BASEL LIFE

12th of September 2019
Congress Center Basel, Switzerland
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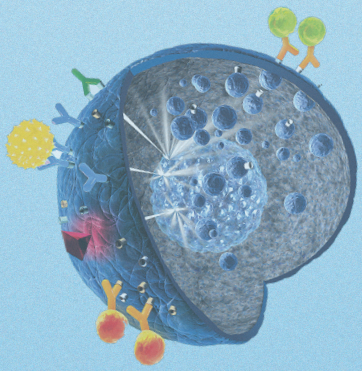
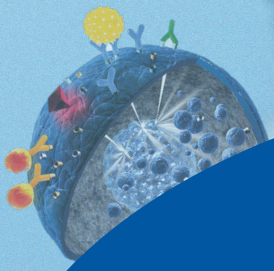
Innovation Forum

CELLULAR ALLERGY





BÜHLMANN

Cellular Allergy Forum

Dear colleagues and guests,

It is our great pleasure to welcome you to this Cellular Allergy Innovation Forum. We are very pleased to present an exceptional programme of outstanding speakers from science, medicine and industry.

Allergic reactions are common phenomena during which the immune system overreacts to typically harmless substances from the environment. These hypersensitivities are mostly mediated by IgE antibodies that recognize the allergen and then trigger a cellular reaction that may lead to a severe and possibly lethal anaphylactic shock. Today we will hear about cutting-edge research on cellular allergy and its implication in immunotherapy together with novel *in vitro* approaches in allergy diagnostics and therapy monitoring. The transition from *in vivo* oral food challenges or skin-prick tests to *in vitro* assays based on basophil activation as well as expected FDA clearances of oral immunotherapies are current game changers in allergy diagnostics and treatment. Additionally, the role of IgE directed immunotherapy (Ligelizumab, Omalizumab, Xolair®) will be discussed. Concomitant monitoring of therapy success with *ex vivo* challenges is expected to alleviate the burden on allergy patients significantly. The basophil activation test provokes a patient-specific allergic reaction in a test tube mediated by PI3 like kinase signaling of blood cells. This potentially allows Bruton's kinase inhibitors, such as Ibrutinib (IMBRUVICA®) to be used not only as treatment for various lymphoma and leukemia, but possibly also for allergy. Therefore, the innovation forum also aims to present novel discoveries in cellular allergy signalling and their importance for novel treatments of allergy.

We wish you all an interesting and inspiring forum.

Kind regards,

Dr. Christian B. Gerhold and Dr. Michael A. Gerspach

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PD Dr. Alexander Eggel

University Hospital Bern, Switzerland

Cellular allergy and novel therapy approaches

Allergen-specific immunoglobuline E (IgE) plays a major role in the manifestation of immediate hypersensitivity reactions and is mainly produced by isotype switched plasma B-cells. It binds to the FcεRI receptor, which is present on allergic effector cells such as basophils and mast cells. Exposure to the cognate allergen mediates the degranulation of these IgE-loaded effector cells resulting in the release of soluble mediators that cause allergic symptoms. Different therapeutic approaches to treat allergic symptoms involve anti-IgE antibodies, a novel class of disruptive anti-IgE inhibitors or the suppression of allergen-induced cell activation by targeting inhibitory receptors on allergic effector cells. You will hear more about the different therapeutic approaches targeting IgE-mediated allergic reactions in Dr. Eggel's talk.

Dr. Wayne Shreffler

Massachusetts General Hospital, Boston, USA

Recent breakthroughs in immunotherapy of allergy

Food allergy can resolve over time periods of a few years, demonstrating that IgE memory can be dynamic. We hypothesize that the development and maintenance of adaptive immunity that results in high affinity IgE and clinical immediate hypersensitivity is regulated by multiple checkpoints. Data from immune profiling of patients with varying clinical sensitivity or in respect to outcomes of immunotherapy will be presented to support this hypothesis. The goal of Dr. Shreffler's team is to better define these checkpoints so that they may become useful therapeutic targets for treatment and prevention of food allergies.

Dr. Christoph Heusser

Novartis Basel, Switzerland

Molecular and functional differences of anti-IgE antibodies ligelizumab and omalizumab

Omalizumab (also known under the name Xolair®) is a therapeutic anti-IgE antibody that is capable of preventing allergic asthma symptoms and inhibiting chronic spontaneous urticaria (CSU). A novel anti-IgE antibody, ligelizumab, shows a 50-100 fold higher affinity for IgE and epitope mapping of both anti-IgE antibodies reveal distinct mode of actions in terms of receptor binding that explain why ligelizumab is highly effective in inhibiting mast cell dependent responses (e.g. skin prick test and CSU), whereas omalizumab is more effective in preventing exacerbations in allergic asthma patients. Dr. Heusser will share his insights on how thorough characterization of these therapeutic antibodies help to improve the outcome of allergic diseases for patients.

Dr. Alexandra Santos

King`s College London, United Kingdom

Novel approaches for allergy diagnosis and immunotherapy monitoring

The oral food challenge (OFC) remains the gold-standard for diagnosing food allergy whereby the allergen is ingested in a medically supervised environment in hospital. This method carries the risk for patients to develop allergic reactions, that are potentially severe. New diagnostic tests such as the basophil activation test (BAT) and the mast cell activation test (MAT) emerged and allow to monitor the response of basophils and mast cells to distinct allergens *in vitro*. These tests are flow-cytometry based with very high specificity to diagnose food allergy and may allow to identify patients at risk of severe allergic reactions preventing serious adverse reactions during OFC. Moreover, BAT and MAT can be useful to monitor the clinical response to immunomodulatory treatments for food allergy. Learn more about current applications of these tests in Dr. Santos`s talk.

