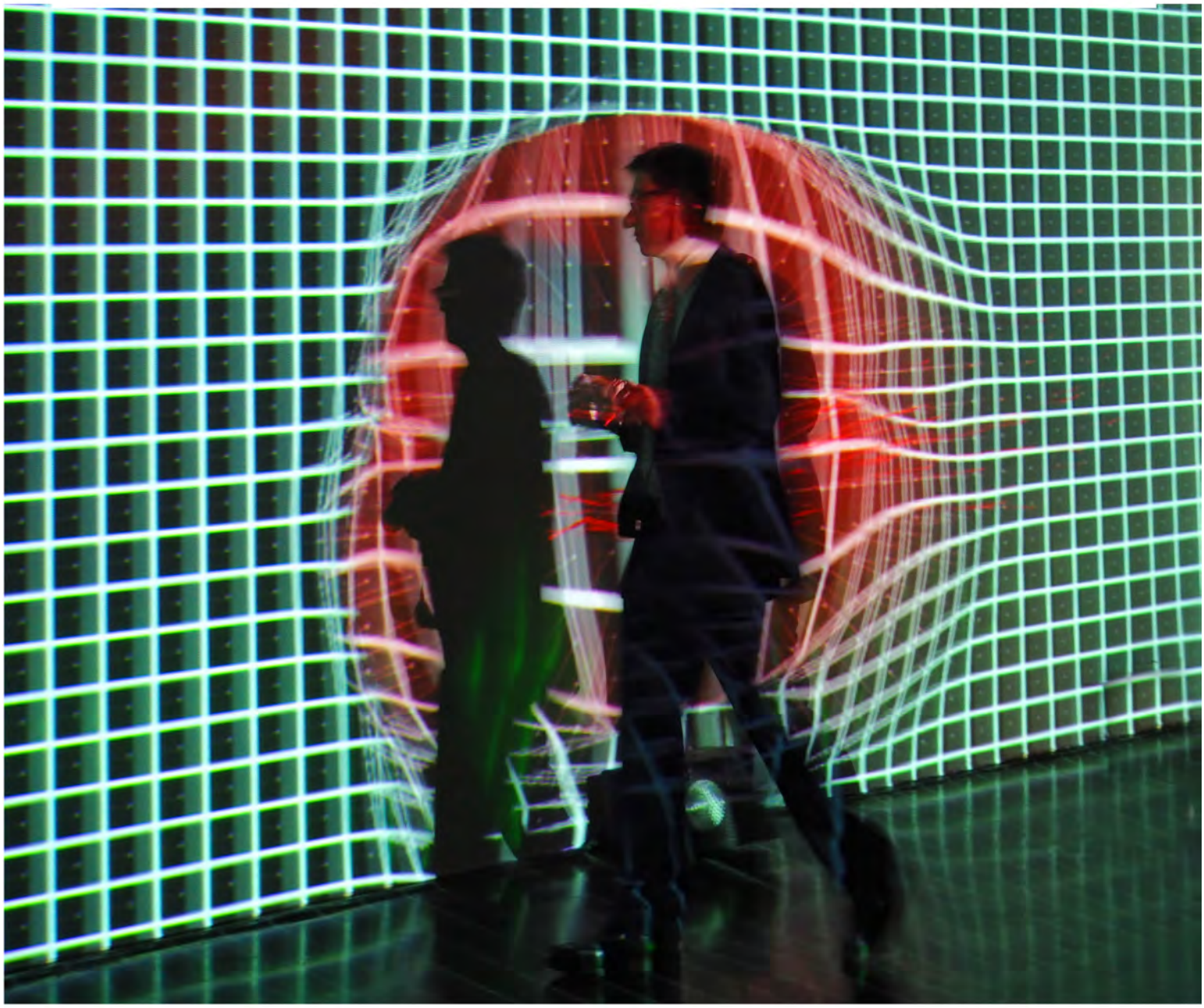
Next Generation ÖGAIng



Schutzhaus zur Zukunft
November 12, 2018

Österreichische Gesellschaft für
Allergologie und Immunologie
Austrian Society for Allergology and Immunology

WELCOME

Dear ÖGAI members,

on behalf of the Austrian Society for Allergology and Immunology and the Local Organizing committee, I cordially welcome you to

NEXT GENERATION ÖGAIng

an experiment with new presentation formats for sharing scientific ideas!

As in many other fields, also in science, “time is money”! Thus, you will ever and anon have to present your results succinctly and more importantly, understandable for the general public. Therefore, we sought for new presentation formats different from the conventional poster and oral presentations which in particular allow the presenters to give an overview on their projects without focusing on experimental details.

So, at this meeting 40 abstracts have been selected for presentation either as a KISS (keep it short and simple) video or in a scientific interview with Edward Knol from the Medical Center Utrecht in the Netherlands.

Furthermore, you will be introduced to the scientific achievements as well as to the awardees of this year´s Clemens von Pirquet Award, the Ursula und Fritz Melchers and the ÖGAI Thesis prizes. On occasion of receiving the „Österreichisches Ehrenkreuz für Wissenschaft und Kunst erster Klasse“ Hannes Stockinger, who is an active ÖGAI member for many years, will give an overview on his scientific achievements.

We hope that Next Generation ÖGAIng will combine innovation, flexibility and creativity to promote the scientific interaction among ÖGAI members in a comfortable atmosphere!

Looking very much forward to an interesting day and exciting outcomes of this experiment!

Barbara Bohle
President of the Austrian Society for Allergology and Immunology
(For the Local Organizing Committee)

ÖGAI MISSION STATEMENT

The Austrian Society for Allergology and Immunology represents Austrian scientists and practitioners interested in the physiology and pathophysiology of the immune response as well as the phenotypic expression, diagnosis and therapy of all diseases involving the immune system.

The principal aims of ÖGAI are to

- foster the understanding of the functioning of the immune system in general as well as the consequences of its aberrations.
- reduce the burden of immunologically-mediated diseases on the individual and also the society, and
- advance the treatment and prevention of these disorders.

Hence, ÖGAI promotes basic and applied research advances and their translation into the clinical practice.

ÖGAI supports excellence in education and training in the fields of allergology and immunology and further provides and also encourages the spread of specific information on the vital importance of the immune system and its disorders, such as allergy, autoimmunity, immunodeficiencies, to the lay, legal and professional public.

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PUBLIC AFFAIRS

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The Austrian Medical Chamber has accredited this meeting with 6 DFP credits (6 Diplomfortbildungspunkte).

VENUE

1150 Vienna, Auf der Schmelz, Verlängerte Guntherstrasse Schutzhaus zur Zukunft

Public transportation

Subway: U3 Station „Johnstraße“
Bus: No. 10a Station „Auf der Schmelz“,
No. 12a Station „Auf der Schmelz“
Tram: No. 9 Station „Guntherstraße“

By car

Stutterheimstraße, Ecke Guntherstraße

Please take care, that neighbouring streets of the Schutzhaus are Limited Parking Zone for 2 hours from 9 a.m. till 10 p.m. Other streets in the 15th district are limited to 3 hours from 9 a.m. till 7 p.m.

You can enter the area from: Gablenzgasse, Stutterheimstraße, Oeverseestraße, Auf der Schmelz

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12:00-13:00	Abstract presentations as KISS Videos
13:00-14:00	***Lunch***
14:00-15:30	ÖGAI-Award Lecture
15:30-17:00	World Cafe in Veranda
17:00-17:30	***Coffee Break***
17:30-18:30	Science Interviews – part 2
18:30-19:00	Presentation and Résumé of World Cafe Results
19:00	Networking evening and awarding of the best presentations

11:00-12:00 Science interviews – part 1

Moderator: Edward Knol

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11:12	Artinger, K.	Co-stimulatory signalling *via* TNF family members CD30 and OX40 promotes disease activity in nephrotoxic serumnephritis
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12:06	Gerner, M.	ROS-induced autophagy regulates CD39 expression on human regulatory T-cells
12:09	Gorris, A.	Caesarean section delivery and the risk of allergic disorders in childhood
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12:45	Shadan Ghandizadeh	ISAC112 allergen microarray, clusters of cross reactivity and clinical history in a retrospective cohort study
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12:51	Üzülmez, Ö.	Transient expression of the major birch pollen allergen Bet v 1 in the tobacco Nicotiana benthamiana using in planta assembled TMV-based provectors
12:54	Villazala-Merino, S.	Bet v 1 oligomer complexed with specific IgE is more efficient in inducing specific T cell activation via CD23-mediated FAP than its monomeric counterpart
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13:00 – 14:00 Lunch

14:00-15:30 ÖGAI-Award Lecture

14:00-14:20 Clemens von Pirquet Prize
K. Niespodziana "PreDicta chip-based high resolution diagnosis of rhinovirus-induced wheeze"

14:20-14:40 Ursula und Fritz Melchers Thesis Prize
L. Aglas "Intrinsic properties of the Bet v 1 fold: impact on immunogenicity and allergenicity"

14:40-15:00 ÖGAI Thesis Prize
L. Pangrazzi "Immunological memory in the bone marrow in old age"

15:00-15:30 Hannes Stockinger „*What next?*"
On the occasion of receiving the Österreichisches Ehrenkreuz für Wissenschaft und Kunst erster Klasse

15:30-17:00 World Cafe in Veranda

17:00-17:30 Coffee Break

17:30-18:30 Science interviews – part 2

Moderator: Edward Knol

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17:42	Sanchez Acosta, G.	Induction of protective blocking antibodies for the birch pollen-related apple allergy
17:48	Schmalz, S.	Exploring the conformational IgE epitopes of the major birch pollen allergen, Bet v 1, by structure based epitope grafting
17:54	Smole, U.	FPR2 controls ILC2 functions in allergic airway inflammation
18:00	Stolz, V.	Molecular and cellular analysis of the nuclear receptor co-repressor 1 (NCOR1) in T follicular helper cells
18:06	Strobl, J.	Low-input RNA sequencing reveals survival program of human skin-resident T cells during complete myeloablation
18:12	Tauber, P.	Stimulation of IL-2 production in T cells using the drug BX-795
18:18	Varkhande, S.	Continual exit of human cutaneous resident memory CD4 T cells that seed distant skin sites
18:24	Vizzardelli, C.	NSG-mice humanized with allergen-specific $CD4^+$ T cells develop allergic airway responses

18:30-19:00 Presentation of World Cafe Results, Résumé and Activities to start

19:00 Networking evening and awarding of the best presentations

BIOSKETCHES

Edward Knol, curriculum vitae, August 2018

Edward Knol is a biomedical scientist and immunologist in the departments of Immunology and Dermatology/Allergology at the University Medical Center Utrecht. He received his PhD training at the University of Amsterdam and had a postdoc position at Johns Hopkins University in Baltimore. His scientific research focuses on allergic diseases, in particularly eczema and food allergy.

The research focusses on

1) improved insights in pathomechanisms,
2) explore new treatment options,
3) improve current diagnostics and establish new diagnostics platforms.

In his career Edward Knol discovered CD63 as the basophil activation marker, described the role of peanut allergen Ara h 2 and described A20/TNFAIP3 dysregulation in eczema. He is involved in several (inter)national collaborations and is Secretary General of the Dutch Society of Immunology (~1400 members).

Within the University Medical Center he holds a teaching position and chairs the education committee of the University Utrecht graduate school Immunity and Infection (60 master and 170 PhD students). He teaches in several courses and is coordinator and examiner of: 1) Course Clinical Immunology for 3rd years students Biomedical Sciences, 2) Course Immune Therapy for 2nd years student Medicine and 3) Course Infection and Immunity for 3rd years Students at the Technical University Eindhoven.

At the international level Edward Knol has organised 3 European Academy of Allergy and Clinical Immunology (EAACI) Winter schools and was the chair of the Scientific Program Committee of the EAACI annual meetings in 2014-2016.

Currently he holds the position of Scientific Media Editor in EAACI. In addition, he is steering committee member of the Federation of Clinical Immunology Societies (FOCIS).

Publications: Scopus ID 7007059464

Austrian Cross of Honor for Science and Art to Hannes Stockinger

The Austrian Society for Allergology and Immunology (Österreichische Gesellschaft für Allergologie und Immunologie – ÖGAI) congratulates Hannes Stockinger for having received the ***Austrian Cross of Honor for Science and Art*** on November 7, 2018. He joined ÖGAI as member in 1983, was Vice Secretary (1992-1994), Secretary General (1994-1996), President-elect (2000-2002), President (2002-2004) Past-President (2004-2006), Chairman of the Expert Committee *Immunological Education and Continuing Education* (2004-present). As President together with his Secretary Gerhard Zlabinger he built up a modern ÖGAI website and logo, initiated medical specialization for immunology in Europe, public awareness and the contact to laypeople support groups, in particular for allergy. He is also very active in ÖGAI-associated societies: he was Treasurer of the *European Federation of Immunological Societies (EFIS*; 2006-2015), he is the designated chairperson of the *Gender Equality and Career Development Committee* of the *International Union of Immunological Societies (IUIS), and* since 2010 he has been the President of the *Federation of Austrian Scientific Societies,* the umbrella organization of Austrian scientific societies, whose 160 member societies comprise approximately 30,000 individual scientists. In 1985 the ÖGAI established the *Thesis Prize* with Hannes Stockinger and Guido Krömer as first awardees of this *Prize*. 1990 he received the *Pirquet-Prize* and 1991 the *Karl-Landsteiner-Prize*. As representative of the ÖGAI he is co-organizing the biannual TATRA Immunology Conference. As EFIS Treasurer he initiated many public awareness projects and programs to support young immunologists, for instance the foundation of the South Eastern European Immunology School that was held recently the 10th time.

