REPORT

IUIS - FAIS Immuno-Algeria 2020

Challenge of Allergy in the molecular era

1st - 12th June, Zoom Course

Organizers

- Prof. Dieter Kabelitz (University of Kiel, Germany, Chair of the IUIS-Education (EDU) Committee)
- Prof. Kamel Djenouhat (Faculty of Medecine, University of Algiers 1, Algeria, Chair of the SAI)
- Prof. Clive Gray (University of Cape Town, FAIS Secretary, IUIS-EDU Committee Vice- Chair)
- Prof. Ridha Barbouche (Institut Pasteur de Tunis, Tunisia, FAIS Board and IUIS-EDU Committee member)
- Prof. Michelle Letarte (SickKids Hospital and University of Toronto, Canada, IUIS-EDU Committee Past-Chair)

Faculty

- Prof. Clive Gray (University of Cape Town, South Africa)
- Prof. Dieter Kabelitz (University of Kiel, Germany)
- Prof. Kamel Djenouhat (Faculty of Medecine, University of Algiers 1, Algeria)
- Prof. Ridha Barbouche (Institut Pasteur de Tunis, Tunis, Tunisia)
- Prof. Rudolf Valenta (Medical University of Vienna, Austria)
- Prof. Yasmine Belkaid (NIH, Bethesda, USA)
- Prof. Jonny Peter (Groote Schuur Hospital, University of Cape Town, South Africa)
- Dr. Sabelo Hadebe (University of Cape Town, South Africa)
- Prof Mehrnaz Mesdaghi (Shahid BeheshK University of Medical Sciences, Tehran, Iran)

- Prof Ulrich Blank (INSERM, Paris, France)
- Prof. Joana Vitte (Marseille University Hospital, Marseille,France)
- Prof Claude Lambert (University Hospital , St. Etienne, France)
- Prof Carsten Schmidt-Weber (Center of Allergy & Environment, Munich, Germany)
- Prof Luis R. Caraballo (University of Cartagena, Columbia)
- Prof. Michelle Letarte (University of Toronto, Canada)

The faculty was composed of an international panel of 15 experts in immunology and allergic diseases. The regional representation is shown in Figure 1

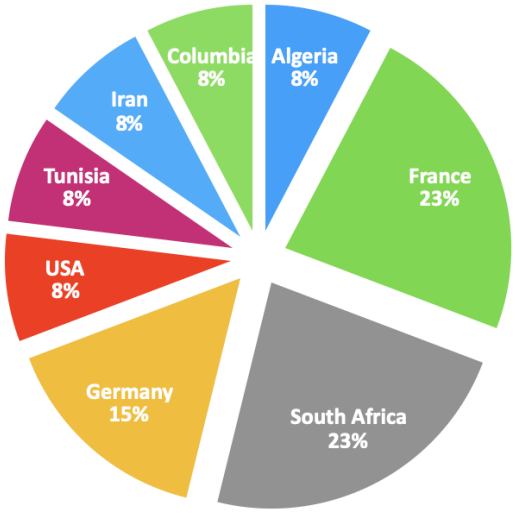

Figure 1: Immuno-Algeria 2020 course faculty

Introduction

The Immuno-Algeria course was set to take place at the El-Aurassi Hotel in Algiers from the 24th - 28th June 2020 and was advertised in early February 2020. We received 118 applications from several African countries. Applicants had to submit a short CV, letter of motivation, abstract, as well as a letter of support from the supervisor. A panel composed of IUIS Education committee members and local organizers reviewed the applications and selected 48 students to attend the course.

It became apparent in April that we could not offer a face-to-face course in view of the global Covid-19 pandemic and the organizers chose to prepare an online course, in fact the first one for the IUIS Education committee. We started having online Zoom meetings and as a first step contacting all lecturers that had agreed to the face-to-face course. Fortunately, several agreed to teach online and we recruited others as well. We also asked all participants to join the online course and 39 accepted, with 36 completing it (23 women, 13 men). Seventeen students were from Algeria, 5 from Tunisia, 2 each from Morocco, Senegal, South Africa, Nigeria and Ghana, and one

each from Kenya, Sudan, Uganda and Zimbabwe. The regional representation of participants is shown in Figure 2.

