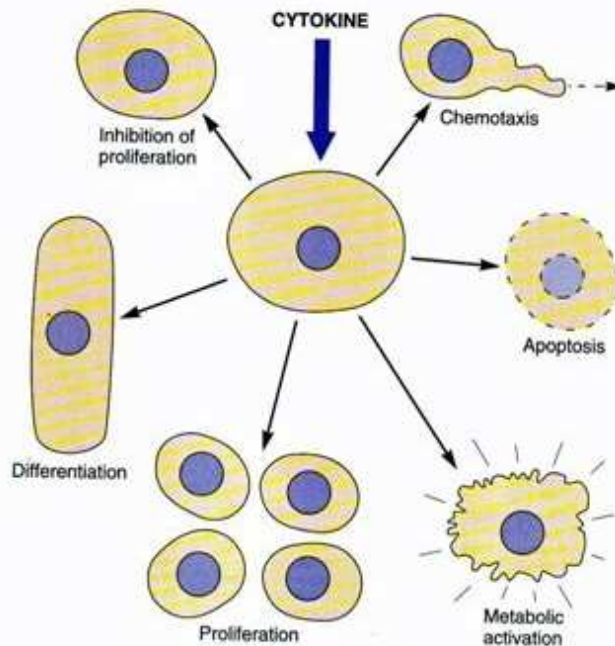


## Les cytokines

Ce sont des protéines de faible poids moléculaire sécrétées par plusieurs types de cellules, qui agissent sur de façon autocrine ou paracrine. Leur production est éphémère et sujette à un contrôle strict.

Les cytokines ont une importance centrale dans la régulation de la réponse immune, le développement embryonnaire et la reconstruction des tissus.



**Figure 31.3 Range of Biological Actions That Cytokines Have on Eucaryotic Cells.** Chemokines are one family of cytokines that induce leukocyte chemotaxis and migration. Other cytokines activate cell metabolism and synthesis. This can lead to the synthesis of a wide range of proteins including cyclooxygenase II, proteolytic enzymes, NO synthase, and various adhesion receptors. In addition, other cytokines can cause proliferation, inhibition of cell proliferation, or apoptosis.

**Table 31.1 The Four Cytokine Families**

| Family                             | Examples   | Functions   |
|------------------------------------|--|---|
| Chemokines                         | IL-8, RANTES, MIP (macrophage inflammatory protein)      | Cytokines that are chemotactic and chemokinetic for leukocytes. They stimulate cell migration and attract phagocytic cells and lymphocytes. Chemokines play a central role in the inflammatory response.        |
| Hematopoietins                     | Epo (erythropoietin), various colony-stimulating factors | Cytokines that stimulate and regulate the growth and differentiation processes involved in blood cell formation (hematopoiesis).  |
| Interleukins                       | IL-1 to IL-16  | Cytokines produced by lymphocytes and monocytes that regulate the growth and differentiation of other cells, primarily lymphocytes and hematopoietic stem cells. They often also have other biological effects. |
| Tumor necrosis factor (TNF) family | TNF- $\alpha$ , TNF- $\beta$ , fas ligand                | Cytokines that are cytotoxic for tumor cells and have many other effects such as promoting inflammation, fever, and shock; some can induce apoptosis.   |

