full article unavailable	
Selection process	The selection process was conducted independently by the authors	

receptor pattern recognition (PRR) [3]. The adaptive immune response is a slow and specific immune response against certain pathogens. The adaptive immune response involves immune cells called B lymphocytes and T lymphocytes, which can recognize and target pathogens specifically. These lymphocytes take time to develop and react to pathogens, but once formed, they can form immune memories that result in a more rapid and effective response if the same pathogen reappears [4].

T cells and B cells as components of the immune system

A key component of the body's immunological response to cancer is the kind of cell known as T cells. T-cell receptors on cancer cells' cell surfaces help cytotoxic T cells (Tc) identify cancer cells and then release cytokines that can kill cancer cells. T helper (Th) cells can also activate Tc cells and boost the immune system's defenses against cancerous cells. T cells are crucial for identifying and killing cancer cells that are immune-evading, like cancer cells with altered expression of cell surface proteins [4]. T cells can run out of energy and lose their ability to fight cancer in individuals with advanced disease, which is a significant barrier. Exhaustion of T cells resulted from the induction of T cells by advanced cancer cells to express a number of additional co-inhibitory receptors, including PD-1, BTLA, LAG-3, TIM-3, T cell immunoglobulin domain, and T-cell immunoglobulin immunoreceptor tyrosine-based inhibitory motif domain (TIGIT) [5]. In addition, cancer cells can also avoid T cells by changing the expression of proteins on their surface, thereby making it difficult for T cells to recognize and fight cancer cells [6].

The immune system, particularly T cells, are unable to recognize cancer cells due to the change in protein expression on the surface of cancer cells. The mechanism involves the inhibition of the peptide-MHC component or the downregulation of the MHC-I protein production. Another method is the mutation or transcriptional suppression of antigen expression, proteasome components, TAP1/TAP2, and 2-microglobulin. Additionally, the microenvironment of cancer cells promotes cells that suppress the immune system. In addition to promoting the development of cancer, the cancer microenvironment can promote the differentiation of macrophages into M2-type cancer-associated macrophages that also release IL-10, which inhibits the CD8+ T cell response. Another collection of heterogeneous cells that thrive in the cancer microenvironment are myeloid-derived suppressor cells. The cytotoxic activity of effector T cells is inhibited by the production of arginase, inducible nitric oxide synthase (iNOS), and TGF-, which decreases the expression of cytotoxic enzymes such perforin and granzyme. Furthermore, T regulator cell differentiation is induced by the cytokines generated. The expansion of T regulatory cells will reduce CD8+ T cell response and accelerate the development of malignancy [5].

B cells, at the same time, are another component of the immune system that plays an important role in the body's immune response to cancer. B cells recognize cancer cells via a cell surface receptor called the B-cell receptor (BCR) and then produce antibodies to fight the cancer cells. B cells can also become memory cells, which can remember cancer cells and amplify the immune response in the event they occur [7]. However, B-cell-focused immune therapies are still in early development and several challenges need to be investigated [8].

One of the main problems is the production of antibodies by B cells that are sometimes not strong enough to destroy cancer cells. In addition, the number of B cells in cancer patients can also be reduced, thereby affecting the body's immune response to cancer [7]. To optimize immune cancer therapy, efforts are needed to develop therapies that are more effective in manipulating T cells and B cells in fighting cancer. One of the most promising recent approaches is an antigen-specific receptor (CAR)-based T-cell therapy that activates Tc cells to fight cancer cells. In addition, the development of more

