

# Prospects for Stimulating Autoimmunity and Developing New T Cells in Cancer Treatment

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**Abstract.** Any adverse problem or weakening of the body's immunity, such as HIV infection, long-term physical and mental stress, nutritional deficiencies, chemotherapy or major surgery, will make cells prone to cancer. The body's immune system also deteriorates with age, which may help understand how people's risk of developing cancer increases significantly as they age. If the body's immune system is no longer strong enough to completely destroy cancer cells, then we move from "eliminating" cancer to "balancing." The immune system is the body's protective network, consisting of immune cells, immune organs, and immune substances. It fights against foreign pathogens and mutated cells in the body to maintain the health of the human body's internal environment.

Strictly speaking, patients with better physical conditions have higher and more powerful T cells, and the more T cells awakened by immune drugs, they are relatively more effective in eliminating tumor cells. Currently, T cell-based immunotherapy includes CAR-T therapy, TCR-T therapy, TILs therapy, and CTL therapy.

**Keywords:** T cells; cancer treatment; autoimmune system; cancer cell.

## 1. Introduction

The distribution and division of immune cells in the human body are of important strategic significance.

T cells and B cells recognize antigens through their respective expressed T cell receptors (TCR) and B cell receptors (BCR), and the adaptive immune response (response). It can be divided into cellular immune response and humoral immune response. T lymphocytes are divided into two categories: CD4 and CD8. The former is a helper T cell, which is the command system of the immune response. It mainly exchanges information with other cells and issues orders through molecules on the membrane surface and secreted cytokines. After the antigen invades the body, if it can enter the blood and reach the spleen and lymph nodes, T and B cells should play their role<sup>[1]</sup>.

## 2. T cell activation

T cells will enter an activated state when stimulated by this pathogenic microorganism and become sensitized T cells. Sensitized T cells have two characteristics: first, they have the ability to attack and kill this pathogenic microorganism; second, they have recognition and memory functions for this pathogenic microorganism<sup>[2]</sup>. The sensitized T cells can recognize the pathogenic microorganism when they encounter it again and continue to attack it.

When B cells are stimulated by pathogenic microorganisms, they will produce a substance that can bind to the pathogenic microorganism and render it inactive. We call this substance an antibody. If such pathogenic microorganisms invade the body again in the future, sensitized T cells (activated T cells) will rush forward to fight them, and antibodies will bind to them, causing them to lose their ability to cause disease. It can be seen that as long as the human body's immune system has seen a certain pathogenic microorganism once, it has immunity to the pathogenic microorganism. This is why people can become immune to this pathogen as long as they take or inject a certain vaccine, or have contracted this infectious disease.

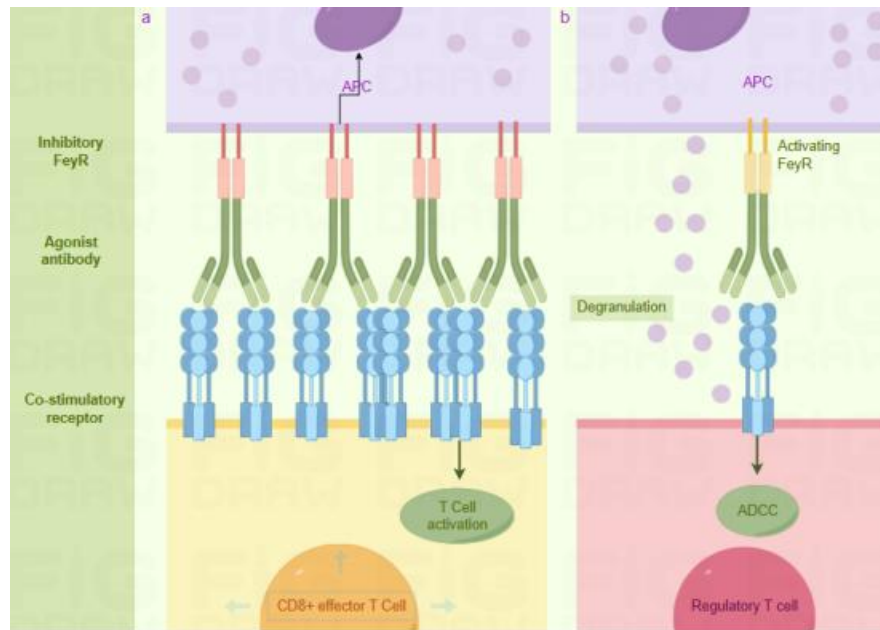


Fig. 1 T Cell

After T cells differentiate and mature in the thymus, they are distributed to immune organs and tissues throughout the body through lymph and blood circulation to perform immune functions. The biggest feature of T cells is that they have a pair of automatic identification systems that can identify whether the enemy is friend or foe. , can accurately identify and destroy cancer cells.

Innate immunity, also known as non-specific immunity, belongs to the innate immune system. It is present after birth. It can respond quickly to various pathogenic microorganisms that invade the human body. This type of immunity belongs to this type of immunity. The body's innate immunity includes tissue barriers and innate immune cells. Adaptive immunity is an important part of the immune system, which consists of cellular immunity and humoral immunity<sup>[3]</sup>.

### 3. Immune activation

The key factor in activating the immune system is genetic recombination. Our general cells are designed according to the blueprints given by genes. RNA first transcribes DNA information, and then goes to ribosomes to manufacture proteins. Basically, we produce it according to the sequence given in the gene, without any creativity in the process. But the production of antibodies is different. There are several sections of genes in our chromosomes that are specifically responsible for producing antibodies. There are many gene sequences in a piece of DNA, which can be roughly divided into three parts, V region, D region, and J region. There are many sets of genes in each region. When we perform recombination, we first randomly select a set of genes from the D and J regions and connect them together, and then select a set of genes from the V region and connect them together, thus forming a VDJ combination.

