Proceedings of ICMMGH 2025 Symposium: Computational Modelling in Biology and Medicine
DOI: 10.54254/2753-8818/91/2025.GU22388

New Advances in the Chimeric Antigen Receptor T Cell Immunotherapy

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Abstract: In the field of cancer treatment, traditional therapies face problems such as side effects and efficacy making the survival rate of advanced cancer patients still low. With the rise of immunotherapy, hematological cancers can benefit greatly from cutting-edge immunotherapy methods, namely chimeric antigen receptor T cell (CAR-T) therapy. However, there are still many obstacles to overcome before CAR-T immunotherapy can be used to treat solid tumors, such as the tumor microenvironment's immunosuppressive effect and antigen heterogeneity and escape. In recent years, continuous innovations in CAR-T technology have driven the progress of this therapy. This article reviews the recent advances of CAR-T technology in tumor therapy and focuses on the prospects and challenges of its application in solid tumor treatment. It shows that by optimizing the design and efficacy strategies of CAR-T cells, the therapy is expected to break through the current bottleneck and bring more effective treatment options in the future. Meanwhile, further clinical studies will help address the limitations of the current technology, including unstable efficacy, high cytotoxicity, and possible immune escape during treatment. In conclusion, CAR-T still has a broad application prospect, but it needs to be thoroughly researched and optimized in various aspects to achieve its wider application in solid tumors.

Keywords: Chimeric antigen receptor T (CAR-T) cell, immunotherapy, tumor microenvironment.

1. Introduction

Cancer is a major disease with a global mortality rate second only to cardiovascular disease, and its treatment still faces multiple challenges. Conventional treatment methods such as surgery, radiotherapy and chemotherapy, although effective in combating cancer to a certain extent, are often associated with severe side effects and limited therapeutic efficacy, especially in advanced cancer patients. In this context, the search for more precise treatments with fewer side effects has become an important direction in cancer research today. As a cutting-edge cancer immunotherapy, CAR-T immunotherapy has made remarkable progress in new cancer treatments, especially in the treatment of hematological malignancies. This method, by using genetic engineering techniques, alters a patient's T cells so that they can recognize and eliminate tumor cells. Therefore, this review will focus on CAR-T immunotherapy, starting from the basic structure of CAR-T and combining the development history of the first three generations of CAR-T technology to discuss in detail the recent technological innovations of this therapy.

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DOI: 10.54254/2753-8818/91/2025.GU22388

Broadly speaking, the technological innovations in this method in recent years have been dominated by the fourth generation that has entered the clinical trial stage and the newer research than the fourth generation, the fifth-generation, which may offer more possibilities for therapeutic efficacy in this field. These advances not only represent a continuing breakthrough in cancer technology with this treatment, but also reflect a profound shift in the concept of cancer treatment.

This review will evaluate the value of these new technological innovations in various aspects, including efficacy, safety, and economic evaluation. It will also reveal the existing problems and future challenges of these innovations. It is hoped that this article will help clinicians and researchers to make sense of the latest research results of CAR-T, and really help them to have a deeper understanding of the recent advances and innovations in this therapy.

2. CAR-T Structure and Development

CAR-T cells consist of three major structures: the extracellular structural domain, the transmembrane structural domain, and the intracellular structural domain (Figure 1). Among them, the extracellular structural domain usually consists of a single-chain fragment variable (scFv) and a hinge region. scFv consists of a variable light chain and a variable heavy chain, and is able to bind antigens on the surface of tumor cells through its specificity. This binding initiates the activation process of CAR-Ts, enabling them to precisely recognize and kill tumor cells [1]. This specific recognition allows CAR-Ts to act exclusively on tumor cells in the tumor microenvironment (TME), minimizing damage to normal cells. The intracellular structural domain consists of a signaling region and a co-stimulatory signaling region. The signaling region significantly enhances the anti-tumor effect by activating T cells, enhancing their immune response, and boosting the ability of CAR-Ts to recognize and kill tumor cells [1]. Co-stimulatory signaling regions, on the other hand, further enhance the tumor-killing ability of CAR-Ts and optimize the overall therapeutic efficacy by promoting the proliferation of T cells and enhancing their effector function [1].

