Predicting probability of tolerating discrete amounts of peanut protein in allergic children using epitope-specific IgE antibody profiling

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ARTICLE SUMMARY

- Existing diagnostic testing is not predictive of severity or the threshold dose of clinical reactivity, and many patients still require an Oral Food Challenge (OFC). While OFCs are very useful for making an allergy diagnosis and determining clinical reactivity, they often cause anaphylaxis, which can increase patient anxiety. and are time and resource intensive.[1]
- An extensive validation was performed across 5 cohorts (all with confirmed oral food challenge results) across six different countries. Cohorts used: BOPI, OPIA, CAFETERIA, CoFAR6, and PEPITES with specimens from Australia, UK, US, Ireland, and Germany.
- This paper reports the first validated algorithm using two key peanut specific IgE epitopes to predict probabilities of reaction to different amounts of peanut in allergic subjects and may provide a useful clinical substitute for peanut oral food challenges.
- Using the algorithm, subjects were assigned into "high", "moderate", or "low" dose reactivity groups. On average, subjects in the "high" group were 4 times more likely to tolerate a specific dose, compared to the "low" group.[1] For example, 88% of patients in the high dose reactivity group were able to tolerate ≥ 144 mg of peanut protein whereas only 29% were able to tolerate the same amount in the low dose reactivity group.[1-2]

CLINICAL CONSIDERATIONS

- The new epitope test offers more granular information to help clinicians stratify treatment and peanut avoidance plans for their patients.
- See below for summary of clinical considerations based on threshold reactivity level.[1]

allergenis peanut diagnostic result	clinical considerations[1]
likely allergic – low dose reactor	• inform or avoid oral food challenge to reduce risk of anaphlyaxis • confirm strict avoidance of peanut • consider immunotherapy to reduce risk of reaction
likely allergic – moderate dose reactor	• consider a single oral food challenge (30 to 100 mg) to reduce anxiety and improve quality of life • less stringent avoidance of peanut regime • consider inclusions of precautionary labeled foods such as 'May contain peanut' • consider immunotherapy to reduce risk of reaction
likely allergic – high dose reactor	• consider a single oral food challenge (100 to 300 mg) to reduce anxiety and improve quality of life • less stringent avoidance of peanut regime • consider inclusions of precautionary labeled foods such as 'May contain peanut' • consider starting immunotherapy at higher doses to shorten time to maintenance dose
unlikely allergic	• oral food challenge to rule out the diagnosis of peanut allergy

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NEWS AND COMMENTARIES

Legends of Allergology and Immunology: Alex Straumann

Major contributions

1. Description of eosinophilic esophagitis as a novel disease entity
2. Characterization of eosinophilic esophagitis as a Th2 type inflammatory disease
3. Analysis of the natural history of eosinophilic esophagitis
4. Demonstration the efficacy of topical corticosteroid therapy in eosinophilic esophagitis
5. Description of a subgroup of patients with eosinophilic esophagitis with a food-induced immediate response
6. Description of non-eosinophilic esophagitis variants

When Alex Straumann celebrated his 50th birthday in 1997, he decided to take the next step in his investigation of patients with eosinophilic esophagitis (EoE) that he described as a new disease entity three years before in German (1). Alex visited me in the Swiss Institute of Allergy and Asthma Research (SIAF) and I was impressed about his careful clinical work as well as the detailed and precise description of his observations. From now on, we were a team working on the pathophysiology and treatment of EoE and developed a life-long friendship. Over the years, more excellent scientists and clinician-scientists joined our team that was essential to take care about the growing numbers of EoE patients and research questions. Now, he enjoys collaborative interactions of a large group of individuals within the Swiss EoE Research Group and EoE Swiss Clinics. Internationally, he is an active member of the TIGER (The International Gastrointestinal Eosinophil Researchers) network. After 25 years of hard work and scientific success, it is time for this commentary on the occasion of Alex' 75th birthday. Alex is indeed a legend and with his work on EoE already today immortal.