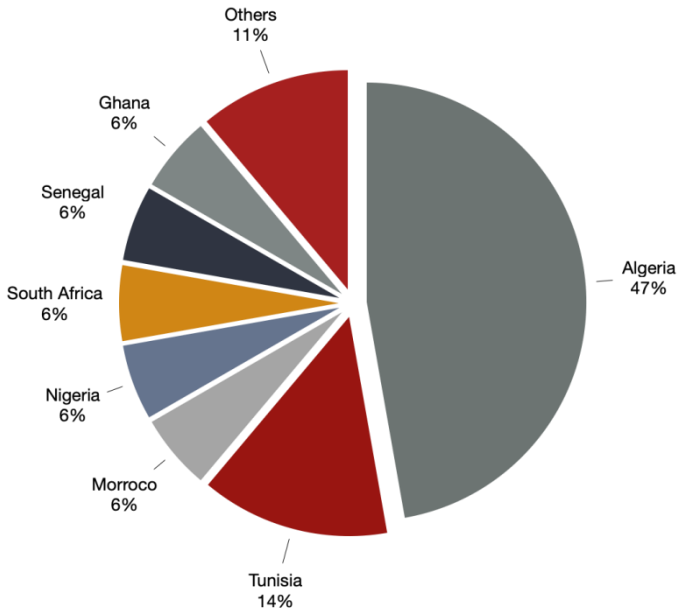

Figure 2: Immuno-Algeria 2020 course participants

The course was prepared within a very short time frame, the organizers faced many challenges to succeed, including the fact that the network in Africa is not always stable and that some participants might face technical issues. Discipline, time management and keeping students motivated were also a challenge.

We chose the Zoom platform and the Immunopaedia website where the team was already taking care of submissions, pre-course learning modules and the assembly of specific course modules. To ensure that all attendees had the immunological knowledge required for advanced content that was going to be discussed during the course, weekly immunology refresher sessions were provided through Immunopaedia during three weeks in May preceding the actual course. For the 2-weeks on-line course, we prepared a program that covered the first two weeks of June with 2-hour morning and afternoon sessions (see full program at the end of this report). The selected professor gave a 45-minute lecture followed by discussion. Then two student participants presented their work in 8-10 minutes and that was followed by a discussion. We had two sessions at the end of the course to complete the student presentations and also organized a round table discussion with several faculty members.

The last session summarized key issues and discussed the pros and cons of online courses and a potential future workshop. That session also included slide presentations on Algeria, music and singing, and display of national costumes by several participants.

Overall it was a successful event and the comments by participants were very positive although everyone still prefers live interactions between staff and participants in selected locations.

Inauguration and welcome address by the organizers

The inauguration of the pre-course started on the 11th of May by Prof. Clive Gray who presented IUIS and Prof. Dieter Kabelitz who introduced the Educational Committee. Prof. Clive Gray also spoke about the current situation and the challenges of this online course. This was followed by a short self-introduction by each participant. Weekly sessions during the three weeks pre-course were held to discuss multiple choice questions related to the topics of the previous week.

Summary of faculty presentations

The following is a collation of articles published on Immunopaedia that summarised 14 out of 16 lectures given during the course. Theses summaries were framed around the different themes covered during the course. These summaries were kindly written by the rapporteurs Sawsan Feki, Khaoula Attia, and Ikram Mezghiche. Video recording of the lectures and student presentations are also available on the Immunopaedia website:

- Online Lectures – Week 1
- Online Lectures – Week 2
- Student Presentations – Week 1
- Student Presentations – Week 2

Introduction to allergy and molecular diagnosis

Immunoglobulin E (IgE)-mediated allergy is the most common immune disorder, with a prevalence as high as 30% of the global population (depending on the allergy). Though allergy symptoms can be mild and manageable, symptoms can often be severe, disabling, and life-threatening.

Professor Rudolf Valenta (University of Vienna, Austria) began his talk (first lecture of the course) discussing important advances in diagnosis and therapy that have occurred in the field of Allergy during the last couple of years. He particularly focused on the importance of the component resolved diagnosis (CRD) as a new form of modern allergy diagnosis based on the molecular aspects of allergens.

