Mechanism of action of γδT cells in eczema

Feng Chen, Chuanxin Cui*

Dermatology Department, China-Japan Union Hospital of Jilin University, Changchun, Jilin, 130033, China

*Corresponding author: Chuanxin Cui

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Abstract: γδT cells are a subset of T cells. Their TCR is composed of γ and delta chains, which are non-restrictive cells of major histocompatibility complexes. Most of the peripheral blood γδT cells express TCRV γ 9 and V Delta 2, which can kill many kinds of anti-tumor cells. As a special cell subset, γδcells have been paid more and more attention by researchers because of their distribution characteristics and non-restrictive antigen recognition. To explore the role of γδ cells in eczema. It is intended to provide a certain experimental basis for comprehensively revealing the role of γδ cells in the early stage of infection and chronic process. T cells were stimulated with BCG and ESAT-6 to amplify γδT cells, and then γδT cells were purified by flow cytometry, and the antigen-presenting cell phenotype was detected. Studies have confirmed that γδ cells play an important role in the body's anti-infective immunity, anti-tumor immunity, autoimmune diseases and the development of eczema.

1. Introduction

Immunotherapy is a new anti-eczema method, and has attracted much attention. Immunotherapy kills eczema cells by expanding immune effector cells in vitro and transferring activated immune cells to the host to fight eczema cells or stimulate immune response [1]. Alpha beta T cells and γδT cells are two main types of T lymphocytes. The difference between these two T cells is that they express different cell surface antigen receptors. Skin is located in the outermost layer of the human body and has a very important defensive and protective function. However, it is often damaged by various external factors [2]. It can monitor surrounding epidermal cells, recognize and respond to related antigens expressed by adjacent keratinocytes, and play an important role in the inflammatory reaction and healing process after skin injury [3]. However, many studies later found that it has a wide range of anti-tumor immunity, so it has gradually become a new direction of basic research and clinical application of cancer treatment. The biological characteristics and functions of γδT cells and their role in tumor therapy are reviewed [4-5].

The γδT cell receptor TCRγδ is a heterodimer composed of a γ chain and a δ chain, and the γ chain and the δ chain are encoded by the γ gene and the δ gene, respectively [6]. Each peptide chain has an immunoglobulin-like domain: an amino terminal variable region domain and two carboxy terminal sTable constant region domains. Human γδT cells do not express lineage markers, and the recognition of antigens does not require the assistance of MHC molecules, ie, no MHC restriction [7]. γδT cells have many unique properties. They differ significantly from alpha-beta T cells in anatomical distribution, developmental pathway, cell phenotype and antigen recognition mechanism. These factors regulate the proliferation, migration and recruitment of injured cells and the functions of inflammatory cells and epidermal cells through autocrine and paracrine actions, so as to promote wound healing. Therefore, γδT cells have become attractive effector cells for immunotherapy of eczema [8]. This article will discuss the classification of γδT cells, the role of γδT cells in the treatment of eczema, the progress of clinical application of γδT cells and the prospects for the future development of γδT cells [9].

2. Methodology

γδT cells not only have non-specific immune characteristics of myeloid cells such as monocytes,

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macrophages, neutrophils and myeloid dendritic cells, but also have specific immune characteristics of B cells and alpha-beta T cells derived from lymphocyte lines. All γδT cells undergo negative selection in the thymus to obtain immune tolerance to their own antigens [10]. Unlike other T cells, some γδT cells do not undergo a positive selection, so γδT cells can rapidly recognize and kill antigens in a non-MHC-restricted manner. Among them, naive cells and central memory cells are mainly distributed in secondary lymphoid tissues, and have no direct effector function. After being stimulated by antigen, central memory cells proliferate more significantly than naive cells. The effector type cells and terminally differentiated cells are mainly distributed in the infected part and the tumor part, and have a direct effect function. Experimental results show that the proportion of human γδT cells in T cells is only 1% to 3% at birth, and rises to 6% at 3 to 12 years old.

γδT cells play various important roles in the immune response. They promote immune responses by interacting with other immune cells and secrete different cytokines, chemokines and growth factors. Therefore, γδTCR has diversity, but the matching of TCRγ and δ chains is highly coordinated, and the Vγ chain cannot be used arbitrarily. Different combinations play a decisive role in the tissue localization, antigen recognition and immune function of γδT cells. Moreover, its surface can express the helper stimulating factor CD8 and help T cell activation. This subtype has inhibitory effects on a variety of epithelial-derived tumors and some leukemias. Effective memory cells proliferate at a low level, but secrete cytokines such as IFN-γ and TNF-alpha. γδT cells in peripheral blood can be recruited to the inflammatory site and rapidly proliferate, secrete cytokines, and differentiate into cytotoxic cells, killing infected cells or cancer cells. In addition, the activation of γδT cells requires a variety of costimulatory molecules, including immunoglobulin (Ig) superfamily co-receptors (such as CD28 or JAML), tumor necrosis factor receptors (such as CD27) and atypical costimulatory molecules such as NKG2D or CD46.