Hannes Stockinger is the Head of the Research Center for Pathophysiology, Infectiology and Immunology at the Medical University of Vienna (2010-present) and Chairman of one of the Center's subunit, the Institute for Hygiene and Applied Immunology (2009-present), where he is appointed as well as a full professor for molecular immunology (2004-present). The Center is with 300 employees (about 200 payed by third-party funds with a mix 75%/25% public/industry) one of the largest translational research facilities of the Medical University of Vienna. As first Dean of the PhD program he built up at this University one of the most successful PhD schools (2003-2010) and he continues to further develop this school as Chairman of the *Committee of the Senate of the Medical University of Vienna for the PhD programs* (2010-present). He also co-founded and managed as CEO the biotech-SME Competence Center for Biomolecular Therapeutics (BMT) that aimed together with Novartis, Baxter and the SMEs Technoclone and Polymun to identify and develop targets for therapeutic treatment of immunological and inflammatory diseases (2002-2012).

Hannes Stockinger has been identifying and characterizing the structure and function of a number of surface receptors on T cells and myeloid cells by monoclonal antibodies, the latter have been distributed to the community and used by health care centers, doctors and researchers for the diagnosis and therapy of immunological diseases and leukemias for decades up to now. Therefore, he is also member of the Cluster of Differentiation (CD) Nomenclature Council. His contribution to the understanding of how GPI-anchored receptor proteins transduce signals across the plasma membrane were fundamental for the identification and characterization of lipid rafts, membrane devices that are now recognized to control signaling across the plasma membrane. The understanding of the function of these lipid entities in the plasma membrane is instrumental for the therapeutic usage of lipid modifying medications such as statins and omega-3-fatty-acids. Currently, he is focusing on the development of: 1) 3G nanodevices to specifically transport drugs and factors to pathologic cells in immunological diseases, 2) novel assays for the diagnosis of bacterial infections and 3) advanced imaging to analyze the dynamic of receptors and signaling molecules in the immunological synapse with the aim to obtain novel insight into the initiation and control of the immune response and thereby to identify nanostructure-markers and targets for precision medicine. During his scientific carrier he published nearly 200 scientific papers including a variety of original papers in the very top journals such as Cell, Science, Nature Methods, Nature Immunology, Science Signaling, the Journal of Experimental Medicine that count for nearly 10,000 citations and an h-factor of more than 50.

AWARDEES

KATARZYNA NIESPODZIANA

Institute for Pathophysiology and Allergy Research
Medical University of Vienna

Clemens von Pirquet Prize for her work

„PreDicta chip-based high resolution diagnosis of rhinovirus-induced wheeze“
Nat Commun. 2018;9:2382

Allergens and infections by rhinovirus (RV), the cause of common cold, are major factors triggering asthma attacks. Whether an asthma attack is really caused by a rhinovirus infection could not be firmly established so far because only nucleic-acid based strategies for virus detection have been available but no serological tests measuring rhinovirus-specific immune responses. In the present study we developed a “PreDicta” chip which contains a large collection of micro-arrayed peptides and proteins representing the currently known rhinovirus species and strains. We measured RV-specific antibody responses in serum samples of 120 children collected during an acute episode of wheeze and at follow-up visit after approximately 11 weeks. Our study shows that one can identify the culprit rhinovirus species in children with wheeze attacks by measuring strain-specific increases of antibodies with only a drop of blood. Thus, it seems that our data have the potential to revolutionize the way how RV-triggered severe respiratory illness will be diagnosed in the future. Furthermore, the chip will be useful for global serological identification of RV species triggering severe respiratory illness and may ultimately pave the road towards RV-specific therapeutic and prophylactic strategies.

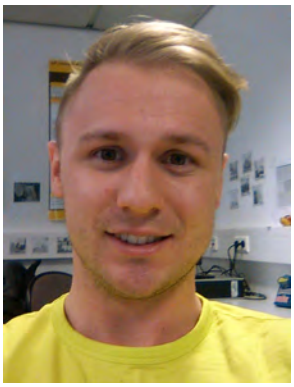
LUCA PANGRAZZI

Institute for Medical Aging Research
Institute of Immunology
University of Innsbruck

ÖGAI Thesis Prize for his work

„Immunological memory in the bone marrow in old age“

Aging leads to a decline of immune function, a process known as immunosenescence, which contributes to a higher incidence and severity of infectious diseases and decreased efficacy of vaccines in the elderly. Due to the involution of the thymus, the numbers of naïve T cells are low in old age. It is therefore important to find new strategies to counteract this problem, in particular through the maintenance of memory cells generated during life. Memory T cells and long-lived plasma cells survive in bone marrow (BM) survival niches for long periods of time. Plasma cells home to APRIL$^+$ cells while effector/memory T cells are in close proximity to IL-7$^+$ and IL-15$^+$ BM cells. Cytomegalovirus (CMV) has been considered one of the most important propagators of immunosenescence. CMV infection leads to a very prominent T cell response, which occupies >20% of the total CD8+ T cell pool. It has been suggested that CMV-driven effector/memory T cell expansions significantly accelerate the age-associated loss of naïve T cells, decreasing *de novo* immune responses.
In the first part of our study, we showed that the expression of IL-7, a cytokine involved in the maintenance of memory T cells, decreases while the levels of IL-15, important for the survival of memory but mostly of highly differentiated/senescent T cells, increase in old age. We described that oxidative stress and inflammation in the BM support the accumulation of senescent T cells, leading to a vicious cycle of inflammation as a consequence. In the second part of the project, the impact of CMV on the phenotype of effector/memory CD8$^+$ T cells and on the production of survival factors for these cells in the BM has been studied. Senescent CD8$^+$ effector memory RA T (TEMRA) cells with a bright expression of CD45RA, high responsiveness to IL-15 and reduced levels of IL-7Rα, accumulate in the BM of CMV$^+$ persons. Increased IL-15 mRNA expression was observed with CMV, and the highest levels were found in old seropositive donors. Thus, our results suggest that inflammation, oxidative stress and chronic viral infections such as CMV may support the accumulation of senescent T cells in the BM, leading to reduced maintenance of adaptive immune cells in the BM survival niches.



LORENZ AGLAS

Department of Molecular Biology
University of Salzburg

Ursula und Fritz Melchers Thesis Prize for his work

„Intrinsic properties of the Bet v 1 fold: impact on immunogenicity and allergenicity“

Allergic reactions to birch (*Betula verrucosa*) pollen are the most prevalent tree pollen allergies in Europe. Over 100 million allergic patients worldwide suffer from birch pollen allergy, and more than 95% of them are sensitized to a protein designated Bet v 1, thus rendering it the major birch pollen allergen. So far, the allergic sensitization-driving property of Bet v 1, which is linked to the induction of a strong Th2 immune response, remains elusive.

The intrinsic properties of the Bet v 1 fold have been investigated in detail and hereby one special feature in particular has attracted attention: the potential of Bet v 1 to act as a promiscuous acceptor for various ligands. The objective of this doctoral thesis was to investigate the influence of ligand binding on the allergenicity of Bet v 1, thereby considering physicochemical and immunological properties. The ligands we chose for this study were, on the one hand, natural pollen-derived compounds, and on the other hand, the microbial-derived compounds lipopolysaccharide (LPS) and lipoteichoic acid, which were selected for their presence as contaminants in aqueous pollen extracts and for their potential to activate toll-like receptors (TLR). We could demonstrate that Bet v 1 is able to bind the pollen-derived compounds but not the TLR-2 and TLR-4 agonists. However, neither one of the investigated compounds did endow Bet v 1 with the capacity to induce Th2 polarization *in vivo*. In contrast, birch pollen extracts were shown to promote Th2 polarization. From these findings we can conclude that TLR-co-stimulation alone is not a decisive aspect in birch pollen sensitization and that Bet v 1 sensitization is rather determined by the complex pollen environment. Hence, a superior role of the intrinsic properties of this allergen on the induction of a Th2-favoured immune response most likely can be excluded. Future studies focusing on the pollen matrix could shed light on the substance(s) contributing to its allergenicity.

PRESENTATION FORMATS

Science Interview:

Edward Knol from the Medical Center in Utrecht/Netherlands will act as your interview partner.
Please be prepared that he may not ask you questions about experimental details but rather about

- the general concept of your work and your scientific aims,
- how you broadly address your research goal,
- what is the relevance of your results for the research field and for the general public,
- which are your biggest challenges, problems and achievements…

The audience is asked to vote for the best two interviews.

Video presentation:

To prepare a KISS (keep it short and simple) video, please follow these guidelines:

- Film your video horizontally with any device you like in 16:9 widescreen and a resolution of 420p, 720p or 1080p in mp4 (MPEG-4) or H.264 format.
- The video maximum length is restricted to 3 minutes.
- You are free to be creative with your video. Consider yourself a movie director.

The audience is asked to vote for the best two videos.

World Café:

All participants are invited to actively discuss a special topic in front of a flip chart in every corner of the veranda. Feel free to move from one topic to the next and to share your ideas with all other participants there. Add your comments to each topic on the respective flip charts.

After having done so for all topics, a jury will summarize all comments and present a résumé and outlook. Hence, you and your ideas/contributions will be the cornerstones of the future development of ÖGAI.

Abstracts – Science Interview Presentations

Abstract Title	*In vivo* induction of IgG antibodies towards Bet v 1 and associated food allergens by a hypoallergenic birch pollen allergy AIT vaccine candidate
Authors Family name, initials	Aglas, L.[1], Grün, M.[1], Stolz, F.[2], Chrusciel, P.[3], Jaakkola, U.-M.[3], Yatkin, E.[3], Jongejan, L.[4], van Ree, R.[4], Ferreira, F.[1]
Affiliation	[1] Division of Allergy and Immunology, Department of Biosciences, University of Salzburg, Austria [2] Biomay AG, Vienna Competence Center, Vienna, Austria [3] Central Animal Laboratory of the University of Turku (UTUCAL), Turku, Finland [4] Academic Medical Center, Amsterdam, The Netherlands
Presenter	Aglas, L.

In course of pre-clinical analysis, we investigated the induction of specific serum IgG (IgG1, IgG2a, and IgG2b) and IgE antibodies in Wistar rats immunized with BM4, a novel AIT candidate for the treatment of birch pollen allergy based on a hypoallergenic variant of the major birch pollen allergen Bet v 1 (www.bm4sit.eu). In addition, the cross-reactivity of the induced BM4-specific antibodies towards Bet v 1 and birch pollen-associated food allergens (Mal d 1 from apple and Cor a 1 from hazelnut) was investigated.
Wistar rats received bi-weekly injections of 80 µg BM4 over a period of 6 months. Animals were grouped into a main group (n=20 rats), sacrificed one week after last injection) and a recovery group (n=10 rats), sacrificed after a 6-week observation period). Endpoint titer of serological BM4-, Bet v 1-, Cor a 1- or Mal d 1-specific antibodies were determined by ELISA.
BM4 was found to effectively induce BM4-specific IgG antibodies, which were cross-reactive with Cor a 1 and Mal d 1. Concerning IgE reactivity, the induced antibody levels were low (main group) or undetectable (recovery group). These results are promising regarding the induction of blocking IgG antibodies and pave the way for a prospective first-in-men clinical trial. In addition, the lack of an IgE response that might decrease the risk of side effects and the potential to treat Bet v 1-related pollen-food syndrome with the same vaccine are advantageous features of the BM4 drug product.

The research was supported by the University of Salzburg Priority Program "Allergy-Cancer-BioNano Research Centre" and the BM4SIT project (grant number 601763) in the European Union's Seventh Framework Programme FP7.

Abstract Title	TGFβ1 mimetic peptide modulates T cell polarization and antibody production in mice sensitized with Phl p 5
Authors Family name, initials	Araujo, GR.[1], Aglas, L.[1], Vaz ER.[2], Machado, Y.[1], Goulart, LR.[2], Ferreira, F.[1]
Affiliation	[1] Department of Biosciences, University of Salzburg, Salzburg, Austria. [2] Laboratory of Nanobiotechnology, Institute of Genetics and Biochemistry, Federal University of Uberlândia, Uberlândia, Brazil
Presenter	Araujo, GR

Transforming growth factor β1 (TGFβ1) is a multifunctional cytokine that has been shown to exert immunoregulatory functions in many different cell types. Hence, peptides that could mimic the active core domain of TGFβ1 would be highly promising candidates for immune modulation of allergy and inflammation. The TGFβ1 mimetic peptide presented herein was selected by phage display technology through competitive elution with the recombinant TGFβ1. The ability of the mimetic to modulate the immune response to Phl p 5 *in vivo* was investigated by flow cytometry, ELISA and mediator release assays. In restimulated splenocytes from mice sensitized with Phl p 5, the mimetic was able to suppress IL-2, IFN-γ, IL-4, IL-5 and IL-13, and induce IL-10 secretion and Treg cell differentiation. Mice treated with the mimetic had lower levels of IgE, IgG1, IgG2a and higher levels of IgA.