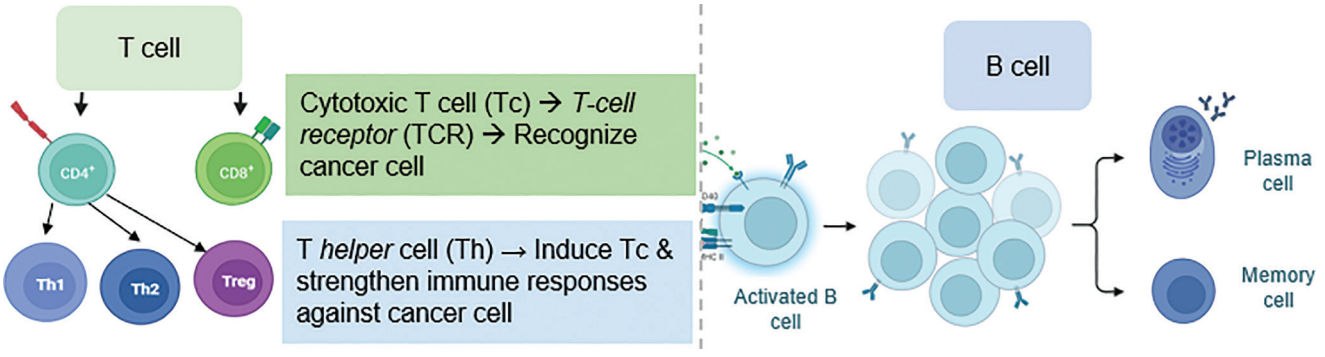

Figure 1. The role of T cells and B cells.

effective and innovative B-cell therapies is also an important goal in treatment [8].

CD8+ T cells: characteristics and role in the immune system

T cells that express CD8 and CD8 proteins on their cell surfaces are known as CD8+ T cells. The bone marrow produces CD8+ T lymphocytes, which develop in the thymus before traveling throughout the body via the blood and lymphatic systems. Target cells can be engaged by CD8+ T cells through cell surface receptors and T-cell receptors, and they can be eliminated by a process known as cytolysis [4]. Additionally, CD8+ T cells can develop into memory cells, which can recall infections or cells that have already been encountered and boost the immune response.

In addition, CD8+ T cells can also produce cytokines, which are signaling molecules used to regulate the activities of other T cells and B cells in the immune system [4]. The main role of CD8+ T cells is to identify and kill cells infected with viruses or cancer cells. When a viral infection or cancer cell growth occurs, CD8+ T cells will be activated by dendritic cells which take up pathogenic or cancer cell parts and display antigen fragments on the surface of dendritic cells. CD8+ T cells will then recognize this antigen through the TCR and become active [4].

CD8+ T cells will produce cytokines and migrate to the area where the target cells are located. Upon reaching that area, CD8+ T cells will kill target cells through the mechanism of cytolysis, namely the release of cytotoxic substances such as perforin and granzyme which damage target cell membranes and cause cell death [4]. In addition to their main role in killing virus-infected cells or cancer cells, CD8+ T cells also have an important role in immune regulation. CD8+ T cells can produce cytokines that regulate the activities of other T cells and B cells in the immune system, thereby helping to coordinate the overall immune response [4].

Cancer immunology

Cancer is a condition that can spread to different body parts and is brought on by unchecked cell development. The immune system frequently fails to identify and destroy cancer cells, allowing them to spread and thrive. Therefore, a deeper comprehension of the immune system's function in cancer may aid in the creation of cancer medicines that are more potent [8]. The immune system has an important role in preventing and treating cancer. Immune cells, such as T cells and NK cells, can recognize and kill cancer cells [1].

These immune cells are known as cytotoxic cells because they can kill potentially damaging cells in the body. In addition, immune cells can also stimulate the production of immune molecules that can help inhibit cancer cell growth [8]. Immune molecules, such as the proteins interferon and interleukin-2, may also play an important role in fighting cancer. These proteins can stimulate immune cells to develop and function better in fighting cancer cells. Additionally, interferons have the ability to activate CD8+ T lymphocytes. Interferon I (IFNI) participates in the development of naive CD8+ T cells into cytotoxic T lymphocytes (CTLs) during contact and co-stimulation of CD8+ T cells with antigen-presenting cells. Additionally, IFNI also stimulates STAT3, which encourages granzyme B production in CTLs and improves their effector activity. With reference to anticancer activity, interferon II (IFNII) is the primary interferon that, through the regulation of survivin and the Ifi202 gene, causes the differentiation, activation, proliferation, and survival of tumor-specific CD8+ T lymphocytes. Moreover, activation through IFNII upregulates the production of granzymes and IL-2 receptors which further enhances the anticancer effector response of CD8+ T cells.(9) In addition, immune molecules can also help activate adaptive immune responses, which involve the formation of immune cells that are specific for cancer cells [8].

