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CYTOKINES

Nomenclature

Cytokines have been classed as lymphokines, interleukins, and chemokines, based on their presumed function, cell of secretion, or target of action. Because cytokines are characterised by considerable redundancy and pleiotropism, such distinctions, allowing for exceptions, are obsolete.

The term interleukin was initially used by researchers for those cytokines whose presumed targets are principally white blood cells (leukocytes). It is now used largely for designation of newer cytokine molecules and bears little relation to their presumed function. The vast majority of these are produced by T-helper cells.

- *Lymphokines*: produced by lymphocytes
- *Monokines*: produced exclusively by monocytes
- *Interferons*: involved in antiviral responses
- *Colony stimulating factors*: support the growth of cells in semisolid media
- *Chemokines*: mediate chemoattraction (chemotaxis) between cells

Classification

Structural

Structural homogeneity has been able to partially distinguish between cytokines that do not demonstrate a considerable degree of redundancy so that they can be classified into four types:

- The four-α-helix bundle family: member cytokines have three-dimensional structures with a bundle of four α-helices. This family, in turn, is divided into three sub-families:
    1. the IL-2 subfamily. This is the largest family. It contains several non-immunological cytokines including erythropoietin (EPO) and thrombopoietin (TPO). They can be grouped into *long-chain* and *short-chain* cytokines by topology. Some members share the common gamma chain as part of their receptor.
    2. the interferon (IFN) subfamily.
    3. the IL-10 subfamily.
- The IL-1 family, which primarily includes IL-1 and IL-18.
- The IL-17 family, which has yet to be completely characterized, though member cytokines have a specific effect in promoting proliferation of T-cells that cause cytotoxic effects.
- The cysteine knot cytokines include members of the transforming growth factor beta superfamily, including TGF-β1, TGF-β2 and TGF-β3.

Functional

A classification that proves more useful in clinical and experimental practice outside of structural biology divides immunological cytokines into those that enhance cellular immune responses, type 1 (TNFα, IFN-γ, etc.), and type 2 (TGF-β, IL-4, IL-10, IL-13, etc.), which favor antibody responses. A key focus of interest has been that cytokines in one of these two sub-sets tend to inhibit the effects of those in the other. Dysregulation of this tendency is under intensive study for its possible role in the pathogenesis of autoimmune disorders. Several inflammatory cytokines are induced by oxidative stress. The fact that cytokines themselves trigger the release of other cytokines and also lead to increased oxidative stress makes them important in chronic inflammation, as well as other immunoresponses, such as fever and acute phase proteins of the liver (IL-1,6,12, IFN-a). Cytokines also play a role in anti-inflammatory pathways and are a possible therapeutic treatment for pathological pain from inflammation or peripheral nerve injury. There are both pro-inflammatory and anti-inflammatory cytokines that regulate this pathway.