Furthermore, serum from mice treated with the mimetic rendered lower levels of Phl p 5-induced basophil degranulation. The TGFβ1 mimetic peptide efficiently modulated important cytokines and antibodies involved in immunopathological processes, induced Treg cell differentiation, and inhibited basophil degranulation, important events that exacerbate the allergic microenvironment. These findings strongly imply a potential use of the TGFβ1 mimetic peptide for the suppression of allergen-specific immune responses.

Abstract Title	Co-stimulatory signalling via TNF family members CD30 and OX40 promotes disease activity in nephrotoxic serumnephritis
Authors Family name, initials	[1]Artinger, K., [1]Kirsch, A.H., [2]Cooper, D.J., [1]Aringer, I., [1] Schabhüttl, C., [3]Eller, P., [2]Lane, P.J., [1]Rosenkranz, A.R., [1]Eller, K.
Affiliation	[1]Clinical Division of Nephrology, Department of Internal Medicine, Medical University of Graz, Graz, Austria [2]Medical Research Council Centre for Immune Regulation, Division of Immunity and Infection, University of Birmingham, Birmingham, United Kingdom [3]Intensive Care Unit at the Department of Internal Medicine, Medical University of Graz, Graz, Austria
Presenter	Artinger, K.

Introduction: The TNF superfamily-members CD30 and OX40 are involved in costimulatory pathways via propagation and survival of $CD4^+$ T cells. This study evaluated the role of CD30 and OX40 in a murine model of glomerulonephritis.

Methods: Nephrotoxic serum nephritis (NTS) was induced in wildtype (WT) mice and mice deficient in CD30 and OX40, in $Rag1^{-/-}$ mice adoptively transferred with $CD4^+$ T cells from WT and CD30/OX40 deficient mice and finally in WT mice treated with anti CD30-ligand and OX40-ligand antibodies or control IgG. Nephritic mice were injected intraperitoneally twice a week starting three days after disease induction.

Results: CD30/OX40 deficient mice developed significantly decreased albuminuria and glomerulosclerosis when compared to WT animals. CD30/OX40 deficient $CD4^+$ T did not induce NTS in $Rag1^{-/-}$, while $Rag1^{-/-}$ mice injected with $CD4^+$ T cells from WT mice developed severe disease. These CD30/OX40 deficient $CD4^+$ T cells differentiated normally towards Th1 and Th17 phenotypes, but did not proliferate to the same extent *in vitro* and in secondary lymphoid organs as compared to $CD4^+$ T cells from WT mice. In line to our data obtained from CD30/OX40 knock-out mice, antibody blockade resulted in decreased albumin/creatinine ratio as well as glomerulosclerosis when compared to control IgG treated mice.

Conclusion: Since not only knock-out animals, but also the treatment with antibodies against CD30-ligand and OX40-ligand lead to an improved disease phenotype, this blockade represents a potential treatment option in the therapy of glomerulonephritis, most likely due to a decreased proliferative capacity of $CD4^+$ T cells.

Abstract Title	Inefficient Early Downstream Signaling Blunts Antigen Sensitivity of CAR-T-cells
Authors Family name, initials	V. Gudipati[1], J. Rydzek[2], I. Perez[1], S. Königsberger[1], M. Hudecek[2], H. Stockinger[1], J. Huppa[1]
Affiliation	[1]Medical University of Vienna, Vienna, Austria, [2]Universitätsklinikum Würzburg, Würzburg, Germany.
Presenter	Gudipati_V

Adoptive immunotherapy employing chimeric antigen receptor (CAR)-modified T-cells has given rise to new hope in oncology as an effective treatment regimen for advanced malignancies. While high rates of complete remission after CAR T-cell therapy can be obtained in patients with B cell malignancies, relapse may occur in significant number of patients, often owing to antigen loss variants. Rational design of CARs with optimized anti-cancer performance mandates detailed knowledge of how CARs engage tumour antigens and how antigen-engagement triggers activation. To gain a deeper insight into the mechanisms of CAR-induced activation and the development of the CAR immunological synapse, we employed total internal reflection fluorescence (TIRF) microscopy. We found the sensitivity of CAR-T-cells towards antigen is reduced by 500 times when compared to T-cell antigen receptor-mediated detection of nominal peptide/MHC complexes. While CAR-antigen binding was efficient, receptor-proximal signalling was significantly attenuated due to reduced recruitment of the tyrosine kinase ZAP70 at ligated CARs. At limiting antigen densities absence of adhesion molecule ICAM1 significantly affects CAR T-cell mediated cytotoxicity indicating that blunted CAR signalling leads to attenuated activation of the integrin LFA-1, thereby compromising cell adhesion. our findings expose fundamental limitations of current one-dimensional CAR designs that has to be overcome for personalized cancer treatment. Furthermore, our findings highlight unique strengths of live molecular imaging for preclinical CAR-development.

Abstract Title	T cell responses to sublingual treatment with recombinant Mal d 1
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Presenter	Kitzmüller, C.

Background: More than 70% of birch pollen-allergic individuals develop birch pollen-related food allergy (BPRFA), most frequently to apple. We recently conducted a randomised double-blind placebo-controlled clinical study of sublingual immunotherapy (SLIT) with recombinant apple allergen, rMal d 1. After 16 weeks, patients receiving rMal d 1 had significantly improved BPRFA. In the current study we analysed changes in the T cell compartment of the rMal d 1-treated patients over the course of treatment.
Methods: We investigated T cell reactivity and the expression levels of the key cytokine IL-4, Il-5, IL-13, IFNγ, IL-10 and TGFβ in response to specific stimulation by thymidine incorporation and RT-qPCR, respectively. Additionally, we analysed changes in the relative numbers of $CD4^+$ memory T cell subsets, namely Th1, Th2, Treg and Tfh, with subset-specific surface markers and flow cytometry.
Results: The proliferative response to rMal d 1 was reduced over the course of treatment, which was accompanied by changes in the expression levels of cytokines, namely a reduction of IL-4, IL-5 and IL-13 and an increase in IL-10. Almost all of the $CD4^+$ memory T cell subsets analysed were unchanged with the notable exception of pro-allergic Th2 cells ($CD27^-$, $CRTh2^+$, $CCR4^+$), which were significantly decreased already after 4 weeks of treatment.
Conclusion: Our results support the model that peripheral tolerance induction and deletion of the allergen-specific terminally differentiated CD27- T cells represent first critical steps to restore tolerance during AIT. SLIT with rMal d 1 is a promising approach to improve birch pollen-related apple allergy.

Supported by: OeNB project 16620, the Austrian Science Fund (projects KLI96 and SFBF4610), Biomay AG, and the Christian Doppler Research Association, Vienna, Austria.

Abstract Title	**Prophylactic treatment with allergen-laden virus-like nanoparticles (VNP) induces tolerance in a mouse model of mugwort allergy**
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Presenter	Kratzer, B.

In high-risk populations, allergen-specific prophylaxis could protect from sensitization and subsequent development of allergic diseases. However, such approaches have the inherent risk to sensitize the intention-to-treat population. Therefore, new and safe vaccine formulations are urgently needed. Allergen-laden virus-like nanoparticles (VNP) could be such a formulation. The major mugwort pollen allergen Art v 1 was targeted either to the surface or to the inner side VNP by genetic engineering and we subjected the vaccine candidates to biochemical and immunological analyses *in vitro*, as well as to humanized allergy mice *in vivo*. Degranulation assays performed with RBL cells sensitized with Art v 1-specific IgE from allergic individuals showed that VNP containing shielded allergen are hypoallergenic when compared to VNP expressing allergen on the surface or soluble allergen. Both VNP versions induced proliferation and cytokine production of allergen-specific T cells *in vitro*. Upon intranasal application in mice, VNP expressing shielded allergen in contrast to surface exposed allergen did not induce allergen-specific antibodies or sensitization, identifying them as promising candidates for prophylactic interventions. Notably, prophylactic treatment with VNP expressing shielded allergen protected mice from subsequent sensitization with mugwort pollen extract. Protection was associated with a Th1/Treg-dominated cytokine response, reduced lung resistance and increased $Foxp3^+$ Treg numbers in lungs. These effects might be mediated by alveolar macrophages and $CD103^+$ DCs, which predominantly took up VNP *in vivo* and are known as Treg inducers. Allergen-laden VNP represent a novel platform to selectively target (allergen-specific) effector T cell functions with a low risk for *de novo* sensitization.

Supported by the Austrian Science Fund (FWF) DK-W1248-B30, SFB-F4609, F4605

Abstract Title	Hepatocyte-intrinsic Ifnar1 signaling drives metabolic reprogramming of liver tissue to shape adaptive immunity via systemic metabolism.
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Presenter	Lercher, A.

Viral infections cause inflammation that shapes metabolism. Yet, the underlying regulatory circuits remain mainly enigmatic. In this study, we employed a model of chronic viral hepatitis and longitudinal transcriptomics, proteomics and metabolomics analyses to dissect metabolic changes in liver tissue. We identified reprogramming of hepatic lipid and amino acid metabolism, which coincided with altered serum metabolite levels during the course of infection. Conditional ablation of *Ifnar1* implicated hepatocyte-intrinsic type I interferon signaling as a central regulator of hepatic metabolic reprogramming and systemic metabolism. *Ifnar1* signaling in hepatocytes specifically targets the urea cycle by transcriptional repression of the enzymes OTC *and* ASS1. This translates to an *Ifnar1*-dependent reduction of the systemic arginine to ornithine ratio. Pharmacological reduction of arginine and ornithine homeostasis suppresses adaptive immunity and ameliorates T cell-mediated hepatitis *in vivo*. These findings shed light on the complex crosstalk between immunity and metabolism during infection and identify interferon-induced modulation of the hepatic urea cycle as a novel endogenous mechanism of immunoregulation.

Supported by ERC grant "CMIL" awarded to AB and a DOC fellowship of the OEAW awarded to AL.

Abstract Title	The energy sensor AMP-activated protein kinase is critical for type 2 T helper cell differentiation and function *in vivo*
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Presenter	Mayer, K.A.

Introduction: T cells must tightly regulate their metabolic processes to cope with varying bioenergetic demands depending on their state of differentiation. The metabolic sensor AMP-activated protein kinase (AMPK) is activated in states of low energy supply and modulates cellular metabolism toward a catabolic state. Although this enzyme is known to be particularly active in regulatory T (Treg) cells, its impact on T helper (Th) cell differentiation is poorly understood.
Results: We show here that pharmacological AMPK activation increases GATA-3 expression in naive CD4+ T cells thereby driving the differentiation of IL-4-producing type 2 T helper cells *in vitro*. Confirming these results, genetic loss of AMPK in T cells ameliorates house-dust-mite (HDM)-induced allergic airway inflammation *in vivo*: conditional AMPK knockout mice (KO) show decreased accumulation of Th2 cells and eosinophils in the lung upon allergen challenge compared to wildtype (WT) controls. Strikingly, the number of lung infiltrating Th1 and Th17 cells was not reduced in KO vs. WT mice. Additionally, we detected lower levels of Th2 cytokines in the supernatant upon *ex vivo* re-stimulation of lung suspensions with HDM-extract in KO vs. WT mice, further highlighting the important role of AMPK in regulating type 2 immunity.
Conclusion: We provide evidence that AMPK is critical in order to fine-tune Th2 dependent effector responses *in vitro* and *in vivo*. Additional research is needed to further elucidate the mechanistic background of our findings.

Abstract Title	The purinergic pathway activated by the proinflammatory stimuli endows M-CSF-dependent folate receptor β (FRβ)$^{+}$ macrophages with potent immunosuppressive capacity
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Presenter	Ohradanova-Repic, A.

If misregulated, macrophage-T cell interactions can drive chronic inflammation thereby causing diseases, such as rheumatoid arthritis (RA). We report that in a proinflammatory environment, granulocyte-macrophage (GM-CSF)- and macrophage colony-stimulating factor (M-CSF)-dependent macrophages have dichotomous effects on T cell activity. While GM-CSF-dependent macrophages show a highly stimulatory activity typical for M1 macrophages, M-CSF-dependent macrophages, marked by folate receptor β (FRβ), adopt an immunosuppressive M2 phenotype. We find the latter to be caused by the purinergic pathway that directs release of extracellular ATP and its conversion to immunosuppressive adenosine by co-expressed CD39 and CD73. Since we observed a misbalance between immunosuppressive and immunostimulatory macrophages in human and murine arthritic joints, we devised a new strategy for RA treatment based on targeted delivery of a novel methotrexate formulation to the immunosuppressive FRβ^{+}CD39^{+}CD73^{+} macrophages, which boosts adenosine production and curtails the dominance of proinflammatory macrophages. In contrast to untargeted methotrexate, this approach leads to potent alleviation of inflammation in the murine arthritis model. In conclusion, we define the macrophage extracellular purine metabolism as a novel checkpoint in macrophage cell fate decision-making and an attractive target to control pathological macrophages in immune-mediated diseases.

Supported by the European Union's Horizon 2020 research and innovation programme under grant agreement No 683356 – FOLSMART and from the 7th Framework Programme under grant agreement NMP4-LA-2009-228827 NANOFOL.

Abstract Title	Skin and *in vitro* tests are positive in every 10th patient with a plausible history of betalactam allergy
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Presenter	Ostermayer, C.

Rationale: Many patients claim "allergy" to betalactam antibiotics, a history which is often wrong and confirmatory tests are required to rule out or confirm this. Provocation tests put patients at risk during testing, while *in vitro* and skin tests can be performed on a rather safe base.

