

## **Introduction:**

Cytokines are a heterogeneous group of proteins, variously termed lymphokines, monokines, interleukines and interferons, which act on cell surface receptors to regulate and modify cell growth, maturation and repair. In addition to their longer term effects on cell growth and differentiation, cell mediated host-defence mechanisms and chronic diseases such as rheumatoid arthritis, cytokines also mediate several acute effects such as the inflammatory response. Cytokines are produced from activated leucocytes, in particular monocytes, and also from activated fibroblasts and endothelial cells. Activation of these cells is one of the earliest cellular responses to tissue injury and is associated with release of a variety of inflammatory mediators, including cytokines, arachidonic acid metabolites, complement split products, lysosomal enzymes and oxygen-free radicals. Cytokines derived from mononuclear phagocytes mediate non-specific immune responses and some parts of the metabolic response to injury . They have local and systemic effects, both mediated by activation of specific receptors. The other principal stimulus to the metabolic response to injury is afferent input from the injured or operative site (*Whiteside, 2003*).

Cytokines play a pivotal role in the coordination and regulation of immune responses. Surgical trauma and anesthesia are associated with a complex dysregulation of the immune system with the activation of both proinflammatory and anti-inflammatory responses. Interleukin-1, tumor necrosis factor (TNF)  $\alpha$  and Interleukin-6 have local and systemic effects

As of 2008, the current terminology refers to cytokines as immunomodulating agents. However, more research is needed in this area of defining cytokines and hormones.

Part of the difficulty with distinguishing cytokines from hormones is that some of the immunomodulating effects of cytokines are systemic rather than local. For instance, to use hormone terminology, the action of cytokines may be autocrine or paracrine in chemotaxis and endocrine as a pyrogen. Further, as molecules, cytokines are not limited to their immunomodulatory role. For instance, cytokines are also involved in several developmental processes during embryogenesis (*Saito et al., 2001*)

Each cytokine has a matching cell-surface receptor. Subsequent cascades of intracellular signalling then alter cell functions. This may include the upregulation and/or downregulation of several genes and their transcription factors, resulting in the production of other cytokines, an increase in the number of surface receptors for other molecules, or the suppression of their own effect by feedback inhibition.

The effect of a particular cytokine on a given cell depends on the cytokine, its extracellular abundance, the presence and abundance of the complementary receptor on the cell surface, and downstream signals activated by receptor binding; these last two factors can vary by cell type. Cytokines are characterized by considerable "redundancy", in that many cytokines appear to share similar functions. It seems to be a paradox that cytokines binding to antibodies have a stronger immune effect than the cytokine alone. This may lead to lower therapeutic doses.