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Review Article

Immunotherapeutics: Advancing precision medicine in cancer treatment

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ABSTRACT

Immunotherapy, also known as biologic therapy or biotherapy, is a medical treatment that utilizes the immune system to combat diseases, including cancer. Over the past few decades, immunotherapy has emerged as an integral part of cancer treatment, with various approaches being explored. This article provides an overview of immunotherapy, its mechanisms of action, and the different types of immunomodulators involved. Activation immunotherapies aim to enhance the immune response, such as cancer vaccines and cellular therapies, while suppression immunotherapies work to reduce or suppress immune activity. The article also discusses the different types of immunotherapies, including cell-based immunotherapies, immunomodulators, vaccines, antibody-based targeted therapies, and oncolytic viruses. Additionally, it highlights the characteristics of an ideal immunomodulator and the limitations associated with these therapies. Monoclonal antibodies, both naked and conjugated, are explored as a specific type of immunotherapy, with examples of their use in treating various cancers. Furthermore, the article touches upon the classification and uses of immunosuppressive agents, particularly in organ transplantation, along with their adverse effects. Overall, this article provides a comprehensive overview of immunotherapy and its diverse applications in disease treatment.

1. Introduction

The field of immunotherapy has experienced remarkable growth and diversification, encompassing a wide range of medical disciplines, including the treatment of infectious diseases, allergies, inflammatory conditions, autoimmune disorders, and cancer.[1] In the context of autoimmune diseases, transplantation, and allergies, the focus of treatment has shifted towards inducing specific tolerance rather than relying solely on immunosuppression or symptom relief through monoclonal antibodies.[2] Recent advancements in our understanding of immunological mechanisms have paved the way for innovative therapeutic strategies aimed at disease prevention and modification. While traditional preventive vaccines have predominantly relied on generating high levels of antibodies to combat invading microorganisms, it is now recognized that established viral infections require the intricate workings of the immune system's cellular components, particularly T cells, to eliminate infected cells.[3] This manuscript seeks to challenge preconceived notions about immune mechanisms for disease prevention and modification by exploring the latest biotechnological advances and insights into prevention and therapy. While recognizing the fundamental role of antibodies in purifying extracellular organisms such as bacteria in bodily fluids, it also highlights the primary role of T cells in clearing intracellular organisms like viruses from within body cells.[2] Immunotherapy, also known as biologic therapy or biotherapy, has emerged as a ground breaking medical approach that manipulates the immune response to combat various diseases, including cancer.[1]

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Drawing inspiration from the pioneering work of William B. Coley, widely regarded as the father of immunotherapy, extensive research has led to the development of diverse immunotherapy strategies for the treatment of cancer.[4] This manuscript delves into the progress made in the field of immunotherapy and the different approaches utilized to induce, enhance, or suppress the immune system's response in the fight against cancer.[5]

2. How it works?

Immunotherapy includes a wide variety of treatments that works in different ways. By boosting the body's immune system in a very general way. Helps to train the immune system to attack cancer cells specifically. Giving immune system components, such as man-made immune system proteins.

2.1. Types of Immunomodulators

Activation immunotherapies, also known as Immunostimulants Activation immunotherapies, which aim to boost the immune system's response, encompass agents like BCG, Levamisole, Thalidomide, Lenalidomide, and Imiquimod.[6] In contrast Suppression immunotherapies, referred to as immunosuppressants. suppression immunotherapies work to lower immune responses and include medications such as glucocorticoids, calcineurin inhibitors, antimetabolites, and specific antibiotics.[7]

Specific active immunotherapy involves the stimulation of cell-mediated and antibody immune responses with a precise focus on a specific antigen, as exemplified by the development of cancer vaccines.[8]

Cancer vaccines are a type of active immunotherapy that aim to activate a person's immune system to fight against cancer.[9] These vaccines can contain either cancer cells, parts of cancer cells, or purified tumor-specific antigens. There are two main categories of cancer vaccines. The first type is cell-based, where a patient's cancer cells are grown together with their own immune system cells and then given back to the same patient.[10] This helps the immune system recognize and target the cancer cells more effectively. The second type is vector-based, where an engineered virus or other carrier is used to introduce cancer-specific proteins and molecules into the patient's body. This helps stimulate the patient's immune system to identify and fight the tumor cells.[11] Examples of cancer vaccines include DNA vaccines, vector-based vaccines, and tumor cell vaccines designed for specific cancers like kidney, ovarian, and breast cancer. These vaccines hold promise in the fight against cancer by harnessing the body's natural defences to combat the disease.