The supernatant from the γδT cells stimulated by anti-γδ was collected, and the secretion of cytokines TNF-α and IFN-γ was detected. The standard was diluted according to the kit to obtain a regression curve. The IFN-γ and TNF-α concentrations of each cell were calculated from the regression equation, and the results are shown in Table 1 and Figure 1.

Table 1 Secretion and killing activity of IFN-γ and TNF-α in γδT cells

γδT cell source	IFN-γ cytokine concentration (pg/mL)	TNF-α cytokine concentration (pg/mL)
Chronic HBV infection	67.83	105.33
Healthy control	98.73	84.19

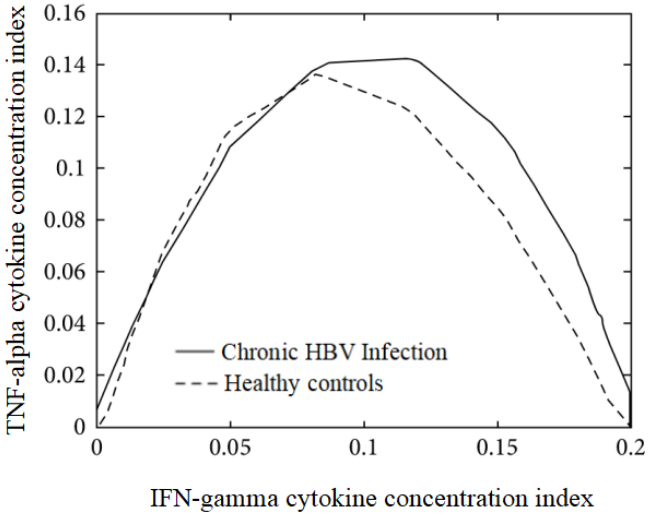

Fig.1. Secretion and killing activity of IFN-γ and TNF-α in γδT cells

Although eczema progresses slowly against the immune system, it is an effective treatment. γδT cells regulate eczema mainly by producing pro-apoptotic molecules and inflammatory cytokines, or

by TCR-dependent pathways. In the treatment of eczema, the main obstacle to the utilization of γδT cells is that there is no continuous and reliable method for amplifying a small amount of γδT cells in current clinical trials. It has the effect of maintaining the functional integrity of the skin barrier. The keratinocytes proliferate and differentiate in the basal layer of the epidermis, and then gradually migrate outward to the spinous layer, the granular layer, the transparent layer, and the stratum corneum, which are constantly updated to maintain the integrity of the barrier. However, antigen presenting molecules such as HLA class I, HLA class II and CD1 are not needed. It has been found that BTN3A1 plays a key role in phosphoric acid antigen-mediated activation of γδT cells. Once TAAs are lost, MHC and/or costimulatory molecules will make eczema cells insensitive to cytotoxicity mediated by alpha beta T cells or unresponsive to induction of specific alpha beta T cells. In addition, in clinical settings, γδT cells are directly activated by phosphorylated antigens or bisphosphonates. Other compounds, such as zoledronate, pamidronate and alkylamine, can indirectly activate γδTlymphocytes.

3. Result Analysis and Discussion

Epidermal γδT cells have dendritic structure and can interact with many surrounding cells at the same time. The factors secreted by them can maintain the activity of keratinocytes. In the absence of γδT cells in the epidermis, the activity of keratinocytes decreases and the apoptosis increases. γδT cells not only have some functions of alpha-beta T cells, but also play the role of immunoglobulin, which is the key component of non-specific immunity. In addition to MHC molecules and heat shock proteins, γδT cells can recognize adenosine triphosphate synthase F1/apolipoprotein A1 (ApoA-1) complex expressed on the surface of eczema cells. This recognition reaction can selectively activate Vγ 9V Delta 2T cells. Therefore, γδT cells can directly recognize molecules expressed in eczema cells without antigen treatment and presentation; in the case of MHC class I molecules reduced or deleted, γδT cells still have anti-eczema effect on target cells. They can efficiently treat antigens and provide costimulatory signals that can strongly induce proliferation and differentiation of naive αβ T cells. Human Vγ9Vδ2T cells can also present CD4+ T cells and antigens that cross-present antigens to CD8+ T cells.