**Table 31.2** Some of the Cytokines That Mediate Natural Immunity

| Cytokine  | Cell Source  | Functions  |
|---|--|--|
| IFNs $\alpha/\beta$<br>(interferons $\alpha/\beta$ )  | T cells, B cells,<br>monocytes/macrophages,<br>fibroblasts   | Antiviral activity, stimulates macrophage activity, modulates MHC class I and II protein expression on various cells, regulates the development of the specific immune response  |
| TNF- $\alpha$<br>(tumor necrosis factor- $\alpha$<br>[cachectin])   | T cells, macrophages and NK cells  | A wide variety of effects due to its ability to mediate expression of genes for growth factors and cytokines, transcription factors, receptors, inflammatory mediators, and acute-phase proteins; plays a role in host resistance to infection by serving as an immunostimulant and mediator of the inflammatory response; cytotoxic for tumor cells |
| TNF- $\beta$<br>(tumor necrosis factor- $\beta$<br>[lymphotoxin])   | T cells, B cells   | Same as TNF- $\alpha$  |
| IL-1 $\alpha$<br>(interleukin-1 $\alpha$ )  | Monocytes/macrophages,<br>endothelial cells, fibroblasts,<br>neuronal cells, glial cells,<br>keratinocytes, epithelial cells | Produces a wide variety of effects on the differentiation and function of cells involved in inflammatory and immune responses; also affects central nervous and endocrine systems  |
| IL-1 $\beta$<br>(interleukin-1 $\beta$ )  | Same as IL-1 $\alpha$  | Same as IL-1 $\alpha$  |
| IL-6<br>(interleukin-6,<br>cytotoxic T-cell<br>differentiation factor,<br>B-cell differentiation<br>factor) | T <sub>H</sub> 2 cells, monocytes/macrophages,<br>fibroblasts, hepatocytes,<br>endothelial cells, neuronal<br>cells          | Activates hematopoietic cells; induces growth of T cells, B cells, hepatocytes, keratinocytes, and nerve cells; stimulates the production of acute-phase proteins  |
| Chemokines<br>(low molecular weight<br>proinflammatory cytokines;<br>IL-8, RANTES, and others)              | Monocytes/macrophages,<br>endothelial cells, fibroblasts,<br>T cells, platelets  | Leukocyte chemotaxis   |

**Table 31.3** Some of the Cytokines That Affect Cell Activation

| Cytokine                                 | Cell Source  | Functions  |
|--|--|--|
| IFN- $\gamma$<br>(interferon- $\gamma$ ) | T cells (T <sub>H</sub> 1, T <sub>C</sub> ),<br>NK cells | Activation of T cells, macrophages, neutrophils, and NK cells; increases class I and II MHC molecules            |
| Lymphotoxin                              | T cells  | Activation of neutrophils and endothelial cells  |
| IL-5                                     | T cells (T <sub>H</sub> 2)                               | Growth and activation of B cells and eosinophils; activation of eosinophil function; chemotactic for eosinophils |
| Migration<br>inhibition<br>factor        | T cells (T <sub>DTH</sub> )                              | Conversion from motile to imotile state (macrophages/monocytes)  |