After a brief introduction about the different clinical manifestations of allergy and the concept of "*allergy march in childhood*" (*progression from sensitisation to an allergen, which may cause disease and progress to severe disease)*, Prof Valenta reported on the traditional aspects of allergy diagnosis (patient history, IgE based blood tests, skin testing, etc.) and discussed mechanisms of allergic inflammation. He then demonstrated how molecular forms of diagnosis and specific

immunotherapy are currently revolutionising diagnosis and treatment of allergic patients and how allergen-specific approaches may be used for the preventive eradication of allergy.

Regarding allergens source and extract, Prof Valenta reported that the first allergen encoding cDNAs were isolated thirty years ago and this was considered as a revolution (at the time) in the characterisation of protein allergens through expression cDNA cloning. In the meantime, the structures of most of the allergens relevant for disease in humans have been solved. New insights have been gained regarding the process of sensitisation to allergens, allergen-specific secondary immune responses, and mechanisms underlying allergic inflammation.

The first demonstration that recombinant allergens can be used for *in vitro* diagnosis of allergy was published in 1991-1992. As a next step, recombinant allergens became available in a fully automated allergy test system (Immunocap) by 1999, leading to the invention of the recombinant allergen-based concept of component-resolved diagnostics (CRD) and immunotherapy (CRIT). The need to test multiple molecules simultaneously resulted in the birth of multiallergen tests (up to 100 allergens at the same time) using microarray technology by 2002.

Prof Valenta suggested that in the future, allergy diagnosis may change and rely on this microarray testing in blood as a first step and then the clinician could complete the anamnestic step in a more precise and relevant way based on blood test results.

Finally, the lecture ended with a discussion on the advantages of molecular allergy diagnosis, in fact, every allergen tells a story: *identification of the genuinely-sensitizing allergen source, understanding clinical cross reactivity, prediction of severity, accurate prescription and monitoring of specific immunotherapy…*

In the afternoon session, Prof Valenta presented on trends to the prediction and then prevention of allergic sensitisation and allergy disease in the future. Furthermore, he showed the basis and the interest of new forms of allergen-specific immunotherapy. Knowledge of the allergen sequence and structure provides information regarding the T cell epitopes presented by MHC molecules and IgE epitopes, and allows for the design of vaccines that target different immune mechanisms: administration of allergen-derived T cell peptides, B cell epitope-containing vaccines (i.e., peptide carrier vaccines).

Reference: Valenta *et al.,* 2018. Molecular Aspects of Allergens and Allergy. Advances in Immunology

Summary by Sawsan Feki

Cellular components of the allergic response

In this summary we highlight talks by **Mehrnaz Mesdaghi (Associate Professor at Shahid Beheshti University of Medical Sciences, Iran), Joana Vitte (Associate Professor & Clinician at Aix-Marseille University and Marseille University Hospitals, France)** and **Sabelo Hadebe (Lecturer at the University of Cape Town, South Africa)** which focused on cellular immunity during allergy.

Innate Immunity

A/Prof Mehrnaz Mesdaghi's talk focused on cellular components of the allergic response, specifically on the role of innate cells. She covered different aspects of allergy starting with the mechanisms of the allergic reaction, the role of mast cells, basophils and eosinophils during allergy, their origin, expression profiles as well as their subtypes.

Mast cells divided into two subtypes: (1) Connective Tissue and (2) Mucosal mast cells, play a huge role in innate immunity and pro-inflammatory responses and release effector molecules upon activation. Their role in allergic responses, is leveraged in the diagnosis of allergy where their fast-acting properties upon allergen exposure induces a local hypersensitivity reaction which is then used as the readout of the skin prick test.

Part of A/Prof Vitte's talk built on the mast cell introduction given by A/Prof Mesdaghi and focused on Mast Cell Activation Syndromes (MCAS). She described tryptase as an indicator of mast-cell activation in systemic anaphylaxis. Currently, there is only one *in vitro* diagnostic available on the market that measures total serum tryptase. She highlighted the symptoms and the diagnostic algorithm for MCAS and its importance, which were later simplified by European Competence Network on Mastocytosis. She stated that though histamine is one of the molecules most associated with the symptomatology of mast cell activation, it is a very delicate marker to detect *in vitro*. As a result, its use for potential diagnostics was almost completely abandoned and replaced by serum tryptase testing.

