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Perspective

Regulatory T cells development and its function

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DESCRIPTION

Regulatory T cells, formerly known as suppressor T cells, are a subpopulation of T cells that modulate the immune system, maintain tolerance to self-antigens, and prevent autoimmune diseases. T cells are immunosuppressive and generally suppress or reduce the induction and proliferation of effector T cells. T cells express the biomarkers CD4, FOXP3 and CD25 and are thought to originate from the same lineage as naïve CD4+ cells. Because effector T cells also express CD4 and CD25, it is very difficult to effectively distinguish T cells from effector CD4+ cells, making their study difficult. Research has established that the cytokine Transforming Growth Factor beta (TGF-β) is essential for the differentiation of T cells from naïve CD4+ cells and is important for maintaining T cell homeostasis. Mouse models suggest that modulation of T cells can treat autoimmune disease and cancer, and may facilitate organ transplantation and wound healing. Their implications for cancer are complicated. T cells tend to be upregulated in individuals with cancer and appear to be recruited to the site of many tumors. Studies in both humans and animal models have shown that high numbers of T cells in the tumor microenvironment are indicative of a poor prognosis, and T cells are thought to suppress tumor immunity, preventing the body's innate ability to control the growth of cancer cells. Immunotherapy research studies how regulation of T cells could potentially be used in cancer treatment (Adeegbe et al., 2013).

Development

All T-cells originate from progenitor cells in the bone marrow that have committed to their lineage in the thymus. All T cells start out as CD4-CD8-TCR- cells in the DN (double negative) stage, where the individual cell rearranges its T cell receptor genes to produce a unique functional molecule that they in turn test against the cells. (Bettelli et al., 2006). In the thymic cortex for a minimal level of interaction with self-MHC. If they receive these signals, they proliferate and express both CD4 and CD8, becoming double-positive cells. Suppressor T cell selection occurs on radioresistant cells expressing MHC II. Class hematopoietically in the marrow or Hassall's corpuscles in the thymus (Curiel 2008). At the DP (double-positive) stage, they are selected by their interaction with cells in the thymus, begin transcription of Foxp3, and become T cells, although they may not begin to express Foxp3 until the single-positive stage, at which point they are functional T cells. Suppressor T cell do not have TCR-restricted NKT expression or γ5 T cells; T cells have greater TCR diversity than effector T cells, biased toward self-peptides (Hori et al., 2003).

Function

The immune system must be able to distinguish between self and non-self. When self-discrimination and self-discrimination fail, immune system destroys the body's cells and tissues,resulting in autoimmune disease (Miyara et al., 2011). Regulatory T cells actively suppress the activation of the immune system and prevent pathological autoreactivity, i.e. autoimmune disease. The decisive role of regulatory T cells in the immune system is demonstrated by a severe autoimmune syndrome, which is the result of a genetic deiciency of regulatory T cells (Nosbaum et al., 2016).

The molecular mechanism by which regulatory T cells exert their suppressor/regulatory activity has not been definitively characterized and is the subject of intense research (Schmetterer et al., 2012). In vitro experiments have provided mixed results regarding the requirement for cell-cell contact with the cell to be suppressed (Singh et al., 2013). The following represent some of the proposed mechanisms of immune suppression,

• Regulatory T cells produce a number of inhibitory cytokines. These include TGF-β, interleukin 35, and interleukin 10. It also appears that regulatory T cells can induce interleukin-10 expression in other cell types.

• Regulatory T cells can produce Granzyme B, which in turn can induce apoptosis of effector cells. Regulatory T cells from Granzyme B-deficient mice have been reported to be less effective suppressors of effector T cell activation.

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• Reverse signaling through direct interaction with dendritic cells and induction of the immunosuppressive indoleamine 2,3-dioxygenase.

• Signaling through CD39 and CD73 ectoenzymes with production of immunosuppressive adenosine.

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