Methods: We performed a retrospective review of a cohort of patient charts, who had visited the "Floridsdorfer Allergie Zentrum" (Floridsdorf allergy center (FAZ), Vienna) for a suspected penicillin or cephalosporin allergy from January 1st, 2016 to December 31st, 2017. A drug-specific history was obtained from all patients. Specific IgE was determined (ImmunoCAP, ThermoFisher, Penicillin G + V, Amoxycillin, Ampicillin, MDM, Cefaclor) and skin prick tests, intradermal tests and patch test (Penicillin G + V, Amoxicillin, Ampicillin, Cefazolin, Cefuroxim, Ceftriaxon) were performed and read after 20 min and after 24 hours. This study was approved by the Ethics committee of the Medical University of Vienna, Austria.

Results: Of 792 patients (562 female and 232 males, average age 42.3 years +/- 21.9 years SD), who were eligible for inclusion into the study, 100 had positive skin- or *in vitro* tests (12.62%). In detail, there were more positive immediate (42 = 5.03% skin test, 44 = 5.5.6% specific IgE) than delayed (19 = 2.40%) reactions. Specific IgE to Penicillin V was the most frequent positive single test result (27 = 3.68%).

Conclusions: Skin and *in vitro* testing are sensitive, easy and safe tools in the confirmation of betalactam-allergy in about every 10th patient.

Abstract Title	Cytomegalovirus contributes to age-related dysfunctions in the maintenance of immunological memory in the bone marrow
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Presenter	Pangrazzi, L.

Cytomegalovirus (CMV) has been considered one of the most important propagators of immunosenescence. CMV infection leads to a very prominent T cell response, which occupies >20% of the total CD8+ T cell pool. Memory T cells home to bone marrow (BM) niches, well organized structures which supports the survival of antigen-experienced adaptive immune cells. T cell survival is promoted by IL-7 and IL-15. IL-7 is important for the maintenance of long-lived memory T cells while IL-15 is mostly needed for more differentiated T cells. High IL-15 levels contribute to inflammation and tissue damage in the elderly, supporting the accumulation of highly differentiated T cells. In a previous study, we showed how pro-inflammatory molecules and oxidative stress play a role in the age-related dysfunction in the maintenance of immunological memory in the BM. In the current study, we describe the influence of CMV on the production of T cell survival factors in the BM and on the phenotype of highly differentiated T cells.The expression of IL-15, IFNγ and TNF in the BM was higher in CMV seropositive donors. Lower IL7R and higher IL-2/IL-15Rβ (CD122) expression on T cells was found in CMV+ compared to CMV- donors. Age-related changes in the expression of both molecules in T cell subsets were observed.Our results suggest that, particularly in the elderly, CMV supports the onset of a pro-inflammatory environment in the BM, leading to impairments in the maintenance of immunological memory and the accumulation of highly differentiated T cells, which further contribute to inflammation.

Abstract Title	Characterization of alum-induced NET-formation in human neutrophils
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Presenter	Reithofer, M.

Alum is the most widely used adjuvant, though the mechanism behind its adjuvanticity is not totally solved. In mice, host-derived DNA has been reported to be involved in the adjuvant effect of alum. Neutrophils are the first cells at the site of injection and in response to strong or particulate stimuli neutrophils have the ability to simultaneously release extracellular DNA and granular material, so-called neutrophil extracellular traps (NETs) which are able to trap and kill microbes.
Here, we investigated alum-induced NET-formation in human neutrophils and its underlying pathway. Neutrophils were stimulated with alum or PMA and ionomycin as positive controls. Strong NET-formation was induced by all stimuli as visualized by fluorescence microscopy showing co-localization of extracellular DNA and different granular proteins. In addition, alum-induced neutrophil elastase activity was found in supernatants. Inhibition of downstream signalling molecules by using a plate-reader assay to quantify released DNA were performed, to reveal the pathway underlying NET-formation. Ionomycin and alum-induced mitochondrial reactive oxygen species (mROS), whereas PMA triggered cytoplasmatic NADPH oxidase-dependent ROS. Alum induced rapid DNA-release similar to ionomycin and dependent on phagocytosis, extracellular calcium and NFκB signalling. Furthermore, a significant dependence on necroptosis signalling similar to crystal-induced NET release was found. During the process of NET formation, increased glycolysis, as well as mitochondrial respiration was observed.
Together, alum potently induces a rapid mROS dependent NET-release in human neutrophils *in vitro,* utilizing energy from glycolysis and mitochondrial respiration. These NETs may represent danger-associated molecular patterns involved in the initial immune response to alum-adjuvated vaccines.

Supported by Austrian Science Fund (FWF): DK W 1248-B13, Austrian National Bank (Project: 17582) and the Medical University of Vienna

Abstract Title	Induction of protective blocking antibodies for the birch pollen-related apple allergy
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Presenter	Sánchez Acosta, G.

Birch-pollen-related apple allergy [BPRAA] affects up to 70% of birch pollen allergic individuals and results from immunological cross-reactivity between the major allergens Betv1 in birch pollen and Mald1 in apple. Interestingly, birch pollen-immunotherapy has no convincing benefits on BPRAA. We recently showed in a double-blind placebo-controlled pilot study that 16 weeks of sublingual immunotherapy with recombinant [r] Mald1 [rMald1-SLIT] significantly improved BPRAA, whereas rBetv1-SLIT did not. To investigate the immune mechanisms underlying the induction of clinical tolerance to apple we characterized the levels, primary specificity and blocking capacity of SLIT-induced Mal d 1-specific IgG antibodies.

SLIT with rMald1 or rBetv1 induced Mald1-specific IgG1, IgG2 and IgG4 levels whereas Mald1-specific IgG3 antibodies were only induced by rBetv1-SLIT. The primary specificity of Mald1-specific IgG4 antibodies was assessed in competition ELISA. Pre-incubation of post-Betv1-SLIT sera with rMald1 and rBetv1 completely abrogated IgG4-binding to rMald1, suggesting that these antibodies bind to common cross-reactive epitopes on Mald1 and Betv1. In contrast, pre-incubation of post-rMald1-SLIT sera with rMald1 but not with Betv1 completely abrogated IgG4-binding to rMald1, indicating that rMald1-SLIT promoted primarily rMald1-specific antibodies. The presence of IgE-blocking antibodies in post-SLIT sera was assessed as their ability to inhibit rMald1-induced activation of basophils from apple-allergic donors. Basophil activation was exclusively inhibited by post-rMald1-SLIT sera, indicative of functional IgE-blocking antibodies and matching the clinical improvement of these patients. All together our findings suggest that clinical tolerance induced by rMald1-SLIT is mediated by the induction of highly specific IgE-blocking antibodies.

The research was funded by the Austrian Science Fund (FWF), projects W1212 and SFB F4610, and the Medical University of Vienna

Abstract Title	Exploring the conformational IgE epitopes of the major birch pollen allergen, Bet v 1, by structure based epitope grafting
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Presenter	Schmalz, S.

Knowledge of the epitopes bound by allergen specific IgE may aid in predicting symptom severity, cross-reactivity and efficacy of allergen immunotherapy. Most conformational IgE epitopes of the major birch pollen allergen, Bet v 1, have not been characterized, yet. We aimed to identify relevant IgE epitopes by grafting epitope sized surface patches of Bet v 1 onto TTHA0849, a non-IgE-binding structural homologue from Thermus thermophilus. Based on a structural alignment, surface-exposed residues of TTHA0849 were replaced by corresponding ones of Bet v 1 while preserving the hydrophobic core. Thereby, we created 16 chimeric proteins (TB1-TB16), each carrying a different Bet v 1-derived surface patch. Codon-optimized synthetic genes were expressed in Escherichia coli as 6xHis-tagged proteins and purified by metal chelate affinity chromatography. The chimeras were characterized via SDS-PAGE, matrix-assisted laser desorption-ionization mass spectrometry (MALDI-MS), circular dichroism (CD) spectroscopy and dynamic light scattering. Until now, two chimeras (TB1 and TB2) were expressed as soluble proteins. Purification yielded 13 mg and 58 mg from 1 liter of bacterial culture. MALDI analysis revealed that the chimeras matched their theoretical masses. The CD spectra showed mixed alpha-beta structures indicating correct folds of the chimeras. Dynamic light scattering of TB2 showed <2% aggregation, while the storage conditions of TB1 are yet to be optimized. Our preliminary data indicate that the structure based design of single-epitope carrying chimeric proteins yielded soluble, folded proteins which will be used in IgE binding assays to characterize the epitope repertoires of sera from birch pollen allergic patients.

Supported by: the Austrian Science Fund (FWF) grant P 30936-B30.

Abstract Title	FPR2 controls ILC2 functions in allergic airway inflammation
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Presenter	Smole, U.

Group 2 innate lymphoid cells (ILC2) are essential for protective immunity against helminths but can also drive airway inflammation to allergens, including house dust mite (HDM). In response to allergen-triggered IL-33, ILC2 secrete high levels of the Th2 cytokines IL-5 and IL-13. More recently, ILC2 have been shown to directly regulate $CD4^+$ T cell activation in a MHC-dependent crosstalk. However, the context- and tissue-specific pathways that regulate ILC2 functions are largely unknown. We demonstrate that signaling of the formyl-peptide receptor 2 (FPR2) on ILC2 is critical for lung-specific allergen- and IL-33-driven ILC2 responses. Blocking FPR2 *in vivo* abrogated cardinal features of the allergic response including airway hyperresponivness, bronchoalveolar lavage eosinophilia, concomitant with reductions in Th2 cytokine levels and lung ILC2 frequency upon HDM- or IL-33-treatment. Sorted ILC2 cultured with IL-2 and IL-33 secreted significantly less IL-5 and IL-13 in the absence of FPR2 signaling. Simultaneous triggering of FPR2 by its ligand, the acute phase protein serum amyloid A1 (SAA1), greatly enhanced ILC2 responsiveness to IL-33. Further, SAA1, a well-established chemoattractant that is highly upregulated in the lungs of allergic asthmatics, enhanced the ILC:T cell crosstalk with increased IL-13 and GM-CSF levels in supernatants of co-cultures of antigen-loaded ILC2 and T cells. Taken together, our preliminary data suggest that ILC2-expressed FPR2 senses the local environment and is required for the full magnitude of their IL-33 responsiveness in the lung. FPR2 signaling enhances the ILC2:T cell crosstalk, increasing cytokine secretion from both ILC2 and $CD4^+$ T cells, thereby possibly perpetuating asthma pathogenesis.

Supported by FWF J3332-B21, ATS funds, and DK W1248

Abstract Title	Molecular and cellular analysis of the nuclear receptor co-repressor 1 (NCOR1) in T follicular helper cells
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Presenter	Stolz, V.

The nuclear receptor corepressor 1 (NCOR1) is a transcriptional regulator bridging repressive chromatin modifying enzymes with transcription factors. NCOR1 regulates many biological processes, including immune cell regulation, differentiation, cell homeostasis and metabolism. Our laboratory has previously shown that NCOR1 promotes the survival of single-positive thymocytes leading to reduced numbers of peripheral T cells. However, its role in the differentiation and homeostasis of peripheral T helper (Th) subsets is not known. NCOR1 has been reported to interact with several members of the BTB-domain containing zinc finger transcription factor family. Among those is also BCL6, a key regulator essential for the differentiation of follicular Th cells (Tfh) cells. Tfh cells are important in providing T cell help to germinal center (GC) B cells and are therefore responsible for GC formation, antibody affinity maturation, isotype switching and also for the establishment of immunological memory. Due to the interaction of BCL6 with NCOR1, it is tempting to speculate that NCOR1 is important for the differentiation of the Tfh lineage. Preliminary data indicate an increase in Tfh and Tfr (T follicular regulatory) cells in mice with a T cell specific deletion of NCOR1 under homeostatic condition and after immunization with OVA. At the same time, GC B cells are decreased. Future analysis will determine whether loss of NCOR1 also affects antibody affinity maturation and isotype switching in GC B cells. Further, we will investigate if and how loss of NCOR1 affects effector functions in Tfh and GC B cells.

Supported by FWF W1212 – PhD program Inflammation and Immunity

Abstract Title	Low-input RNA sequencing reveals survival program of human skin-resident T cells during complete myeloablation
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Presenter	Strobl, J.

Myeloablative conditioning preceding allogeneic hematopoietic stem cell transplantation (HSCT) presents a unique situation in the human system to compare survival capacities of central and peripheral T cells. To determine factors mediating long-term tissue residency, we analyzed T cells isolated from peripheral blood and skin of patients receiving HSCT by flow cytometry and low-input RNA sequencing. T cells purified in full myeloablation and central immunosuppression (day of transplantation) were compared to cells isolated before and until 1 year after transplantation in the very same patients. Additionally, long-term skin-residency was visualized in skin sections after HSCT with sex-mismatched donors by X/Y-fluorescence-*in-situ*-hybridization.

While >90% of peripheral blood T cells are eliminated by HSCT, merely 50% of skin T cells are affected by myeloablative conditioning therapy. Notably, CD69+ and CD103+ αβ memory T cells remain stable and functionally competent populations in the epidermis and dermis with recipient T cells still constituting >30% of total T cells 2 years after transplantation. These skin-resident cell subsets down-regulate tissue egress molecules while enhancing transcription of tissue retention genes, maturation markers and pro-inflammatory cytokines. Instead of a glucose-based metabolism common for effector T cells, skin cells at the day of transplantation upregulate lipid scavenger receptors, likely relying on exogenous free fatty acid uptake for long-term survival.