Cellular therapies represent a distinct form of immunotherapy. They involve the utilization of single agents obtained from cancer patients, which are then modified in a laboratory setting to enhance their capacity to identify and eliminate tumor cells effectively. This approach is tailored to augment specific aspects of the immune system, ultimately triggering the death of tumor cells. In contrast, traditional vaccines aim to stimulate the body's immune system to respond to specific antigens.[12] An example of cellular therapy is Lymphocyte Activated Killer Cell (LAK) therapy, showcasing the innovative methods employed to bolster the body's defences against cancer.[13]

Adjuvant immunotherapy involves the use of certain materials that, when administered alongside an antigenic protein or other substances like monoclonal antibodies and cancer vaccines, enhance the immune response within the body. For instance, the BCG vaccine is a notable example of this approach. Adjuvants play a vital role in amplifying the effectiveness of various immunotherapies, contributing to a more robust and targeted immune response.[14]

Non-specific immunotherapy differs from specific immunotherapies in that it does not directly target cancer cells. Instead, it focuses on boosting the overall immune system's response. Cytokines, which are chemicals produced by certain immune system cells, play a crucial role in regulating the growth and activity of various immune cells and blood cells in the body. They are administered through injections under the skin, into a muscle, or into a vein. One group of cytokines is called interleukins, which act as messengers between white blood cells[15] Interleukin-2 (IL-2), in particular, helps immune cells to proliferate more rapidly. In 1992, a synthetic version of IL-2 gained approval from the USFDA, marking the first true immunotherapy for solo use in cancer treatment. However, IL-2 treatment can lead to side effects like flu-like symptoms, weight gain, nausea, vomiting, diarrhoea, and even low blood pressure, which may require additional medications.[16] Rare but potentially severe side effects include irregular heartbeat, chest pain, and other heart issues. Another group of cytokines, interferons (IFN), discovered in the late 1950s, are essential in assisting the body's resistance against viral infections and cancer. These interferons come in different types, named after the first three letters of the Greek alphabet: IFN-α, IFN-β, and IFN-gamma.[17] While non-specific immunotherapies like cytokines and interferons may not directly target cancer cells, they play a significant role in bolstering the immune system's ability to defend against both infections and cancer.

3. Types of Immunotherapies

The main types of immunotherapies now being used to treat cancer. As of June 2017, the USFDA has approved 32 different immunotherapies for patients with cancers including melanoma, lung cancer, bladder cancer, kidney cancer, lymphoma, Leukemia, and prostate cancer. These immunotherapies enhance the cancer fighting activity of the

immune system in a variety of ways, which can be roughly divided into the five following classes:

Cell-based immunotherapies physically supplement patient immune system with immune cells. These include bone marrow transplants and newer more sophisticated cell transplants, such as CAR-T cells. [18]

Immunomodulators can act directly on immune cells to promote anticancer activity. The first immunomodulator (the cytokine IFN-α) was approved by the FDA in 1986 for Leukemia. [19] While the first checkpoint inhibitor (the anti-CTLA-4 ipilimumab) was approved in 2011 for advanced melanoma.

Vaccines help educate or arouse the immune system against a potential threat in 1990. A tuberculosis vaccine called BCG (bacillus Calmette Guerin), became the first to be FDA approved in the United States, for the treatment of bladder cancer. The vaccine Sipuleucel-T was approved for prostate cancer patients in 2010.

Antibody-based targeted therapies can target cancer cells directly, or other cells/protein that help support tumor survival. The first antibody (the anti-CD20 rituximab) was approved in1997 for lymphoma. [20] There are now over a dozen antibody-based immunotherapies approved for various cancers, including modified versions with anti-cancer drugs attached.

Oncolytic viruses can be modified to infected cancer cells and cause them to burst, which attracts the attention of the immune system. The oncolytic virus T-Vec was approved for patients with advanced melanoma in 2015. [21]

3.1. Mechanisms of immunomodulators

A drug can influence the immune system by either suppressing or enhancing various critical steps, including antigen recognition and phagocytosis, lymphocyte proliferation and differentiation, antibody synthesis, antigen-antibody interactions, and the release of immune response mediators. Furthermore, it may also modify the response of target tissues involved in the immune process.

