GAMMA DELTA LYMPHOCYTES

DEFINITION:

γδ T cells constitute a small proportion (< 5%) of T lymphocytes, and are different from conventional αβ T lymphocytes. [1] These lymphocytes are unique in their T cell receptor usage, location, and functions in the body.

Stress reception by γδ T cells as a result of traumatic epithelial injury, malignancy, and/or infection induces their activation; and then is activated their function to repair tissue, induce inflammation, recruit leukocytes, and lyse cells.[1]

Many of these functions are mediated via the production of cytokines and growth factors upon γδ T cell activation. T cells require a delicate balance between their need for acute inflammatory mediators to function normally and the detrimental impact imparted by chronic inflammation. [2]

→ **Location**

γδ T cells are more abundant in tissues than in circulation [3]. They are scarce in lymphoid tissues and abundant at mucosal sites such as skin, tongue, intestine and reproductive organs.

γδ T cells are responsible for maintaining the homeostasis of the epithelium via the production of secreted factors, which can act in a paracrine manner to sustain a large impact. In this manner, γδ T cells not only modulate inflammation but also are sensitive to changes in the cytokine milieu caused by chronic inflammatory diseases. [2]

RECEPTORS:

All T cells express either an α:β receptor or a γ:δ receptor but never both. These two types of T-cell receptor define two fundamental, distinctive, and ancient T-cell lineages that are present in all jawed vertebrates. [3]

Most γδ T cells recognize a wide variety of self- and nonself antigens such as metabolites of isopentenyl diphosphate (also known as phosphoantigens), small peptides, MHC-class I chain-related protein A (MICA), MHC-class I chain-related protein B (MICB) and mycobacterial heatshock proteins[1]

Although γδ T cells do not require self-MHC-restricted priming, they can distinguish “foreign” or transformed cells from healthy self-cells using activating and inhibitory killer Ig-like receptors. Antigen recognition by γδ T cells does not require antigen processing and presentation by antigen presenting cells (APCs) and these cells can react rapidly in response to stress by spontaneously producing cytokines.γδ T cells have the ability to produce proinflammatory cytokines as well as anti-inflammatory cytokines.[1]

An important characteristic from γδ T cells is that their receptor recognition is not dependent on MHC molecules and their bound peptides but they can be involved [3]. They can also act as professional antigen-presenting cells.[1]

GENOME ORGANIZATION

The δ gene segments are situated within the α-chain locus on chromosome 14, between the Vα and Jα gene segments. This location means that DNA rearrangement within the α-chain locus inevitably results in the deletion and inactivation of the δ-chain locus. [3]

The human γ-chain locus is on chromosome 7. The γ-chain and δ-chain loci contain fewer V gene segments than the α-chain or β-chain loci. Consequently γ:δ T-cell receptors are less diverse than α:β T-cell receptors. Rearrangement at the γ and δ loci proceeds as for the α

and β loci, with the exception that during δ-gene rearrangement two D segments can be incorporated into the final gene sequence. This increases the variability of the δ chain in two ways. First, the potential number of combinations of gene segments is increased. Second, extra N nucleotides can be added at the junction between the two D segments, as well as at the VD and DJ junctions.

Relation between tumor cells and γδ T cells :

Effector Function of γδ T Cells in Cancer Tumor-infiltrating lymphocytes (TILs) play an important role in anti-tumor immunity, and the adoptive transfer of TIL is considered a promising approach for cancer immunotherapy. γδ TCR-expressing T lymphocytes infiltrate into a variety of the tumors, where they are known to have effector and regulatory functions. The capacity of γδ T cells to infiltrate murine and human tumors and recognize tumor antigens, their ability to secrete cytotoxic molecules like granzyme and perforin and their potential to an activate adaptive immune response make them promising candidates for adoptive cellular therapy.[1]
Collectively, these findings suggest that the pro-inflammatory cytokines produced by γδ T cells and their interactions with other immune cells help in mounting an effective anti-tumor response.[1]
They can also promote tumor growth under certain circumstances. The pro-tumorigenic role of γδ T cells is dependent on their regulatory function in the tumor microenvironment and secondary lymphoid tissues. [1]

γδ T Cells as Adoptive Cellular Therapy

The efficacy of conventional chemotherapy and radiotherapy for cancer treatment depends on a sustained anti-tumor immune response from innate and adaptive immune cells. During chemotherapy, dying tumor cells can prime immune cells (immunogenic cell death) and induce immune tolerance (tolerogenic cell death). A deficiency of γδ T cells had been reported in several malignancies such as breast cancer and hematological, liver and gastric tumors, suggesting that adoptive transfer of these cells may have a beneficial effect in controlling the tumor. In human PBMCs, Vg9Vd2 T cells are relatively more abundant and easy to manipulate in vitro, and are well characterized in response to the phosphoantigens. [1]

In vivo manipulation of γδ T cells with zoledronate has shown a beneficial outcome in the cancer patients. Infusion of ex vivo activated and expanded γδ T cells in cancer patients have also shown anti-tumor activity.[1]Some components have been tried as a treatment and they showed an increase of γδ T cells and tumor reduction but not its complete elimination.[1]

REFERENCES:
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