A/Prof Mesdaghi's also talked about basophils, the similarities and the differences with tissue mast cells, she highlighted their important role as initiators of chronic allergic inflammation and the fact that they are a major source of IL4. She also gave an example of the basophil activation test of a patient who is allergic to antibiotics. She then described the role of eosinophils, their cytokine and cell surface expression profile and types of granules and degranulation markers. *Did you know that eosinophils can also serve as antigen presenting cells because they present antigen on MHC class II molecules ?*

Adaptive Immunity

Dr Sabelo Hadebe's talk highlighted the importance of T cell responses in allergy and how each T helper cell phenotype contributes to asthma pathology. He began his talk discussing how the interaction between dendritic cells (DCs) and CD4 T cells leads to the development of T helper 2

(Th2) CD4 T cell responses (*instigators of allergic asthma*). One of the first cells, to be triggered by allergen are the epithelium cells and they are initiators of this allergic response. DCs present antigens to naive CD4 T cells, basophils can also present antigens to T cells and are considered a major source of IL-4. He then described the development of Th2 cells through induction a complex set of transcriptional factors, which commit CD4 T cells to the Th2 lineage. He then described the important role type 2 innate lymphoid cells (ILC2) in asthma. ILC2's in addition to producing IL-4, IL-13 and other Th2 cytokines, they also have the capacity to present allergens to CD4 T cells. He talked about the role of Th17 cells in asthma and presented studies that describe how these cells can also produce IL-4. Further, he highlighted other studies that provide evidence for the contribution of Th1 cells to severe asthma. Currently, many therapeutic antibodies used for asthma therapy target Th2 and Th17 cells.

Dr Hadebe ended his presentation by explaining the function of regulatory T cells in asthma and how they are generated. Early dysfunction of T regs, active tolerance and allergen ignorance are all mechanisms of T regs suppression in asthma.

References:

- Weller & Spencer 2017. Functions of tissue-resident eosinophils. Nat Rev Immunol.
- Persson & Uller 2013. Primary lysis of eosinophils as a major mode of activation of eosinophils in human diseased tissues. Nat Rev Immunol.
- Valent *et al.,* 2019. Proposed Diagnostic Algorithm for Patients with Suspected Mast Cell Activation Syndrome. J Allergy Clin Immunol Pract.
- Arock *et al.,* 2020. New developments in the field of mastocytosis and mast cell activation syndromes: a summary of the Annual Meeting of the European Competence Network on Mastocytosis (ECNM) 2019. Leuk Lymphoma.
- Weiler *et al.,* 2019. AAAAI Mast Cell Disorders Committee Work Group Report: Mast cell activation syndrome (MCAS) diagnosis and management. J Allergy Clin Immunol.
- Hadebe *et al.,* 2018. C-Type Lectin Receptors in Asthma. Front Immunol.
- Walker &McKenzie 2018. T_H2 cell development and function. Nat Rev Immunol.
- Bacher & Scheffold A 2018. The effect of regulatory T cells on tolerance to airborne allergens and allergen immunotherapy. J Allergy Clin Immunol.
- Lambrecht *et al.,* 2019. The Cytokines of Asthma. Immunity.
- Zakeri & Russo 2018 Dual Role of Toll-like Receptors in Human and Experimental Asthma Models. Front Immunol.

Summary by Khaoula Attia

IgE & its receptors as a pharmacological targets

This summary highlights a talk by Professor Ulrich Blank (INSERM, Paris, France) entitled "**IgE and its affinity IgE receptor as a pharmacological target**". In the first part of his presentation, Professor Ulrich gave a general overview of IgE and its high-affinity receptor in the context of type I hypersensitivity reactions. He then described the different therapeutic strategies developed (or under development) that target IgE and its receptor interactions to treat hypersensitivity. He explained that the simplest and most direct therapeutic strategy was to block the binding of the IgE with its receptor. For that purpose, a humanized monoclonal antibody (mAb) was developed by Novartis in 2003 "*Omalizumab*", that targets IgE (anti-IgE antibody) and was designed to inhibit the interaction between IgE and its receptor. Currently, Omalizumab is only used to treat severe cases of allergies. The expensive cost and the very strict protocol for patients' selection are some of the major limiting factors that prevent its widespread use. Follow up products of Omalizumab are currently under development by Novartis, one of which is Ligulizumab (QGE031) with an 80 fold higher affinity than Omalizumab.