Table 1:

Phase of Immune Response	Suppressants	Enhancers
Antigen recognition & processing	Corticosteroids Cyclophosphamide	BCG vaccine Tetramisole
Amplification	L-Asparaginase Corticosteroids Cyclophosphamide 5-Fluorouracil	Concanavalin A Tetramisole
Antibody formation	Corticosteroids Cyclophosphamide Cyclosporin A	Lipopolysaccharide Tetramisole
Immune affecter response	Corticosteroids Cyclophosphamide Cyclosporin - A Methotrexate	Tetramisole

An ideal immunomodulator should have the following characteristics: It should boost both specific and general immune responses, aiding vaccines as an adjuvant. It should work when taken orally, be compatible with other medications, and have a defined chemical composition with known biological effects. Additionally, it should allow for a quick withdrawal period with minimal tissue residues.

On the flip side, immunomodulators should avoid toxicity, antigenicity, pyrogenicity, and long-lasting side effects in the body to be considered truly beneficial.

3.2. Monoclonal antibodies

Many copies of a specific antibody can be made in the lab. These are called as monoclonal antibodies(mAbs or moAbs). These antibodies can be useful in fighting diseases because they can design specifically to only target a certain antigen, such as one that is found on cancer cells. Over the past 15 years, the USFDA has approved about a mAbs to treat certain cancers.

4. Types of Monoclonal Antibodies

Monoclonal antibodies (mAbs) come in two distinct categories, each serving a unique purpose. Naked mAbs function independently and offer various mechanisms of action. Some stimulate a person's immune responses against cancer cells, while others work by obstructing specific proteins crucial for cancer cell growth. An example of a naked mAb is Herceptin, targeting the HER2/neu protein and applied in the treatment of breast and stomach cancer. [22]

On the other hand, conjugated mAbs are attached to chemotherapy drugs, radioactive particles, or toxins. They are sometimes referred to as tagged, labelled, or loaded antibodies, based on what they are linked to. When mAbs are combined with radioactive particles, they become radiolabelled antibodies, used in radioimmunotherapy (RIT). Examples like Ibritumomab and Tositumomab directly deliver radioactivity to cancerous B-cells and are employed in non-Hodgkin lymphoma treatment. [23] Chemotherapy drug-linked mAbs are referred to as Chemolabeled antibodies. Additionally, mAbs linked to cell toxins are known as immunotoxins, though none are currently approved for cancer treatment, despite ongoing research efforts.

It's important to note that the use of monoclonal antibodies may lead to side effects such as allergic reactions, nausea, diarrhoea, skin rashes, and flu-like symptoms, including chills, fatigue, fever, and pain. [24]

5. Immunosuppressive Agents

Immunosuppression involves an act that reduces the activation or efficacy of the immune system. Some portion of the immune system itself have immunosuppressive effects on other parts of the immune system, and

immunosuppression may occur as an adverse reaction to treatment of other condition.[25] An immunosuppressant is any agent that causes immunosuppression, including immunosuppressive drugs and some environmental toxins. One of the primary uses of immunosuppressant drugs is to lower the body's ability to reject a transplanted organ, such as a liver, heart or kidney.[26]

5.1. What are they used for?

Almost everyone who receives an organ transplant must take immunosuppressant drugs. If the new organ came from an identical twin, however, one may not have to take them. When one gets an organ transplant, our body knows that the new organ is foreign. This triggers a response by the body's immune system to attack it. The immunosuppressant drugs suppress the body's ability to do this. The drugs allow the transplanted organ to remain healthy and free from damage. The goal is to adjust these drugs to prevent rejection and to minimize any side effects of the drugs.

Immunosuppressive drugs play a crucial role in the treatment of various conditions. They are classified into several categories, each with its specific drugs. Selective inhibitors of cytokine production and function, such as Cyclosporin, Everolimus, Sirolimus, and Tacrolimus, help manage immune responses.[27] Immunosuppressive metabolites, like Azathioprine, Mycophenolate mofetil, and Mycophenolate sodium, are also used. Antibodies, including Alemtuzumab, Antithymocyte globulins, Basiliximab, Daclizumab, and Muromonab-CD3, are employed to modulate the immune system.[28] IL-2 receptor antagonists like Basiliximab and Daclizumab are used to inhibit certain immune responses. Additionally, corticosteroids such as Methylprednisolone, Prednisolone, and Prednisone are employed in immunosuppression.