Our results combine data of a unique clinical setting with in-depth cell profiling and imaging techniques. Thus, we were able to identify long-lived and radio-resistant skin-resident T cells and their distinct survival program compared to circulating T cells.

Supported by a DOCmed fellowship of the Austrian Academy of Sciences

Abstract Title	Stimulation of IL-2 production in T cells using the drug BX-795
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Presenter	Tauber, PA.

We investigated the immunomodulatory properties of BX-795, an inhibitor of 3-phosphoinositide-dependent kinase-1 (PDK1) and TANK-binding kinase-1 (TBK1), in T cells. We assessed proliferation, T cellular activation and polarization by measuring methyl-^{3}H-thymidine uptake and evaluation of CD69, CD25, CD154 and CD49e expression on $CD3^{+}CD4^{+}$ T cells as well as cytokine secretion by multiplexing of supernatants from murine or human T cells after activation. Interestingly, BX-795 increased secreted IL-2 levels upon TCR ligation in the human Jurkat T cell line, in human PBMCs and upon allergen-specific stimulation in murine splenocytes. This IL-2 promoting effect was confirmed on the mRNA level. Notably, analysis of TCR proximal phosphorylation revealed an inhibitory effect on ζ-chain phosphorylation in Jurkat T cells upon activation. Somehow paradoxically, in Jurkat triple parameter reporter (TPR) cells (expressing NFAT, NFκB and AP-1 fluorescent reporters) stimulated with α-CD3/α-CD28 beads BX-795 increased NFAT, NFκB and AP-1 reporter protein expression and secreted levels of IL-2 (4.0±0.38-fold, $p < 0.01$). In addition, in human PBMCs and allergen-specific murine T cells, BX-795 treatment resulted in an almost complete shut-down of Th2 cytokines. Most notably, BX-795 reduced secreted levels of IL-4 (88.3±6.5%, $p<0.05$), IL-5 (35.8±23.2%, $p<0.05$) and IL-13 (75.8±8.7%, $p<0.001$) but also IL-10 (80.8±13.1%, $p<0.001$) at 48 hours in allergen-specific murine T cells. In summary, elucidating the exact molecular mechanisms underlying enhanced IL-2 secretion might allow selective stimulation of this major Treg-driving cytokine in the future. The combination of IL-2 stimulation and Th2 cytokine inhibition makes BX-795 a promising candidate for the treatment of allergic diseases.

Supported by the Austrian Science Fund (FWF) projects SFB F4609-B19 and DK W 1248-B13 and the Medical University of Vienna

Abstract Title	Continual exit of human cutaneous resident memory CD4 T cells that seed distant skin sites
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Presenter	Varkhande, S.R.

As a barrier organ the skin harbors immune cells that not only provide protection against a myriad of pathogens but also support tissue homeostasis and repair. A large proportion of these immune cells in skin are resident memory T_{RM} cells and are thought to permanently reside in the tissue.
However, *in vitro* skin explant cultures indicated that $CD4^+CLA^+CD103^+$ T_{RM} can downregulate CD69 and exit the tissue. Using a multidimensional mass cytometry approach (CyTOF) we discovered a novel population of circulating $CD4^+CLA^+CD103^+$ T cells in the blood of healthy humans with a unique skin-tropic phenotype reminiscent of skin T_{RM}. Phenotypic and transcriptional similarities determined by conventional flow cytometry and RNA sequencing further highlighted the close relationship between $CD4^+CLA^+CD103^+$ T_{RM} and circulating $CD4^+CLA^+CD103^+$ cells. Their unique cytokine production profile of IL-22 and IL-13, and low IFN-g indicates a function in skin homeostasis and repair. The presence of this unique population in circulation suggests recirculating T_{RM} mobilized potentially to seed remote tissue sites.
To test the migratory behavior of mobilized T_{RM} (mT_{RM}) *in vivo*, we transferred human skin onto immunodeficient mice that carried an engineered human skin graft devoid of T_{RM} and followed T cell migration. We found that CLA^+CD103^+ T_{RM} could be mobilized from the skin, enter circulation and seed a distant skin site, while preserving their phenotype. Further, mT_{RM} from human blood could seed an engineered human skin graft underlining their skin tropism. Thus, we propose that circulating $CD4^+CLA^+CD103^+$ cells in human blood represent a migrating population of skin T_{RM}.

Funding: National Institute of Health (NIH) (R01AI127726) awarded to D.J.C. and I.K.G.

Abstract Title	NSG-mice humanized with allergen-specific CD4+ T cells develop allergic airway responses
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Presenter	Vizzardelli, C.

We have successfully employed non-obese diabetic severe-combined-immunodeficient $\gamma c^{-/-}$ (NSG) mice engrafted with PBMC from allergic patients as *in vivo* model of respiratory allergy. Allergic airway inflammation in this model is mainly mediated by allergen-specific $CD4^+$ T-cells. As their frequency in PBMC of allergic individuals is very low and $CD8^+$ T-cells may trigger graft-versus-host-disease (GvHD) we sought to improve this model by employing T-cell lines (TCL) enriched for allergen-specific $CD4^+$ T-cells.

Betv1-specific TCL were established from birch pollen-allergic patients. The ratio of CD4/CD8 T-cells was analysed by flow cytometry. Allergen-reactivity was confirmed in proliferation assays. T-cell-specificities were identified with overlapping synthetic 12-mer peptides. Allergen-induced cytokine responses were assessed with qPCR and intracellular staining. Betv1-specific TCL plus autologous antigen-presenting cells were injected intraperitoneally. After 17 days, engraftment was assessed by flow cytometry. Airway hyperresponsiveness (AHR) and bronchial inflammation were analysed after intranasal challenges with allergen or PBS.

After injection of TCL harbouring $CD4^+$ T-cells reactive with various epitopes of Betv1 and showing a Th2 phenotype, $CD4^+$ T-cells were detected in cell suspensions of lungs and spleens. $CD8^+$ T-cells did not expand *in vivo*. Mice challenged with allergen showed significantly higher AHR and larger numbers of eosinophils, neutrophils and basophils in bronchoalveolar fluids than those challenged with PBS. Lung histology revealed peribronchial inflammation in mice challenged with allergen.

NSG-mice engrafted with allergen-specific $CD4^+$ TCL develop allergic airway responses. This improved *in vivo* model may be useful in the assessment of novel therapeutic allergy vaccines targeting allergen-specific T-lymphocytes.

This work was supported by Austrian Science Fund, project SFB F4610.

Abstracts – Video Presentations

Abstract Title	Protection against beta-lactoglobulin from milk can be achieved in its holo-form only in a BALB/c mouse model
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Presenter	Afify, S.M.

Background: Prevention of milk allergy is an urgent problem that has attracted the attention of food scientists and physicians. In previous studies we proved that the unloaded apo-form of the lipocalin beta-lactoglobulin (BLG) from milk promoted Th2 cells and inflammation, whereas the holo-form acted immunosuppressive. In this study, we tested in BALB/c mice whether nasal application of holo-BLG can actually prevent allergy to BLG.

Methods: BALB/c mice were sensitized twice intraperitoneally with BLG adjuvanted with aluminum hydroxide after being nasally treated 3 times in biweekly intervals with the unloaded apo-form of BLG, or holo-BLG loaded with quercetin-iron complexes, or water as sham-treatment. Then mice were intraperitoneally challenged with apo-BLG. Subsequently, body temperature drop was recorded as a sign of a systemic allergic reaction. Specific antibodies in serum as well as cytokines of BLG-stimulated splenocytes were analyzed by ELISA. MHC Class II I-Ad+ and CD86+ expression on CD11c+ dendritic cells from spleens were analyzed by flow cytometry.

Results: Intranasal prophylactic treatment with holo-BLG prevented allergic sensitization to BLG. Mice pretreated with water or apo-BLG had significantly elevated BLG–specific antibodies (IgG1, IgG2a, IgA and IgE) and cytokine levels (IL5, IL13, IL10 and IFNγ) and significantly upregulated MHC Class II I-Ad and CD86+ on CD11c+ dendritic cells in the spleens, compared to the group treated with holo-BLG. Pretreatment with holo-, but not apo-BLG prevented body temperature drop upon allergen-challenge.

Conclusion: Prophylactic treatment with holo-BLG provided specific protection against sensitization to BLG and prevented the onset of allergy.

Supported by the Austrian Science Fund FWF, grant SFB F4606-B28, and by Biomedical Int. R+D GmbH, Vienna, Austria

Abstract Title	The cutaneous microbiome changes significantly in the course of allogeneic hematopoietic stem cell transplantation
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Presenter	Bayer, N.

The success of allogeneic hematopoietic stem cell transplantation (HSCT) remains limited due to severe side-effects, such as infections and graft versus host disease (GVHD). Recent studies suggest that dysbiosis of intestinal microbes is associated with an increased risk of GVHD and poor outcome, while the role of the cutaneous microbiome remains elusive.

We obtained patient material (peripheral blood, skin scales, stool and skin biopsies) at 5 time points before myeloablative conditioning and up to one year after HSCT (n= 20). The cutaneous and intestinal microbiome is analyzed with 16S rRNA and whole metagenome sequencing. *In vivo* interactions of bacteria with immune cells are monitored by combining monoclonal antibodies with fluorescent *in situ* hybridization (FISH). Bacterial numbers/mm^2 and distance calculations from CD45+ and HLA-DR+ cells are assessed via StrataQuest Analysis Software.

16S sequencing was established from healthy stool and skin samples and showed an expected mixture of commensal bacteria. Visualization of bacteria via 16S rRNA-FISH in HSCT patients revealed a decrease in bacteria/mm² skin in the epidermis as well as the upper (<500μm) and lower (>500μm) dermis at day 0 and day 14 after transplantation. At day 100 bacterial numbers were comparable to baseline before transplantation. Although often in close contact with CD45+cells, no intracellular bacteria were observed.

This study gives us the unique possibility to examine the repopulation kinetics and crosstalk between the immune system and the residing microbiome. Furthermore, we will establish risk profiles for GVHD development and occurrence of infections based on the individual skin and gut microbiome.

Abstract Title	ROS-induced autophagy regulates CD39 expression on human regulatory T-cells
Authors Family name, initials	Marlene C. Gerner, Liesa Ziegler, Ralf L.J. Schmidt and Klaus G. Schmetterer
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Presenter	Gerner, M.

Treg are a subpopulation of $CD4^+$ T-cells, associated with immunosuppression and preservation of self-tolerance. Treg can suppress proliferation and cytokine production of effector T-cells through various mechanisms including the degradation of ATP into the suppressive molecule Adenosine through the ectoencymes CD39 and CD73. Increased CD39 expression on tumor-infiltrating Treg has been described in multiple human malignancies. Therefore, CD39 has also been considered as a relevant immune checkpoint in tumor immunology. The regulation mechanisms of CD39 on $CD4^+$ T-cells have not been fully determined so far. Previous studies have established a role for autophagy in the expression of CD39 on tumor cells. Thus, we investigated signals leading to the *de novo* induction of CD39 on iTreg and assessed the influence of autophagy modulators (rapamycin, chloroquine, hydroxy citrate and ROS-modulators) in this process.
Our studies show that CD39 was strongly up-regulated by atRA/TGF-beta. Inhibition of autophagy further increased CD39 expression and led to a stronger suppressive function *in vitro.* In contrast, induction of autophagy significantly reduced CD39 expression during induction of Treg by atRA/TGF-beta. These principles also applied to peripheral blood tTreg. Only $CD39^-$ tTreg showed significant ROS-production and induction of autophagy, whereas $CD39^+$ tTreg did not. Furthermore, CD39 expression on tTreg could be modulated by autophagy modulators similar to atRA/TGF-beta iTreg. First results also show, that patients with autophagy-defects express higher rates of CD39 on tTregs compared to age- and sex-matched healthy donors confirming the role of autophagy on CD39 expression on tTregs *in vivo.*

Acknowledgements: This work was funded by the Austrian Science Funds project FWF 29654.

Abstract Title	Caesarean section delivery and the risk of allergic disorders in childhood
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Presenter	Gorris, A.

Introduction: Recent studies have proposed a strong association between caesarean section (CS) and an increased prevalence of allergic diseases in the offspring. While these observations have been confirmed in large cohorts in industrialized countries, evidence on the risk of allergic disorders after CS in developing countries is lacking.
Objectives: The objective of this study was to assess the association between the mode of birth and allergic diseases in children aged 3 to 12 years in Ecuador.

Methods: A cross-sectional study of 189 children living in Quito, Ecuador, was carried out. Parents were questioned using an anonymous, standardized questionnaire according to the ISAAC project to assess the presence of asthma, allergic rhinitis, allergic dermatitis and food allergies in their children. The children's age, sex, place of birth, mode of birth (CS or vaginal), socioeconomic status and ethnic origin were documented. Other parameters included gestational age, breast-feeding, smoking status during pregnancy and allergic diseases of the parents.