An alternative to humanized antibodies is vaccination; this strategy is based on the immunization of patients with parts of the IgE antibody that binds to the specific receptor (Cε3). This vaccination strategy aims to induce a humoral immune response (anti-IgE antibodies). Pre-clinical vaccines studies on monkeys have been conducted, and results seem interesting so far, with IgE levels in monkeys serum dropping by 50% after injection with IgE-Ce3 peptides. The current challenge with anti-allergenic vaccination is inducing a robust and durable immune response specific for self-antigens.

Another alternative strategy and potentially much cheaper would be the design of small molecular weight chemical inhibitors of the IgE allergic response. There are different therapeutic strategies possible such as inhibitors that target either the free serum IgE or the bind IgE on the cell surface. Genentech in particular is working on this approach.

Last but not least, another alternative would be inhibitors that interact with cell signalling of the high affinity IgE cell receptor that leads to the effector cell degranulation. Potential problems may be the specificity the IgE receptor shares with many signalling enzymes and other cell receptors. Another challenge is that chronic allergic inflammation involves activation of many other cells and receptors. This implies that this therapeutic strategy may be very feasible, only if we can achieve a high specificity of action with the minimal secondary effects possible.

Summary by Ikram Mezghiche

Allergic activity of IgE binding molecules

Professor Luis Caraballo gave a talk on "**The experimental strategies to evaluate the allergenic activity of IgE-binding molecules."** Allergens are characterized by two important properties; the first being the allergenicity and the second being the allergenic activity. The later represents the capacity of an allergen to induce allergic inflammation, a process that can be dependent or independent of IgE activity. As a result, the IgE binding property of an allergen only evaluates a part of the allergenic activity and must be considered as an initial step in studying the allergenic properties.

Professor Caraballo insisted that the traditional way of thinking of an allergy response focused only on the frequency of IgE antibody binding, which was a limited perspective that restricted the scope of allergy research for a long time. In fact, the characterisation of clinically relevant allergens only starts with detecting IgE antibody binding capacity. However, more properties that can influence the whole spectrum of allergenic activity, and these properties are critical to selecting individual allergens for component-based immunotherapy and preventive vaccines.

Despite the large number of discovered and registered allergens, we have a limited understanding of the allergenic activity and clinical importance for most of them. For instance, the allergenic activity of most indoor IgE antibody binding components has not been investigated, despite the major advances in the field of allergology over the last 20 years, specifically in component-resolved diagnostics and immunotherapy. Some of the experimental protocols researchers used to determine the allergenic activity and clinical relevance of IgE antibody binding molecules include (but not limited to):

- the intrinsic proinflammatory mechanism of action
- provocation tests (*in vivo* or *in vitro*)
- animal models of experimental allergy
- Human case-control studies or avoidance studies, and immunotherapy trials.

In summary, the allergenic activity and clinical relevance have so far only been studied for few allergens. Identification of the clinical relevance of allergens will be an important step towards the engineering of innovative molecular allergy vaccines.

Reference: Caraballo *et al. ,* 2020. The allergenic activity and clinical impact of individual IgE-antibody binding molecules from indoor allergen sources. World Allergy Organization Journal

Summary by Ikram Mezghiche

Microbial dysfunction and allergy

Yasmine Belkaid (adjunct professor at the University of Pennsylvania and NIH Distinguished Investigator in Mucosal Immunology Section) gave a lecture about the control of immunity and allergy by Microbiota.

She first talked about the role of the immune system and that its dysfunction leads to many diseases including allergies. Humans have co-evolved with microbiota, and we are a composite of not only bacteria but fungi, viruses and many other microbes. The microbiota is responsible for controlling host physiology including metabolism, and the change of microbiota composition due to lifestyle, infections, age, genetics…etc. can influence behaviour and cognitive function.