These immunosuppressive drugs find application in treating a variety of conditions, including arteritis, autoimmune diseases, Behcet's Disease, Crohn's Disease, Lupus, Rheumatoid Arthritis, and more. However, they can come with potential adverse effects such as allergic reactions, hypotension, fever, thrombophlebitis, and other side effects that need to be carefully monitored and managed during treatment.[29]

5.2. Management of side effects of Immunosuppressive therapy

Advise taking medication after eating something. Emphasize importance of good nutrition and hydration. Utilize antiemetic/antinausea medications as needed.

5.3. Cancer Vaccines

The goal is to treat cancer or to prevent it from coming back after other treatments.

5.4. Vaccines to prevent cancer

Some strains of the human papilloma virus (HPV) have been linked to cervical, anal, throat, and some other cancers. Vaccines against HPV may help protect against some of these cancers.[30] People who have chronic (long-term) infections with the hepatitis B virus (HBV) are at higher risk for liver cancer. Getting the HBV vaccine to help prevent this infection may therefore lower some people's risk of getting liver cancer.[31]

5.5. Vaccines to treat cancer

Cancer treatment vaccines are different from the vaccines that work against viruses. These vaccines try to get the immune system to mount an attack against cancer cells in the body.[32] Instead of preventing diseases, they are meant to get the immune system to attack a disease that already exists.

Cancer treatment vaccines come in various forms, each designed to target the disease differently. These types include tumor cell vaccines, antigen vaccines, dendritic cell vaccines, and DNA vaccines.[33] Additionally, vector-based vaccines employ special carriers like viruses, bacteria, yeast cells, or other structures to deliver antigens or DNA into the body[34]. While these vaccines show promise in fighting cancer, they can lead to side effects such as fever, chills, fatigue, back and joint pain, nausea, wheezing, headache, breathing problems, and elevated blood pressure.[35]

5.6. How cellular immunotherapies are changing the outlook for cancer patients

Adoptive cell therapy also known as cellular immunotherapy, is a form of treatment that uses the cells of our immune system to eliminate cancer.[36] Some of these approaches involve directly isolating our own immune cells and simply expanding their numbers, whereas other involve genetically engineering our immune cells (via gene therapy) to enhance their cancer-fighting capabilities. Our immune system can recognize and eliminate cells that have become infected or damaged as well as those that have become cancerous. In the case of cancer, immune cells are known as killer T cells are particularly powerful against cancer, due to their ability to bind to markers known as antigens on the surface of cancer cells. Cellular immunotherapies take advantage of this natural ability and can be developed in different ways.

1. Tumor-Infiltrating Lymphocyte (TIL) Therapy
2. Engineered T Cell Receptor (TCR) Therapy
3. Chimeric Antigen Receptor (CAR) T Cell Therapy
4. Natural Killer (NK) Cell Therapy

Today, cell therapies are constantly evolving and improving and providing new options to cancer patients. Cell therapies

are currently being evaluated, both alone and in combination with other treatments, in a variety of cancer types in clinical trials.

6. Tumor-Infiltrating Lymphocyte (TIL Therapy)

Cancer patients have naturally occurred T cells that are often capable of targeting their cancer cells. These T cells are some of the most powerful immune cells in our body and come in several types. The "killer" T cells especially can recognize and eliminate cancer cells in a very precise way.[37] The existence of these T cells alone, however, is not always enough to guarantee that they will be able to carry out their mission to eliminate tumors. One potential roadblock is that these T cells must first become activated before they can effectively kill cancer cells, and then they must be able to maintain that activity for a sufficiently long time to sustain an effective anti-tumor response. This TIL approach harvests naturally occurring T cells that have already infiltrated patients' tumors, and then activates and expands them.[38] Then, large numbers of these activated T cells are re-infused into patients, where they can then seek out and destroy tumors.

