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Review:

Ethical considerations of cellular immunotherapy for cancer*

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Abstract: With the rapid development of immunology, molecular biology, and associated technologies such as next-generation sequencing, cellular immunotherapy has recently become the fourth major cancer treatment. Immunotherapies based on T cells, natural killer cells, and dendritic cells play key roles in cancer immunotherapy. However, their application in clinical practice raises several ethical issues. Thus, studies should focus on proper adherence to basic ethical principles that can effectively guide and solve related clinical problems in the course of treatment, improve treatment effects, and protect the rights and interests of patients. In this review, we discuss cellular immunotherapy-related ethical issues and highlight the ethical practices and current status of cellular immunotherapy in China. These considerations may supplement existing ethical standards in cancer immunotherapy.

Key words: Cancer; Cellular immunotherapy; Ethical issue
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1 Introduction

Cancer immunotherapy was evaluated as one of the top ten scientific and technological breakthroughs in *Science* in 2013 (Couzin-Frankel, 2013). After five more years of thorough research, methods such as cellular immunotherapy, immunological checkpoint inhibitors, and tumor vaccines have opened a new chapter in cancer immunotherapy and achieved encouraging results in clinical settings. However, potential ethical issues have emerged in clinical research, such as the informed consent of patients in clinical trials, especially consideration of the potential benefits and risks involved, and the balance between researchers' personal academic development and patients' interests. Therefore, researchers should discuss the ethical issues in cancer immunotherapy, especially those involved in cellular immunotherapy, to improve clinical efficacy based on adherence to ethical principles and the protection of patients' rights and interests.

2 Current status of cancer cellular immunotherapy

T cells, natural killer (NK) cells, and dendritic cells (DCs) play important roles in the anti-tumor immune response. At present, chimeric antigen receptor T (CAR-T) cell technology has achieved efficacy in the treatment of blood tumors and melanoma. NK cells, combined with immunological checkpoint inhibitors, cytokines, and CAR-NK, have shown

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good prospects for application to cancer immunotherapy. In 2010, the DC vaccine, as the first tumor therapeutic vaccine approved by the United States Food and Drug Administration (FDA), gradually caught the attention of researchers (Sims, 2012). Although cancer immunotherapy has rapidly progressed in the last 10 years, numerous scientific problems persist. Thus, researchers must continuously strengthen basic research and accelerate clinical transformation to benefit more patients.

2.1 T cell therapy

At present, two main methods of T cell immunotherapy are available. One method amplifies tumor-infiltrating lymphocytes (TILs) in vitro and then transfers them back to the patient for cancer therapy. The other, through gene modification, enables T cells to express receptors, mainly the T cell receptor T (TCR-T) and CAR-T that recognize tumor antigens.

Muul et al. (1987) discovered that TILs isolated from melanoma tissue specifically recognize tumor cells in vitro. Rosenberg et al. (1988) revealed that adoptive immunotherapy of autologous TILs can mediate tumor regression in melanoma patients. Clinical trials have confirmed that TILs can induce persistent remission in patients with metastatic melanoma. Recently, TILs were shown to recognize neoantigens in melanoma patients. The highly specific responses of T cells against neoantigens can significantly enhance their anti-tumor effects (Verdegaal et al., 2016). Given the presence of exon mutations in melanoma, encoded epitopes specifically activate TILs and serve as TIL targets, making TILs effective in treating melanoma. However, difficulties in TIL separation and negative regulatory factors, including Tregs, in the tumor microenvironment limit the application of TILs in cancer immunotherapy.

TCRs can recognize the antigen peptide/major histocompatibility complex (MHC) on antigen-presenting cells (APCs), mediating T cell activation and proliferation. Therefore, recognition of tumor antigens with TCRs has become an effective method for adoptive immunotherapy of T cells. Morgan et al. (2006) first discovered that TCR-T cells targeting the melanoma antigen recognized by T-cells 1 can induce tumor regression. TCR-based adoptive T cell therapy targets mainly tumor-associated antigens (TAAs). TCR transformation methods, targeting neoantigens in tumor progression, have attracted much attention (Strønen et al., 2016). However, the high specificity and large individual variation among neoantigens present new challenges for screening appropriate TCR-T-targeted neoantigens (Gubin et al., 2015).