Prof. Dr. Jean-Philippe Girard

IPBS Toulouse, France

How allergens become allergic - the role of the alarmin cytokine IL-33 in allergen sensing

Allergic inflammation is central to causing allergic diseases such as asthma. IL-33, a tissue-derived nuclear cytokine, was found to play a crucial role in the rapid and efficient induction of allergic type-2 responses. Prof. Dr. Girard's research group was able to identify that many allergens contain proteases that cleave full-length IL-33 to mature forms eliciting the activation of group 2 innate lymphoid cells via the IL-33/ST2 signalling axis. The capacity of IL-33 to sense the proteolytic activity of a large variety of environmental allergens may explain the critical role of this unique cytokine in asthma susceptibility.

Prof. Dr. Matthias Wymann

University of Basel, Switzerland

Orchestrating signalling in allergic inflammation

Allergic (type I hypersensitivity) reactions are initiated by IgE-allergen complexes that bind to the high affinity IgE receptor, FcεRI. The clustering of FcεRI triggers a protein tyrosine cascade that leads to the phosphorylation of adapter proteins, which provide docking sites for phosphoinositide 3-kinase (PI3K). For activation, the catalytic subunit of PI3Kγ (p110γ, must be bound to an adapter subunit, which is either p84 or p101. Prof. Dr. Wymann's group has shown that the p84-p110γ complex promotes mast cell degranulation, while p101-p110γ does not. Therefore, selective targeting of PI3Kγ adapter complexes could provide attenuation of anaphylaxis without an impairment of host defence mechanisms. Highly specific PI3Kγ inhibitors have been developed and genetic models to explore non-redundant p84 or p101 function in allergy, inflammation and obesity have been established.

Dr. Augustin Amour

GSK, Stevenage, United Kingdom

PI3K signalling in allergic asthma

The lipid kinase phosphoinositide 3-kinase delta (PI3Kδ) plays a key role in immune receptor signalling that mediates the activation, proliferation and recruitment of cells associated with antigen-driven inflammation. Therefore, PI3Kδ is a promising therapeutic target for respiratory diseases such as allergic asthma. Dr. Amour is involved in the development of selective inhibitors that show promising effects on allergic effector cells derived from asthmatic patients as well as in murine models of allergen-induced airway inflammation. Based on the *in vitro* and *in vivo* data, a clinical trial of an inhaled PI3Kδ-inhibitor was conducted in steroid naïve asthmatic patients, which provides informative data on the application of PI3K modulators in asthma.

Prof. Dr. Bruce Bochner

Northwestern Medicine, Chicago, USA

Use of BTK inhibitors to prevent cellular and clinical allergic responses

Bruton's tyrosine kinase (BTK) is involved in FcεRI-dependent activation of mast cells and basophils in allergic reactions. As BTK inhibitors such as ibrutinib and acalbrutinib are presently used in treating lymphoma or chronic lymphatic leukemia (CLL) patients, Prof. Dr. Bruce Bochner's group was interested whether these small molecule inhibitors are also potent at blocking allergic reactions. Murine studies showed that pretreatment with BTK inhibitors are capable of preventing a fatal anaphylactic shock. These results are corroborated in human studies by significant reduction of wheal and flare areas in skin-prick tests and the abolishment of basophil activation in a BAT upon BTK inhibitor treatment, suggesting that these oral pharmacological agents may allow to dampen or even eliminate allergic reactivity in humans.

Notes

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Chairs

Dr. Michael A. Gerspach (BÜHLMANN Laboratories AG, Switzerland)
Dr. Christian B. Gerhold (BÜHLMANN Laboratories AG, Switzerland)

Part 1: Novel strategies for allergy treatment and monitoring

09.00 Introduction

09.15 Cellular allergy and novel therapy approaches
PD. Dr. Alexander Eggel (University Hospital Bern, Switzerland)

09.45 Recent breakthroughs in immunotherapy of allergy
Dr. Wayne Shreffler (Massachusetts General Hospital, Boston, USA)

10.15 Break

10.45 Molecular and functional differences of anti-IgE antibodies ligelizumab and omalizumab
Dr. Christoph Heusser (Novartis Basel, Switzerland)

11.15 Novel approaches for allergy diagnosis and immunotherapy monitoring
Dr. Alexandra Santos (King's College London, United Kingdom)

11.45 Break

Part 2: Cellular signalling in allergy and beyond

12.00 How allergens become allergic – the role of the alarmin cytokine IL-33 in allergen sensing
Prof. Dr. Jean-Phillipe Girard (IPBS Toulouse, France)

12.30 Orchestrating signalling in allergic inflammation
Prof. Dr. Matthias Wymann (University of Basel, Switzerland)

13.00 Lunch Break & Industry Symposia

14.30 PI3K signalling in allergic asthma
Dr. Augustin Amour (GSK, Stevenage, United Kingdom)

15.00 Use of BTK inhibitors to prevent cellular and clinical allergic responses
Prof. Dr. Bruce Bochner (Northwestern Medicine, Chicago, USA)

The programme indicated maybe subject to change!
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