7. Engineered T Cell Receptor (TCR Therapy)

Unfortunately, not all patients have T cells that have already recognized their tumors. Other patients might, but for several reasons, these T cells may not be capable of being activated and expanded to enough to enable rejection of their tumors. This approach also involves taking T cells from patients, but instead of just activating and expanding the available anti-tumor T cells, the T cells can also be equipped with a new T cell receptor that enables them to target specific cancer antigens. By allowing doctors to choose an optimal target for each patient's tumor and distinct type of T cells to engineer, the treatment can be further personalized to individuals and ideally provide patients with greater hope for relief[39].

8. Chimeric Antigen Receptor (CAR T Cell Therapy)

The previously mentioned TIL and TCR therapies can only target and eliminate cancer cells that present their antigen in a certain context (when the antigens are bound by the major histocompatibility complex, or MHC). Recent advances in cell-based immunotherapy have enabled doctors to overcome this limitation. Scientists equip a patient's T cells with a synthetic receptor known as a CAR, which stands for chimeric antigen receptor.[40] A key advantage of CARs is their ability to bind to cancer cells even if their antigens are not presented on the surface via MHC, which can render more cancer cells vulnerable to their attacks. However, CAR T cells can only recognize antigens that themselves are naturally expressed on the cell surface, so the range of potential antigen targets is smaller than with TCRs. In October 2017, the USFDA approved the first CAR T cell therapy to treat adults with certain types of large B-cell lymphoma.[41] One approach currently in clinical trials is using stem cells to create a limitless source of off-the-shelf CAR T cells.

9. Natural Killer (NK Cell Therapy)

More recently, adoptive cell therapy strategies have begun to incorporate other immune cells, such as natural killer NK cells.[42] One application being explored in the clinic involves equipping these NK cells with cancer- targeting CARs.

9.1. Common side effects associated with the currently approved cell immunotherapies.

Acute kidney injury, Bleeding episodes, Chills, Heart arrhythmias, Cytokine storm, Vomiting, Constipation, Edema, Encephalopathy, Fatigue, Pyrexia, Hypoxia, Hypotension, Tachycardia, Febrile neutropenia, Nausea, Tremors, Fever, Headache, Hypogammaglobulinemia, Delirium,[43,44]

9.2. Recent approach in immunotherapy

9.2.1. Allergen immunotherapy

Immunotherapy can also be used to treat allergies. While allergy treatments (such as antihistamines or corticosteroids) treat allergic symptoms, immunotherapy can reduce sensitivity to allergens, lessening its severity. Immunotherapy is partly effective in some people and ineffective in others, but it offers allergy sufferers a chance to reduce or stop their symptoms.[45] The therapy is indicated for people who are extremely allergic or who cannot avoid specific allergens. IgE-mediated food allergy is a global health problem that affects millions of persons and affects every aspect of life for the patients.[46] A promising approach to treat food allergies is the use of oral immunotherapy (OIT). OIT consist in a gradual exposure to increasing amounts of allergen can lead to many subjects tolerating doses of food sufficient to prevent reaction on accidental exposure. Dosages increase over time, as the person becomes desensitized. This technique has been tested on infants to prevent peanut allergies. Allergen-assisted immunotherapy (ASIT) has become the gold standard for the causative treatment for IgE-mediated allergic diseases for a large variety of allergens.[47] One may curiously await the new developments, which will further enhance our understanding of allergy mechanisms and improve ASIT for the next generations of patients and physicians.[48]

10. Helminthic Therapies

Whipworm ova (Trichuris suis) and Hookworm (Necator americanus) have been tested for immunological diseases and allergies.[49] Helminthic therapy has been investigated as a treatment for relapsing remitting multiple sclerosis, Crohn's diseases, allergies and asthma.[50] The mechanism of how the helminths modulate the immune response, is unknown. Helminth's relationship to humans as hosts should be classified as mutualistic or symbiotic.

11. Types of Immunotherapy Treatment

Whenever we are on our cancer treatment journey, we may want information on the types of immunotherapies available today. Here it describes some of the different approaches to cancer immunotherapy and how they are used to treat a wide variety of cancers. Please note that these treatments do not include all cancers immunotherapies currently available but represent some promising approaches that are currently approved by the FDA or being tested in clinical trials.

