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Crystal Structure of the Trimeric Complex of Interleukin-13, IL-13 Receptor $\alpha 1$ and the Binding Domain of the Inhibitory Antibody Fab13.2. Kevin Parris, John Dumas, Marion Kasaian, Amy Tam, Tim Cook, Lioudmila Tchistiakov, Xiang-Yang Tan, Kimberly Marquette, James Wilhelm, Laura Lin, Lidia Mosyak, Wyeth Research, Cambridge, MA 02140.

Interleukin 13 is a pleiotropic cytokine generated early in immune responses driven by T helper 2 cells and plays a critical role in mediating T helper 2-type immunosuppressive activities. Administration of recombinant IL-13 has been shown to induce the pathophysiological features of asthma, whereas neutralization of IL-13 ameliorated/attenuated the asthma phenotype. IL-13 has also been shown to play a prominent role in parasitic infections, atopic dermatitis and cancer. To gain insight into the mechanism of IL-13 regulation, we utilized the Fab fragment of an IL-13 inhibitory antibody (mAb13.2) as a tool to facilitate crystallization of IL-13 singly (1.8Å) and in complex with IL-13 $\alpha 1$ receptor (2.2Å). We find that IL-13 $\alpha 1$ grasps IL-13 in a pincer-like fashion where the Ig3 domain interacts with C-terminal end of the D-helix and the Ig1 domain interacts with loops near the N-terminal end of the D-helix. This interaction with Ig1 induces beta-strand structure onto two loops of the IL-13 molecule forming an extended beta sheet across the two molecules. The Fab fragment binds to the C-helix, where the IL-4 receptor would normally bind.