

Therapeutic and Mechanistic Perspectives of Protein Complexes in Severe Persistent Asthma.

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Allergic asthma, a very common form of asthma, is a worldwide public health problem with increasing incidence, morbidity, and/or mortality rates during the past three decades. Severe persistent allergic asthma (SPA) is a chronic inflammatory/immune/genetic disorder of the airway that is characterized by bronchial hyper-responsiveness and/or variable airflow limitation. Approximately 250 million people are affected by asthma worldwide and 10% are considered to be refractory to standard asthma treatment (also called SPA) [1]. These patients are known to have repeated exacerbations requiring multiple courses of systemic corticosteroids and as a result, are at risk for increased side effects (i.e. Cushing's syndrome, obesity, hypertension). Several new medications known as biologic agents (also called Humanized monoclonal antibody treatment) have been approved for the treatment of severe asthmatics [1-4].

The main manifestations of asthma, including bronchial eosinophil infiltration, airway hypersensitivity, elevated serum total and/or specific immunoglobulin E (IgE) levels, mucus hypersecretion and airway remodeling, are strongly associated with increased T helper 2 (Th2) cell responses to inhaled harmless allergens [3-6]. In addition, Th2 cytokines (i.e., TGF, TNF, TSLP, CXCL8, ECP, IL-10, IL-33, IL-25, IL-1 β , sCD200, IL-2, IL-4, IL-5, IL-17) play a key role in the induction and exacerbation of allergic asthma and/or asthma-COPD overlap syndrome (also called ACOS) [4]. With the cross-linking of allergen-specific IgE molecules bound to high-affinity IgE receptors (Fc ϵ R) on mast cells, basophils and eosinophils, the receptors are activated, resulting in cell degranulation, the release of

soluble proinflammatory mediators, such as thermogenic proteins/adipokines and histamine and leukotrienes and the exacerbation of the atopic asthma [1,3-7]. We showed lower serum circulating vitamin D levels were found in patients with severe allergic asthma than in the control group, which was attributed to impaired 25-hydroxy vitamin D synthesis and/or metabolism with the use of systemic steroids [2,3,6,7].

In conclusion, the results of our studies suggest that omalizumab (also called Anti IgE) treatment may play a role in the regulation of proinflammatory cytokines metabolism, reducing the need for systemic steroids. However, large-scale, prospective, randomized clinical studies are needed to establish a definite conclusion.

Abbreviations and Acronyms: IL: interleukin, Ba: Basophils, IgE: Immunoglobulin E, BMI: body mass index, CRP: C-reactive protein, ECP: Eosinophil cationic protein, Eu: Eosinophils, DC: Dendritic cell, TNF: tumor necrosis factor, Treg: regulatory T cell, Mc: Mast cells, Mac: Macrophages, ICS: inhaled corticosteroid, ACT: asthma control test, TSLP: thymic stromal lymphopoietin, Tc: T lymphocytes, TGF: transforming growth factor, FVC: forced vital capacity, FEV1: forced expiratory volume in 1 second, NPF: normal pulmonary function, GM-CSF: granulocyte-macrophage colony-stimulating factor, NK cell: natural killer cell, Neut: neutrophils, ILC2: type 2 innate lymphoid cell, SPA: severe persistent asthma, LABA: long-acting beta-2 agonist.

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