Transactions on Materials, Biotechnology and Life Sciences
ISSN: 2960-1932, eISSN: 2960-2319 | Volume 7
MISBP 2024

Current Advances and Future Outlook of Cancer Immunotherapy

Yuhang Du
Dalian NO.24 High School, Dalian, China
dyh0812@outlook.com

Abstract. In the following discourse, I will delve into the array of immunotherapeutic approaches. Presently, immunotherapy stands at the forefront of cancer treatments within medical facilities, representing a significant shift in the way to approach the management and eradication of malignant diseases. It encompasses the employment of ICI (Immune checkpoint inhibitors), CAR-T cells (Chimeric Antigen Receptors), and cancer vaccines. Each of these methods represents a different facet of the immune system's potential to combat cancer, and each has its unique mechanism of action and clinical application. To begin with, ICI (Immune checkpoint inhibitors) are a groundbreaking class of drugs that have revolutionized cancer treatment. These inhibitors work by targeting specific proteins on immune cells and cancer cells that act as checkpoints, effectively turning off immune responses. By blocking these checkpoints, CAR-T cell therapy, on the other hand, is a form of immunotherapy that involves genetically modifying a patient's own T cells to recognize and destroy cancer cells. This is achieved by introducing a gene for a chimeric antigen receptor into the T cells, which enables them to target specific antigens on the surface of cancer cells. Cancer vaccines are another promising avenue in immunotherapy. Unlike traditional vaccines that prevent infectious diseases, cancer vaccines are designed to treat existing cancer or prevent its recurrence.

Keywords: Immune system; immunotherapy; CAR-T therapy; immune checkpoint inhibitor; cancer vaccines.

1. Introduction

Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts. In 2022, there is an incidence of cancer in both sexes. It is among the most common diseases in the world. This type of disease is more common in the elderly, according to the data from WHO(World Health Organization) [1]. It's affected by family history, diet, obesity, smoking, and alcohol. Fortunately, there are still several ways to treat cancer, such as surgery, chemotherapy, radiotherapy, targeted therapy, and Immunotherapy. Research has shown that the multidisciplinary Integrated Care Collaboration model can improve the diagnosis and treatment of cancer. Immunotherapy is one of the most advanced cancer treatments available today. It's also one of the cancer treatments which are actively investigating. Immunotherapy is a treatment that uses your immune system to fight cancer. Some immunotherapy helps the immune system find and kill the cancer cells. Unlike chemotherapy, Immunotherapy always builds a strong line of defense to kill the cancer cells, but it won't harm other cells. It also depends on the type of cancer and its different stages. For now, more and more drugs are produced to help the immune system kill cancer cells without other side effects, such as ICI, CAR-T cells, and cancer vaccines.

2. Immune checkpoint inhibitors

Immune checkpoint inhibitors have been one of the most innovative Immunotherapy in recent years. The immune system has so many types of immune cells. The most well-known cells are T-cells(T-lymphocytes). The T-cells transfer in your blood to kill the cancer cells. It plays a crucial role in the treatment of cancer. They can find the abnormal cells through interaction between T-cell receptors(TCR, PD-L1&PD-1, CTLA-4) and major histocompatibility complex. After reorganization, the abnormal cells T-cells will release the cytokines to eliminate the tumor cells. T-cells also have receptors to restrain their function. When these receptors are on, The T-cells can no longer destroy

the abnormal cells [2].So, It is the same thing. Cancer cells trick T-cells to protect themselves from being destroyed by T-cells. So, the scientists made a checkpoint inhibitor to block the cancer cells and trigger the stop signals in the T-cells. Then, the T-cells will recognize the abnormal cells and work the same as before. Most of the time, humans use mice for experiments. Here's why scientists are experimenting with mice. First, Mice are up to 80 percent genetically similar to humans. Also, it's small and easy to manage. Here, I used a mouse model to explain the situation. Immune checkpoint inhibitors (ICI) kill the cancer cells by targeting proteins like CTLA-4 and PD-1/PD-L1.Even though it has shown significant efficacy, it's still limited by immune-related adverse events(IrAEs).To better understand and develop the treatment means. The scientists have created three different kinds of animal models [3].