She then mentioned the most important features of microbiota and mechanisms by which they can promote, control the development and function of the immune system. The quality of haematopoiesis is also related to the quality of microbiota. She described a study which isolated skin microbes, sequenced them and then associated microbial profile with the pathologies of the skin, this study detected immune signatures associated with homeostasis and disease.

She also highlighted the role of microbiota in allergies and gave the example of atopic dermatitis. She described how data from skin microbiome sequencing in association with immune signature from homeostasis and disease models can be used to identify microbes associated with disease. *S.aureus* for example can sometimes become pathogenic and cause severe atopic dermatitis when patients are mono-colonised by inducing Th2 and Th17 responses.

She ended her lecture by discussing the relationship between early life microbiota and allergic responses. Maternal factors and postnatal factors affect the composition and quality of microbes, overuse of antibodies could create a massive dysregulation of microbiota leading to allergic and inflammatory disorders.

References:

- Belkaid & Segre 2014. Dialogue between skin microbiota and immunity. Science.
- Chen *et al.,* 2018. Skin microbiota–host interactions. Nature
- Collins & Belkaid 2018. Do the Microbiota Influence Vaccines and Protective Immunity to Pathogens? Engaging Our Endogenous Adjuvants. Cold Spring Harb Perspect Biol.
- Durack & Lynch 2019. The gut microbiome: Relationships with disease and opportunities for therapy. JEM

Summary by Khaoula Attia

Non-invasive allergy biomarkers & next-gen immunotherapies

This summary highlights lectures by Professors Carsten Schmidt-Weber and Claude Lambert that discussed **non-invasive methods to diagnose and monitor allergy response**, and a lecture by Professor **Rudolph Valenta** on "**Next generation of allergen-specific immunotherapies: molecular approaches**".

After a brief historical introduction, Prof Schmidt-Weber (Germany) started his lecture by reporting on the need for markers of endotyping (underlying pathobiological mechanism), disease prediction and therapy monitoring in the field of allergic diseases.

Endotyping is essential for medical practice, as it enables in-depth characterisation of pathobiological mechanisms associated with clinical symptoms . For example, transcriptomic analysis of skin biopsies from people with different skin diseases (e.g. eczema, psoriasis) allows the identification of molecules that are differentially expressed depending on the disease. Combining transcriptomic analysis with clinical data/phenotypes could inform the identification of potential biomarkers of a certain clinical presentation. Prof Schmidt-Weber gave an example of endotyping between eczema and psoriasis which identified High iNOS and low CCL27 as a potential classifier for psoriasis which was superior to clinical presentation alone.

For disease prediction, Prof Schmidt-Weber gave the example of airway allergy, where there is a need for non-invasive markers to improve diagnosis at an early stage (early intervention → chance for cure) and in chronic disease (endotyping→ targeted therapy). This has led to the creation of the ADAPT Consortium to combine biomarkers and clinical findings into a single risk score (ADAPT Algorithm→prevention).

Another area of allergy where non-invasive markers are needed is during early life. In this part of his lecture, Prof Schmidt-Weber highlighted the difficulties associated with the molecular characterisation of different asthma phenotypes in childhood (in comparison with adulthood). Additionally, challenges in the identification of predictors for persistent asthma and transient wheeze, respectively. Regarding airways secretions, he demonstrated that analysis of molecules secreted by epithelial cells in nasal samples seems to be more reliable than markers from infiltrating cells. He gave the example of experimental biomarkers in nasal secretions for diagnosis of allergic rhinitis, which performs locally much better than systemically. Thus, demonstrating that local analysis dynamics are in general more powerful than systemic assessment. He also gave an overview of the studied nasal biomarkers from different sources (epithelial cells, infiltrating cells and both) during asthma.

Finally, he ended his talk by describing numerous non-invasive/ minimally-invasive biomarker candidates (from serum, micro biopsies, exhalates, secretions, excretions) which have been suggested and tested for primary prevention, differential diagnosis, endotyping and secondary prevention of allergic and non-allergic diseases.