Alex is primarily a clinician with remarkable observational skills. Clearly, he must have had a good clinical education. In fact, in 1975, he completed his medical training in Bern (Switzerland) and was a fellow in Internal Medicine at the University of Basel. In 1984, he was board-certified as a Gastroenterologist. But what makes him so special compared to the majority of other clinicians? I think it is his inherent curiosity leading to comprehensive anamneses and to meticulous endoscopic examinations is really the key. Another important point is that he is not shy and likes to communicate with basic scientists and clinicians from other disciplines. Finally, Alex is persistent and never gives up. Therefore, he struggles for a project until the work can be published. These characteristics of Alex are worth to be copied by young clinician-scientists as they are at least helpful for long-term successful scientific work.

It is not possible to appreciate all contributions of Alex in the last 25 to 28 years. Owing to space limitations, I need to select just a few milestones in his work on EoE. After the discovery of the disease in adults, he has worked several years on discovering its pathophysiology. Because of the presence of eosinophils, his hypothesis was that EoE has an underlining immunological mechanism. His approach was to use the esophageal biopsies and to analyze the inflammatory cell infiltrate and cytokines that are present in EoE. Indeed, besides eosinophils (Figure 1), these tissues are characterized by increased numbers of T cells producing Th2 cytokines and mast cells (2). These observations resulted in a landmark paper, since the inflammatory infiltrate and cytokine pattern exhibited a strong similarity to asthma. During this time, Alex also investigated the natural history of EoE. At this time, it had not been clear at all if EoE is a chronic disease and whether the inflammation could be a risk factor for the development of cancer in the esophagus. The results of this study demonstrated that EoE is a chronic inflammatory disease and, since patients suffer mostly from dysphagia and food impaction, require treatment (3).

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In the subsequent years, Alex made many efforts to develop novel therapies for EoE, keeping clinical presentations, immunological mechanisms and the need of the patients in focus. Several investigator-driven studies were performed for this purpose. While a direct anti-eosinophil approach had been less successful (4), topical therapy with corticosteroids demonstrated high efficacy in reducing inflammation and symptoms in EoE patients (5). The latter study was the basis for the future development of topically applied corticosteroids that are now available for the therapy of EoE patients.

Studying EoE patients for almost 3 decades resulted in observations that suggested that not all patients with EoE symptoms suffer from the same disease. For instance, some EoE patients respond to food with an immediate reaction of the esophagus (6). While these patients appear to be a subgroup of EoE patients, a recently published study suggests the existence of non-eosinophilic variants of esophagitis that all suffer from classical EoE symptoms (7). Interestingly, all these variants are characterized by distinct gene expression patterns, suggesting different types of inflammatory responses (8).

In 2017, Alex closed his doctor's practice in Olten, in which he had worked for about 32 years, after his 70th birthday. He is now a consult physician in the Department of Gastroenterology of the University Hospital Zurich. Alex mentors young fellows interested in EoE (Figure 2), works on new research projects, facilitates collaborations and works as a consultant for many pharmaceutical companies which develop drugs for the treatment of EoE.

ACKNOWLEDGEMENTS

Hans-Uwe Simon has known Alex Straumann for over 25 years. There was no student–supervisor relationship. It has been a close collaboration between them to which both contributed with what they could offer. Since the contributions were different, the collaborative interactions were characterized by strong synergy.

CONFLICTS OF INTEREST

None.

