Research on the Role of γδT Cells in Psoriatic Myocardial Injury

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Abstract. γδT cells are an important T lymphocyte subtype found in 1986, mainly distributed in mucosa-associated lymphoid tissues, in which γδT cells in the intestine are the major T cell subtypes distributed in this tissue. Numerous studies have shown that after the body is infected by bacteria, viruses and parasites, γδT cells can rapidly proliferate and exert immune function through induction of apoptosis, ADCC, antigen presentation and immune regulation.

Introduction

According to different T cell receptors (TCRs), T cells are mainly divided into αβ and γδT cells. In the thymus, both αβ and γδT cells are derived from a common double negative cell precursor. αβT cells generally express CD4 or CD8 lineage markers, and recognition of antigens depends on major histocompatibility complex (MHC) molecules on the surface of antigen presenting cells (APCs). 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. The TCR of γδT cells is composed of γ chain and δ chain, and the diversity of Vγ and Vδ gene loci recombination constitutes different subclasses of γδT cells. In addition, γδT cells are also divided into multiple functional subtypes according to their functional differences. Each functional subtype directly participates in or regulates the body response through different functions, and plays an important role in disease occurrence and host defense. A new review on the subclasses of γδT cells and their biological effects is reviewed.

Structure and Distribution Characteristics of γδT Cells

The peptide chains constituting the TCR have four types of α, β, γ, and δ. According to the peptide chain, the TCR is divided into TCRαβ and TCRγδ, and accordingly, the T cells are classified into αβT cells and γδT cells. The γ chain and δ chain genes of TCR are composed of four regions: V, D, J, and C. The V region is a functional region of the TCR recognition antigen peptide-MHC complex. γδT cells are divided into many subtypes according to the expression of TCR variable region gene products, since T cell subsets often only use a limited part of the receptor library, that is, only a specific combination of VγVδ and junction region sequences is used. The TCRγδ structure is relatively monotonous, but due to the recombination of the junction region (J region), TCRγδ has diverse potentials, such as Vγ9δ2 in peripheral blood and Vγ7Vδ4/6 in digestive tract mucosa. The cytokines and functions secreted by γδT cells of different subtypes in different parts are not identical.

γδT Cell Recognition Antigen Characteristics

γ δ T cells have both the function of αβT cells and the role of immunoglobulins, which are key components of non-specific immunity. The antigen recognition of γδT cells has the following characteristics: (1) The molecular structure and antigen binding properties of γδT cells are more

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similar to those of immunoglobulins, and can directly recognize antigens; (2) Most of the antigens recognized by γδT cells are small molecular weight non- Protein molecules and lipid components can also recognize atypical MHC class I molecules, viral surface proteins and HSP60; (3) γδT cell recognition antigens are MHC-free, and the peptides need not be processed into small peptides. It is recognized in its intact form, so it can respond rapidly to antigens. (4) γδT cells distributed in different tissues can express different TCRs to recognize antigens of different nature, and γδT cells in the same tissue express the same TCR. Identify antigens of the same nature [1].

γδT Cells and Infection Immunity

Main Biological Functions. γ δ T cells have both non-specific immunological characteristics derived from myeloid cells such as monocytes, macrophages, neutrophils and myeloid dendritic cells, as well as B cells and αβ T cells derived from lymphocyte lines. Specific immunological characteristics, the main biological functions of γδT cells in anti-infective immunity are: (1) Direct lysis of target cells: Activated γδT cells can directly lyse target cells by granzyme-perforin pathway, or via Fas- FasL and IFN-γ induce apoptosis in target cells [2]; (2) Antibody-dependent cytotoxicity: ADCC acts through certain membrane surface receptors such as FcγR, and enhances cytotoxicity by secreting IL-2 Effects; (3) Immunization by activating, inhibiting, or recruiting other immune cells: such as dendritic cells, granulocytes, macrophages, Langerhans cells, αβ T cells, and B cells are all resistant to γδT cells Infection function is closely related; (4) Antigen presentation: Partially activated γδT cells can differentiate into APC, highly express MHC class II molecules and CD80, CD86 and CCR7, etc. Presenting to αβT cells to elicit a specific immune response; (5) Immunomodulatory function of γδT cells: Activated γδT cells can inhibit Foxp3(+) Tregs proliferation [13], and can also produce IL-10, TGF- β plays an immunomodulatory role [14]; (6) Immune surveillance: The surface of memory γδT cells can prevent the spread of viruses, resist opportunistic infections, and exert immunological surveillance through high expression of CCR7, CD161.

