Moving -omics and Machine Learning into Clinical Practice in Asthma and Allergy Medicine

Evan Kimber
Editorial Assistant

Citation: EMJ Allergy Immunol. 2021;6[1]:22-24.

COMPELLING discussions took place at the European Academy of Allergy and Clinical Immunology (EAACI) Hybrid Congress 2021, exploring the emergence of machine learning (ML) in current practice and potential avenues within allergy research. Keeping to an underpinning focus on asthma but touching on eczema and other allergic conditions such as α-Gal syndrome, conversations began with a consideration of metabolomics and biomarkers, progressing to discuss phenotype characterisation, with an overall clinical focus. Applications of ML upon early-life microbe exposure and the development of the immune system were tackled, before concluding with the basophil activation test (BAT) and its use in studying allergen sensitisation.

The session opened with Maria Escribese of the University of San Pablo, Madrid, Spain, who summarised current standing in metabolomics and focussed on the challenges and next steps for utilising biomarkers. Next, Adnan Custovic, Imperial College London, UK, discussed the implementation of ML in understanding asthma heterogeneity, followed by Jenni Lehtimäki of the University of Helsinki, Finland, who provided insight on ML analytic studies that investigate the development of the immune system and risk of allergies based on early exposure to microbes. Concluding with the use of BAT centred on α-Gal allergy was Bernedette Eberlein of the Technical University of Munich, Germany.

LESSONS LEARNED FROM METABOLOMICS

Reminding us that asthma is a multifactorial, chronic syndrome involving genetic and environmental interaction, Escribese began by emphasising the complexity of the disorder. Her presentation gave an update on the unmet needs in asthma and challenges facing biomarker-based treatment in allergic disease, highlighting the idea that clinical phenotypes are governed by underlying endotypes. Current practice uses IgE and eosinophilia as biomarkers, but adipokine and periostin are showing promise and are expected to be widely adopted soon.

"Metabolomics has provided unique and novel insights into asthma profiling at the molecular level," stated Escribese, addressing targeted or untargeted classifications and mentioning

'breathomics' as the first approach incorporating metabolic biomarkers into clinical practice. Returning to the overall ML focus in this session, this breath-based initiative captures, identifies, and quantifies volatile organic compound patterns in human breath, which is useful for diagnosis of a wide spectrum of medical problems. Escribese stressed that this method allows identification of new biomarkers for monitoring intervention, patient classification, and biological drug management, promising that it will prove useful for explaining the underlying mechanisms associated with diseases and could help identify novel therapeutic interventions.

EXPLANATORY AND PREDICTIVE MACHINE LEARNING APPLIED TO ASTHMA

Energising proceedings, Custovic brought an enormous passion to his presentation, which examined a shift from diagnosis-based to mechanism-based treatment. He tied together ML for asthma diagnosis, assessing severity and future risk, and patient stratification, stating: "In the last decade or so, the development of high-throughput technology has really transformed the way we do research, and offers tremendous opportunity to unravel the complexities of asthma."

"In the last decade or so, the development of high-throughput technology has really transformed the way we do research, and offers tremendous opportunity to unravel the complexities of asthma."

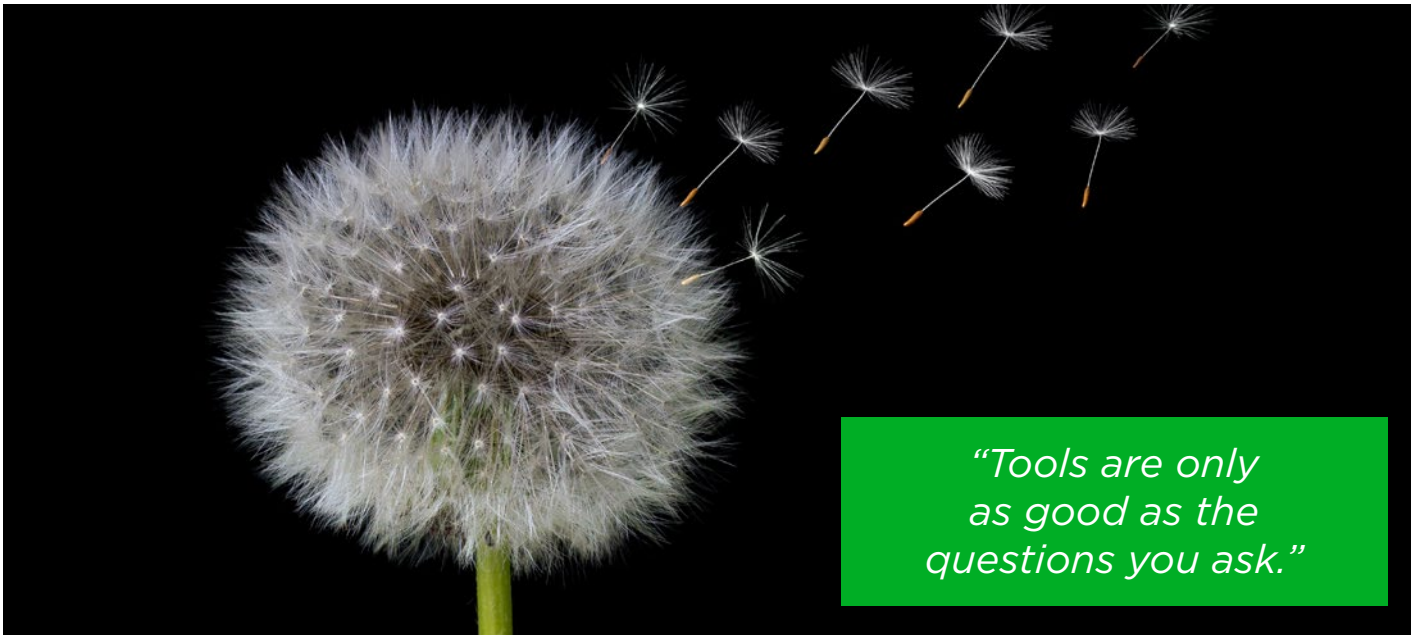
Custovic spotlighted the vast amount of data ML can analyse and interpret where traditional methods would find processing challenging, driving the movement away from hypothesis-driven study towards data-driven approaches. Splitting ML into two categories, he outlined that explanatory ML aims to understand patterns in data, meanwhile predictive ML makes predictions without attempting to explain the data. Predictive ML applied to children and adults to forecast the diagnosis of asthma, using algorithms applied to complex data, has produced a noteworthy correlation network, examining structural homology and IgE dynamics. Patients with severe asthma express a higher connectivity among these components, but with weak interaction; in moderate asthma there are fewer connections but stronger bonds between components.