12. Adoptive Cell Therapy

Adoptive cell therapy is a type of cancer treatment that reactivates, enhances, and expands naturally occurring cancer fighting immune cells before reinfusing them into patients.[51]

13. Cancer Vaccines

Preventive vaccines can protect against cancer development. Whereas therapeutic vaccines can stimulate immune responses against existing tumors.[52]

14. Immunomodulators

Immunomodulators are a form of immunotherapy that manipulate the "gas pedals" and "brakes" of the immune system to fight cancer.[53]

15. Targeted Antibodies

Targeted antibodies are a type of immunotherapy that can disrupt cancer cell activity and alert the immune system to attack cancer.[54]

16. Oncolytic Virus Therapy

Oncolytic virus therapy uses modified viruses that can infect and destroy tumor cells.[55]

17. Conclusion

This article gives a thorough explanation of immunotherapy, including its methods of action, the various types of immunomodulators involved, and its uses in the treatment of cancer. It draws attention to the variety of immunotherapy and its potential to advance cancer patients' access to precision medicine.

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19. Conflict of Interest

None.

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References

1. Sahu M, Suryawanshi H. Immunotherapy: The future of cancer treatment. *J oral Maxillofac Pathol*. 2021;25(2):371.
2. Buss NA, Henderson SJ, Mcfarlane M, Shenton JM, De Haan L. Monoclonal antibody therapeutics: history and future. *Curr Opin Pharmacol*. 2012;12(5):615–22.
3. Paterson P, Meurice F, Stanberry LR, Glismann S, Rosenthal SL, Larson HJ. Vaccine hesitancy and healthcare providers. *Vaccine*. 2016;34(52):6700–6.
4. Mccarthy EF. The toxins of William B. Coley and the treatment of bone and soft-tissue sarcomas. *Lowa Orthop J*. 2006;26:154–8.
5. Derynck R, Turley SJ, Akhurst RJ. TGFβ biology in cancer progression and immunotherapy. *Nat Rev Clin Oncol*. 2021;18(1):9–34.
6. Anagnostou T, Ansell SM. Immunomodulators in Lymphoma. *Curr Treat Option in Oncol*. 2020;21(4):28. doi:10.1007/s11864-020-0720-8.
7. Trunečka P. Imunosuprese po transplantaci jater, současnost a budoucnost. *Vnitrni lekarstvi*. 2013;59(8):671–7.
8. Sahin U, Türeci Ö. Personalized vaccines for cancer immunotherapy. *Science*. 2018;6382:1355–60.
9. Sahin U, Türeci Ö. Personalized vaccines for cancer immunotherapy. *Science*. 2018;6382:1355–60.
10. Reardon DA, Mitchell DA. The development of dendritic cell vaccine-based immunotherapies for glioblastoma. *Seminars Immunopathol*. 2017;39(2):225–39.
11. Sakurai F, Tachibana M, Mizuguchi H. Adenovirus vector-based vaccine for infectious diseases. *Drug Metab Pharmacokinet*. 2022;42:100432. doi:10.1016/j.dmpk.2021.100432.
12. Paterson P, Meurice F, Stanberry LR, Glismann S, Rosenthal SL, Larson HJ. Vaccine hesitancy and healthcare providers. *Vaccine*. 2016;34(52):6700–6.
13. Zhang L, Wang F, Yi H, Ermakova SP, Malyarenko OS, Mo J. The role of T-LAK cell-originated protein kinase in targeted cancer therapy. *Mol Cell Biochem*. 2022;477(3):759–69.
14. Dibajnia P, Cardenas LM, Lalani AA. The emerging landscape of neo/adjuvant immunotherapy in renal cell carcinoma. *Human Vaccines Immunotherapeutics*. 2023;19(1):2178217. doi:10.1080/21645515.2023.2178217.
15. Dudakov JA, Hanash AM, Den V, Brink MR. Interleukin-22: immunobiology and pathology. Annual review of immunology. *Ann Rev Immunol*. 2015;33:747–85.
16. Yuan Y, Kolios AGA, Liu Y, Zhang B, Li H, Tsokos GC. Therapeutic potential of interleukin-2 in autoimmune diseases. *Trends Mol Med*. 2022;28(7):596–612.
17. Pestka S, Krause CD, Walter MR. Interferons, interferon-like cytokines, and their receptors. *Immun Rev*. 2004;202:8–32.
18. Singh AK, Mcguirk JP. CAR T cells: continuation in a revolution of immunotherapy. *Lancet Oncol*. 2020;21(3):168–78.