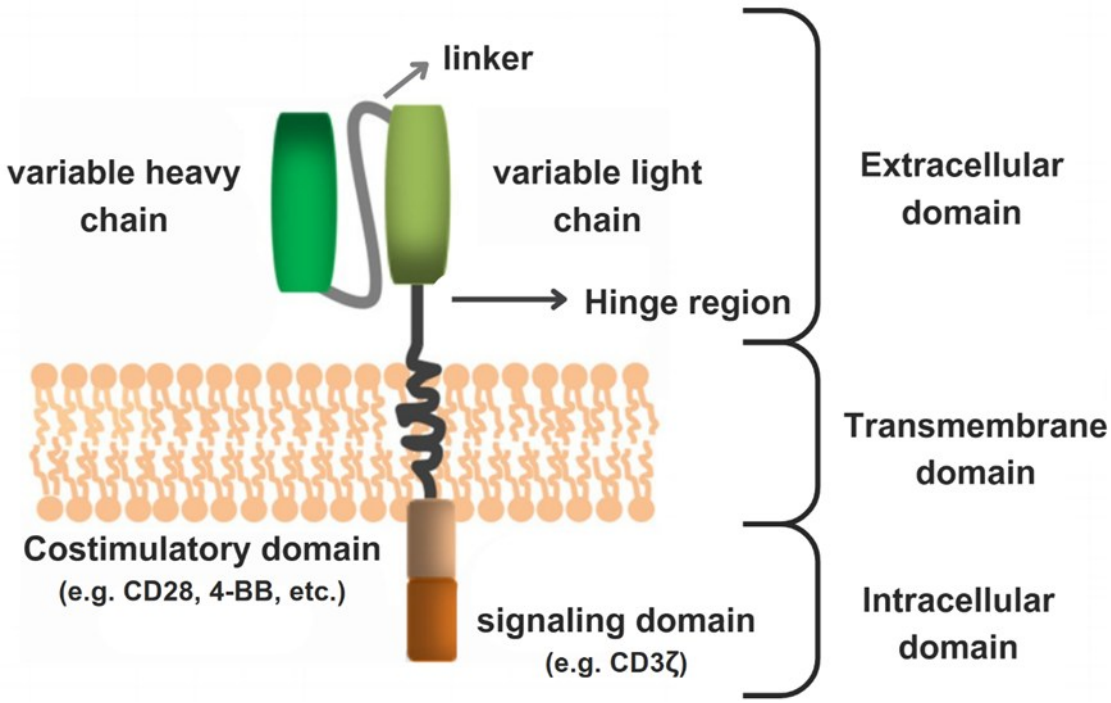

Figure 1: Schematic diagram of CAR structure [2].

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Structure is compatible with function, structure determines function, and function influences structure. CAR-T therapies have undergone a continuous technological evolution from the first to the third generation (Figure 2). The first-generation consists only of a CD3ζ signaling region and an antigen recognition region, a design that limits the proliferative capacity and anti-tumor effects of T cells, resulting in a more limited clinical efficacy. The main reason is the lack of necessary co-stimulatory signals, which fails to effectively enhance the proliferation, survival and effector functions of T cells, resulting in insufficient anti-tumor activity [3]. Second-generation have enhanced the proliferation and anti-tumor effects of T cells by introducing co-stimulatory signaling domains. Since the FDA approval of this therapy in 2017, second-generation has become a key tool in the treatment of hematologic malignancies, especially in acute lymphoblastic leukemia (ALL) and diffuse large B-cell lymphoma (DLBCL), etc., which have shown good efficacy, and some patients are even able to achieve long-term clinical remission [4,5]. Therefore, second-generation CAR-T has become the current standard regimen for the treatment of hematological tumors. Third-generation further enhances T cell survival and persistence based on the second generation by adding multiple co-stimulatory signaling domains. This improvement allows T cells to expand more efficiently and increase their ability to kill tumor cells. However, some researchers have argued that multiple co-stimulatory elements like the third generation may lead to a lower threshold for T cell stimulation, which may also induce excessive cytokine release [3]. Disappointingly, third-generation CAR-T did not show in vivo therapeutic benefit and failed to outperform second-generation in leukemia and pancreatic cancer models [4].