Recognition of cancer cells by the immune system

The process of recognizing cancer cells begins when specific antigens from cancer cells are generated and processed. This antigen is then expressed on the surface of cancer cells along with major histocompatibility class I molecules (MHC). CD8+ T cells can then recognize this antigen and bind to cancer cells that produce it via the TCR receptor. After CD8+ T cells identify cancer cells, they will start a chain of immunological reactions to eliminate the cancer cells. By proliferating and differentiating into cytotoxic effector cells, CD8+ T cells can grow and kill cancer cells in a variety of ways, including by releasing cytokines and cytotoxic granules like perforin and granzyme [6].

Upon recognition, CD8+ T cells can generate effector responses that include the release of cytokines and chemokines that trigger cancer cell death. In addition, CD8+ T cells can produce memory cells that can survive for a long time and provide long-term protection against cancer cells that reappear [3]. However, CD8+ T cells can also experience inhibition mechanisms, such as up-regulation of inhibitory receptors such as PD-1 and CTLA-4. This inhibitory mechanism can inhibit the immune response and allow cancer cells to continue to survive in the body [10].

Mechanisms of cancer immune evasion

Cancer immune evasion mechanisms are strategies used by cancer cells to evade detection and destruction by the immune system. Cancer cells have several mechanisms that

allow them to evade or suppress immune responses. These mechanisms can be divided into three general categories: first, molecular inhibition of immune cells; second, cellular inhibition of immune cells; and third, inhibition of communication between cancer cells and immune cells [11]. Molecular inhibition of immune cells is one of the mechanisms most commonly used by cancer cells. In this mechanism, cancer cells secrete special proteins that bind to immune cell receptors. This causes the immune cells to become inactive or inhibits the activation of the immune cells. These cytokines are mostly immunosuppressive which induce T cell anergy, such as IL-10 and TGF-β. IL-10 suppresses T cells by downregulating TAP proteins which consequently downregulates MHC class I expression and causes the evasion of cancer cells recognition. Moreover, IL-10 inhibits the differentiation and maturation of dendritic cells. Hence, CD8+ T cells are unable to recognize cancer cells. Another protein that is upregulated in cancer cells is Fas ligand which may induce apoptosis in Fas-expressing T cells [11]. In addition, cancer cells can also issue signals that trigger the formation of suppressive immune cells, such as regulatory T cells [11]. These proteins are produced by myeloid-derived suppressor cells that thrives within cancer microenvironment, such as arginase, iNOS, and TGF-β. They act as a signal for differentiation of regulatory T cells which will cause the inhibition of CD8+ T cells effector response [11].

Cellular inhibition of immune cells is the second mechanism used by cancer cells to evade detection by the immune system. In this mechanism, cancer cells reduce the ability of immune cells to attack and destroy cancer cells. Cancer cells can interfere with immune cells' capacity to recognize them by manipulating their surface chemicals. Additionally, cancer cells can boost the production of substances that prevent immune cells from functioning [11]. The mechanism of immune cell recognition evasion is through the aforementioned lack of MHC class I antigens and the upregulation of class I HLA-G antigen which further impairs the responses of both NK and T cells [11]. Inhibition of communication between cancer cells and immune cells is a third mechanism used by cancer cells to evade immune responses. In this mechanism, cancer cells reduce the number of signals or molecules released by immune cells [6, 11]. The current mechanism is through the production of vascular endothelial growth factor (VEGF), TGF-β, prostaglandin-E2 (PGE2), and IL-10 from cancer cells which decreases the function of anti-cancer immunity. PGE2 is known to promote differentiation of dendritic cells into myeloid-derived suppressor cells in cancer microenvironment which produces various proteins and cytokines that inhibit the production of various cytotoxic enzymes by effector T cell. Moreover, PGE2 upregulates the production of IL-10 that inhibits CD8+ T cell response.(5, 12) This mechanism causes immune cells to be unable to communicate with cancer cells so that cancer cells cannot be detected and destroyed [6, 11].

