



Editorial

Anti-IgE treatment in asthma: Galectin-3 as a predictive marker



A number of targeted therapies have been developed in recent years in order to improve the treatment specificity and efficacy in patients affected by severe diseases. For example, a number of monoclonal antibodies have been generated to target cell surface molecules preferentially expressed by tumor cells or cell populations involved in disease processes. MAbs specific for TNF or IL-1 have been successfully employed in the treatment of rheumatoid arthritis and other autoimmune/inflammatory diseases; in addition, targeting of altered enzymatic proteins involved in cell activation/proliferation has dramatically improved the prognosis of chronic myeloid leukemias and is also promising in some solid tumors. Personalized medicine represents another major advance toward a more proper and efficacious patient treatment. Aim of this approach is the use of therapies tailored to individual patients. The choice of appropriate therapies requires informative diagnostic tests. In this context, genetic information has provided important tools not only for a precise diagnosis of diseases such as primary immunodeficiencies, cystic fibrosis and cancer but also for predicting the efficacy of certain drugs (pharmacogenomics). In this issue, Pierluigi Mauri and colleagues, by applying a sophisticated proteomic approach, show that Galectin-3 represents a reliable predictive marker of the efficacy of the treatment of severe asthma with the anti-IgE mAb Omalizumab [1].

IgE-mediated allergy is a well known and common cause of asthma and the anti-IgE mAb Omalizumab has been approved for the treatment of patients with severe, uncontrolled allergic asthma. The efficacy of this treatment has been confirmed in a number of controlled studies. Notably, histological evaluation of the bronchial remodeling after 12 months of treatment, revealed the existence of two groups of patients: responders, displaying a reduction of the reticular basement membrane (RBM) thickening, and non-responders, showing no substantial variation or even increased RBM thickening. Since this may greatly impact on the evolution of the pulmonary function, the identification, in bronchial specimens, of candidate biomarkers of response appeared particularly relevant. To this aim, the authors applied to the study of bronchial specimens a multidimensional protein identification technology (MudPIT) that allows the rapid identification and quantification of hundreds of proteins from a single sample. Comparative analysis of the protein profiles in responders versus non-responders provided a first remarkable information, namely the existence of

substantial differences in the composition of smooth muscle proteins in the two groups. Thus, actins and myosins decreased in responders to Omalizumab, but not in non-responders. Remarkably, this is the first report showing a therapy-induced reduction in the muscular component of asthma remodeling. It is conceivable that this reduction may substantially impact on the improvement of lung function. Analysis of the extracellular matrix (ECM) main proteins, including vimentin, periostin and other proteins revealed that they were present in comparable amounts in bronchial biopsies from both responders and non-responders. In contrast Galectin-3 was exclusively present in samples from responders and its levels were quite stable when analyzed before and after treatment with Omalizumab. Thus, Galectin-3 represents an useful and reliable marker predictive of the effect of the anti-IgE treatment on bronchial basal membrane thickening, thus allowing to identify responders. What is the mechanism whereby Galectin-3 may be involved in responsiveness to Omalizumab? The Authors suggest that Gal-3, by promoting the disruption of the high affinity IgE-FcεR1 interaction, facilitates the dissociation of the complex, leading to improved efficacy of anti-IgE mAb in Gal-3-positive patients.

In conclusion, this study provides evidence that Gal-3 may represent an useful marker to identify patients who will respond to anti-IgE treatment with modulation of bronchial remodeling involving both major smooth muscle proteins and collagen/fibronectin deposition. While the present study is focused on bronchial specimens, it is conceivable that Gal-3, being a matrix protein, may be detected in serum or urine, thus allowing the identification of severe asthma patients who would benefit from anti-IgE therapy.

Reference

- [1] Mauri P, Riccio AM, Rossi R, Di Silvestre D, Benazzi L, De Ferrari L, Dal Negro RW, Holgate S, Canonica GW. Proteomics of bronchial biopsies: Galectin-3 as a predictive biomarker of airway remodeling modulation in omalizumab-treated severe asthma patients. *IMLET* 2014;162:2–10.

Lorenzo Moretta
Vito Pistoia

Istituto Giannina Gaslini, Genova, Italy

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