There are three different kinds of mouse models in ICI. The first one is the Mouse model for adverse events. It developed a mouse model to investigate inflammatory toxicities in response to dual checkpoint blockade (anti-CTLA-4 and anti-PD-1 antibodies). This model showed that the mouse developed significant IrAEs [4]. Which means this model is successful. The second model is the myocarditis Model. This model developed the genetics of different mice. This model reappears the myocarditis from ICI on the mouse model. This model showed that combining CTLA-4 and PD-1 inhibitors led to T-cells and macrophages. It's similar to clinical manifestations of myocarditis patients. The third animal model is about autoimmunity and inflammation. This research also explored the use of ICIs in autoimmune diseases. For example, in this model, targeting receptors VISTA(PD-1H) can prevent graft-versus-host disease(GVHD) [5]. Immune checkpoint inhibitors have shown unbelievable results in cancer treatment. There are so many different immunotherapy drugs being developed. In the future, Immunotherapy will be the most common cancer treatment method. However, for now, there are still some issues with Immunotherapy, such as autoimmune reactions and toxicities. The scientists also developed new ways to combinate the different treatments with ICIs.

There are three main categories of approved. PD-1 inhibitors: Cemiplimab, Nivolumab, and pembrolizumab. Ipilimumab, which blocked the CTLA-4, will allow the T-cells to continue their work. Atezolizumab, avelumab, and durvalumab are inhibitors that block PD-L1 and treat some cancers, such as Bladder and Breast cancer [6]. Next generation of ICIs: For example, LAG-3 is a monoclonal antibody. Preliminary data from a phase I/II clinical trial using LAG525 with or without natalizumab in patients with advanced malignancies were published. Of 240 patients, 119 received LAG525 as monotherapy and 121 as combination therapy. Seventy-nine percent of patients receiving LAG525 monotherapy and 67% of patients on combination therapy discontinued therapy due to disease progression. Eleven of 121 patients in the combination group achieved a partial response (PR), and one had a complete response (CR). Data regarding response to monotherapy were not available. TIM-31 is another inhibitor that is in clinical trials. It will come out soon [7].

3. CAR-T cells

T-cells are one of the most critical cells in the immune system. It can recognize the abnormal cells. T-cells have the protein receptor on themselves. They will immediately attack the abnormal cells and release the toxic chemicals when they find the abnormal cells. But it has not always happened that successfully. Some abnormal cells can fool the immune system into showing that they are normal cells or by sprouting so many antigens on their surface, which means even though the immune system finds out it is an abnormal cell, it can still escape the attack. Humans have the T-cells in our body. However, modified inactive viruses are used for the CAR-T-cells. This virus cannot cause disease but can introduce genetic information into the T-cells. After that, the T-cells changed their shape and produced some special protein receptors called Chimeric Antigen Receptors (CARs) on their surface. This kind of T-cells is manufactured cells. They grew in the lab, and it's also targeted to the different specific cancers. They can find corresponding cancer cells and kill them (Fig.1) [8].