The limitations of the first three generations of CAR-T are mainly due to the fact that patients with hematologic malignancies face relapse, loss of CAR-T persistence, and tumor resistance to apoptosis after treatment, as well as antigen escape from the tumor. In contrast, their limitations in solid tumors are more prominent.

1)Lack of tumor-specific antigens (TSAs): unlike hematological tumors, where most targets are single and specific, there are few TSA in solid tumors, and most of the antigens currently highly expressed in tumors are tumor-associated antigens (TAA), which are also expressed in normal tissues. This poses a high off-target risk and safety becomes a key issue [5,6].

2)Immunosuppression in the TME: The TME is characterized by immunosuppressive mechanisms that are extremely harmful to T cell survival and immunological efficacy, as well as low pH, low oxygen, and high osmolality [5]. In the meantime, the TME contains immunosuppressive cells including M2-type macrophages, myeloid-derived heterogeneous cells (MDSC), and Tregs Within solid tumors, these immunosuppressive cells release cytokines including IL-10 and TGFβ, which lessens the anti-tumor activity of CAR-T upon reinfusion [5,6].

3)Endogenous T-cell suppressive signaling: There is an endogenous regulatory mechanism for the immune activity of T cells. When T cells are overactive, molecules such as PD-1 and CTLA4 play a role in maintaining immune homeostasis. After CAR-Ts are activated by antigen, PD-1 and CTLA4 bind to relevant ligands and inhibit T cell proliferation and secretion of relevant cytokines. Thus, endogenous T cell inhibitory signaling also reduces the antitumor activity of CAR-T.

In addition, side effects such as cytokine release syndrome (CRS) and neurotoxicity, which have been somewhat improved but still occur from time to time in second- and third-generatio reatments, may pose a threat to the life safety of patients [7]

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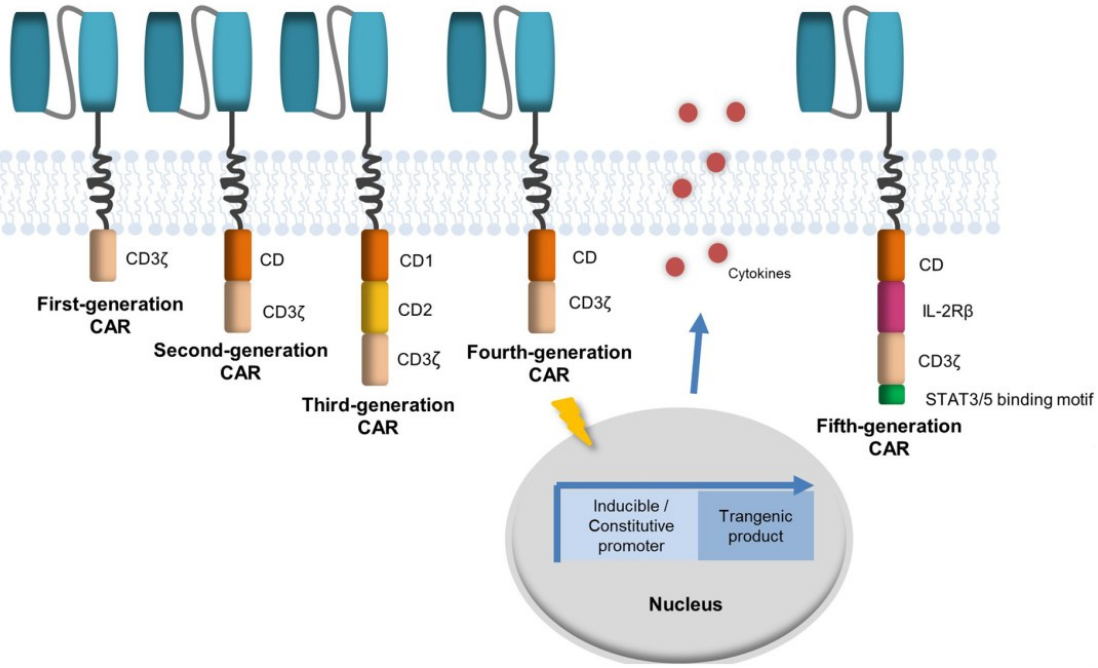

