Cytokines & other signaling molecules

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Cytokines are a category of signaling proteins and glycoproteins that, like hormones and neurotransmitters, are used extensively in cellular communication. While hormones are secreted from specific organs to the blood, and neurotransmitters are related to neural activity, the cytokines are a more diverse class of compounds in terms of origin and purpose.

Produced by a wide variety of hematopoietic and non-hematopoietic cell types and can have autocrine, paracrine and endocrine effects.

The cytokine family consists mainly of smaller, water-soluble proteins and glycoproteins with a mass between 8 and 30 kDa.

Cytokines are critical to the development and functioning of both the innate and adaptive immune response.

They are often secreted by immune cells that have encountered a pathogen, thereby activating and recruiting further immune cells to increase the system's response to the pathogen.

Also involved in several developmental processes during embryogenesis

Classification:

Cytokines have been classed as lymphokines, interleukins, and chemokines, based on their presumed function, cell of secretion, or target of action.

Interleukins

Interleukins are a group of cytokines that were first seen to be expressed by white blood cells (leukocytes, hence the *-leukin*) as a means of communication (*inter-*). It has since been found that interleukins are produced by a wide variety of bodily cells.

Cytokines are a unique family of growth factors. Secreted primarily from leukocytes, cytokines stimulate both the humoral and cellular immune responses, as well as the activation of phagocytic cells. Cytokines that are secreted from lymphocytes are termed lymphokines, whereas those secreted by monocytes or macrophages are termed monokines. A large family of cytokines are produced by various cells of the body. Many of the lymphokines are also known as interleukins (ILs), since they are not only secreted by leukocytes but also able to affect the cellular responses of leukocytes. Specifically, interleukins are growth factors targeted to cells of hematopoietic origin. The list of identified interleukins grows continuously with the total number of individual activities now at 22 (13 are listed in the Table below).

Interleukins	Principal Source	Primary Activity
IL1-a and -b	macrophages and other antigen presenting cells (APCs)	costimulation of APCs and T cells, inflammation and fever, acute phase response, hematopoiesis
IL-2	activated TH_1 cells, NK cells	proliferation of B cells and activated T cells, NK functions
IL-3	activated T cells	growth of hematopoietic progenitor cells
IL-4	TH_2 and mast cells	B cell proliferation, eosinophil and mast cell growth and function, IgE and class II MHC expression on B cells, inhibition of monokine production
IL-5	TH_2 and mast cells	eosinophil growth and function
IL-6	activated TH_2 cells, APCs, other somatic cells	acute phase response, B cell proliferation, thrombopoiesis, synergistic with IL-1 and TNF on T cells

IL-7	thymic and marrow stromal cells	T and B lymphopoiesis
IL-8	macrophages, other somatic cells	chemoattractant for neutrophils and T cells
IL-9	T cells	hematopoietic and thymopoietic effects
IL-10	activated TH_2 cells, $CD8^+$ T and B cells, macrophages	inhibits cytokine production, promotes B cell proliferation and antibody production, suppresses cellular immunity, mast cell growth
IL-11	stromal cells	synergisitc hematopoietic and thrombopoietic effects
IL-12	B cells, macrophages	proliferation of NK cells, INF-g production, promotes cell-mediated immune functions
IL-13	TH_2 cells	IL-4-like activities
Interferons	**Principal Source**	**Primary Activity**
INF-a and -b	macrophages, neutrophils and some somatic cells	antiviral effects, induction of class I MHC on all somatic cells, activation of NK cells and macrophages
INF-γ	activated TH_1 and NK cells	induces of class I MHC on all somatic cells, induces class II MHC on APCs and somatic cells, activates macrophages, neutrophils, NK cells, promotes cell-mediated immunity, antiviral effects

Interleukin-1 (IL-1)

1. IL-1 is one of the most important immune response - modifying interleukins. The predominant function of IL-1 is to enhance the activation of T-cells in response to antigen. The activation of T-cells, by IL-1, leads to increased T-cell production of IL-2 and of the IL-2 receptor, which in turn augments the activation of the T-cells in an autocrine loop.
2. IL-1 also induces expression of interferon-γ (IFN-γ) by T-cells. This effect of T-cell activation by IL-1 is mimicked by TNF-α which is another cytokine secreted by activated macrophages.
3. There are 2 distinct IL-1 proteins, termed IL-1-α and -1-β, that are 26% homologous at the amino acid level.
4. The IL-1s are secreted primarily by macrophages but also from neutrophils, endothelial cells, smooth muscle cells, glial cells, astrocytes, B- and T-cells, fibroblasts and keratinocytes.

Interleukin-2 (IL-2)

1. IL-2, produced and secreted by activated T-cells, is the major interleukin responsible for clonal T-cell proliferation.
2. IL-2 also exerts effects on B-cells, macrophages, and natural killer (NK) cells. The production of IL-2 occurs primarily by CD4+ T-helper cells. As indicated above, the expression of both IL-2 and the IL-2 receptor by T-cells is induced by IL-1.

Interleukin-6 (IL-6)

1. IL-6 is produced by macrophages, fibroblasts, endothelial cells and activated T-helper cells. IL-6 acts in synergy with IL-1 and TNF-(in many immune responses, including T-cell activation.
2. In particular, IL-6 is the primary inducer of the acute-phase response in liver.
3. IL-6 also enhances the differentiation of B-cells and their consequent production of immunoglobulin.
4. Glucocorticoid synthesis is also enhanced by IL-6.

TNF-α

1. Unlike IL-1, IL-2 and TNF-a, IL-6 does not induce cytokine expression; its main effects, therefore, are to augment the responses of immune cells to other cytokines.
2. TNF-a (also called cachectin), like IL-1 is a major immune response - modifying cytokine produced primarily by activated macrophages.
3. Also activates programmed cell death through interaction with TNF receptors on cell.

Interferon-g (INF-γ)

1. IFN-α, IFN-β and IFN-ω are known as type I interferons: they are predominantly responsible for the antiviral activities of the interferons.
2. IFN-g is secreted primarily by CD8+ T-cells. Nearly all cells express receptors for IFN-g and respond to IFN-g binding by increasing the surface expression of class I MHC proteins, thereby promoting the presentation of antigen to T-helper (CD4+) cells.
3. IFN-g also increases the presentation of class II MHC proteins on class II cells further enhancing the ability of cells to present antigen to T-cells.