

Precision Medicine in Allergic Disorders

Cevdet Ozdemir, MD¹
Mübeccel Akdis, PD, MD, PHD²
Cezmi A. Akdis, MD^{2,3,*}

Address

¹Memorial Health Group, Department of Pediatric Allergy, Atasehir Hospital, Istanbul, Turkey

²Swiss Institute of Allergy and Asthma Research (SIAF), University of Zurich, Davos, Switzerland

³Christine Kühne-Center for Allergy Research and Education, Davos, Switzerland
Email: akdisac@siaf.uzh.ch

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The Era of Precision Medicine in Allergic Disorders

It is fully acknowledged in medical education that *“There is no single disease as a general term that covers every patient, but there is individual characteristics and variations between patients and the treatment should focus on the individual patient not the disease.”* This individual variability among patients has aroused the necessity for subcategorizations, tailoring, or customization of diseases. This concept has been brought up as *“Ut quod ali cibus est aliis fuat acre venenum,”* which means *“What Is Food to One May Be Fierce Poison to Others”* by Titus Lucretius Carus a Roman poet and philosopher for the description of food allergy (Wikipedia). Allergic patients have individual stories, different molecular mechanisms, different visible characteristics and disease outcomes under the influence of genetic background, and epigenetic control by micro- and macro-environment. Accordingly, the three keywords, endotype, phenotype, and biomarker are becoming the basis of a lot of future discussions and thousands of publications with the upcoming efforts to revolutionize patient care and public health in the direction of precision medicine and precision health [1, 2]. An endotype is a subtype of a disease condition defined by a distinct pathophysiological mechanism, whereas a disease

phenotype defines any observable characteristic of a disease without any implication of a mechanism. Another key word linked to disease endotyping is biomarker that is measured and evaluated to examine any biological or pathogenic processes, including response to a therapeutic intervention [3]. It is very ostentatious and optimistic to expect that one treatment option can be applicable to entire population, especially in disorders like allergy, asthma, chronic rhinosinusitis, and atopic dermatitis in which multiple developmental and triggering insults are key players [1, 2]. Phenotyping, endotyping, genotyping, and therotyping (therapy response) are gaining more and more attention to better understand the diseases to develop better prevention and daily patient care, where biologics are emerging and individualized pharmacotherapy and allergen-specific immunotherapy stand as an essential precision medicine approaches [4, 5].

The field of allergy/immunology in general, and asthma in particular, has considerably advanced along the path of Precision Medicine, but there is a long way to go at the level of individual patients. The precision in the clinic needs the development of three main components. (1) It is essential and

urgent to develop new disease taxonomy including new terms to describe recent findings in subgroups of allergic diseases, CRS, and asthma. (2) Full patient and medical environment (pharmacy, invoices going to insurance companies) monitoring using novel digital technology should be established. (3) Research should continue and algorithms should be developed on disease phenotypes, endotypes, and biomarkers preferentially at the point of care. All of these approaches will enable to customize and better define treatment responders, foresee risk development, and design disease-modifying strategies [6, 7].

First, better characterization of the allergic patient is essential. For example, in respiratory allergies, while some patients may suffer from upper airway symptoms as in allergic rhinitis, another group of patients may suffer from only lower airway symptoms in asthma. It is also highly possible to observe both upper and lower airway allergies in the same patient [8]. While some of these respiratory sufferers are due to seasonal triggers, others are due to perennial ones. In seasonal sufferers, pollens are known to be the most prevalent triggers, and their symptoms may be triggered either by tree pollens, grass pollens, or by both. Similar examples can be suggested for pet owners. It is possible in those who own both cat and dog in the same household, symptoms may develop due to cat allergy in one or only dog allergy in the other. It is possible to be sensitized against both allergens in the third case or the allergen can be fully independent of dog and cat and can be *alternaria* or house dust mite.

The identification of allergen source can be more detailed in food allergies. Mild atopic dermatitis stands on one edge, whereas anaphylaxis, a life-threatening disease stands on the other edge in food allergic infants. As an example, while an infant is allergic to cow's milk protein, he or she may tolerate baked products or sooner become tolerated. Unfortunately, some infants will never be able to tolerate cow's milk in the following years, and even stay allergic with a risk of anaphylaxis to baked products. Variations in the clinical course of food allergic infants open a broad area for precision medicine. Another issue is to find out which patient is allergic to more than one food allergen and what will be the clinical outcome and progress of tolerance development.

Allergen immunotherapy (AIT) and avoidance approaches will be fully different in all of the above. By component resolved diagnosis (CRD), a representative diagnostic method of precision medicine, it is possible to foresee this outcome and progress. Data obtained by CRD will provide decision points when to perform food provocations and challenges. CRD also gives insights about tolerability to fresh or baked forms of food allergens in the patient. Furthermore, CRD also provides information about cross-reactivities among same allergen families, and guide clinicians to avoid unnecessary food elimination diets, which may result in growth retardation and low quality of life.

AIT is a specific way of treatment of allergic disorders, targeting the underlying mechanisms and altering the natural disease course by inducing a long-lasting clinical and immunological tolerance to allergens [9–14]. By defining the main allergen molecule that triggers allergic disorders will enable to take true avoidance measures and provide exact AIT plans. AIT as understood by its name is a specific modality of treatment that stands as a prototype of precision medicine. Customization through precision medicine renders identification of which patient will benefit from AIT and which allergen should be chosen during therapy. Clinical follow-up to assess the efficacy of AIT can be possible with the precision medicine methods. It will be a very important decision to make whether to start AIT or a biological in certain patients in the short future.

Multiple omics including proteomics, transcriptomics, or metabolomics, providing big data analysis, is coming to the sight more and more in individual patients' basis as well as in big patient cohorts. Through the analysis of big data, it will be possible to develop management guidelines for allergic disorders, and clinical utility of precision algorithms. In addition, it is not so difficult to foresee that electronic health care data of patients, statistics of insurance companies, and pharmacies as well as internet searches, will provide an artificial intelligence for the outcomes, seasonal status, viral infection status, and pollen status of geographical regions and subgroups of patients.

In conclusion, precision medicine will be the future of all diseases, because the individualization of the patient care will enable precision diagnosis, improved prognosis, low-treatment costs, better selection of treatment responders, and better design of disease-modifying and prevention strategies [2].

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