Figure 2: Development of CAR-Ts [2].

3. Evaluation of Specific Innovations snd Application Value of Fourth-generation CAR-T

3.1. Chemokines

Numerous cell types, including stromal cells, innate immune cells, and even tumor cells, express chemokines. The receptors expressed on T cells frequently do not match the chemokines produced in the TME. Several research have designed homologous chemokine receptors, mostly on CAR-Ts, to take advantage of this phenomena. T cells' chemotactic behavior was improved when Kershaw et al. engineered a CXCR2 receptor for its homologous cytokine CXCL8 [8]. The cognate chemokine CCL2, which is significantly expressed in malignant pleural mesothelioma, was targeted by CCR2 on CAR-Ts in a different study. Compared to untransduced CAR-Ts, engineered CAR-Ts exhibited improved migration and 12.5-fold higher cytotoxicity.

Li et al. modified the chemokine receptor CXCR5 onto the surface of CAR-Ts targeting EGFR for the treatment of non-small-cell lung cancer (NSCLC). The results of in vivo CAR-T tracer experiments showed that CAR-Ts modified with CXCR5 could migrate and penetrate directionally to tumor foci and significantly cleared the tumors, while greatly reducing the potential extra-tumor toxicity [9].

3.2. Improvement of CAR-T Recognition of Antigens

Wendell Lim et al. implanted the synNotch system in CAR-Ts, and under the regulation of synNotch, CARs recognizing relevant TAA would only be expressed on T cells migrating into tumors without attacking cells in normal tissues, which greatly improved the specificity of CAR-T recognition of antigens [10].

CD133 is commonly used as a target for cancer stem cells. A phase 1 clinical trial successfully showed that CD133+ tumors were eliminated, but CD133- tumor recurrence was observed [5].

Kim et al. demonstrated that KIAA1114 is a unique and stable marker for CSCs and that Kiatomab, a KIAA1114-specific monoclonal antibody, showed therapeutic potential in a mouse tumor model,

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suggesting that KIAA1114 could be used as a novel target antigen for CSC CAR-T immunotherapy [5].

Hirabayashi et al. conducted a study on dual-target CAR-T for neuroblastoma (NB) model. This study targeted two NB-associated antigens, GD2 and B7-H3, and provided CD28 and 4-1BB co-stimulation, achieving rapid and sustained anti-tumor effects in mice and preventing tumor immune escape due to low antigen density [11].

