

Chemokines: Proteins Secreted by Cells that Influence the Immune System

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EDITORIAL NOTE

Chemokines are a type of tiny cytokine that cells produce as a signalling protein. Chemotactic cytokines get their name from their capacity to cause directed chemotaxis in surrounding responder cells. Chemokines are proteins that behave like cytokines but have different structural and behavioural features. Chemokines are all about 8-10 kilodaltons in mass and have four cysteine residues in conserved sites that are important for establishing their 3-dimensional shape. These proteins have been referred to as the SIS family of cytokines, the SIG family of cytokines, the SCY family of cytokines, the Platelet factor-4 superfamily, or intercrines in the past. Some chemokines are pro-inflammatory and can be generated during an immune response to recruit immune system cells to an infection site, whereas others are homeostatic and control cell migration during normal tissue maintenance or development. Chemokines have been discovered in all vertebrates, as well as in some viruses and bacteria, but none in other invertebrates.

Chemokines are divided into four distinct subfamilies: CXC, CC, CX3C, and C. All of these proteins have biological effects by interacting with chemokine receptors, which are G protein-linked transmembrane receptors present on the surfaces of their target cells. Chemokines' main function is to act as a chemoattractant, guiding cell migration. Chemokine-attracting cells follow a signal of increased chemokine concentration back to the chemokine's source. Some chemokines regulate immune system cells during immune surveillance procedures, such as sending lymphocytes to lymph nodes to screen for pathogen invasion by interacting with antigen-presenting cells in these tissues. Homeostatic chemokines are generated and released without the need for their source cells to be stimulated.

Some chemokines play a role in development, promoting angiogenesis or directing cells to regions that offer important signals for cellular maturation. Other chemokines are inflammatory and are generated by a variety of cells in response to bacterial infection, viruses, and physical damaging agents such as silica or urate crystals in gout. Pro-inflammatory cytokines like interleukin 1 are known to increase their secretion. Inflammatory chemokines are chemoattractants for leukocytes, attracting monocytes, neutrophils, and other effector cells from the bloodstream to infection or tissue damage sites. Inflammatory chemokines activate cells to trigger an immune response or aid wound healing. Many distinct cell types emit them, and they serve to guide cells in both the innate and adaptive immune systems.

Many signalling cascades are activated as a result of these events, resulting in reactions such as chemotaxis, degranulation, superoxide anions production, and changes in the avidity of cell adhesion molecules called integrins within the cell containing the chemokine receptor. Following ligand interaction, chemokine receptors connect with G-proteins to convey cell signals. The activation of G proteins by chemokine receptors results in the activation of phospholipase C, an enzyme (PLC). PLC cleaves phosphatidylinositol (4,5)-bisphosphate (PIP₂) into two second messenger molecules, inositol triphosphate (IP₃) and diacylglycerol (DAG), which initiate intracellular signalling processes, DAG activates protein kinase C (PKC), and IP₃ stimulates calcium release from intracellular reserves. Chemokine receptors are G protein-coupled receptors that are present on the surface of leukocytes and have seven transmembrane domains.

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