Proliferation analysis of cultured T lymphocytes showed that the algebra of CD4+ T cell proliferation was 6.33% in the sixth generation. As shown in Figure 2 below.

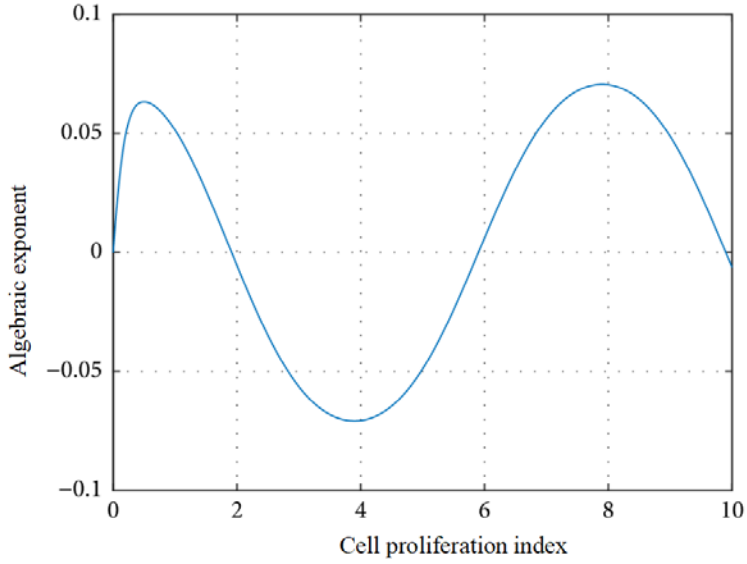

Fig.2. Proliferation response of CD4+ T cells by different culture methods

γδT cells can directly recognize malignant cells and use human immunity to reject them. It is generally believed that γδ T cells mainly exclude eczema cells by the following means. First, cytokines lead to death. γδT cells exert anti-eczesia activity by producing various chemokines and cytokines such as TNF-α and IFN-γ. IFN-γ can directly inhibit eczema growth, stimulate

macrophages, and block angiogenesis. The maintenance of epidermal homeostasis requires a dynamic balance of proliferation and apoptosis of keratinocytes. When the epidermis is stressed and traumatized, the homeostasis changes, and the regulation of keratinocyte proliferation and apoptosis maintains epidermal homeostasis and promotes tissue repair. γδT cells activate macrophages and release IL-15 by producing IFN-γ. The secreted IL-15 promotes the accumulation of γδT cells at the infected site to participate in local anti-inflammation, and also recruits centralized granulocytes to play an anti-infective role by releasing IL-17. Activation signals are transmitted to cells to kill tumor cells. Like CD226, CD96 recognizes the killing effect mediated by CD155 molecules on the surface of cancer cells.

γδT cells are considered to be members of innate immune cells and have been shown to play an important role in immune surveillance and eczema, including the immunodefense of melanoma, the role of leukemia, lymphoma, neuroblastoma, and other types of cancer. Therefore, they have become attractive target cells for adoptive cell transfer therapy. In humans, this activity manifests in a variety of tumors in vitro, including prostate cancer cells. Currently, one of the focuses of recent research is the adoptive transfer of ex vivo activated and expanded γδT cells. γδT cells are regarded as a bridge between innate and adaptive immunity. They can exert cellular immune effects by releasing cytotoxic molecules such as perforin and granulase, expressing Fas-FasL inducing apoptosis and secreting IFN-γ, and also release cytokines such as IL-2, IL-4 and so on to regulate humoral immunity. γδT cells fight rotavirus infection by increasing the expression of TLR2, TLR4 and TLR9 and releasing IFN-γ and TGF-beta. It can be seen that γδT cells can participate in the immune response process by altering the expression of their own receptors and regulating other immune cells.

4. Conclusions

As an important part of the body's immune defense line, γδT cells recognize eczema antigens in their unique way in the anti-eczema immune response. On the one hand, they directly act on tumor antigens, on the other hand, they play an anti-eczema role by regulating the innate immunity and acquired immunity of the body. Although the number of γδT cells is small in vivo, they can be stimulated by phosphate both in vitro and in vivo, and play an important role in the body's anti-eczema immunity. Immunotherapy based on γδT cells has been used in many clinical trials. It has been shown to be effective in the treatment of solid eczema such as breast cancer, renal cancer, colorectal cancer and some blood eczema. In addition, it is necessary to explore better antigens to help us stimulate γδT cell expansion in vitro to prepare a large number of cells for adoptive cell transfer. Future research should focus on the possible advantages of combining γδTcell immunotherapy with conventional chemotherapy or other therapeutic approaches such as anti-angiogenic drugs.

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