anti-IL-13 antibody (lebrikizumab) results in improvement of $FEV_1$, and a reduction in nitric oxide (NO) in the exhaled breath (26). NO and superoxide are metabolites that are constitutively present in healthy cells and tissues. NO can react with superoxide to generate a form of toxic oxygen, peroxynitrite. Increased NO in exhaled air is a hallmark feature of asthma, and evidence suggests that the NO contributes to the pathology of asthma by directly destroying tissues (27). The fact that IL-4 contributes to the pathology of asthma is demonstrated by the fact that administering an anti-IL-4 antibody (dupilumab) to asthma patients results in improved $FEV_1$ and decreased exhaled NO (28).

### 5. Chronic Obstructive Pulmonary Disease

COPD is mainly caused by long-term cigarette smoking (29,30). The disease involves a decreased ability to breath, as measured by $FEV_1$ per second, with consequent disability and death. Cytokines that mediate COPD include IL-6, TNF-alpha, IL-1beta, while the immune cells most responsible for this disease are macrophages, neutrophils, and T cells. While COPD and asthma both involve the airways (bronchial tree) and alveoli, COPD is distinguished in that its pathology is mostly caused by *neutrophils*, while that of asthma is caused mostly by *eosinophils*. FDA provides guidance for trial design and endpoints for clinical trials on COPD (31).

### 6. Crohn's Disease and Ulcerative Colitis

CD and UC are two autoimmune diseases of the large intestines. The term *inflammatory bowel disease* (IBD) is used to refer to both of these diseases (32,33). Both diseases result in abscesses in the colon. CD also involves abscesses in the distal ileum. Both diseases result in weakening of the tight junctions between intestinal epithelial cells, distortion of the crypts, disappearance of the mucus layer that coats the lumen side of the epithelial cells, pathological infiltration of white blood cells in the lamina propria (the tissue immediately beneath the layer of epithelial cells), intestinal bleeding, and diarrhea.

CD is characterized as a Th1-mediated disease, while UC is a Th2-mediated disease (34). UC patients express increased IL-5, and have NKT cells that express increased IL-13. IL-5 and IL-13 are Th2-type cytokines. Biopsies from both CD and UC patients show increased levels of

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