19. Tuncer AM, Hiçsönmez G, Gümrük F, Sayli T, Güler E, Cetin M. Serum TNF-alpha, gamma-INF, G-CSF and GM-CSF levels in neutropenic children with acute leukemia treated with short-course, high-dose methylprednisolone. *Leukemia Res*. 1996;20(3):140–9.
20. On S, Chang A. Treatment of lymphoma with rituximab and chemotherapy during pregnancy. *Leukemia lymphoma*. 2022;63(12):2897–904.
21. Soliman H, Hogue D, Han H, Mooney B, Costa R, Lee MC, et al. Oncolytic T-VEC virotherapy plus neoadjuvant chemotherapy in nonmetastatic triple-negative breast cancer: a phase 2 trial. *Nature Med*. 2023;29(2):450–7.
22. Cameron D, Piccart-Gebhart MJ, Gelber RD, Procter M, Goldhirsch A, Azambuja ED, et al. 11 years' follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive early breast cancer: final analysis of the HERceptin Adjuvant (HERA) trial. In: & Herceptin Adjuvant (HERA) Trial Study Team; 2017. p. 1195–1205.
23. Johnston PB, Bondly C, Micallef IN. Ibritumomab tiuxetan for non-Hodgkin's lymphoma. *Expert Rev Anticancer Ther*. 2006;6:861–9.
24. Gaudinski MR, Berkowitz NM, Idris AH, Coates EE, Holman LA, Mendoza F, et al. A Monoclonal Antibody for Malaria Prevention. *Study Team*. 2021;385:803–14.
25. Zenlea T, Peppercorn MA. Immunosuppressive therapies for inflammatory bowel disease. *World J Gastroenterol*. 2003;95(7):455–6.
26. Trunečka P. Imunosuprese po transplantaci jater, současnost a budoucnost. *Vnitrni lekarstvi*. 2013;59(8):671–7.
27. Parlakpinar H, Gunata M. Transplantation and immunosuppression: a review of novel transplant-related immunosuppressant drugs. *Immunopharmacol Immunotoxicol*. 2021;43(6):651–65.
28. Ponticelli C. Basiliximab: efficacy and safety evaluation in kidney transplantation. *Expert Opin Drug safety*. 2014;13(3):373–81.
29. Desbois AC, Wechsler B, Resche-Rigon M, Piette JC, Huong D, Amoura Z. Immunosuppressants reduce venous thrombosis relapse in Behçet's disease. *Arthritis Rheumatism*. 2012;64(8):2753–60.
30. Genovese C, Fauci VL, Squeri A, Trimarchi G, Squeri R. HPV vaccine and autoimmune diseases: systematic review and meta-analysis of the literature. *J Prevent Med hygiene*. 2018;59(3):194–9.
31. Su J, Brunner L, Oz EA, Sacherl J, Frank G, Kerth HA, et al. Activation of CD4 T cells during prime immunization determines the success of a therapeutic hepatitis B vaccine in HBV-carrier mouse models. *J Hepatol*. 2023;78(4):717–30.
32. Rausch S, Schwentner C, Stenzl A, Bedke J. mRNA vaccine CV9103 and CV9104 for the treatment of prostate cancer. *Hum Vac Immunother*. 2014;10(11):3146–52.
33. Baharom F, Ramirez-Valdez RA, Khalilnezhad A, Khalilnezhad S, Dillon M, Hermans D, et al. Systemic vaccination induces CD8+ T cells and remodels the tumor microenvironment. *Cell*. 2022;185(23):4317–32.
34. Sakurai F, Tachibana M, Mizuguchi H. Adenovirus vector-based vaccine for infectious diseases. *Drug Metab Pharm*. 2022;42:100432.
35. David SB, Gez SB, Rahamim-Cohen D, Shamir-Stein N, Lerner U, Zohar AE, et al. Immediate side effects of Comirnaty COVID-19 vaccine: A nationwide survey of vaccinated people in Israel. *Eur Communicable Dis Bull*. 2020;27:2100540.
36. Mishra AK, Malonia SK. Advancing cellular immunotherapy with macrophages. *Life Sci*. 2023;328:121857.