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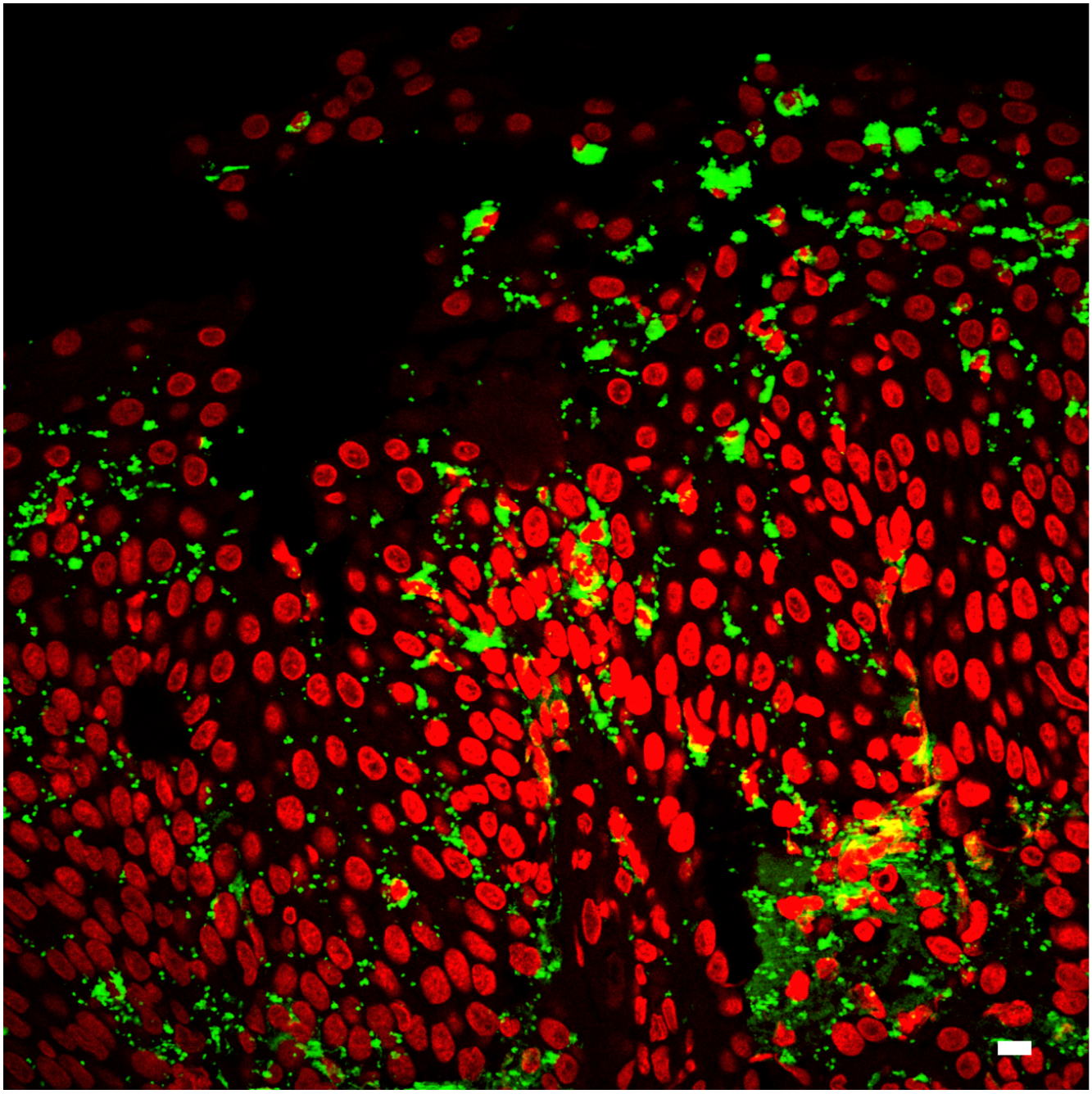
FIGURE LEGENDS

Figure 1. EoE is characterized by an infiltration of eosinophils in the esophageal epithelium. Eosinophils were stained with a fluorescence-labelled lineage-specific antibody (anti-EPX) and the tissue was analyzed by confocal microscopy. EPX is an eosinophil granule protein. It should be noted that EPX is not only present within eosinophils, but also in the extracellular space, suggesting eosinophil degranulation.

Figure 2. Alex Straumann (right) und Luc Biedermann (left) in the Endoscopy Unit at the Department of Gastroenterology of the University Hospital Zurich (2022).

Fig 1



EPX
Nucleus

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