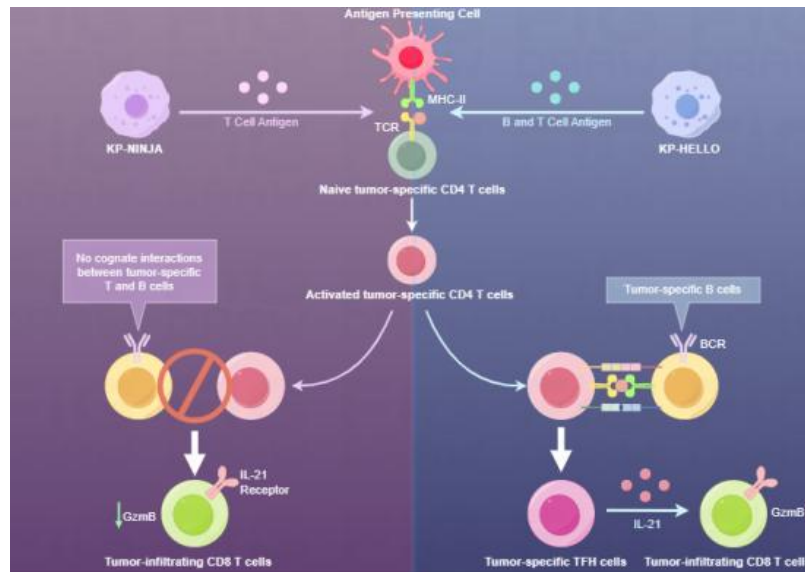


Fig. 2 Immune activation

In every B cell the DNA is in random motion, twisting around in the cell fluid. At a certain moment, a gene in the J region and a gene in the D region happened to be very close to each other. At this time, two Rag proteins happened to catch up<sup>[4]</sup>. So the two proteins moved toward the middle, and the sequences between the genes at the two ends became one. After the gene is cut, it connects the two ends together, so a D and a J are connected together, and the other V and J between them are thrown away. Next, the connections between V and D are the same. Because this cutting relies on the random movement of gene sequences and proteins, in this cell, it may be that the first J and the first D are connected. In another cell, the second J may be connected to the third D. So this random connection and cutting creates the effect of random card drawing. The immune system can be activated.

#### 4. Challenges and prospects for the application of novel T cells

For patients with sensitive gene mutations found by genetic testing, targeted therapy is the first choice<sup>[5]</sup>. Sensitive genes in medical terms refer to genes such as EGFR, ALK, and ROS1. As long as we can find targeted drugs that are available and accessible, we will try our best to choose targeted treatments in the first line within the economic affordability. Even for lung cancer patients with existing gene mutations and high PDL1 expression, targeted drugs are the first choice, and immunotherapy will be considered after drug resistance.

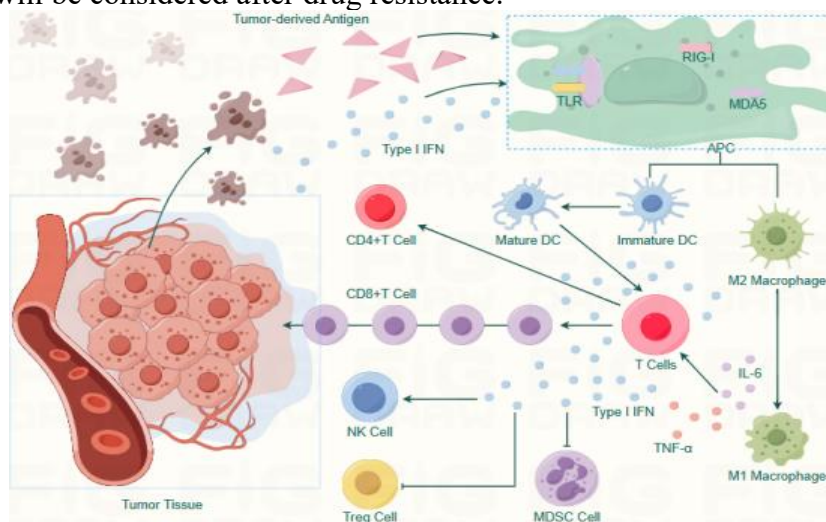


Fig. 3 RNA sensing model under anti-tumor immunity

Studies have shown that MSI-H and microsatellite-high instability tumors respond well to immunotherapy. Patients with high tumor mutation burden (TMB) have better outcomes. The higher the expression of PD-L1 (TPS  $\geq$  50%) in tumor cells, the more likely they are to experience tumor shrinkage. Therefore, these indicators should be tested as much as possible before immunotherapy. If the financial situation is good, large panel testing can be performed, which covers immunotherapy-related indicators. Those with average finances may also consider detecting PD-L1 expression through immunohistochemistry. If the physical condition is poor, patients with high PD-L1 expression ( $\geq$ 50%) can be treated with immune monotherapy, which is also recommended by the NCCN guidelines.

## 5. Summary

There are currently 8 types of PD1/PD-L1 inhibitors. The imported O drugs and K drugs are slightly more expensive, but they are all indicated for non-small cell lung cancer. The current drugs approved by NCCN guidelines for small cell lung cancer are the PD-L1 inhibitors durvalumab and atezolizumab. The prices of the four domestic immunotherapy drugs in China are not high. Sintilimab and camrelizumab are approved for non-squamous non-small cell lung cancer, and tislelizumab is approved for lung squamous cell carcinoma.

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