

Structure and Function Analysis of the IL-13 Receptor (IL-4R α /IL-13R α 1)

Mark A. Schroeder

Ryan P. Andrews

Gurjit K. Khurana Hershey

Department of Pediatrics, Division of Pulmonary Medicine, Allergy and Clinical Immunology, Children's Hospital Medical Center, Cincinnati, OH 45229

IL-13 is a Th2-derived pleiotropic cytokine that plays an integral part of the allergic response in asthma independent of IL-4. It shares many biological activities with IL-4 including the induction of IgE synthesis and CD23 expression by B cells. In addition, IL-13 mediates its effects via a complex receptor system, which includes an IL-4 receptor alpha chain (IL-4R α) and at least two other cell surface proteins, IL-13R α 1 and IL-13R α 2, which specifically bind IL-13. IL-13R α 1 binds IL-13 with low affinity, but when complexed with IL-4R α , it forms a high affinity functional receptor that can signal. There is little known about the interaction between the subunits of the IL-13 receptor. Previous work in our lab has shown that human IL-13R α 1 complexes with human IL-4R α , but not murine IL-4R α . Thus, the heterodimeric interaction between IL-4R α and IL-13R α 1 is species-specific. In contrast, the signaling molecules required for IL-13 responsiveness, including Stat6 and Jak1, are not species-specific and IL-13 itself is not species-specific. Based on this information and our preliminary data we hypothesized that the species-specificity between IL-4R α and IL-13R α 1 is secondary to intermolecular contact requirements of these two components. In order to elucidate the requirements for IL-13 receptor activation and signaling in murine B cells we generated cDNA constructs encoding chimeric IL-4R α containing the human extracellular and murine intracellular domain or vice versa, and transfected these into the murine B cell line, A201.1, which have been stably transfected with human IL-13R α 1. The transfectants were analyzed for IL-4 and IL-13 dependent CD23 expression. The characterization of the transfectants is currently in progress.