Precision Medicine in Airway Diseases: What Can We Offer in the Clinic?

Authors: Abigail Craig, EMJ, London, UK

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AN EXCITING session, delivered at the European Respiratory Society (ERS) International Congress 2023, held in Milan, Italy, saw field experts present recent research surrounding precision medicine in airway diseases. Chaired by Apostolos Bossios, Karolinska University Hospital, Stockholm, Sweden; Emer Kelly, St. Vincent's University Hospital, Dublin, Ireland; and Omar Usmani, National Heart and Lung Institute (NHLI), Imperial College London, UK, presentations discussed the value of 'omics', cellular signatures, novel chronic obstructive pulmonary disease (COPD) classifications, and the identification of treatable traits in improving patient care.

EARLY DIAGNOSTICS: OMICS AND CELLULAR SIGNATURES

Sanjay Haresh Chotirmall, Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore, began the session by considering the value of omics and cellular signatures in the early diagnosis of airway diseases. He emphasised the need for new approaches in this field, suggesting that multi-omic technologies and cellular signatures show promise. Specifically, these technologies could aid in classifying patients based on their clinical phenotypes, sub-phenotypes, endotypes, and treatable traits, thus generating patient sub-groups with a common characteristic that could be successfully targeted by intervention.

Explaining how multi-omics can help in the clinic, Chotirmall highlighted the very clear endotypes that have been identified through this technology. Novel phenotypes of bronchiectasis and COPD were presented, with the crucial role played by multi-omics in these discoveries highlighted. When considering the value of multi-omics in constructing novel-phenotypes in airway diseases, the U-BIOPRED cohort led the way through the integration of multi-omic data related to the molecular phenotypes of asthma onto one common platform.

Chotirmall also suggested that multi-omics could help in the clinic through biomarker discovery, through the identification of new mechanisms, and by permitting a more in-depth analysis of overlap patients. For example, a recent publication including 100 patients with COPD utilised a range of 'omic' technologies to validate key pathways in neutrophilic dominant COPD. Multi-omic technologies have already made a dramatic difference to therapy when considering, for example, the treatment of cystic fibrosis, in which, according to Chortimall, we have now revolutionised the treatment through the use of potentiators and correctors based on genomics. Finally, Chotirmall hypothesised that multi-omics would aid in the stratification (prognosis, prediction, and progression) of patients. By understanding all these data, clinicians can more easily identify patients whose data is going to progress. For example, in a cohort of patients with COPD, data on lung microbiota was combined with metabolomics to successfully identify disease progression.

Chotirmall concluded by addressing some of the challenges associated with bringing multi-omics to the bedside, namely cost, lack of facilities and expertise, standardisation, and clinical utility and validation across cohorts, before stressing that emerging technologies show great promise.

ARE NOVEL CHRONIC OBSTRUCTIVE PULMONARY DISEASE CLASSIFICATIONS HELPFUL?

Shyamali Dharmage, University of Melbourne, Australia, discussed novel COPD classifications and whether they are helpful in offering better care for patients. The definition of COPD has undergone substantial changes since it was first defined in 1969. Recently, a number of sub-classifications have been developed with sub-types and aetio-types, based on risk factors that can occur at any age, which were introduced in 2023. They emphasised that, with five sub-types proposed, each associated with different risk factors and aetiologies, COPD is not just a smoker's disease.

Dharmage continued by discussing the evolving taxonomy of pre-COPD. Using repeated lung function data between the ages of 7–53 years, a report was able to generate lung function trajectories. The patterns reveal three types of trajectory in each measure that can contribute to the development of COPD by middle-age. Overall, this suggested that there is a long lag of deteriorating lung function before reaching the diagnostic cut-off for COPD. Pre-COPD was first defined as a stage of increased risk in 2020, and the pre-COPD framework has since been formalised.

Lastly, Dharmarge explained the usefulness of these classifications. As the classifications are currently conceptual, they lack precision. Furthermore, this system for sub-grouping patients is inherently flawed as the subtypes do not consider the multifactorial nature of COPD or the interactions between risk factors. However, these classifications provide opportunity to promote the multifactorial nature of COPD, strengthen the case for prevention and early diagnosis, and suggest a way forward in identifying endotypes of early disease. A decision support tool, currently under development, aims to help clinicians understand which patients in the pre-COPD stage are at risk of developing COPD.

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NON-TYPE 2 ASTHMA: THE UNMET NEED

Richard Costello, Royal College of Surgeons in Ireland (RCSI), Dublin, Ireland, sought to review the clinical, physiological, and immunologic features of Type 2 (T2) low asthma. Currently, T2 high asthma is well characterised as airway injury resulting in physiological changes and the production of IL-4, IL-5, and IL-13 by T helper 2 cells and T2 innate lymphoid cells lymphocytes. The definition of T2 low asthma is rather unsatisfactory; limited to an absence of T2 inflammation. Costello subsequently suggested that there is little mechanistic evidence to support the concept of T2 low asthma as an independent condition.

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Costello stressed that previous exposure to corticosteroids could affect T2 status of the patient. Looking at cross-sectional data from several studies, between 40–50% of patients were T2 low. In contrast, when researchers record T2 status over time, between 70–90% of patients were T2 high at some point. Costello then highlighted the results of INCA SUN, a multicentre study of patients with severe asthma, recorded over 32 weeks. The researchers investigated whether clinician decision making would be altered by using digital data rather than traditional prescription data. Importantly, exposure to inhaled corticosteroids was precisely measured throughout this study. Across the study period, patients were most commonly T2 high, but when considering individuals over time at successive visits, the percentage of patients that were T2 high increased.

When considering this result in tandem with corticosteroid use, T2 low status was significantly associated with higher inhaled corticosteroids ($p=0.011$). Thus, knowing the patient's previous corticosteroid exposure is crucial in understanding their T2 status.

Costello concluded that this evidence suggests there is very little mechanistic evidence to support the concept of T2 low asthma as an independent condition. In fact, most T2 asthma can be explained through the combined effects of corticosteroid treatment and the non-specific nature of asthma symptoms. He stressed that the recognition of one type of asthma, caused by damage to the airway resulting in inflammation and a change in the airflow, will make patient management easier.

The final talk, delivered by Clémence Martin, Cochin Hospital, Paris, France, considered treatable traits in bronchiectasis. Following diagnosis, patient management is centred around treatable traits, such as the underlying cause, infection, breathlessness, comorbidities, and exacerbations. Martin concluded that precision medicine will aid in patient characterisation, which in turn will improve treatment and selection for clinical studies. Regarding bronchiectasis, cystic fibrosis transmembrane conductance regulators and other ion channels show promise as therapeutic targets.

CONCLUDING REMARKS

It is clear that the application of precision medicine in airway disease will have a largely positive impact in the clinic, offering opportunities for improved patient classification and the early identification of disease. ●