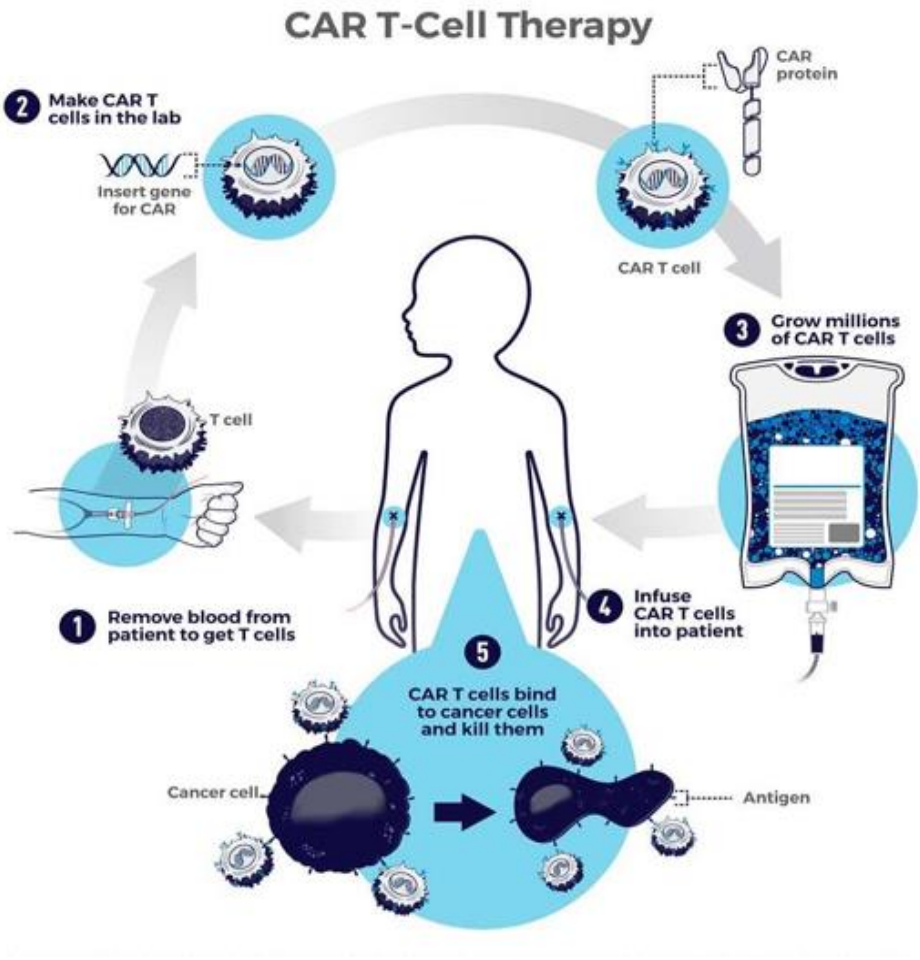

Figure 1. CAR-T cells therapy [9].

There are currently over 1200 clinical trials globally exploring various aspects of CAR T-cell therapy, indicating a robust research and development pipeline. The CAR T-cells are used in children's most common cancer, acute lymphoblastic leukemia (ALL). Over eighty percent of children will be cured after intensive chemotherapy. But unfortunately, the cancer will return after chemotherapy or stem-cell transplants. In 2017, they tried to use CAR-T-cells on the patient of ALL. In the following five years, there was no cancer return. But it also has other side effect. It will lead to a mass die-off of antibody-producing B cells and infections. One of the most frequent and severe side effects is cytokine release syndrome(CRS). But it can be treated by Acterma. It can block the IL-6 [9]. In the future, the CAR T-cells will develop in solid tumors. The number of receptors of the T-cells will increase. So more types of cancers can be treated. Scientists are developing next-generation CAR T-cell therapies that aim to reduce side effects, lower or eliminate cancer recurrence, and better target treatment-resistant cancer. CAR-T cell therapy may improve treatments for autoimmune diseases and help reduce the risks of organ rejection in those who receive organ transplants.Overall speaking CAR-T cell therapy has great hope for the future. Ongoing research is aimed at improving safety, effectiveness, and availability.

4. Cancer Vaccines

Vaccines are worked by training the immune system to find the abnormal cells. Because sometimes these kinds of cells can fool the immune system. Which means they cannot find the abnormal cells. All cells have the protein inside or outside of the cells [10]. Different cells have different proteins. Suppose the scientists picked a piece of the protein of cancer cells. Then, the immune system can react. It sounds easy, also. The fridges of hospitals have the most common types of cancer vaccines. But sadly, it was not helpful during the trial. So, the scientists will focus on the patients with different

vaccines. It depends on the other cancer cells. Because the cancer cells will mutate, the protein in the cancer cells will be changed. These changed proteins are called neoantigens.