Role of CD8+ cells in lung cancer

CD8+ T-cell expression is associated with a good prognosis in adenocarcinoma [13] non-small cell lung carcinoma (NSCLC) stage IV (14), and NSCLC CD4+ T cells [15, 16]. However, another study found that NSCLC patients with CD8+ T cells had a worse prognosis [17, 18]. Another study found no relationship between CD8+ T cells and the outcome of NSCLC patients [19]. Therefore, the prognostic role of CD8+ T cells is still inconclusive. Antigen recognition by CD8+ T cells in lung cancer is highly dependent on the expression of class I MHC molecules by cancer cells. Cancer cells that lack or do not express MHC class I tend to avoid recognition by CD8+ T cells and can avoid killing by CTL. In addition, the involvement of CD8+ T cells in anti-cancer activity also depends on the activation, proliferation, and differentiation of cells which are regulated by signals provided by the tumor and the accompanying microenvironment [4].

Cancer microenvironment plays a big part in the involvement of CD8+ T cells anticancer activity. The anticancer activity of CD8+ T cells can only be exerted after the recruitment of CD8+ T cells into the cancer microenvironment. The recruitment requires the interaction of CD8+ T cells chemokine receptors with chemokines produced by the cancer cells. A chemokine and chemokine receptor that is found to be high in lung cancer to facilitate the recruitment of CD8+ T cells into cancer microenvironment is the fractalkine chemokine (CX3CL1) and its receptor CX3CR1. This recruitment allows CD8+ T cells to further differentiate and activate into their effector cells, cytotoxic T lymphocytes, which are able to exert the anticancer activity. Moreover, studies have reported high production of fractalkine correlates with reduced cancer growth [20, 21].

The mechanism of action of CD8+ T cells in controlling lung cancer involves several complex stages. First, CD8+ T cells must be able to recognize cancer cells as foreign or abnormal. This occurs when cancer cells secrete specific tumor antigens that can be recognized by CD8+ T cells [4]. One of the most important effector mechanisms is the production of the protein perforin and granzyme. The perforin protein is used by CD8+ T cells to penetrate the cancer cell wall and enter the cancer cell. After entering into cancer cells, granzyme will damage cell structure and destroy cancer cells effectively [4]. In addition to perforin and granzyme production, CD8+ T cells can also activate other cellular killers mechanisms, such as cytokine production and natural killer (NK) cell activation. Meanwhile, NK is a type of natural killer cell that can destroy cancer cells without requiring antigen recognition [4].