4. Introduction of New Co-stimulatory Molecules

Conventional CAR-T therapies have focused on antigen recognition and effects of T cells, and in solid tumor therapy, single antigen recognition may not be able to overcome immune escape mechanisms in the TME. Therefore, Nishimura et al. (2024) study proposed TOP CAR, in which they introduced TMIGD2, a known co-stimulatory molecule, into CAR-Ts, which could enhance T cell activation and proliferation, and enhance their anti-tumor effects, especially in the presence of a high number of tumor cells and high antigenic heterogeneity [12]. In addition, the team also used B7-H3 as the target antigen of CAR-Ts, which is an immunomodulatory molecule highly expressed in a variety of solid tumors. By targeting B7-H3, CAR-Ts were able to efficiently recognize and kill tumor cells while reducing the damage to normal cells. This design not only improves the targeting of CAR-Ts in solid tumors, but also improves the persistence and anti-tumor ability of the cells [12]. In animal models and preliminary preclinical studies, TOP CAR showed higher anti-tumor activity and persistence compared to conventional CAR-Ts, especially against solid tumors. It was shown that the TMIGD2 co-stimulatory structural domain significantly enhanced the proliferation and survival of T cells, increasing their ability to kill tumor cells, thereby enhancing the overall efficacy of CAR-Ts. This finding provides a new direction for CAR-T therapy, especially in the treatment of solid tumors, showing more significant advantages, and is expected to provide a more effective and safer strategy for future tumor immunotherapy [12].

4.1. Release Immunosuppression

The absence of immune stimulating substances, immunosuppressive cells, and immunosuppressive cytokines are the primary causes of TME's immunosuppressive effects. One important aspect influencing the efficacy of CAR-T in solid tumors is immunosuppression in TME.

Fourth-generation CAR-T enhances the immune response by modifying CAR-Ts to overexpress pro-inflammatory cytokines [13]. IL-2 and IL-12 regulate Tregs and MDSCs and promote T-cell proliferation. Pro-inflammatory effects are amplified by T cells that release the cytokines IL-12 and IL-21. The survival of mice with subcutaneous tumors was improved by local administration of IL-12 using CAR-Ts that target VEGFR-2. IL-7 and CCL19-expressing CAR-Ts improved anti-tumor activity and boosted T and dendritic cell infiltration in the TME. When CAR-Ts identify and come into contact with tumor antigens, they produce these cytokines, which attract and activate more immune cells including NK cells and macrophages to strengthen the immune response. For example, Lei et al. (2024) developed 7×19 CAR-T by engineering CD19-specific CAR-Ts to autocrine IL-7 and CCL19 upon exposure to CD19 antigen [14]. Preclinical studies determined the anti-lymphoma activity of 7×19 CAR-T, demonstrating superiority over conventional anti-CD19 CAR-T with enhanced tumor targeting and anti-tumor activity [14]. Adults with relapsed/refractory LBCL (R/R LBCL) participated in a multicenter clinical trial that was carried out by the research team. According to the data, individuals with R/R LBCL who received 7×19 therapy experienced long-lasting remissions with a controllable safety profile [14]. Moreover. A group of researchers from the University of Pennsylvania created and carried out a phase I clinical trial to assess CAR-T huCART19-IL18 in patients with relapsed or refractory non-Hodgkin's lymphoma using a novel

DOI: 10.54254/2753-8818/91/2025.GU22388

fourth generation CAR that can secrete the pro-inflammatory cytokine IL-18 [15]. The results showed that out of 7 evaluable patients, 100% achieved clinical response, 4 patients (57%) had complete remission and 3 (43%) partial remission. 4 patients in complete remission did not experience relapse during follow-up and all patients survived [15]. All demonstrated good safety and initial efficacy during dose escalation. Overall, huCART19-IL18 demonstrated significant potential in the treatment of relapsed or refractory CD19+ non-Hodgkin's lymphomas, especially in patients resistant to conventional CAR-T [15].