Results: After adjusting for confounding factors, children born by CS were significantly more susceptible to suffer from chest wheezing (OR 3.70, 95% CI 1.59-8.33), physician-diagnosed asthma (OR 16.7, 95% CI 2.27-100) and atopic dermatitis (OR 2.78, 95% CI 1.39 – 5.56) than children born vaginally. No association was found between the mode of birth and rhinitis (OR 1.47, 95% CI 0.63 – 3.45) or food allergy (OR 2.63, 95% CI 0.88 – 7.69).

Conclusions: Delivery by CS strongly increases the risk to develop asthma and allergic dermatitis in Ecuadorian children.

Abstract Title	Identification of macadamia nut allergens and their role in cross-reactivity among tree
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Presenter	Kabasser, S.

The nuts of Macadamia integrifolia are gaining increasing popularity as ingredients in nut mixes, cakes, biscuits and many other food products. As other tree nuts, they contain valuable nutrients (e.g. unsaturated fatty acids and antioxidants) which contribute to a healthy diet. However, macadamia nut has been reported to be a potent elicitor of allergic reactions with mild to severe clinical symptoms. There is still no information regarding the identity of the relevant allergens and their cross-reactivity to pollen or other food allergens. Therefore, we aimed at the identification of allergens from macadamia nuts and evaluation of their cross-reactivity with allergens from other tree nuts. Proteins were extracted from defatted macadamia flour and subsequently purified by affinity, ion exchange, and size exclusion chromatography. Protein extract as well as individual purified proteins were tested for IgE binding by ELISA using sera from patients allergic to macadamia and/or several tree nuts. Preliminary results showed that we purified three IgE binding macadamia proteins. A protein of approx. 60 kDa (a putative legumin) as well as a macadamia vicilin, and an unknown 14 kDa allergen were recognized by IgE of most of the tested sera. Further biochemical analysis and immunological characterization of the purified proteins will be performed to evaluate the relevance of these proteins for diagnosis of macadamia allergy based on the concept of component-resolved diagnosis. In addition, the analysis of their IgE cross-reactivity with allergens from different tree nuts will be performed to elucidate clinically relevant and irrelevant sensitizations to different nuts.

Supported by funds of the Oesterreichische Nationalbank (Austrian Central Bank, Anniversary Fund, project number: 17560).

Abstract Title	Alum and MPLA as triggers for NET release in human neutrophils *in vitro*
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Presenter	Karacs, J.

The most widely used vaccine adjuvants are insoluble aluminium salts, especially. aluminium hydroxide (alum). Besides alum, the TLR-4-ligand monophosphoryl-lipid A (MPLA), a detoxified derivate of LPS, is used as adjuvant in allergen-specific immunotherapy (AIT). Neutrophils represent the first line of defence against invading microbes. Besides phagocytosis and oxidative burst, neutrophils have the ability to simultaneously release cellular DNA and granular material in response to strong microbial or particulate stimuli. These neutrophil extracellular traps (NETs) are not only able to trap and kill microbes, but this modified endogenous DNA may also represent a danger-associated molecular pattern (DAMP) that activates APCs. Therefore, adjuvant-induced NETs may play an important role in the initiation of immune responses to AIT vaccines.

Here, we use a human *in vitro* model to investigate the role of neutrophils and NETs in the initiation of immune responses in the presence of alum and/or MPLA. The formation of NETs was visualized by fluorescence microscopy and quantitatively assessed by DNA release assays. Stimulation of GMCSF-primed neutrophils with optimum concentrations of alum induced strong DNA release, whereas MPLA or LPS were less potent stimuli. Confocal fluorescence microscopy confirmed these differences. Alum-induced NETs showed typical co-localization of DNA and granular proteins, while only few neutrophils released NETs upon stimulation with MPLA or LPS.

So far, our data indicate that alum particles are strong triggers for NET release, while MPLA weakly induces NET formation. Further experiments will include original vaccine preparations, address signalling pathways and potential synergistic effects of adjuvants leading to NET induction.

Supported by FWF DK1248-B30, Medical University of Vienna and Austrian Austrian Central Bank (Anniversary Fund Project 17285).

Abstract Title	Characterization of host proteins interacting with the lymphocytic choriomeningitis virus L protein
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Presenter	Khamina, K.

RNA-dependent RNA polymerases (RdRps) play a key role in the life cycle of RNA viruses and impact their immunobiology. The arenavirus lymphocytic choriomeningitis virus (LCMV) strain Clone 13 provides a benchmark model for studying chronic infection. A major genetic determinant for its ability to persist maps to a single amino acid exchange in the viral L protein, which exhibits RdRp activity, yet its functional consequences remain elusive. To unravel the L protein interactions with the host proteome, we engineered infectious L protein-tagged LCMV virions by reverse genetics. A subsequent mass-spectrometric analysis of L protein pulldowns from infected human cells revealed a comprehensive network of interacting host proteins. The obtained LCMV L protein interactome was bioinformatically integrated with known host protein interactors of RdRps from other RNA viruses, emphasizing interconnected modules of human proteins. Functional characterization of selected interactors highlighted proviral (DDX3X) as well as antiviral (NKRF, TRIM21) host factors. To corroborate these findings, we infected Trim21-/- mice with LCMV and found impaired virus control in chronic infection. These results provide insights into the complex interactions of the arenavirus LCMV and other viral RdRps with the host proteome and contribute to a better molecular understanding of how chronic viruses interact with their host.

Supported by Hochschuljubiläumsstiftung of the City of Vienna (ABe). ABh and KK were supported by DOC Fellowships from the Austrian Academy of Sciences. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Abstract Title	Investigating oncogenic functions of STAT5B in innate(-like) lymphocytes
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Presenter	Klara Klein

Natural killer (NK) cells are important effectors in antiviral and antitumor responses, which are tightly controlled by JAK-STAT signalling. STAT5B, one of two STAT5 paralogs, plays an essential role in NK cell biology. Interestingly, activating mutations in *STAT5B* have been reported in T and NK cell malignancies. We have previously shown that mice, expressing the most frequent human *STAT5B* mutant (hSTAT5B^{N642H}) in hematopoietic cells, develop severe CD8^{+}T cell neoplasms. However, NK cells have not yet been investigated in this model and we aim to explore the effects of mutant STAT5B on innate lymphocytes. We could not observe significant increase in NK cells in diseased hSTAT5B^{N642H} compared to non-mutant hSTAT5B mice. However, we could observe a temporary increase of hSTAT5B^{N642H} compared to hSTAT5B NK cells upon bone marrow transplant, which was eventually overruled by T cell expansion. To circumvent T cell disease, we transplanted hSTAT5B or hSTAT5B^{N642H} bone marrow depleted of T cells, stem cells and lymphoid progenitors. After four months one of the recipient mice transplanted with hSTAT5B^{N642H} cells developed a disease characterized by expansion of NKT cells, which was serially transplantable and responsive to JAK1/2 inhibitor treatment. Our data show that hSTAT5B^{N642H} expression can give rise to NKT leukemia, once rapidly transformed CD8^{+}T cells are eliminated. Therefore, we established a novel mouse model for studying NKT cell malignancies. However, further research is ongoing to address the question if and how mutant STAT5B may contribute to NK cell transformation and how hyperactive STAT5B signalling affects innate lymphocyte function.

Supported by FWF: SFB-F61 and PhD program ''Inflammation and Immunity'' (IAI) FWF W1212

Abstract Title	Antibodies in the PIPEline: Fast generation of different isotypes sharing the same variable region against birch pollen major allergen Bet v 1
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Presenter	Köhler, V. K.

PIPE cloning is a cutting-edge method for the rapid creation of antibodies of different classes sharing the same variable region (Ilieva et al., 2017). In allergy research, antibodies are urgently needed for mechanistic studies, especially different isotypes with identical specificity to an allergen epitope. Birch pollen allergy, with the single major allergen Bet v 1, is an ideal model to study the role of IgE versus IgG_1 or IgG_4 on a molecular basis. We therefore aimed at utilising PIPE cloning for the creation of antibodies of different classes against Bet v 1.

PIPE cloning was used to combine heavy and light variable region sequences targeting Bet v 1 (Levin et al., 2014) with ε, γ_1 and γ_4 heavy constant region sequences, respectively, and a κ light constant region sequence. Plasmids coding for IgE, IgG_1 and IgG_4 were expressed in Expi 293F cells. Antibodies were purified by affinity chromatography and integrity checked with SDS-PAGE. Concentration was measured with a BCA protein assay and specificity tested with a Bet v 1 dot blot (all antibodies) and ISAC112 microarray (IgE).

SDS-PAGE confirmed specific isolation and correct assembly of antibodies. All produced antibodies bound specifically to Bet v 1. Overall yields from 30 ml were in the range of several hundred micrograms (IgE) to milligrams (IgG_1, IgG_4). We hereby successfully established an antibody PIPEline for recombinant antibodies of several classes against Bet v 1. These antibodies will be useful for studying class-specific antibody function in immediate type allergy and allergen immunotherapy to birch pollen.

Supported by the Austrian Science Fund FWF grants MCCA W1248-B30 and SFB

F4606-B28 to EJJ.

Abstract Title	Soluble FcεRI disrupts cell-bound IgE comparable to omalizumab
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Presenter	Kopanja, S.

The truncated portion of high-affinity IgE receptor (FcεRI) α subunit is released upon receptor cross-linking as a soluble form (sFcεRI) and is able to bind circulating IgE with strength comparable to the commercial humanized anti-IgE antibody omalizumab. The long-term application of omalizumab is shown to disrupt preformed IgE:FcεRI complexes on basophils. Furthermore, both omalizumab and sFcεRI bind to the same IgE-binding site. We investigated the competition between those two molecules for IgE, as well as the effect of sFcεRI long-term application.
MelJuSo (human melanoma-derived) cell line transfected with the trimeric or tetrameric isoform of FcεRI (αγ/αβγ) were loaded with chimeric IgE (cIgE) overnight, followed by a pulse per day of either sFcεRI (62.5 nM) or omalizumab (62.9 nM) for three days. Cell-bound cIgE levels were analysed by flow cytometry (n=5). Competition for IgE binding was assessed by ELISA detection of formed cIgE:sFcεRI complexes after incubation of sFcεRI (200 nM) and omalizumab (0-400 nM) in presence of cIgE.
Both molecules were able to disrupt cIgE:FcεRI complexes on MelJuSo-αγ/αβγ cells by 98.2% and 95.6% respectively for sFcεRI, and 98.8% and 97.7% for omalizumab. Additionally, we show that omalizumab and sFcεRI are competitors for the IgE binding site.
Comparable properties of sFcεRI long-term application with omalizumab imply a potential role of sFcεRI as an endogenous modulator of IgE-mediated responses.

Supported by the Austrian Science Fund (FWF): DK W 1248-B30 and the Medical University of Vienna.

Abstract Title	IgE sensitization profiles to kiwifruit cultivars in patients with pollen-food syndrome
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Presenter	Nagl, C.

Since the introduction of kiwifruit (KF) in routine diet, the prevalence of KF allergy (KFA) is increasing. Until recent times, the KF production throughout most of the world was based on the green-fleshed cultivar Actinidia deliciosa and the cultivar A. chinensis (gold KF). Latterly, the cultivar A. arguta (red KF) became available on the international market. The aim of our study is to characterize the allergenicity of different KF cultivars in an Italian population.

The study population included 17 patients aged 12-22 years affected by pollinosis, participating in the follow-up study “Panallergens in Pediatrics”, selected on the basis of the presence of allergic symptoms after ingesting green KF. Protein extracts were prepared from the total fruit of A. deliciosa and from the peel and seeds of A. deliciosa, A. chinensis and A. argute. Patients´ sera were tested for IgE binding by immunoblot.

Allergenic profiling of KF extracts: total protein, peel and seed extracts were obtained from KF cultivars and separated by Comassie stained SDS PAGE. When testing selected sera from KF allergic patients diverse IgE recognition patterns were detected including allergenic proteins in the range from 10 to 55 kDa.

KF is regarded as an allergenic plant food relevant for pediatric and adult patients. However, up to now, it is not known how different cultivars may result in an altered allergen specific response. Here, we present some comparisons of KF allergenicity. Further investigations will assess the differences in allergenicity of individual KF cultivars.

Abstract Title	A novel role for neutrophils in IgE-mediated allergy: Evidence for antigen presentation in late-phase reactions.
Authors Family name, initials	Dominika Polak[1], Christine Hafner[2], Caterina Vizzardelli[1], Peter Briza[3], Claudia Kitzmüller[1], Gabriela Sánchez-Acosta[1], Nazanin Samadi[1], Adelheid Elbe-Bürger[4], Peter Steinberger[5], Maria Gschwandtner[6], Wolfgang Pfützner[7], Gerhard J. Zlabinger[5], Beatrice Jahn-Schmid[1], and Barbara Bohle[1]
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Presenter	Polak, D.

Human neutrophils are abundant in allergic late-phase responses (LPR) and so far considered to contribute to allergic inflammation by the release of cytokines, chemokines and pathogenic compounds. In addition, it was reported previously that human neutrophils may acquire features of antigen-presenting cells. In particular, the cytokines GM-CSF, IL-3 and IFN-γ upregulated the expression of MHC class II molecules on neutrophils. Notably, all three cytokines are present in LPR. Therefore we speculated that neutrophils act as antigen-presenting cells (APC) for local allergen-specific effector T-cells.

