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Review article

Interleukin-15 in autoimmunity

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ABSTRACT

Interleukin-15 (IL-15) is a member of the IL-2 family of cytokines, which use receptor complexes containing the common gamma (γ_c) chain for signaling. IL-15 plays important roles in innate and adaptative immune responses and is implicated in the pathogenesis of several immune diseases. The IL-15 receptor consists of 3 subunits namely, the ligand-binding IL-15Rα chain, the β chain (also used by IL-2) and the γ_c chain. IL-15 uses a unique signaling pathway whereby IL-15 associates with IL-15Rα during biosynthesis, and this complex is '*trans*-presented' to responder cells that expresses the IL-2/15Rβγ_c receptor complex. IL-15 is subject to post-transcriptional and post-translational regulation, and evidence also suggests that IL-15 *cis*-signaling can occur under certain conditions.

IL-15 has been implicated in the pathology of various autoimmune diseases such as rheumatoid arthritis, autoimmune diabetes, inflammatory bowel disease, coeliac disease and psoriasis. Studies with pre-clinical models have shown the beneficial effects of targeting IL-15 signaling in autoimmunity. Unlike therapies targeting other cytokines, anti-IL-15 therapies have not yet been successful in humans. We discuss the complexities of IL-15 signaling in autoimmunity and explore potential immunotherapeutic approaches to target the IL-15 signaling pathway.