There are two different ways to make these personalized vaccines. First, collect tumor samples from the patient. Then, the doctors will analyze the tumor cells. In the tumor cells, it carries the message RNA(mRNA). These mRNA carries the genetic material. mRNA is extracted and sequenced along with cellular DNA. To identify the instructions for the tumor's unique protein(neoantigen). Select the cells that stimulate the immune system the most and let the dendritic cells find them. This is called customized mRNA vaccines. And also there is another way to make personalized vaccines. The doctor will put the protein of the cancer cells into the dendritic cells. They are injecting these dendritic cells back into the body. The T-cells scan these abnormal dendritic cells. And kill the cancer cells. Personalized vaccines work. But it's costly and time-consuming. So the scientists now are developing the "off-the-shelf" treatment. This means all of these steps will happen in your own body. Patients are given drugs of dendritic cell activators. Then, radiotherapy is used to kill some cancer cells. Dying cancer cells will release the proteins [10]. These proteins will be eliminated by the dendritic cells. The cancer proteins are shown to the T-cells to irritate T-cells to kill the cancer cells. This approach is still being researched and tested. If the trial is successful a vaccine that boosts your immune system. That will be a big step in the fight against cancer.

5. Conclusion

There are so many different ways to treat the cancer. But cancer remains one of the most common causes of morbidity and mortality. Even though some patients are cured for now the cancer will return or they will face high treatment costs and serious sequelae. That's why it is so important to develop an effective treatment. Immunotherapy is by far the least harmful and most effective treatment. The main purpose of immunotherapy is to train the patient's immune system to kill the cells by themselves. Not like chemotherapy, Immunotherapy will only focus on the abnormal cells in the patient's body, but chemotherapy will target all the cells in the patient's body. So in the future immunotherapy will be the most popular treatment. Now scientists are studying how to reduce the cost of immunotherapy so that more cancer patients can use this technology, and apply this technology to other diseases. The other side effects are also important in cancer treatment, for immunotherapy, it will decrease the other side effects to the minimizing side effects.

References

[1] Hao Yijia, Han Xuexiang. Research progress of cancer mRNA-LNP vaccine[J/OL]. Chemistry of Life,1-13[2024-09-04].

[2] Tian Jiping, Zhang Jian, Zhou Jinpei, et al. Research progress on small molecule inhibitors of PD-1/PD-L1 at immune checkpoints[J]. Journal of China Pharmaceutical University,2019,50(01):1-10.

[3] Wang Yucong, Xu Yinghui, Li Hongwei, et al.PD1/PD-L1 immune checkpoint inhibitors in the treatment of non-small cell lung cancer[J]. Journal of Jilin University (Medical Science),2019,45(04):965-970.

[4] Marin-Acevedo JA, Kimbrough EO, Lou Y. Next generation of immune checkpoint inhibitors and beyond[J]. J Hematol Oncol. 2021,19;14(1):45.

[5] Yao Chao, Qian Cheng. Opportunities and challenges of CAR-T cells in tumor therapy[J]. Chinese Journal of Cancer Biotherapy,2017,24(01):6-11.

[6] Lin Caiyao, Muhammad Kalim, Liang Keying, et al.CAR-T therapy and its application progress in tumor immunotherapy[J]. Chinese Journal of Cell Biobiology,2018,40(03):412-417.

[7] Osama E. Rahma et al. Phase Ib study of pembrolizumab and trebananib (angiopoietin-2 inhibitor [Ang-2]): Preliminary analysis of the colorectal cancer (CRC) cohort. JCO 2019,37, e14160-e14160.

[8] Chen Shaofeng, Zhu Zhipeng, Wu Yanfeng. Chinese Journal of Cancer Biotherapy,2019,26(07):802-809.

[9] Information on: https://en.wikipedia.org/wiki/CAR_T_cell.

[10] Wei Zhimeng, Dang Sheng, Li Guangchen, et al.mRNA vaccines and drugs: the new darling of cancer immunotherapy[J/OL].Progress in Biochemistry and Biophysics,1-23[2024-09-04].