37. Donnell JS, Teng MWL, Smyth MJ. Cancer immunoediting and resistance to T cell-based immunotherapy. *Nat Rev Clin Oncol*. 2019;16(3):151–67.
38. Granhoj JS, Witness A, Presti M, Met Ö, Svane IM, Donia M, et al. Tumor-infiltrating lymphocytes for adoptive cell therapy: recent advances, challenges, and future directions. *Expert Opin Biol Ther*. 2022;22(5):627–41.
39. Leidner R, Silva NS, Huang H, Sprott D, Zheng C, Shih YP, et al. Neoantigen T-Cell Receptor Gene Therapy in Pancreatic Cancer. *New Engl J Med*. 2022;386(22):2112–9.
40. Holstein SA, Grant SJ, Wildes TM. Chimeric Antigen Receptor T-Cell and Bispecific Antibody Therapy in Multiple Myeloma: Moving Into the Future. *J Clin Oncol Official J Am Soc Clin Oncol*. 2023;41(27):4416–29.
41. Mulholland N, Chandra J, Sanderson R, Kuhnl A. Chimeric Antigen Receptor T-Cell Therapy and Imaging Applications for Large B-Cell Lymphoma. *Radiology*. 2023;307(5):e221362. doi:10.1148/radiol.221362.
42. Wu SY, Fu T, Jiang YZ, Shao ZM. Natural killer cells in cancer biology and therapy. *Mol Cancer*. 2020;19(1):120. doi:10.1186/s12943-020-01238-x.
43. Johdi NA, Sukor NF. Colorectal Cancer Immunotherapy: Options and Strategies. *Front Immunol*. 2020;11:1624.
44. Lacouture M, Sibaud V. Toxic Side Effects of Targeted Therapies and Immunotherapies Affecting the Skin, Oral Mucosa, Hair, and Nails. *American journal of clinical dermatology*. 2018;19(1):31–39.
45. Šošić L, Paolucci M, Flory S, Jebbawi F, Kündig TM, Johansen P. Allergen immunotherapy: progress and future outlook. *Expert Rev Clin Immunol*. 2023;19(7):745–69.
46. Anvari S, Miller J, Yeh CY, Davis CM. IgE-Mediated Food Allergy. *Clin Rev Aller Immunol*. 2019;57(2):244–60.
47. Sindher SB, Long A, Chin AR, Hy A, Sampath V, Nadeau KC. Food allergy, mechanisms, diagnosis and treatment: Innovation through a multi-targeted approach. *Allergy*. 2022;77(10):2937–48.
48. Akinfenwa O, Domínguez AR, Vrtala S, Valenta R, Campana R. Novel vaccines for allergen-specific immunotherapy. . *Curr Opin Aller Clin Immunol*. 2021;21:86–99.
49. Elliott DE, Weinstock JV. Helminthic therapy: using worms to treat immune-mediated disease. *Adv Exp Med Biol*. 2009;666:157–66.
50. Shields VE, Cooper J. Use of helminth therapy for management of ulcerative colitis and Crohn's disease: a systematic review. *Parasitology*. 2022;149(2):145–54.
51. Wang Z, Cao YJ. Adoptive Cell Therapy Targeting Neoantigens: A Frontier for Cancer Research. *Front Immunol*. 2020;11:176. doi:10.3389/fimmu.2020.00176.
52. Li Y, Wang M, Peng X, Yang Y, Chen Q, Liu J, et al. mRNA vaccine in cancer therapy: Current advance and future outlook. *Clin Transl Med*. 2023;13(8):e1384. doi:10.1002/ctm2.1384.
53. Aribi M, Mennechet FJD, Boukoffa C. Editorial: The role of vitamin D as an immunomodulator. *Front immunol*. 2023;14:1186635. doi:10.3389/fimmu.2023.1186635.
54. Dumontet C, Reichert JM, Senter PD, Lambert JM, Beck A. Antibody-drug conjugates come of age in oncology. *Nature Rev Drug Disc*. 2023;22(8):641–61.
55. Mondal M, Guo J, He P, Zhou D. Recent advances of oncolytic virus in cancer therapy. *Hum Vac Immunotherap*. 2020;16(10):2389–402.

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