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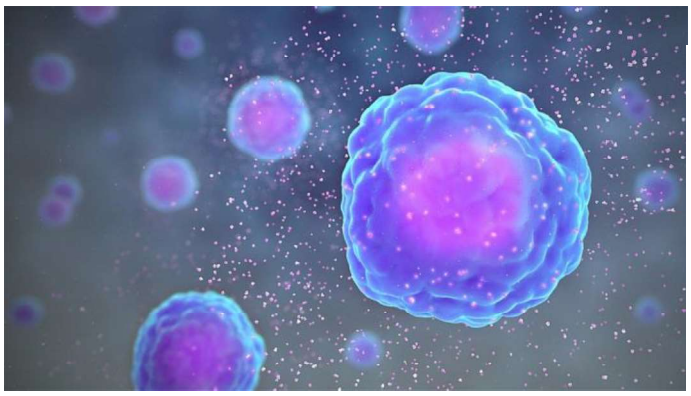
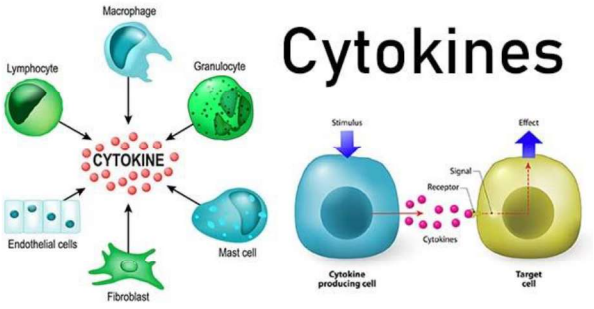
CYTOKINES

Cytokines are a broad and loose category of small proteins (~5–20 kDa) important in cell signaling. Cytokines are peptides and cannot cross the lipid bilayer of cells to enter the cytoplasm. Cytokines have been shown to be involved in autocrine, paracrine and endocrine signaling as immunomodulating agents. Their definite distinction from hormones is still part of ongoing research.





Cytokines include chemokines, interferons, interleukins, lymphokines, and tumour necrosis factors, but generally not hormones or growth factors (despite some overlap in the terminology). Cytokines are produced by a broad range of cells, including immune cells like macrophages, B lymphocytes, T lymphocytes and mast cells, as well as endothelial cells, fibroblasts, and various stromal cells; a given cytokine may be produced by more than one type of cell.They act through cell surface receptors and are especially important in the immune system; cytokines modulate the balance between humoral and cell-based immune responses, and they regulate the maturation, growth, and responsiveness of particular cell populations. Some cytokines enhance or inhibit the action of other cytokines in complex ways. They are different from hormones, which are

also important cell signaling molecules. Hormones circulate in higher concentrations, and tend to be made by specific kinds of cells. Cytokines are important in health and disease, specifically in host immune responses to infection, inflammation, trauma, sepsis, cancer, and reproduction.

Discovery

Interferon-alpha, an interferon type I, was identified in 1957 as a protein that interfered with viral replication. The activity of interferon-gamma (the sole member of the interferon type II class) was described in 1965; this was the first identified lymphocyte-derived mediator.[4] Macrophage migration inhibitory factor (MIF) was identified simultaneously in 1966 by John David and Barry Bloom. In 1969, Dudley Dumonde proposed the term "lymphokine" to describe proteins secreted from lymphocytes and later, proteins derived from macrophages and monocytes in culture were called "monokines". In 1974, Stanley Cohen published an article describing the production of MIF in virus-infected allantoic membrane and kidney cells, showing its production is not limited to immune cells. This led to his proposal of the term cytokine. Ogawa described the early acting growth factors, intermediate acting growth factors and late acting growth factors.

Difference from hormones

Classic hormones circulate in nanomolar (10-9 M) concentrations that usually vary by less than one order of magnitude. In contrast, some cytokines (such as IL-6) circulate in picomolar (10-12 M) concentrations that can increase up to 1,000 times during trauma or infection. The widespread distribution of cellular sources for cytokines may be a feature that differentiates them from hormones. Virtually all nucleated cells, but especially endo/epithelial cells and resident macrophages (many near the interface with the external environment) are potent producers of IL-1, IL-6, and TNF-α. In contrast, classic hormones, such as insulin, are secreted from discrete glands such as the pancreas. The current terminology refers to cytokines as immunomodulating agents. A contributing factor to the difficulty of distinguishing cytokines from hormones is that some immunomodulating effects of cytokines are systemic rather than local. For instance, to accurately utilize hormone terminology, cytokines may be autocrine or paracrine in nature, and chemotaxis, chemokinesis and endocrine as a pyrogen. Essentially, cytokines are not limited to their immunomodulatory status as molecules.