According to Wenzel et al. (65), half of asthma patients have increased Th2-type inflammation, where there is increased expression of IL-4 and IL-13. Most asthma patients can be successfully treated with the combination of inhaled glucocorticoids plus long-acting beta-agonists, but about 20% of asthma patients do not respond to this therapy. In a study of patients with asthma that was not controllable by the combination of these two kinds of drugs, it was found that administered *dupilumab* was dramatically effective. Efficacy was measured by a test for lung function (forced respiratory volume in 1 s test; FEV_1 test), and by questionnaires filled out by the study subjects (SNOT-22 score; ACQ5 questionnaire).

Efficacy of *dupilumab* was also shown by plasma-level assays for two chemokines, TARC and eotaxin-3. TARC is also known as CCL17, and eotaxin-3 is also called CCL26. TARC is the ligand for CCR4, a receptor that occurs on T cells (66). TARC is thymus and activation-regulated chemokine. According to Wenzel et al. "[l]evels of TARC, eotaxin-3, and IgE ... remained unchanged with placebo. In contrast, with dupilumab, TARC and eotaxin-3 levels were decreased at week 1 and remained lower than baseline values through week 12. With dupilumab, the IgE level was also lower than the baseline value at week 4."

The literature establishes a mechanism of action that connects increased plasma levels of the cytokines IL-4 and IL-13, as a cause of constriction of smooth muscle of the airways. Asthma is a pulmonary disorder that is characterized by increased susceptibility to bronchospasms. Direct activation of smooth muscle by IL-4 or IL-13 is sufficient to induce airway hyper-responsiveness (AHR). In the words of Perkins et al. (67), "[t]hese observations demonstrated that AHR can be induced through direct, in vivo effects of IL-4R signaling on smooth muscle and were consistent with previous in vitro evidence that IL-4R signaling can increase smooth muscle contractility."

Airway smooth muscle cells express receptors for IL-4 and IL-13. These cytokines act on the smooth muscle cells to induce contractile and relaxant responses, proliferation, and the ability of smooth muscle cells to generate chemokines such as eotaxin and TARC (68). TARC acts on the chemokine receptor CCR4, which is expressed on T cells (69). TARC attracts T cells into the asthmatic airways. Plasma and bronchial fluids, in asthma patients, have elevated levels of TARC.

The following narrative helps establish a role for TARC, as expressed by airway smooth muscle cells, in the mechanism of airway smooth muscle contraction in asthma.

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