To solve MHC restriction in TCR-T, a new structure named CAR was constructed by fusing an antigen–antibody recognition region with a TCR signal molecule containing an extracellular domain, a transmembrane domain, and an intracellular domain (Gross et al., 1989). T cell activation requires the presence of co-stimulatory molecules, and only fully activated T cells can secrete cytokines and promote T cell proliferation and anti-tumor responses. The structure of CAR has been continuously optimized over the last 30 years. Third-generation CAR-T is equipped with two co-stimulatory molecules to elicit a strong anti-tumor immune response in vivo (Helmby, 2009). CAR-T has achieved results in the treatment of hematological tumors. Previous studies have shown that CD19 CAR-T can effectively target B cell malignant tumors (Kochenderfer et al., 2015), and the success rate in treating advanced relapsed acute lymphoblastic leukemia reaches 90% (Maude et al., 2014). On August 31, 2017, KYMRIAH®, the first CAR-T treatment drug, was approved by the US FDA, opening a new era of cellular immunotherapy for tumors. However, the limited specific TAA targets and difficulties in identification of intracellular TAAs and CAR-T homing limit the application of this drug on solid tumors. Encouragingly, the recently generated 7X19 CAR-T cells have achieved remarkable efficacy in treating solid tumors, including mastocytoma, lung adenocarcinoma, and pancreatic carcinoma (Adachi et al., 2018).

2.2 NK cell therapy

The anti-tumor effect of NK cells was first observed by Ruggeri et al. (2002). Patients with acute myeloid leukemia undergoing blood cell transplantation had a significantly improved survival rate following adoptive transfer of activated NK cells (Miller et al., 2005). Results from several clinical trials indicated the important role of NK cells in controlling and eradicating several types of human tumors, such as lymphoma, leukemia, and oophoroma (Cheng et al., 2013). NK cells, named for their ability to lyse infected

cells and tumor cells without presensitization, play a significant role in the innate immune response. They are considered the most effective subset of immune cells involved in the immunological surveillance and clearing of diseased cells (Robinson et al., 2016). Under general conditions, NK cells that express killer cell immunoglobulin-like receptor (KIR) with specificity for a particular MHC class I molecule will be inhibited, protecting autologous cells from destruction. NK cell cytotoxicity is triggered by abnormal cells that lack expression of self MHC class I molecules. These NK cells secrete granulozyme and act to kill the target cells or release cytokines, such as interferon, to modulate innate and adaptive immune responses. However, the abnormal immune environment in cancer patients may restrain the proliferation and function of autologous NK cells. Allogeneic NK cells derived from peripheral blood, umbilical cord blood, and hematopoietic stem cells of healthy donors are being used more frequently in NK cell therapy.

The major limitations of NK cell therapy include the low proportion of NK cells in peripheral blood cells and technical problems of culture and amplification of NK cells in vitro. In NK cells, immune checkpoint inhibitors, such as KIRs, NKG2A (Ruggeri et al., 2016), T cell immunoreceptor with Ig and ITIM domains, and Tim-3 (Anderson et al., 2016), have been discovered. These inhibitors can release a cell brake signal and activate NK cells. Several studies demonstrated that programmed cell death-1 (PD-1) is highly expressed in NK cells in patients with multiple myeloma, and administration of the antibody of PD-1 can enhance the anti-tumor effect of NK cells (Benson et al., 2010). Furthermore, as an important adjuvant immune therapy, cytokines can promote the proliferation and activation of immune cells. Several clinical trials have assessed the effects of administration of interleukin (IL)-2, IL-15, and IL-18 on NK cells (Childs and Carlsten, 2015). The results showed that cytokines can promote the activation and cytotoxicity of NK cells, but combined drug therapies still require further research.