Looking at ML applications for longitudinal data, Custovic touched on latent variable modelling and discussed future action for asthma: "ML and data-driven methodology allow us to understand the underlying pathophysiology and offer us pointers as to where to go next." He concluded by underlining that no single data source or method can uncover the complex mechanisms involved in asthma heterogeneity, and that without understanding mechanisms we cannot improve patient outcomes. He closed by highlighting the requirement for a shift towards a more integrated cross-disciplinary and cutting-edge analytic approach, incorporating ML-based science in large datasets and facilitated by collaboration from all parties involved in study.

RURAL VERSUS URBAN UPBRINGING AFFECTING LATER ALLERGY

Lehtimäki elaborated on analysis conducted in Denmark comparing the allergy profiles of children born in, and spending critical periods of their development in, rural and urban areas. Including observation of asthma, eczema, and allergic rhinitis, the differences in microbe exposure and health outcomes were recorded at 1 week, 1 month, 6 months, and 1 year, only including those who remained for the full year.

The ML aspect of this study was seen through the use of a single-variable simplification of data, describing markers of rural or urban development by creating a sliding gradient scale and outlining composition of a participant's microbiota of the airways and gut. Describing a sparse partial least-squares model, Lehtimäki noted higher asthma, eczema, and aero-allergen sensitisation levels in children raised in an urban environment, and observed a superior immune response in rural-born children.



Speaking about an innovative study that involved vacuuming infant beds to collect dust, Lehtimäki expanded on investigation of the composition of the samples collected, implementing a similar ML method to create a single-variable scale of the microbiota found in the beds. Children with an urban background and no siblings had less-diverse microbes in the sample and an increased likelihood of developing asthma and allergic rhinitis at 6 years.

"It seems both the microbes you are exposed to, and the microbes which are colonising your airways and gut, are important in defining later health," was the summary delivered by Lehtimäki, going on to state: "And it might seem the rural ones are protecting." This presentation of ML findings has sparked debate into how cities must be changed to allow more access to diverse green space to mimic a rural environment upbringing and potentially reduce later allergy.

USING BASOPHIL ACTIVATION TESTS TO DIFFERENTIATE ALLERGY AND SENSITISATION

Eberlein began by contextualising the discovery of α-Gal syndrome and the delayed anaphylaxis it causes with consumption of red meat. The ML aspect here involved exploiting the known association with tick bites and IgE, using BAT to identify triggers. This method is a cellular *in vitro* test for IgE-mediated reactions, involving basophil identification and measuring activation flow cytometrically.

The diagnostic workflow followed was initiated with selection of patients with a history of urticaria and anaphylaxis, progressing to stratify based on IgE diagnostics and skin prick-to-prick testing with products such as raw beef and pork. Cellular BAT was then applied in a provocation test, producing evidence of an association between α-Gal serum IgE positivity with IgE levels and recent tick bites. Findings showed that patients can be sensitised to α-Gal without having a clinically manifested allergy; the diagnostic workflow is an example of ML being used to confirm diagnosis and determine individual allergen sensitivity.

The usefulness of BAT was emphasised by Eberlein, who discussed potential for use as a generalised clinical test and the possibility of creating an algorithm used in a mobile application to calculate risk, using co-factors like alcohol consumption and exercise. Strengths lie with the ability of the test to identify triggers and sources of α-Gal-containing substances, differentiate sensitisation and allergy, as well as elucidate mechanisms of the syndrome.

CONCLUSION

A host of advanced machine-driven initiatives were brought forward in this session, and will no doubt change the way allergy research is conducted in the near future. But a human element will always remain present in investigations, according to Custovic, who assured: "Tools are only as good as the questions you ask."