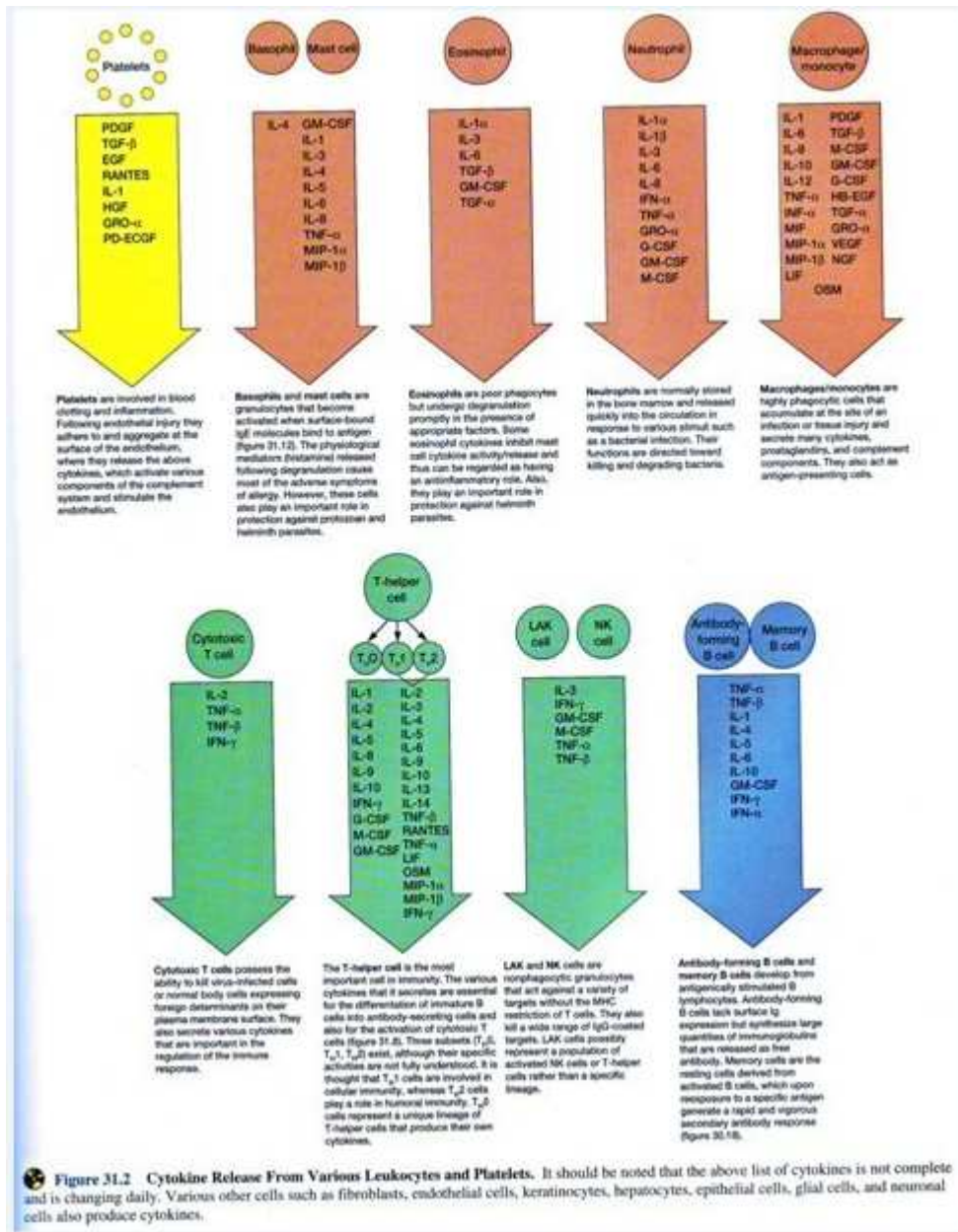


Figure 31.2 Cytokine Release From Various Leukocytes and Platelets. It should be noted that the above list of cytokines is not complete and is changing daily. Various other cells such as fibroblasts, endothelial cells, keratinocytes, hepatocytes, epithelial cells, glial cells, and neuronal cells also produce cytokines.

## Les cellules présentatrices d'antigènes

Les cellules présentatrices d'antigènes (Antigen presenting cells, APC) sont des cellules qui absorbent des protéines, modifient ces dernières et ensuite présentent des fragments d'antigènes aux lymphocytes B et T ainsi qu'au MHC de la classe II afin d'activer les cellules. Les macrophages, les lymphocytes B, les cellules dendritiques, et les cellules de langerhans peuvent agir comme APC. Ces cellules internalisent les antigènes par phagocytoses et les re-expriment avec les molécules de MHC.

Une réponse inappropriée des Th aux produits du soi peut provoquer une réaction auto-immune.

**Remarque** : La réaction immune cellulaire n'est pas indépendante de la réaction immune humorale. Les cellules du système phagocytaire (surtout les macrophages) sont impliquées dans la réponse humorale. De même, divers facteurs solubles produits pendant la réponse immune accentue en retour la réponse de la cellule phagocytaire (feed-back).

### ***Réactions auto-immunes***

Exceptionnellement, les molécules provenant d'un individu peuvent provoquer des réactions (productions d'anticorps) chez le même individu. C'est le cas des maladies auto-immunes.

Exemple: diabète insulino-dépendant. L'insuline est une hormone produite par les cellules beta des îlots de Langerhans du pancréas. Elle joue un rôle important dans le stockage du glycogène dans le foie et la conversion des sucres en graisses dans les adipocytes. La destruction des cellules beta peut survenir à la suite des réactions auto-immunes. Ceci entraîne une insuffisance de la production de l'insuline provoquant ainsi une hyperglycémie avec plusieurs perturbations secondaires dans le sang.