Recently, CAR-NK cell therapy has been proven to be effective in tumor immunotherapy (Hermanson and Kaufman, 2015). CAR-NK cells have good prospects for clinical application because of their advantages, including a short life cycle, fewer off-target effects, and extensive types and sources of CAR cells. CAR-NK-92 cells targeting mainly cluster of differentiation 19 (CD19), CD20, and human epidermal growth factor receptor 2 have been approved by the US FDA to enter clinical trials (Glienke et al., 2015; Zhang et al., 2017). However, the effects of CAR-NK cell therapy are yet to be confirmed in such trials.

2.3 DC-based therapeutic vaccines

DCs are considered the most potent APCs, helping the activation and proliferation of T cells and enhancing their anti-tumor activity. The first clinical trial of ex vivo DCs on B cell lymphoma (Hsu et al., 1996) has since led to the development of novel vaccine strategies. The US FDA has approved Sipuleucel-T for treatment of metastatic prostate cancer. The use of DC-based therapeutic vaccines has led to considerable progress in treating cancers, including melanoma, malignant gliomas, and renal carcinoma (Anguille et al., 2014).

Distinguished by the use of tumor antigen-presenting DCs, DC-based vaccines can be divided into ex vivo generated DCs and in vivo DC targets. DCs differentiate mostly from $CD14^+$ monocytes and $CD34^+$ progenitor cells. Using granulocyte-macrophage colony-stimulating factor/IL-4 at proper intervals to induce differentiation, DCs can be induced to maturity by Toll-like receptor (TLR) agonists, TLR4, TLR7, TLR9, or a cocktail of pro-inflammatory cytokines including tumor necrosis factor-α, IL-1β, IL-6, and prostaglandin E2 (Hansen et al., 2013). Mature DCs can typically be loaded with a variety of tumor antigens, such as antigenic peptides, TAAs, tumor cell lysates, or apoptotic tumor cells. Studies have shown that polypeptide antigens provide a high level of targeting. Wilms' tumor 1, a kind of polypeptide antigen, combined with DC vaccines and chemotherapy, has been proven to be safe and efficient in the treatment of melanoma (Fukuda et al., 2017) and advanced colon cancer (Shimodaira et al., 2015). DCs that induce the uptake of tumor antigens in vivo, mainly by using antibodies against DC antigens bound to tumor antigens to induce DCs to present tumor antigens, have also proved to be effective. As different DC subsets exhibit different anti-tumor immune responses, effective DCs must be specifically selected and generated for precision therapy. Recent studies have addressed the possibility that therapies combining DC

vaccines with immunological checkpoint inhibitors, cytokines, targeting drugs, or T cell immunity may be more efficacious than DC monotherapy (Mao et al., 2015; Jackson et al., 2016).

3 Ethical issues and countermeasures related to cancer cellular immunotherapy

Based on adaptive and acquired immune mechanisms, a variety of immunotherapies and the combined use of cancer-related research and clinical trials have shown continuous development. Cancer immunotherapy adds to the improvement of the treatment of cancer patients. However, in the development of tumor immunotherapy, especially cellular immunotherapy, a number of significant ethical issues must be settled to protect the rights of patients.