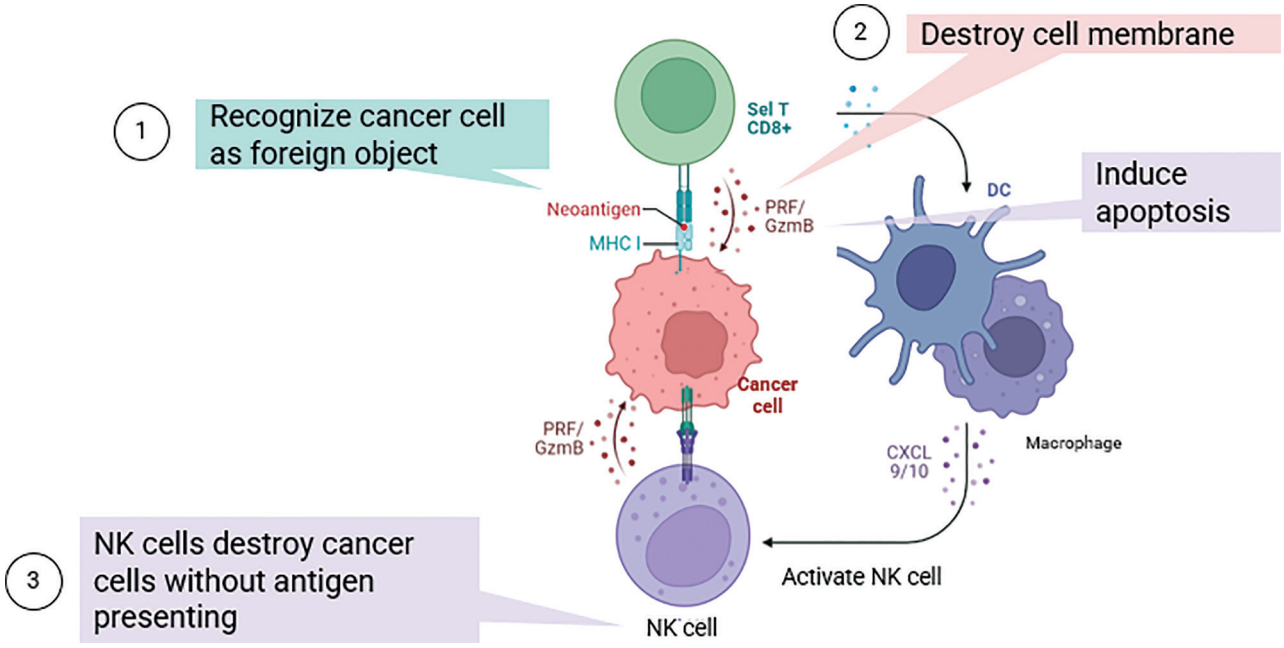

Figure 2. Mechanism of action of CD8+ cells against cancer cells.

Immunological checkpoints can also impede T lymphocyte activity. Many cancers express PD-L1, which can bind to PD-1 and mediate tumor immune escape activity. As a result, inhibiting PD-1 can restart T cell function. Because PD-1 is expressed not just by T cells but also by NK cells, B lymphocytes, macrophages, and dendritic cells, it may play a role in tumor microenvironment alterations and the antitumor immune system. Preclinical research has discovered that PD-1 inhibitors can suppress and stimulate cell growth as well as programmed cell death or apoptosis in a variety of tumor cells, including melanoma, renal cell carcinoma (RCC), and NSCLC [10].

The transmembrane protein that is produced by both CD4+ and CD8+ T lymphocytes is CTLA-4, which is also known as CD152. CTLA-4 suppresses T cell activation. CTLA-4 binds CD80/CD86 in order to block T cell activation signals; this action is useful to prevent autoimmune disorders under physiological settings. CTLA-4 inhibition can target inhibitory signals on CD8+ T cells and lower the inhibitory effect of Treg, increasing the anticancer effect of T cells. The most recent phase III clinical trial is the MYSTIC trial, which is testing durvalumab or in combination with tremelimumab as therapy in advanced NSCLC patients. The median increase in OS with durvalumab monotherapy in patients with PD-L1 expression was reported to be ≥ 25% compared to chemotherapy [22].

In addition, there are also mucin domain-3 (Tim-3, CD366) and T Cell Immunoglobulins which are inhibitors of T cell surface molecules expressed by CD4+, CD8+ T cells, and Treg. Tim-3 or HAVCR2, was expressed by various innate immune cells, including monocytes, NK cells, dendritic cells, and macrophages. In a patient with PD-L1 negative SCLC who was resistant to PD-1/CTLA-4 antibody and cisplatin/etoposide, anti-TIM-3 monotherapy produced a partial response. Nonetheless, phase II and III trials are required to evaluate the efficacy of TIM-3 inhibitors [23].