GM-CSF, IL-3 and IFN-γ enhanced the life-span, allergen uptake and expression of HLA-DM and HLA-DR of neutrophils from allergic individuals. Isolated lysosomal proteases rapidly degraded the major birch pollen allergen (Bet v 1) into fragments containing relevant T-cell epitopes. Neutrophils pulsed with Bet v 1 induced proliferation of Bet v 1-specific T-cell clones specific for various epitopes distributed over the entire amino acid sequence of Bet v 1. Together, these data indicate that cytokine-activated neutrophils are fully capable of processing and presenting allergens. To proof the relevance of these *in vitro* data, we established an in vivo system and detected HLA-DR-positive neutrophils in allergen-induced cutaneous LPR of allergic individuals.

Our data demonstrate that neutrophils serve as APC for allergen specific T-cells. Thus, we identified a novel role for in the late phase reaction of IgE-mediated allergy.

Supported by the Austrian Science Funds, project W1248 and SFB F4610.

Abstract Title	PIPE cloning: Fast and efficient production of human monoclonal antibodies specific for the major milk allergen beta-lactoglobulin
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Presenter	Pranger, C. L.

Food-allergic reactions can affect various organs (skin, respiratory or gastrointestinal tract, or cardiovascular system) and may lead to severe conditions (Sicherer 2002). On average, 2-3% of children are suffering from IgE-mediated immediate type allergy to cow milk during the first year of life (Luyt et al., 2014), however it can be "outgrown" after 3-4 years. Specific tools for exploring the induction of tolerance in milk allergy are still missing, especially the role of IgG1 and IgG4 seems to be important in this mechanism. In this study, we used Polymerase Incomplete Primer Extension (PIPE) cloning (Ilieva et al., 2017) to generate human IgE, IgG1 and IgG4 antibodies containing the variable region against the major milk allergen beta-lactoglobulin (BLG) (Jylhä et al. 2016).
The final antibody was assembled using the PIPE cloning method, transformed into E. coli, validated by colony-PCR and finally expressed in the Expi293F cells for production. After purification by affinity chromatography, total yields were measured with BCA protein assay.
One transfection round yielded 2.2 mg of IgE, 0.8 mg of IgG1 and 1.9 mg of IgG4 antibodies. Correct assembly was validated by SDS-PAGE and their specific binding to BLG was confirmed in dot blot, ELISA and ISAC 112 allergen microarray.
In summary, PIPE-cloning is an efficient and fast method to produce functional human antibodies and their subclasses in high quantity. The newly generated antibodies will be useful tools to investigate the mechanism of milk allergy.

The work was supported by Austrian Science Fund (FWF), grants MCCA W1248-B30 and SFB F4606-B28 to EJJ.

Abstract Title	Deciphering T cell heterogeneity in prenatal human skin
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Presenter	Reitermaier, R.

In healthy individuals skin hosts a large numbers of T cells that allow an efficient immune response, but can also cause inflammation and autoimmune diseases. Small numbers of T cells were identified in prenatal human skin. However, this scarcity hampered their isolation and comprehensive characterization. We succeeded to isolate meaningful T cell numbers with preserved classical T cell markers with an automatic tissue dissociator and a dissociation kit. Like in adult skin, many T cell subsets were found by flow cytometry. Surprisingly, prenatal skin contained substantial numbers of γδ T cells, while in adult skin they represented only a minor population. Most prenatal skin T cells showed a naive phenotype and CD31 expression profiling indicated that about 40% thereof derive directly from the thymus. Besides small numbers of tissue resident, central and effector memory T cells, memory T cells re-expressing CD45RA and regulatory T cells, in addition to naive T cells, were the overwhelming T cell populations in prenatal skin. Furthermore, we identified an innate-like T cell subset distinct from conventional T cells. Special culture conditions facilitated the expansion of sizable numbers of prenatal T cells still displaying the post-isolation phenotype after 4 weeks of culture. The cytokine secretion profile of skin culture supernatants suggests a role of prenatal T cells in maternal immune tolerance. Results of this work may help to better understand skin diseases characterized by T cell activation and proliferation in the future.

Abstract Title	Cross-blocking activity of specific antibodies induced by SLIT with rBet v 1
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Presenter	Rodrigues Grilo, J.

We have recently performed a sublingual immuntherapy (SLIT) with the recombinant major birch pollen allergen rBet v 1. Twenty individuals received a daily dose of 25 *µ*g of rBet v 1 and 20 individuals received placebo for 16 weeks. Compared to the placebo group, SLIT with rBet v 1 induced significant levels of Bet v 1-specific IgG4 antibodies. Furthermore, the post-SLIT sera prevented the IgE-mediated activation of basophils indicating the induction of Bet v 1-specific blocking antibodies. Various tree pollens contain Bet v 1-homologous major allergens such as Aln g 1 (alder), Car b 1 (european hornbeam), Cas s 1 (chestnut tree), Cor a 1 (hazel), Fag s 1 (european beech), Ost c 1 (hop-hornbeam), Que a 1 (white oak), which through IgE-cross-reactivity cause allergic reactions in birch pollen-allergic patients. Here, we sought to investigate if SLIT with Bet v 1 induced antibodies can prevent IgE-mediated reactions to these homologous pollen allergens. We first tested the presence of IgG4 antibodies against the different pollen allergens by ELISA. We found that SLIT with rBet v 1 induced a significant increase of IgG4 against all Betv1 homologous pollen allergens except for Car b 1 and Cor a 1. Currently, the capacity of the post-SLIT sera containing specific IgG4 antibodies to inhibit basophil activation by the different homologs ist tested. Primary experiments provide evidence for a cross-blocking capacity of sera collected post SLIT with rBet v 1.

Supported by: Austrian Science Fund (FWF) projects: SFB F4610, KLI 96 & W1248, and the Medical University of Vienna

Abstract Title	ISAC112 allergen microarray, clusters of cross reactivity and clinical history in a retrospective cohort study
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Presenter	Shadan Ghandizadeh

Background: Management of allergic diseases would profit from better understanding of the relation between IgE reactivity patterns, components of allergens and clinical manifestations. Comprehensive assessment of clinical history of allergic patients together with molecular allergy diagnosis allow better assessment of cross reactivity and co-sensitization patterns.
Aims: This study aims to clarify the molecular characteristics of allergens recognized by IgE in allergic patients and to define clusters of allergens predictive for clinical symptoms.
Methods: By a 'molecules-to-clinic' approach,1058 patients with recorded clinical history were diagnosed by the ISAC112 allergen microarray. Clusters of cross-reactive allergens or co-sensitization were assessed and compared concerning clinical features. Skin prick tests were conducted to confirm ISAC112. We performed cluster analysis and multivariate regression analysis using SPSS 24.
Results: Overall, 18 molecular clusters of co-sensitizations and IgE cross-reactivity including at least two allergens were identified. Patients were grouped into ISAC negative, single and multiple cluster positives. Positive reactions to the Bermuda and Timothy grass pollen cluster and to the cluster of tree pollen and PR-10 related food allergens were most prevalent among our patients. Sensitization to allergens within these clusters was significantly more prevalent in males. Multivariate analysis of the clinical history and cross reactivity clusters revealed significant associations (p-value<0.05) between gastroesophageal reflux, gastritis and pulmonary disease and tree pollen, PR-10 related food proteins, grass pollen allergens and house dust mite allergens.
Conclusion: Based on our data we suggest that medical history may be related to individual IgE profiles as assessed by clusters of molecular allergens.

This work is supported by the Austrian Science Fund FWF, SFB-F4606-B28.

Abstract Title	The skin as an effector site of antigen-specific memory NK cells residing in the liver
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Presenter	Stary, V.

Evidence suggests that NK cells can develop highly specific memory to a variety of haptens and viral antigens in mice and in non-human primates. Despite description of memory-like features of human NK cells, the existence and consequences of antigen-specific NK cell memory still needs to be proven.

We isolated NK cells of human livers and blood from individuals vaccinated against hepatitis A and/or B and characterized them phenotypically and functionally in killing assays against antigens the patients had been vaccinated. In parallel, we evaluated the distribution and function of NK cells in epicutaneous patch test lesions of nickel-sensitized patients, an effector site of adaptive immune responses.

In contrast to NK cells of the peripheral blood, $CD49a^{+}CD16^{-}$ liver NK cells performed antigen-specific killing of hepatitis A/B-pulsed autologous B cells matching the patients' vaccination status. Blood-derived and $CD49a^{-}CD16^{+}$ liver NK cells did not exert antigen-specific cytotoxicity but were highly capable to lyse K562 in contrast to their $CD49a^{+}$ counterpart. Antigen-specific lysis by NK cells decreased when blocking the perforin/granzyme B pathway. Although absent in healthy human skin, 57.8 ± 5.1 % of total NK cells in nickel-induced epicutaneous patch test lesions exhibit the phenotype of antigen-specific NK cells of the liver ($CD49a^{+}CD16^{low}$) and were capable of specific lysis of nickel-pulsed autologous target cells.

These results suggest that antigen-specific memory NK cells in humans are present in the liver and participate in adaptive immune responses as antigen-specific effector cells in inflamed skin.

Supported by FWF

Abstract Title	Transient expression of the major birch pollen allergen Bet v 1 in the tobacco *Nicotiana benthamiana* using *in planta* assembled TMV-based provectors
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Presenter	Üzülmez, Ö.

Birch is the main pollen-allergen-producing tree in mid- and northern Europe. Its major allergen, Bet v 1, is considered an important inducer of tree pollen and related plant food allergies. Here, we present a platform technology for expressing plant-derived allergens in a plant system.

Agrobacterium tumefaciens, a plant pathogen, contains a Ti plasmid enabling the delivery of T-DNA into plant cells. We used two tobacco mosaic virus (TMV)-based provectors that harbor either T-DNA encoding Bet v 1 on a 3'-module or viral proteins on a 5'-module. A third provector delivered phiC31 integrase for recombining the 5'- and 3'-modules. Plants were infiltrated under vacuum while submerging leaves into a suspension of agrobacteria transformed with the corresponding plasmids. The mRNA synthesis of Bet v 1 was achieved after a successful recombination which brought the subgenomic promoter, polymerase, and allergen sequences together.

Recombinant (r) allergen, including a C-terminal hexa-histidine tag, was extracted from the leaves and isolated using Ni-NTA loaded beads. The purified rBet v 1 was able to bind both the mouse monoclonal anti-Bet v 1 antibody Bip 1 and IgE from birch pollen allergic patients' sera. After optimizing infiltration rates and incubation times of the plants, the highest expression yield of rBet v 1 was 12 mg per kg fresh leaf.

We made use of this *in planta* expression system for the first time to produce a plant-derived allergen. We will apply this system for more complex allergens in the future. Supported by Austrian Science Fund doctoral program W1248-B30.

Abstract Title	Bet v 1 oligomer complexed with specific IgE is more efficient in inducing specific T cell activation via CD23-mediated FAP than its monomeric counterpart
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Presenter	Villazala, S.

CD23, the low affinity receptor for IgE, mediates facilitated antigen presentation (FAP). FAP begins with the binding of IgE-allergen complexes to CD23. Those complexes are endocytosed and peptides derived from those antigens are eventually displayed on the cell surface. Specific T cells recognise those peptides and get activated, thereby amplifying a pre-existing immune response. Our aim was to study the effects of different types of IgE-Bet v 1 complexes on FAP. First, Epstein Barr virus transformed B cells were incubated with different concentrations and ratios of chimeric Bet v 1 specific IgE (CB1 IgE) and recombinant Bet v 1 in monomeric or oligomeric form. Primed cells were incubated with Jurkat T cells, which expressed a T cell receptor (TCR) specific for Bet v 1 and a luciferase reporter gene. Equimolar concentrations of CB1 IgE-oligomer Bet v 1 complexes induced higher specific T cell activation and also at lower concentrations (25 to 125 fold) when compared to CB1 IgE-Bet v 1 monomer complexes, independently of their ratio. Blocking of CD23 using anti-CD23 antibody completely abrogated specific T cell activation triggered by IgE-Bet v 1 complexes. Secondly, PBMCs from patients allergic to birch were isolated and then incubated with different equimolar concentrations of Bet v 1 monomer and oligomer for a week. Specific T cells from those patients also proliferated if stimulated with lower concentrations of Bet v 1 oligomer than monomer. These data indicate that the oligomerisation state of IgE-allergen complexes greatly enhances CD23-mediated FAP and subsequent allergen-specific T cell activation.

The research was funded by the Austrian Science Fund (FWF): DK W 1248-B13, SFB F4602, SFB F4604, SFB F4605, SFB F4608, SFB F4609, SFB4613 and the Medical University of Vienna

Abstract Title	JAK1 is indispensable for natural killer cell survival
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Presenter	Witalisz-Siepracka, A.