Prof Claude Lambert (University of Saint Etienne, France) presented an interesting lecture on **T cell analysis in hypersensitivity**. He began his talks with a brief introduction of type I and IV hypersensitivity mechanisms, the role of the cytokine imbalance in the pathogenesis of the delayed type of hypersensitivity and by extension the role of T cell subsets in these reactions.
Prof Lambert discussed how flow cytometry could be used to monitor T cells in allergy diseases, specifically :

- T cell maturity: naive, central memory, effector memory and terminally differentiated effector cells
- Tissue homing (chemokine receptors)
- Functional polarisation and activity following non-specific (PHA, PMA/ionomycin) or a specific (antigen e.g. allergen peptides) stimulation.

He then emphasised the importance of quality assurance when performing flow cytometry assays as it may negatively affect analysis. He also gave a hands-on (online) practical example of flow cytometry analysis using a specialised flow cytometric software.
His second lecture focused on the use of flow cytometry to investigate immediate hypersensitivity. He began the lecture by using clinical cases of urticaria and quick oedema to explain the mechanisms of type I hypersensitivity. He specifically focused on the structure, activation and degranulation of the two main cells involved in this type of reaction: basophils and mast cells. In this summary, we shall focus on the use of the basophil activation test (BAT), a functional *ex vivo* test to investigate type I hypersensitivity. Basophils were first identified as **circulating IgE+ cells**, and determination of activated basophils by flow cytometry was first described with CD63. Now alternative basophil markers have been identified such as **CD203c (basophil-specific ectoenzyme E-NPP3)**, basophil lineage specific marker, which in combination with IgE identified activated basophils. Other described basophil markers include: **CD123+HLADR-**, **CRTH2+CD3-**, **CCR3+CD45+**, CCR3+CD3-, among others. *What is the clinical utility of the test?* He explained the basic principle of the test (*sampling, allergen stimulation, labelling, flow cytometric analysis using identification and activation markers of basophils*) and the possible technical issues when performing it (*controls, gating strategy, interpretation etc.*). BAT is a multifaceted and promising tool for the allergologist, who can use it to :

- Diagnose patients with food, insect venom, and drug allergies.
- Monitor patients on allergen immunotherapy,
- Monitor Anti-IgE treatment
- Study the natural resolution of allergy.

However, the proper performance of the BAT test requires special attention, which to many could be challenging due the technical expertise required.

Professor **Rudolph Valenta** began the talk by highlighting the importance of molecular diagnosis in providing specific and personalised allergenic immunotherapy (AIT) for patients. Molecular allergy diagnosis has revolutionised the identification of causal allergens in multi-sensitized patients, which eventually leads to a better targeted vaccination. Specific diagnosis also leads to targeted

treatment and favourable patient outcomes. He also highlighted the importance of molecular allergy in monitoring the efficiency of treatments in patients. One way to monitor immunotherapy is to measure specific IgE levels using microarrays. Current vaccination in allergic patients is accompanied with a decrease in specific allergen IgE levels and an increase in IgG1 and IgG4 levels.

The future perspectives of molecular diagnosis aim to:

- Diagnosis individuals earlier in life and facilitate prophylactic treatment
- Predict the development of allergy by detecting IgE in sensitised but asymptomatic children
- Predict genetic susceptibility for allergen-specific IgE sensitisation in not yet sensitized children

The elucidation of the molecular structures of the allergens and the determination of IgE and T cell epitopes recognized by allergic patients facilitate the design of vaccines that target different immune mechanisms. Some of the novel strategies being investigated are synthetic peptides targeting allergen-specific T cells, recombinant hypoallergenic allergen derivatives, and recombinant peptide carrier-based vaccines. These new strategies are under clinical trials and aim to decrease the number of injections of allergens in patients. Beside therapeutic vaccination, the trend now is to develop prophylactic vaccination: a personalized therapy, administered after the early identification of sensitization profiles in children, and will hopefully be available a decade from now.