Immunological therapy for lung cancer

Pulmonary immuno-oncology is a field of lung cancer treatment that relies on the body's immune system to fight cancer cells. This approach is different from conventional approaches that rely on chemotherapy or radiotherapy to destroy cancer cells. Pulmonary immuno-oncology has become a very exciting area of research in recent years, and several immuno-oncology therapies have been approved by the FDA (Food and Drug Administration) for use in patients with lung cancer [8]. One of the most commonly used immuno-oncology therapies is the use of immunological checkpoint inhibitors, such as pembrolizumab, nivolumab, and atezolizumab. Immunological checkpoint inhibitors work by blocking certain immunological checkpoint molecules, such as PD-1 or PD-L1, that allow cancer cells to evade attacks from the immune system [8, 10].

T cells can recognize cancer cells as aberrant and kill them by blocking molecular immunological checkpoints [24]. Several clinical trials have demonstrated that immune checkpoint inhibitors can increase survival in lung cancer patients.

Reck et al. (2016) discovered that pembrolizumab significantly enhanced survival in patients with PD-L1-positive squamous cell lung cancer as compared to conventional chemotherapy in the KEYNOTE-024 study [25]. Other clinical studies, namely CheckMate 227 and IMpower150, also showed positive results with the use of immunological checkpoint inhibitors. in patients with lung cancer [26, 27].

In addition to immunological checkpoint inhibitors, several other immuno-oncological therapies are being developed, such as the use of therapeutic T cells and therapeutic vaccines. T cell therapy is a therapy that involves taking T cells from a patient, processing these T cells in a laboratory, and then reinjecting them into the patient's body to fight cancer cells. Therapeutic vaccines are vaccines designed to stimulate the body's immune system to fight cancer cells [28]. Although pulmonary immuno-oncology therapy has shown positive results in some patients with lung cancer, there are several challenges in its use. Several factors such as tumor resistance to immuno-oncology therapy, serious side effects, and high cost may hinder the use of this therapy in patients with lung cancer [24]. This is especially true as lung cancer is known to have low infiltration of tumor-infiltrating lymphocytes. The mechanism is through the downregulation of HLA I expression which prevents lymphocytes, mainly CD8+ T cells, to infiltrate its microenvironment. Thus, the challenge lies in the ability of pulmonary immuno-oncology therapy to recruit and activate CD8+ T cells into lung cancer microenvironment to exert its anticancer activity [29].

Effect of immunological therapy on CD8+ T cell activity

The effect of immunological therapy on CD8+ T cell activity primarily involves the activation and proliferation of CD8+ T cells to enhance the immune response against cancer cells. One common immunological therapy approach is using immunomodulating agents such as checkpoint inhibitors or cancer vaccines. Checkpoint inhibitors block molecules that limit T cell activity, such as PD-1 and CTLA-4, thereby activating T cells to attack cancer cells. Cancer vaccines, on the other hand, stimulate the immune system to recognize and attack cancer cells by exposing cancer antigens to dendritic cells or T cells [22].

At the cellular level, immunological therapy can affect CD8+ T cell activity through several mechanisms. To begin, immunomodulators can activate T cells by activating intracellular signaling pathways such as the JAK-STAT and NF-B pathways, which enhance gene expression and T-cell proliferation. In addition, checkpoint inhibitors can reduce inhibition by PD-1 or CTLA-α molecules. Thus enabling CD8+ T cells to more easily interact with cancer cells and trigger an immune response [4]. During tumor growth, cancer cells secrete various immunosuppressive factors such as TGF-β and IL-10, which can inhibit T cell activity. Immunological therapy can change this environment by decreasing the production of immunosuppressive factors and increasing the production of pro-inflammatory cytokines such as IFN-γ and TNF -α, which stimulate the activity of T cells and CD8 [6].

Conclusion

CD8+ T cells play an important role in the body's immune system to fight lung cancer cells.The mechanism of action of CD8+ T cells in controlling lung cancer includes antigen recognition, effector mechanisms (granzyme and perforin), cytokine production, and activation of natural killer (NK) cells. *Checkpoint inhibitors* inhibit molecules that limit T cell activity, such as PD-1 and CTLA-4, thereby activating T cells to attack cancer cells.

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Institutional Review Board Statement

Not applicable.

Informed Consent Statement

No informed consent was necessary.

Data Availability Statement

Data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare no conflict of interest.

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