Common γ-Chain Family Cytokines Regulate Immune System Functions

γ-Chain Cytokines Have Unique & Overlapping Effects on Different Immune Cell Types

Cytokines belonging to the common γ-chain receptor (γc) family include IL-2, IL-4, IL-7, IL-9, IL-15, and IL-21. Members of this family signal through receptor complexes that contain the γc and βc subunits. The γc subunit associates with different cytokines specific receptor subunits to form unique homogeneous receptors for IL-2, IL-4, IL-7, IL-9, and IL-15, or with both IL-2/IL-15 R and IL-2/IL-15 R to form heterodimeric receptors for IL-2 or IL-15, respectively. γc family cytokines generally activate three major signaling pathways that promote cellular survival and proliferation, the PI 3-Kinase pathway, the Ras-MAPK pathway, and the JAK-STAT pathway. Differences in the regulation of the cytokines or their unique receptor components, along with the activation of different STAT proteins, may account for some of the distinct effects mediated by γc family cytokines.

Signaling through γc family cytokines plays a major role in regulating the development, survival, proliferation, and differentiation of most of the immune system. The importance of γc family cytokines for the establishment and maintenance of the immune system is emphasized by the fact that mutations in γc (or β2) in humans are associated with a disease known as X-linked severe combined immunodeficiency (XSCID), which is characterized by the absence of T cells and natural killer (NK) cells, and the presence of non-functional B cells. Animal models have demonstrated that the lack of IL-2 and γc in B cell development in this disease can be partially attributed to the respective lack of IL-7 and IL-15 signaling, while the loss of both IL-4 and IL-21 signaling leads to deletion of B cell function. Similar studies revealed that in contrast to humans, B cell development in mice also requires IL-7 signaling. Several additional unique and overlapping effects of the γc family cytokines on different immune cell types have been documented. A number of these effects are highlighted here to demonstrate the central role that γc family cytokines play in controlling immune system functions. Understanding the mechanisms by which these cytokines act and how their signaling pathways can be regulated may have therapeutic implications not only for a variety of immunodeficient disease states, but also for disorders resulting from aberrant exaggerated immune system activation.

FAMILY CYTOKINE INDUCED EFFECTS ON:
- T Cells
- B Cells
- NK Cells or NK Cells
- Mast Cells or Basophils
- Eosinophils
- Epithelial Cells

IL-2
- Activates 
- T Cells 
- Promotes Follicular Helper T Cell Development & Graft vs. Host Disease
- Enhances Cytotoxicity of CD8+ T Cells & NKT Cells
- Promotes B Cell Development & Survival
- Enhances Cytotoxicity of CD8+ T Cells & NKT Cells
- Promotes NK Cell Activation

IL-4
- Activates T Cells
- Promotes T Cell Proliferation & Differentiation
- Promotes IL-21 Production & Class Switching
- Inhibits T Cell Responses
- Promotes B Cell Development & Survival
- Promotes IL-21 Production & Class Switching

IL-7
- Activates T Cells
- Promotes T Cell Proliferation & Differentiation
- Promotes IL-21 Production & Class Switching
- Inhibits T Cell Responses
- Promotes B Cell Development & Survival
- Promotes IL-21 Production & Class Switching

IL-9
- Activates T Cells
- Promotes T Cell Proliferation & Differentiation
- Promotes IL-21 Production & Class Switching
- Inhibits T Cell Responses
- Promotes B Cell Development & Survival
- Promotes IL-21 Production & Class Switching

IL-15
- Activates T Cells
- Promotes T Cell Proliferation & Differentiation
- Promotes IL-21 Production & Class Switching
- Inhibits T Cell Responses
- Promotes B Cell Development & Survival
- Promotes IL-21 Production & Class Switching

IL-21
- Activates T Cells
- Promotes T Cell Proliferation & Differentiation
- Promotes IL-21 Production & Class Switching
- Inhibits T Cell Responses
- Promotes B Cell Development & Survival
- Promotes IL-21 Production & Class Switching

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