γδT Cells and Bacterial Infection. Mycobacterium tuberculosis can invade all organs of the body and is most common in the lungs. A number of previous studies have found that in the early stages of infection, γδT cells secrete toxic IFN-γ to kill infected macrophages and promote granuloma formation. Recently, Kubota et al [3] found that Vδ2T cells can produce granulolytic enzymes and perforin at the time of infection to reduce the activity of intracellular and extracellular M. tuberculosis, and can produce IFN-γ-induced macrophage initial killing, and activate the infected site. The antigen-presenting ability of dendritic cells triggers specific immunity. Gong et al studied the infection of Mycobacterium tuberculosis and found that γδT cells have immunomodulatory ability. They can interact with Tregs by phosphorylation-activated Vγ2Vδ2T cells. After a short course of IL-2 treatment, they induce CD4 (+). CD25(+) Foxp3(+) T cells can inhibit the number of Vγ2Vδ2T cells increased by M. tuberculosis infection, and can down-regulate CD4(+) CD25 induced by IL-2 after addition of phosphorylated antigen-activated Vγ2Vδ2T cells (+) Amplification of Foxp3(+) T cells. It can be seen that γδT cells participate in the killing of Mycobacterium tuberculosis from multiple time points and multiple pathways.

Typhoid typhoid bacillus infection mainly involves the systemic mononuclear phagocytic system, lesions prominent in the intestinal lymphoid tissue, mesenteric lymph nodes, liver, spleen and bone marrow. Pieper studied the chicks infected with Salmonella and found that γδT cells expressing CD8αα in blood and spleen after rapid infection of Salmonella rapidly proliferated and increased the transcription of Fas, IL-2Rα and IFN-γ. Li et al used a model of intestinal infection of Salmonella typhimurium to show that γδT cell subsets of intestinal epithelial lymphoid tissues play an important role in immune surveillance and clearance of infected epithelial cells by expressing NKG2D, CD8αα, FasL and IFN-γ, and also with epithelial cells. Secretion of keratinocyte growth factor, promote the regeneration of epithelial cells and limit the further invasion of pathogens. It can be seen that the effect of γδT cells is limited, mainly in the early stage of defense. However, the interaction between phagocytic cells and γδT cells with phagocytic function during typhoid

infection cannot eliminate typhoid bacillus, and whether there is damage to the phagocytic environment. These are worth exploring.

Coli is the most important and abundant bacteria in the intestine. The study found that γδT cells activated by E. coli infection further activate macrophages and release IL-15 by producing IFN-γ. The secreted IL-15 promotes the accumulation of γ δ T cells at the site of infection and participates in local anti-inflammatory, and also releases IL by itself. -17 Concentrated granulocytes to play an anti-infective function; Recently, Wu et al [4] used confocal microscopy, transmission electron microscopy and functional antigen presentation analysis to find that human peripheral blood γδT cells can pass antibody opsonin and CD16 molecules. The E. coli is mediated and captured, and then the expressed MHC class II molecule exerts an antigen presenting function. Therefore, γδT cells, like APC, act as a link between non-specific and specific immune responses, on the one hand, as effector cells directly involved in the killing of pathogens, and on the other hand, they play a role in regulating cell function and trigger specific immunity to join the infection immunization process.