4.2. Knockdown of Endogenous Suppressor Molecules

Fourth-generation CAR-T therapies have used such as CRISPR/Cas9 to, on the one hand, knock down the major histocompatibility complex (MHC)-associated genes, which further reduces immunogenicity, and the T-cell receptor (TCR) genes of allogeneic T-cells, preventing them from eliciting an immune rejection response from the host. Conversely, CTLA-4 and PD-1, two T-cell inhibitory signaling molecules, were eliminated. By removing these endogenous inhibitory molecules, CAR-Ts are able to better perform their killing function in the TME and are less subject to inhibition mediated by the corresponding ligands on the surface of the tumor cells, thus enhancing the persistence and anti-tumor activity of CAR-Ts. This strategy has shown positive results in preclinical studies. For example, the NCT02793856 clinical trial in China used T cells with CRISPR/Cas9 edited PD-1 to treat NSCLC and achieved a 5-year survival rate of 15.5%-23%. In another phase I clinical trial (NCT03399448), CRISPR/Cas9 was used to edit T cells to target the NY-ESO-1 antigen. The results showed that the engineered T cells were more cytotoxic and the treatment was well tolerated with fewer side effects and no CRS. two patients showed a significant clinical response with a significant reduction in tumor size, and the other patient had a 50% reduction in abdominal tumor mass for 4 months with few side effects [16]. Tmunity is also using gene editing to knock out endogenous T cells in the TCR and PD-1 receptor in T cells, and then express TCRs targeting the NY-ESO-1 antigen. TCR cell therapies developed using this technology have shown positive efficacy in clinical trials.

4.3. Anti-Apoptotic Protein Upregulation

Up-regulation of anti-apoptotic proteins helps to enhance the ability of CAR-Ts to survive low oxygen or high cytokine concentrations, thereby improving their persistence in the TME. The development of CAR-Ts overexpressing Bcl-xL, Bcl-2, and other members of the Bcl-2 family has been demonstrated by researchers at Harvard Medical School to significantly improve the persistence and function of CAR-Ts in vivo. These cells may also be used in conjunction with the BH3 mimetic venetoclax to further enhance tumor growth in mice [17].

4.4. Expression of Fusion Proteins of Immune Checkpoint Inhibitors (ICIs)

CAR-Ts were constructed to express fusion proteins of ICIs with other functional proteins, such as PD-1 antibodies with cytokines or co-stimulatory molecules. Such fusion proteins can not only block the inhibitory signals of immune checkpoints such as PD-1, but also further enhance the activity and proliferation of CAR-Ts through the action of co-stimulatory molecules or cytokines, thus improving their efficacy in the treatment of solid tumors.

4.5. Improved Aafety and Controllability

Fourth-generation employs suicide gene systems such as the inducible cysteoaspartase (iCasp9) system. These systems are capable of inducing apoptosis of CAR-Ts through specific external

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activation signals when they overproliferate, thus avoiding adverse reactions [18]. For example, researchers conducted a clinical trial of iCasp9-modified CAR-Ts for the treatment of leukemia and lymphoma. The trial included several patients with relapsed or refractory leukemia and lymphoma. Some of the patients were able to control their tumor cells and went into remission after receiving the treatment. Moreover, when some adverse effects that may be related to the over-proliferation of CAR-Ts occurred, the activation of the iCasp9 system with a specific drug successfully induced the apoptosis of CAR-Ts, thus alleviating the adverse effects, which were well tolerated by the patients.

5. Improvement of Side Effects

5.1. In Situ Polyethylene Glycolization Modification

Michael J, et al. proposed a novel strategy for in situ polyethylene glycolization (PEGylation) of CAR-Ts [19]. The study constructed in situ PEGylated CAR-Ts by introducing an azide group modification on the surface of CAR-Ts and covalently attaching long-chain PEG to the surface of CAR-Ts using a click chemistry reaction [19]. It was found that macrophage overactivation during CAR-T immunotherapy is a key factor in the development of CRS and neurotoxicity. Therefore, PEG, as a physical spacer, successfully blocked the interaction between CAR-Ts, macrophages and tumor cells, reducing the overactivation of macrophages and the secretion of toxic cytokines, thus alleviating the symptoms of CRS and neurotoxicity [19]. In addition, in situ PEGylation expanded the safety window of CAR-T, reduced lethal neurotoxicity, and avoided problems commonly associated with IL-6R/IL-6 blocking antibody therapy [19]. Studies have also ensured that CAR-T interactions with tumor cells are preferred over interactions with macrophages, thereby avoiding over-activation of macrophages while effectively killing tumor cells [19].