References:

- Baumann et al., 2013. Nasal levels of soluble IL-33R ST2 and IL-16 in allergic rhinitis : inverse correlation trends with disease severity. Clin Exp Allergy.
- Quaranta *et al.,* 2014 Intraindividual genome expression analysis reveals a specific molecular signature of psoriasis and eczema. Sci Transl Med.
- Valenta *et al.,* 2018. Chapter Five – Molecular Aspects of Allergens and Allergy. Advances in Immunology
- Zissler et al., 2016. Current and future biomarkers in allergic asthma. Allergy

Summary by Sawsan Feki & Mezghiche Ikram

Drug hypersensitivity - a focus on TB/HIV endemic settings

Prof. Peter began his talk with a basic overview of drug hypersensitivity and the immunological mechanisms associated with these conditions. Followed by an overview of the TB/HIV burden in SA and finally with inspiring and intriguing questions and gaps that we still need to address in the future.
It is important to note that the immunological mechanisms behind immune-mediated adverse drug reactions (IM-ADR) are still to be investigated. Although we know today that most of drug reactions are due to the pharmacological properties of the drug, an IM-ADR occurs in 20% of cases and should not be neglected. These reactions might be both antibody and/or T cell-mediated.

In Africa, the most common drug hypersensitivity reaction (DHR) inducing drugs are anti-microbial drugs prescribed in the context of TB (such as rifampicin or isoniazid)and HIV (anti-retroviral (ARV) drugs). Reactions can be very diverse and include different phenotypes with varying severity levels. It is of major importance to have tools that permit the prediction of a DHR before drug administration. Human leukocyte antigen (HLA) risk alleles have a very good negative predictive value for DHR, and thus may be used as a preventive measure. An example of which is HLA-B*57:01 genotyping in patients in order to prevent hypersensitivity towards abacavir (HIV ARV). Other interesting risk alleles are drug metabolism genes such as cytochromes or also t cell receptor encoding genes, specifically the genes encoding the hypervariable region CDR3 which is the most implicated in drug recognition.

Summary by Ikram Mezghiche

IMMUNO-ALGERIA 2020: Program of the online course

	PROGRAM of On-line Sessions			
WEEK 1	**Morning: 9-11am**	**Moderators**	**Afternoon: 2-4pm**	**Moderators**
1st June	Zoom review of week 3; followed by Introduction to allergy and molecular diagnosis, pre-recorded lecture by **Rudi Valenta**	Clive Gray	Discussion with **Rudi Valenta**	Dieter Kabelitz
2nd June	Cellular Components of the allergic response: **Mehrnaz Mesdaghi**	Kamel Djenouhat	Role of T cell responses in allergy: **Sabelo Hadebe**	Dieter Kabelitz
3rd June	IgE and its high affinity receptor as pharmacological target: **Ulrich Blank**	Ridha Barbouche	IgE response: links between allergens and helminth infections: **Luis Caraballo**	Michelle Letarte
4th June	Tryptase and histamine in anaphylaxis and (MCAS) Mast Cell Activation Syndromes: **Joana Vitte**	Kamel Djenouhat	Next-generation of allergen-specific immunotherapies: molecular approaches (pre-recorded + discussion): **Rudi Valenta**	Michelle Letarte
5th June	Non-invasive biomarkers for allergy: **Carsten Schmidt-Weber**	Dieter Kabelitz	Experimental strategies to evaluate the allergenic activity of IgE-binding molecules: **Luis R Caraballo**	Michelle Letarte
WEEK 2				
8th June	Drug hypersensitivity - a focus on TB/HIV endemic settings: **Jonny Peter**	Clive Gray	Control of immunity and allergy by Microbiota: **Yasmine Belkaid**	Dieter Kabelitz
9th June	Molecular dissection of immunological defects underlying Hyper-IgE syndrome: **Ridha Barbouche**	Kamel Djenouhat	Bradykinin angioedema: An example of differential diagnosis of allergy: **Kamel Djenouhat**	Ridha Barbouche
10th June	Flow cytometry in allergy diagnosis. (Session 1): **Claude Lambert**	Dieter Kabelitz	Flow cytometry in allergy diagnosis. (Session 2): **Claude Lambert**	Michelle Letarte
11th June	Current and future perspective on adjuvants for allergen immunotherapy: **Carsten Schmidt-Weber**	Clive Gray	Round Table Discussion with Faculty (Hadebe, Valenta, Blank, Mesdaghi, Schmidt-Weber, Djenouhat) and students	Winfried Pickl
12th June			General Discussion and Feedback: Organisers and students	Michelle Letarte

Course Pictures: Impressions of faculty and participants