Listeria monocytogenes Listeria monocytogenes is a pathogen of zoonotic diseases. After infection, it mainly manifests as sepsis, meningitis and mononuclear cells. When infected, activated macrophages can activate γδT cells, make them cytotoxic, kill killing macrophages, maintain the stability of normal macrophages, and control the occurrence of chronic inflammation. Rhodes et al after infection of γδT cell-deficient mice with Listeria, mouse hepatocytes showed severe and extensive hepatocyte necrosis mediated by CD8 + T cells secreting TNF-α, and activated macrophages Secretion of IL-10 by cells and CD8 + T cells in contact with Vγ4T cells can attenuate liver damage, and Vγ4T cells can also control the expansion of CD8 + T cells and regulate and reduce the secretion of TNF-α by IL-10. Meeks et al found that in the early stage of Listeria infection, there was a large amount of IL-17 production, and γδT cells were the main source of IL-17. The researchers speculated that γδT cells may recruit concentrated granulocytes by secreting IL-17. Accelerate the removal of bacteria. It can be seen that γδT cells can participate in the immune process through various pathways, and the effect of producing various cytokines to regulate other immune cells is particularly prominent.

The Role of γδT Cells in Psoriatic Myocardial Injury

Psoriasis is a common, chronic, inflammatory, multi-system disease characterized by skin and joint damage. The prevalence of the natural population is about 2%, but there are differences among different populations. Immunosuppressive drugs are effective in treating the disease. Bone marrow transplantation can transfer psoriasis to bone marrow recipients. The plaque lesions have cloned T-cell receptor (TCR) rearrangement and other evidence that silver Psoriasis is an immune-mediated disease, but the molecular mechanisms that initiate this immune disorder are still unclear.

Humans have recognized the relationship between psoriasis and genetic basis for nearly 100 years [5]. The genetic factors of psoriasis and the in-depth study of genetic etiology are based on epidemiological investigations.

Research on twins provides strong evidence for the genetic basis of psoriasis. The alleles of the single-oval twins are identical, and half of the alleles of the fraternal twins are identical. Even if many other genes are involved in the pathogenesis of psoriasis, the chance of unilateral twins sharing the disease should be better than that of fraternal twins. Studies of twins have shown that the occurrence of psoriasis is determined by genetic factors. Multiple studies have found that 35% to 73% of monozygotic twins have psoriasis at different times, but all studies have confirmed that monozygotic twins are 3 times more likely to have psoriasis than fraternal twins.

Many family studies and demographic surveys also provide genetic evidence for the onset of psoriasis, including single-gene recessive inheritance, double-gene recessive inheritance, extrinsic autosomal dominant inheritance, and multi-factor and multivariate models of environmental factors. Wait. Demographic studies have shown that parents are suffering from psoriasis, the probability of having psoriasis in their children is 41%, the chance of developing a child with a parent is 14%, and

the likelihood of siblings suffering from a sibling is 6%. Parents and siblings are not ill with 2% of the disease, the same results as those of Waston et al. Some domestic scholars also conducted a genetic epidemiological survey of 721 patients with psoriasis vulgaris and their families using questionnaires and follow-up. RESULTS: Of the 721 patients, 212 (29.4%) had a positive family history; men with a family history had an onset age earlier than those without a family history; fathers and/or mothers with a predator of psoriasis had a premature age earlier than their parents. The prevalence of early-stage (starting age < 40 years old) relatives was higher than that of late-type (first-grade age ⩾ 40 years), and the average starting age of women in early-onset was earlier than that of males. The heritability of the first- and second-degree relatives of the witness was 71.07%±2.05% and 36.77%±5.17%, respectively. The conclusion is that psoriasis belongs to polygenic genetic diseases, and genetic factors play an important role in the pathogenesis.

Conclusion

In recent years, the mechanism of action of γδT cells in infection immunity has been a hot topic, but the immune mechanism of γδT cell-mediated infection is still not fully understood. Current research focuses on antigen recognition, cytolytic action, ADCC, immune regulation, and immune surveillance. The interrelationship between various immune mechanisms and the ability to treat partial immunodeficiency diseases as a means of adoptive therapy also require more in-depth research.

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