5.2. Specific Innovations and Application Value Assessment of Fifth-Generation

5.2.1. Fine Regulation of Cell Activation and Expansion

Martin Oft, et al. have each published two research papers on the orthogonal IL-2/IL-2Rβ system, and have succeeded in developing a modified IL-2 and IL-2Rβ receptor pair capable of specifically activate and expand CAR-Ts expressing orthogonal IL-2Rβ in vivo, avoiding activation of non-target cells [19,20]. Martin Oft et al. developed STK-009 by mutating IL-2Rβ and PEG modification of IL-2, which is able to specifically activate hoRb-expressing CAR-Ts, resulting in a recurrent lymphoma model that achieved a 100% complete tumor response with no tumor recurrence [20]. Milone, et al. on the other hand, utilized orthogonal IL-2 (hoIL2) to specifically activate CAR-Ts, which also showed remarkable efficacy in a mouse model of leukemia, with CAR-Ts rapidly expanding and clearing tumors [21]. More importantly, this system allowed precise regulation of CAR-T activation, avoiding side effects such as CRS triggered by over-activation [20,21]. Through the introduction of the orthogonal IL-2/IL-2Rβ system, researchers have successfully improved the safety and efficacy of CAR-T immunotherapy, providing a new treatment strategy for relapsed or refractory tumors.

5.2.2. Enhancing CAR-T Efficacy

The ability of CAR-T treatment to produce a sustained remission is still restricted. Currently, in order to address this issue, Dana-Farber Cancer Research created CAR-Enhancer therapy, which preferentially delivers low-affinity IL-2 molecules to the surface of CAR-Ts through the construction of fusion proteins (fused with immune regulatory molecules) to enhance the efficacy of CAR-Ts. cell surface, enhancing the activity of CAR-Ts can eradicate tumor cells and enhance the memory of CAR-Ts, which is expected to solve the problem of cancer recurrence after the use of CAR-T [22].

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5.2.3. Solid Tumor Therapy

Recently, Andras Heczey's team conducted a clinical study of IL-15-enhanced GPC3 CAR-T immunotherapy for solid tumors, and the results showed that the experimental group had a tumor control rate of 66%, a response rate of 33%, a good safety profile, and an increase in the expansion, intratumor survival, and antitumor activity of GPC3-CAR T cells in patients [18].

5.2.4. Hematologic Oncology Treatment

One of the challenges of CAR-T for blood cancers is antigen escape. In 28%-68% of cases, cancer cells reduce or lose this CD19 marker, making treatment less effective. Recently, City of Hope et al. developed a novel compound, CCI-38, that is capable of targeting and inhibiting YTHDF2. Studies have confirmed that CCI-38 treatment is effective in inhibiting cell growth or survival in a number of different B-cell malignancies . In addition, data demonstrated that CCI-38 was able to significantly improve clinical outcomes in patients who relapsed (tumors with low CD19 abundance) after treatment with CD3/CD19 dual-antibody or CD19 CAR-T therapies.

5.2.5. Facing Challenges

Fourth-generation therapies have made some breakthroughs in anti-tumor efficacy, but their safety and stability still face significant challenges. First, although certain clinical trials have shown enhanced efficacy through strategies such as the introduction of pro-inflammatory cytokines and reduced the risk of CRS in some cases, side effects such as CAR-T-associated encephalopathy syndrome (CRES), tumor lysis syndrome, and secondary tumors have not yet been completely resolved, and in severe cases, they may even be life-threatening. Second, although CRISPR/Cas9 can enhance the precision of CAR-Ts, off-target effects remain a central challenge limiting their safety and efficacy. In addition, while studies of multi-antigen-targeted CAR-T have demonstrated the potential to overcome tumor escape, the technical complexity and the risk of associated side effects need to be further validated. Although PEG modification technology can reduce side effects to a certain extent, long-term use may induce the generation of anti-PEG antibodies, leading to a decrease in efficacy and failure to sustainably improve side effects and enhance the safety of CAR-T.