3.1 Ethical issues related to qualifications and access of research units and researchers

With the rapid development of cancer cellular immunotherapy technology, an increasing number of medical institutions and researchers have joined in the development of new therapies. If immunotherapy research units have weak admission criteria and their immunotherapy equipment does not meet prescribed cellular immunotherapy technical requirements, patients who suffer from diseases and who lack professional judgement may blindly join clinical trials. This will delay the most appropriate treatment opportunity, which will violate the principle of non-harm in medical ethical principles, such as in the case of the "Wei Zexi incident" in China (Su and Han, 2016). Because of the large differences among individual patients in cellular immunotherapy and the high risk of serious complications such as cytokine storms, if the admission requirements for researchers are weak and their professional abilities are limited, they may not adequately be able to predict and explain potential risks to patients, or make timely professional judgments in unexpected situations, and thus will not able to guarantee the safety of patients. If the moral access requirements of researchers are reduced, they will only pursue research results and ignore the interests of patients, or fail to inform patients about the risks faced during the treatment process, or publish the research data without consent, which will seriously violate the ethical principles of fairness, justice, and respect for autonomy and privacy.

To strengthen the management of medical institution access, the first step is to ensure technical entry requirements, for example, to guarantee a suitable immunotherapy environment and equipment, including software and hardware support. At the same time, medical teams with appropriate operational qualifications should also be recruited. Medical teams will also benefit from professional training or relevant treatment experience. Moreover, admission by the administration office of hospitals is required. Institutions intending to conduct immunotherapy should feature an accurate evaluation and supervision system, and the department should supervise and manage the technical path and clinical application standards. At the ethical level, admitted medical institutions should carry out long-term supervision and evaluation of new technologies. Immunotherapy techniques are updated frequently. Thus, medical institutions should also constantly monitor the safety and effectiveness of existing technologies and update the standards of treatment methods in a timely manner.

Researchers and medical staff engaged in cancer immunotherapy should possess considerable research aptitude and relevant professional qualifications issued by a certification authority. This should enable timely and accurate countermeasures to be taken for emergencies in the course of treatment. Also, strict standards of approval and admittance should be formulated for the ethics of researchers and medical staff to reduce improper benefit correlation in the treatment process and maximize the right to life and health of patients.

3.2 Ethical issues related to subject recruitment

Cellular immunotherapy, as a promising tumor therapy, has brought great survival hope to many tumor patients. However, because of the different indications for different treatment options, choosing the right subject is an important factor in the safety and effectiveness of the treatment. Based on basic ethical requirements, researchers and research institutions should reasonably and comprehensively evaluate the risks and benefits to the participants and maximize the protection of patients' rights. The main risk to patients in clinical trials is the risk of pain and complications caused by treatment. The benefits refer

mainly to avoiding injury and obtaining a certain curative effect, or understanding whether the advantages outweigh the disadvantages. Therefore, when selecting subjects, researchers should inform them in such a way that they can understand the risks they may face, the possible benefits they may gain, and the reasons why the benefits outweigh the risks.

In clinical trials, the failure of patients to distinguish between the two concepts of clinical treatment and medical research may easily lead to therapeutic misunderstanding. If the patients believe that they can still obtain the clinical treatment services and treatment effects from clinical trials, they fail to fully understand the nature of scientific research, which will violate the principle of informed consent in scientific research. In recent years, many problems in drug clinical trials reported in China have been caused by therapeutic misunderstanding. Therefore, the strengthening of informed consent, the standardization and interpretation of the use of technical terms, and the strengthening of ethical review are needed to ensure that the ethical principles of medical research are not violated.

When enrolling subjects, first, an overall estimate should be obtained for the disease progression of each patient, and if necessary, relevant examinations should be carried out to determine whether the corresponding immunotherapy can be performed. Second, subject enrollment should be based on the principles of informed consent and respect, and be voluntary. Informed consent includes the investigator providing adequate information to the subject, ensuring that the subject understands the information correctly, and the subject voluntarily agreeing with and choosing the therapy. Given the possible side effects of cellular immunotherapy, such as a cytokine storm, patients undergoing immunotherapy face certain risks and should know the specific risks involved. Before the investigator determines the treatment plan, patients should be informed about the likely progress and prognosis of sickness, optional treatment plans, and the anticipated effects and possible adverse reactions of these treatments. The final plan must be implemented only when the patient decides and signs the informed consent form after learning all the pros and cons and optional treatment plans. The informed consent form should be patient-centered, and the language used must be easy to understand to avoid guiding the choice of the patients.