Fifth-generation have not yet received adequate clinical validation in extensive clinical trials and are still in the early stages of clinical trials.

5.2.6. Common Challenges

High cost of personalized customization: This method needs to be individually customized for each patient, which involves cell collection, genetic modification, expansion and transfusion, and requires a large number of high-cost consumables and professional technicians, resulting in expensive treatment costs that are difficult to be afforded by ordinary patients.

Limited production scale: Currently, the production of CAR-Ts is mostly individualized, making it difficult to achieve large-scale industrialized production, which makes it difficult to reduce costs. Meanwhile, the global supply of viral vectors is tight, limiting capacity expansion.

Treatment durability and recurrence: The sustainability of efficacy in solid tumor treatment is still a problem. It is challenging for CAR-Ts to sustain anti-tumor activity for an extended length of time, particularly in the event of tumor recurrence, due to the heterogeneity of the TME and the immune escape phenomena.

Despite the high remission rate after CAR-T treatment of hematologic malignancies, achieving sustained remission remains challenging, and patients often experience disease recurrence.

DOI: 10.54254/2753-8818/91/2025.GU22388

The efficacy of CAR-T in tumor treatment is influenced by many factors, such as the activation and expansion of T cells in vivo, killing effect and durability, and is also closely related to tumor type and individual patient differences. In the face of highly complex solid tumors, it is difficult to balance these factors with a single CAR-T immunotherapy.

6. Conclusion

The field of CAR-T is rapidly evolving, with fruitful results but also challenges. In terms of technology iteration, it has evolved from the first generation to the third generation, and the fourth and fifth generation technologies are now bringing new breakthroughs and innovations, and the development of these technologies forms the basis for the continuous progress of CAR-T immunotherapy. In the application of tumor therapy, CAR-T shows unique advantages, but also encounters difficulties such as immune escape and drug resistance, etc. Moreover, the maturity of different generations of technologies in clinical practice varies significantly, such as the fifth-generation technology is still in the early stage of research and development, with insufficient accumulation of clinical data, which restricts the full recognition of its potential and effective exploration of clinical transformation.

With an eye to the future, CAR-T present two key directions of development. On the one hand, the combination with cancer vaccines has become a much-anticipated trend. By integrating multiple pathways of action, this combination is expected to break the dilemma of tumor immune escape and drug resistance, especially in the field of solid tumor treatment, which shows greater potential for application and provides new ideas and hope for overcoming the difficult challenge of solid tumors. On the other hand, personalized treatment will become the core strategy for CAR-T development. With the help of comprehensive analysis of patients' tumor tissues, such as gene sequencing and proteomics, we can accurately grasp the individual differences in patients' gene mutation profiles and antigen expression characteristics, so as to screen out tumor antigens with a high degree of specificity and immunogenicity as the targets, and then customize the CAR-T cell products that are most suitable for the patients' individual conditions. This personalized design concept is not only in line with the development trend of precision medicine, but will also continue to evolve and improve in the subsequent immunotherapy process, providing patients with more accurate and efficient treatment options.

Although the new generation of CAR-T has brought more cures to patients, it is still necessary to dig deeper on the basis of the existing technology to realize its wide clinical application and maximize its value. For example, future research should focus on optimizing gene editing tools to minimize the potential risk of off-target effects; carefully designing dynamic regulatory mechanisms to effectively reduce the incidence of adverse reactions and improve the safety of treatment; actively developing new modification materials to replace PEG and enhance the stability of CAR-Ts, so as to comprehensively improve the safety, stability and personalized treatment capability of CAR-T in multiple dimensions. This will comprehensively improve the safety, stability and personalized treatment capability of CAR-T from multiple dimensions, promote the steady progress of CAR-T in the field of tumor treatment, bring good news to more patients, and create a new situation of tumor immunotherapy.

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