3.3 Ethical issues about the sources of immune cells

The cells used for immune therapy can be divided into autologous or allogeneic cells according to their origin. These include mainly peripheral blood-derived cells, umbilical cord blood-derived cells, hematopoietic stem cell-derived cells, and cell line-derived cells. Because immune cells need to be treated in vitro and have adoptive reinfusion processes, ensuring the accuracy of cell source, treatment and quality control can effectively comply with the non-harm principle in medical ethics. Therefore, the specific experimental scheme should be regulated according to common guiding principles. For example, the specific source of non-cell lines must be identified, and the specific tissue origin and cell type, cell morphology, and the exact information related to the markers should also be provided. Detailed immunological detection methods and results are needed for immunotherapy of allogeneic cells. In addition, the history, the number of descendants from the parent library, and the number of permitted generations are needed for cells such as NK-92, and their cell phenotype and functional stability must be maintained. If cells are to be cultured in vitro, strict monitoring of cell cultures and detection is required. Ensuring the high quality of the cells used in cancer cellular immunotherapy can avoid violation of the ethical principle of non-harm.

3.4 Ethical issues related to experimental design and evaluation criteria

Given the complexity and diversity of cancer cellular immunotherapy, difficulty arises from establishing a unified clinical trial design standard, safety evaluation criteria, and a fully appropriate effectiveness evaluation system. According to the requirements of Good Clinical Practice (GCP), clinical trials should be randomized double-blind trials that require a blank control. On the other hand, in cancer cellular immunotherapy, setting a blank control is contrary to the ethical principles proposed in the Helsinki Declaration (World Medical Association, 2013). Denying tumor patients in the control group any treatment is not conducive to their recovery. Double-blind trials require complete secrecy of patients and operators, conflicting with the ethical advocacy principle and the patients' right to know. Therefore, implementing a double-blind study as required by GCP is impractical. Compared with a drug review and clinical trial

protocols, the lack of uniformity of principles for cancer cellular immunotherapy programs at home and abroad is the main cause of confusion in immunotherapy treatment (Yang et al., 2016).

Establishing a safety evaluation system for cellular immunotherapy is an essential requirement for ensuring the interests of patients. Safety evaluation criteria should be applied throughout the whole treatment process (Ying et al., 2012). A cellular immunotherapy program requires a mass of cell experiments and in vitro tests. These increase the risks in cell separation preparation, culture quality tests, and gene-editing technology. In the whole process of treatment implementation, the operator should strictly abide by standardized laboratory management requirements. Therefore, improving and optimizing the related technologies and formulating the corresponding standardized requirements and technical standards for immune cell therapy as early as possible are primary factors in ensuring patient safety (Yu et al., 2005). Immunotherapy effects are closely related to the immune function of the individual. The operator should establish the best indications of immunotherapy for different disease categories according to their professional knowledge and previous treatment experience and strictly control the contraindications to ensure the safety of patients during treatment.

The effectiveness of most cellular immunotherapy protocols should be demonstrated in animal models before starting clinical trials. Because of the differences in the immune system among species, the specific evaluation indicators and systems for a certain treatment should be derived from preclinical studies and clinical trials. The use of strict effectiveness evaluation criteria can guarantee the precise treatment of tumors.

3.5 Construction of ethical and moral culture

The Declaration of Helsinki mentions that "Medical researchers should obey moral standards and protect patients' right to health. In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society" (World Medical Association, 2013). A minority of researchers lack respect for life; examples of such disrespect include using nonstandard treatments that increase the risk of therapy for patients, and paying more attention to their own academic development and economic interests than to the patient's interests. Patients may be not promptly informed when there is information that affects their continued participation in the trial. These issues encountered in clinical trials of cancer cellular immunotherapy challenge the ethical and moral culture of researchers. Given the particularity of the patients in cancer cellular immunotherapy, the development of complementary scientific ethics and moral culture should be reinforced. In the development of cancer cellular immunotherapy, strengthening ethical construction is an important part of scientific research. Respect and reverence for life can comprehensively improve the researcher's moral culture.

4 Ethical practice in cellular immunotherapy in China

Cancer cellular immunotherapy has been studied in China for a long time, but the relevant ethical norms are not well constructed. In recent years, the level of medical institutions engaged in cellular immunotherapy in China was uneven, examination of researchers' qualifications was not strict enough, and there were serious therapeutic misunderstandings when patients were treated with cellular immunotherapy. In 2016, Ze-xi WEI, a student of Xidian University, Xi'an, Shaanxi, China, died in the late stage of synovial sarcoma after receiving cell immunotherapy provided by a tertiary hospital, thereby exposing cancer cellular immunotherapy to public scrutiny. Although the Health Planning Commission has stopped biological immunotherapy and defined it and prevented clinical application, a vague understanding persists in China of the clinical research and irregularities in cancer cellular immunotherapy. China has issued several policies and regulations for the scientific development of cancer cellular immunotherapy technology.

In 1999, the China FDA issued "Guidelines for the Clinical Trial of Human Gene Therapy," which regulates the relevant content of somatic cell therapy. In 2003, China promoted the "Guidelines for Human Cell Therapy Research and Preparation Quality Control Technology" to establish standard operating procedures for application materials, somatic cell collection,

culture and in vitro operation, quality inspection and pre-clinical trial safety, and efficacy evaluation of adoptive cell transfer treatments, such as lymphokine-activated killer and TIL cells, and to provide a reference standard for somatic treatment in China. In 2013, based on the current development of ethics in China and documents, such as "Human Somatic Cell and Gene Therapy Conditions," formulated by the US FDA Center in 1991 for biological products evaluation and research, the FDA of China issued the "Quality Control Points for Clinical Research of Human Somatic Cell Therapy and Gene Therapy," which defined the basis of the research, identification of therapeutic cell populations, and safety and effectiveness of the evaluation of preclinical trials. It served as a foundation for examining the ethical issues related to cancer cellular immunotherapy in China. In December 2017, the "Guidelines for the Research and Evaluation of Cellular Therapeutic Products (Trial)" issued by the FDA of China provided guidelines for the development of clinical application rules for cancer cellular immunotherapy. At present, a number of clinical trials related to cellular immunotherapy, including those for lung cancer, stomach cancer, colorectal cancer, and liver cancer, have been reviewed and approved by the Chinese Ethics Committee (Table 1).

Table 1 Cancer cellular immunotherapies approved by the Ethics Committee in China

Agent	Mechanism/combining agent	Disease	Phase	Patient	NCT number
CAR-T	PSCA, MUC1, PD-L1, or CD80/86 targeting CAR-T cells	Lung cancer	1	30	03198052
	EGFRvIII, IL13Rα2, Her-2, CD133, EphA2, GD2 targeting CAR-T cells	Recurrent malignant gliomas	1	50	03423992
	Anti-MUC1 CAR-T cells	MUC1-positive solid tumor	1, 2	20	02617134
	Anti-CD19 CAR-T cells	Refractory/relapsed B cell malignancies	1, 2	100 20	03191773 02652910
	Anti-CD19, CD22 CAR-T cells	Relapsed and refractory lymphoma	1, 2	10 12	03468153 03593109
	GPC3-T2-CAR-T cells	GPC3 expression HCC	1	30	03198546
	EpCAM CAR-T cells	Nasopharyngeal carcinoma and breast cancer	1	30	02915445
CAR-NK	Anti-MUC1 CAR-pNK cells	$MUC1^+$ relapsed or refractory solid tumor	1, 2	10	02839954
	Anti-CD33 CAR-NK cells	Relapsed/refractory $CD33^+$ AML	1, 2	10	02944162
	Anti-CD7 CAR-NK cells	$CD7^+$ leukemia and lymphoma	1, 2	10	02742727
γδ T cells	Cryosurgery, IRE surgery, and surgery	Breast cancer	1, 2	30	03183206
	Cryosurgery or IRE surgery	Liver cancer	1, 2	30	03183219
	Cryosurgery or IRE surgery	Lung cancer	1, 2	30	03183232
	Cryosurgery or IRE surgery	Pancreatic cancer	1, 2	30	03180437
NK cells	NK and NKT cells	Non-small cell lung cancer	1	30	03198923
	NK cells	Small cell lung cancer	2	120	03410368
	High-activity NK cells	Non-small cell lung cancer metastatic	1, 2	20	03007875
DCs	TACE	Advanced liver cancer	1, 2	40 40	02873442 02862613
	Chemotherapy	Advanced lung cancer	1, 2	40	02873416
	Radical surgery	Gastric cancer	2	120	03410732

PSCA, prostate stem cell antigen; MUC1, mucin 1; PD-L1, programmed cell death ligand 1; EGFRvIII, epidermal growth factor receptor vIII; IL13Rα2, interleukin 13 receptor α2; EphA2, EPH receptor A2; GD2, ganglioside D2; GPC3, glypican-3; EpCAM, epithelial cell adhesion molecule; IRE, irreversible electroporation; TACE, transcatheter arterial chemoembolization; HCC, hepatic cell carcinoma

China has made continuous progress in the construction of cellular immunotherapy systems, but compared with developed countries, it still needs to form a normative system, especially in relation to the ethical issues in treatment. In future, the main work in the construction of ethics related to cancer cellular immunotherapy in China will be to further systematize the standards for targeted clinical trials of tumor cellular immunotherapy, the preparation and quality control of immune cells, the evaluation of the efficacy of immunotherapy, and the admission of patients and researchers, and the formulation of national standard operating procedures.

5 Conclusions

With the continuous development of cancer cellular immunotherapy technologies and the introduction of relevant national normative policies, cancer immunotherapy will help more patients. Thorough implementation of relevant ethical guidelines during the entire clinical research process to achieve respect, fairness, and "lack of harm" can effectively protect patients' rights.

Contributors

Sang-sang REN and Jing-wen DENG were responsible for writing the article. Meng HONG, Yan-li REN, and Hai-jing FU were responsible for data collection. Yan-ning LIU and Zhi CHEN were responsible for reviewing the paper.

Compliance with ethics guidelines

Sang-sang REN, Jing-wen DENG, Meng HONG, Yan-li REN, Hai-jing FU, Yan-ning LIU, and Zhi CHEN declare that they have no conflict of interest.

This article does not contain any studies with human or animal subjects performed by any of the authors.

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中文概要

题　目：肿瘤细胞免疫治疗相关伦理学探讨

概　要：本文旨在对细胞免疫治疗相关的伦理学问题进行探讨，并通过分析我国细胞免疫治疗相关伦理学实践及现状，为规范我国肿瘤细胞免疫治疗的伦理标准提供参考。随着免疫学、分子生物学等学科的飞速发展和高通量测序等技术的普及，肿瘤免疫治疗已成为第四大肿瘤治疗方法。肿瘤细胞免疫治疗，如各种基于 T 细胞、自然杀伤（NK）细胞和树突状细胞（DC）的免疫治疗在其中发挥了重要作用。随着临床实践的开展，一些相关的伦理学问题逐渐暴露出来。如何在治疗过程中坚持基本伦理原则，有效指导并解决相关临床问题，提高治疗效果，保护受试者权益，是目前亟需研究的重要课题。本文对与之相关的伦理学问题进行探讨，并通过分析我国细胞免疫治疗相关伦理学实践及现状，以期为规范我国肿瘤细胞免疫治疗的伦理标准提供参考。

关键词：肿瘤；细胞免疫治疗；伦理问题