Janus kinase 1 (JAK1) is a member of JAK-STAT signaling pathway, which is critical in regulation of immune responses. In humans, deficiency of JAK1 leads to primary immunodeficiency, whereas ''loss of function'' mutations are associated with young age malignancies. JAK1 transmits the signal downstream of interleukin (IL) 15, which is a crucial survival factor for natural killer (NK) cells. NK cells are innate lymphocytes with a unique ability to directly recognize and kill virally-infected or transformed cells. JAK1/JAK2 inhibitor *Ruxolitinib* has been shown to reduce NK cell numbers, maturation and function. However, the exact contribution of JAK1 and JAK2 to NK cell survival and development has not been investigated. To address this question we have generated mice with conditional deletion of JAK1 or JAK2 in NKp46^{+} cells. We could show that deletion of NK cell-intrinsic JAK1 significantly reduces NK cell numbers in the bone marrow and impairs their development. In line, we observed almost a complete loss of NK cells in the spleen, blood and liver, proving a crucial role of JAK1 in NK cell survival. As expected NK cell-deficient *Jak1*$^{fl/fl}$*Ncr1Cre* mice show impaired tumor growth control. Importantly, deletion of JAK2 in NK cells had no effect on their survival or maturation. In summary, JAK1 is a key survival factor for NK cells, whereas JAK2 is dispensable, suggesting that usage of specific JAK2 inhibitors in patients would leave the NK cells untouched. Moreover we provide the community with an excellent tool to study the effects of NK cell deficiency.
Supported by FWF: SFB-F61

Abstracts – accepted for print

Abstract Title	Mice and Men: A comparison of Bet v 1-specific adaptive immune responses
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Presenter	Akinfenwa, A.O.

The major allergen from Birch pollen, Bet v 1, is responsible for severe respiratory symptoms as well as manifestations of food and skin allergy. As part of a strategy to develop non-allergenic forms of Bet v 1 for use in the prevention of birch pollen allergic disease, we designed and synthesized Bet v 1-derived peptides with 30- 42 amino acids in length and with an overlap of 5 amino acids in between them selected from the N-terminal to the C-terminal of the Bet v 1 sequence to ensure complete coverage of the allergen sequence and any possible epitopes recognized by mice and humans. A comparative study of Bet v 1epitopes recognized by IgE and IgG antibodies from mice sensitized to Bet v 1 and birch pollen allergic patients was mapped with the peptides by using direct ELISA and indirect mapping with peptide-specific blocking antibodies raised in rabbits.

The results reveal differences in patterns of epitope recognition and thus antibody formation between mice and humans. IgG1 and IgE antibodies from mice recognized identical epitopes in both the N-terminal and C-terminal peptides indicating antibodies are formed against sequential epitopes in mice. Human IgG and IgE antibodies however did not recognize any epitopes in the peptides as these antibodies are formed against conformational or non-sequential epitopes. These results along with comparative T-cell epitope mapping which we will conduct will help in translating results from our murine allergy research model for subsequent preventive trials in humans using Bet v 1 derived peptides.

Supported by the Austrian Science Fund (FWF) SFB project F4605 and the MCCA PhD-program.

Abstract Title	Torque Teno Virus Quantification for Immunologic Monitoring after Kidney Transplantation
Authors Family name, initials	Doberer, K.[1], Strassl, R.[1], Herkner, H.[2], Görzer, I.[3], Kläger, J.[4], Haupenthal, F.[1], Dermuth, F.[1], Puchhammer, E.[3], Bond, G.[1]
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Presenter	Doberer, K.

The continuous evolution of immunosuppressants has allowed for constant improvements of survival rates following kidney transplantation (KTx). Yet, the life-quality of KTx-patients is strongly limited by frequent routine visits for immunosuppressant trough level measurements, but more importantly by multiple infectious and immunologic complications due to inaccurate immunosuppression. One potent candidate to monitor the immunocompetence of the host might be the apathogenic and ubiquitous Torque Teno Virus (TTV). We could previously show that its peripheral load is slightly reduced in longterm allograft recipients experiencing chronic rejection episodes when compared to none-rejectors (N=86) and predicts infections in KTx-patients as early as three months before the event (N=169).

In our latest setting, patients transplanted between 01/01/2012 and 31/12/2017 were enrolled. A total of 113 allograft recipients with biopsies between month 4 and 12 post-KTx were eligible for TTV testing. TTV levels were significantly lower in rejectors ($3.1x10^7$ vs $2.26x10^8$, p=0.043) and predicted rejection episodes 48 days (median) prior to the event and 121 days (median) after KTx.

“Underimmunosuppression” might be due to insufficient dosing and/or insufficient Calcineurin-inhibitor (CNI-)through levels, rapid metabolization of immune-suppressants or non-adherence to prescribed drugs.

We suppose that these parameters are closely linked to the actual immunocompetence of the host and therefore enroll all KTx-patients since 01/01/2018. All informed consenting patients, routinely tested for TTV, are equipped with a medication event monitoring system for adherence monitoring. CNI doses and through levels are prospectively measured, the data will be linked to a parallel pharmacogenomic testing. A first interim-analysis is currently ongoing.

Supported by OeNB (Jubiläumsgrant AP17917) and “Austrian Science Fund” (KLIF 604-B31).

Abstract Title	Disease tolerance to sepsis is orchestrated by B cells and neutrophils
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Presenter	Gawish, R.

Sepsis is a severe condition characterized by uncontrolled activation of systemic inflammation, coagulation and subsequent organ failure. Next to the well-studied strategies of “avoidance” and “resistance”, mechanisms of disease tolerance aim to improve the host fitness irrespective of the pathogen burden. We have recently established a model, were mice are long-term protected from sepsis-induced organ damage, allowing us to study mechanisms of disease tolerance uncoupled from bacterial load dependent effects.

We could so far show that neutrophils and platelets are the main contributors to sepsis-induced liver failure by promoting micro thrombus formation. Tolerant animals showed reduced neutrophil extravasation into organs, an expansion of splenic B-cells and an increase of total IgM in the serum. Interestingly, B and T cell deficient ($Rag2^{-/-}$) animals fail to establish disease tolerance and this seems to be independent of neutrophil migration into peripheral organs.

Taken together, we propose a dual role for B cells, on the one hand promoting the organ damaging properties of neutrophils in a primary infection and on the other hand being important inducers of disease tolerance via IgM, that might suppress neutrophil migration into organs. The understanding of the complex interplay between neutrophils and B cells during the development of disease tolerance might possibly allow for novel therapeutic approaches in patients suffering from sepsis.

Supported by SFB-F54 (Cellular mediators linking inflammation and thrombosis)

Abstract Title	Identification and characterization of HDAC1 interaction networks in Th17 cells
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Presenter	Hamminger, P.

The differentiation and function of $CD4^+$ T helper (Th) subsets has to be tightly regulated, since their dysregulation is linked with immune-mediated diseases. Th cell differentiation is accompanied by reversible changes in histone acetylation, mediated by the opposing activity of histone acetyltransferases (HATs) and histone deacetylases (HDACs), however many non-histone targets are emerging, indicating that HAT/HDACs act beyond the regulation of chromatin. Results of my laboratory demonstrate an essential role for HDAC1 in regulating Th17 cell effector function and that loss of HDAC1 in T cells protects mice from the development of experimental autoimmune encephalitis. This clearly indicates essential roles for HDAC1 in the control of T cell-mediated autoimmunity. Since HDAC1 is part of larger multiprotein complexes, it is tempting to speculate that the crucial role of HDAC1 is mediated by targeting factors that are key regulators of Th17 cells. The aim of my PhD thesis project is to test this hypothesis.

Supported by: ÖAW (Austrian Academy of Sciences), FWF (Der Wissenschaftsfonds), IAI (Inflammation and Immunity PhD Program)

Abstract Title	Generation of a Jurkat based fluorescent reporter cell line to evaluate the interaction of lipid antigens with the human iNKT cell receptor
Authors Family name, initials	Humeniuk, P.[1], Geiselhart, S.[1], Battin, C.[2], Webb, T.[3], Steinberger, P.[2], Paster, W.[2], Hoffmann-Sommergruber, K.[1]
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Presenter	Humeniuk, P.

In contrast to conventional T lymphocytes, invariant natural killer T (iNKT) cells recognize lipid antigens presented by the class I MHC homolog CD1d. Their T cell receptor (TCR) consists of an invariant α-chain (Vα14-Jα18 in mice and Vα24-Jα18 in humans) paired with a restricted repertoire of β-chains. Upon activation iNKT cells secrete Th1, Th2 and Th17-type cytokines, thus they can significantly affect immune responses. Consequently, iNKT cells have been identified as important players in different types of immune responses. An iNKT reporter system was engineered by introducing the human iNKT TCR into a human leukemic Jurkat T cell line carrying an NF-kB-driven fluorescent transcriptional reporter construct (Jkt-iNKT). BW-CD1d, a human CD1d transfected thymoma cell line, was generated and used as antigen presenting cells. Reporter induction (NF-kB-driven eGFP-expression) in Jkt-iNKT cells was measured by flow cytometry. The specificity and sensitivity of our system was compared to IL-2 production by murine DN32.D3 iNKT cell hybridomas, following activation by α-Galactosylceramide (α-GalCer)-loaded recombinant CD1d molecules, as well as co-culture assays utilizing BW-CD1d cell lines. Jurkat cells stably expressing the human iNKT TCR receptor (Jkt-iNKT) were shown to specifically react with iNKT antigens presented in the context of CD1d. The detection limit for α-GalCer was similar for Jkt-iNKT and DN32.D3 cell lines. Our Jurkat-based iNKT cell reporter cell line is a useful tool to study the capacity of lipid antigens to activate human iNKT TCR. In addition, our reporter system is remarkably faster and more cost-effective, compared to traditional iNKT cell assays.

Supported by grants SFB F4603 and W1248 (Austrian Science Fund) to K. Hoffmann-Sommergruber and P. Humeniuk, respectively.

Abstract Title	A new classification system for IgG4 autoantibodies
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Presenter	Koneczny, I.

IgG4 autoimmune diseases are characterized by the presence of antigen-specific autoantibodies of IgG4 subclass, and contain well-characterised diseases such as MuSK myasthenia gravis, pemphigus and thrombotic thrombocytopenic purpura. Recently several new diseases were identified, and by now fourteen antigens associated with IgG4 subclass are known. The IgG4 subclass is considered as immunologically inert and functionally monovalent. In the context of IgG4 autoimmunity, pathogenicity of IgG4 is associated with blocking of enzymatic activity or protein-protein interaction of their target antigen. Pathogenicity of IgG4 autoantibodies has not yet been systematically analysed in IgG4 autoimmune diseases. Here we establish a modified classification system based on Witebsky's postulates to determine IgG4 pathogenicity in IgG4 autoimmune diseases, analyse published characteristics and pathogenic mechanisms of IgG4 in these disorders and also investigate the contribution of other antibody entities to pathophysiology by additional mechanisms. As a result, three classes of IgG4 autoimmune diseases emerged: class I where IgG4 pathogenicity is validated by use of subclass specific autoantibodies in animal models and/or *in vitro* models of pathogenicity, class II where IgG4 pathogenicity is highly suspected but lack a final validation by use of subclass specific antibodies *in vitro* models of pathogenicity or animal models, and class III with insufficient data or a pathogenic mechanism associated with multivalent antigen binding. Five IgG4 antibodies were validated as class I, five as class II and four as class III. Antibodies of other IgG subclass or Ig class were present in several diseases, and could contribute additional pathogenic mechanisms.

Supported by an Erwin Schrödinger Fellowship (J 3545-B13) by the Austrian Science Fund (FWF).

Abstract Title	Why do IgE profiles differ in humans and horses? Analyzing pollen allergen exposure on pastures and paddocks in collaboration with the Austrian Pollen Information Service.
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Presenter	Korath, A. D. J.

Background: In our recent study we revealed that IgE patterns in ISAC allergen microarray (Einhorn et al, Allergy 2018) differed between horses and humans, suggesting different allergen exposure.

Aims: We therefore aimed to collect pollen and plants from horse paddocks and meadows and compare to the pollen counts assessed for humans by the Austrian pollen Information Service.
Methods: Pollen were collected, on paddocks and pastures in four different horse stables, using pollen traps in April and in June 2018. The surrounding vegetation was examined botanically to correlate the pollen with the occurrence of allergenic plants.

Results: The overall pollen count was higher in early summer. In spring mostly pollen from Picea, Quercus and Fagus were found and in summer Poaceae, Urticaceae, Sambucus and Plantago pollen. The same pollen species as relevant for humans occur in the equine environment, however largely differing in terms of quantitative composition.

Conclusions: This study will provide evidence whether Information from the Austrian Pollen Information Service can be useful for owners of sensitized horses.

This study is supported by Austrian Science Fund FWF (grant SFB F4606-B28 to EJJ).

Abstract Title	Fcμ receptor as a new costimulatory molecule for T cells
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Presenter	Meryk, A.

Fc receptor for IgM (FcμR) deficient mice display dysregulated function of neutrophils, dendritic cells and B cells. The relevance of FcμR on human T cells is still unknown. We found that FcμR is mostly stored inside the cell and that surface expression is tightly regulated. Decreased surface expression on T cells from elderly individuals is associated with alterations in the methylation pattern of the FCMR gene. Binding and internalization of IgM stimulates transport of FcμR to the cell surface to ensure sustained IgM uptake. Concurrently, IgM accumulates within the cell and the surface expression of other receptors increases, among them, the TCR and costimulatory molecules. This leads to enhanced TCR signaling, proliferation and cytokine release, in response to low, but not high doses of antigen. Our findings indicate that FcμR is an important regulator of T cell function and reveals a new mode of interaction between B and T cells.

Supported by the EU H2020 project "An integrated approach to dissect determinants, risk factors, and pathways of ageing of the immune system" (ImmunoAgeing), the EU's Seventh Framework Programme "Advanced Immunization Technologies" (ADITEC) and the FWF Austrian Science Fund (P28694-B30 and DOC fellowship)

Abstract Title	Human bone marrow adipocytes display distinct immune regulatory properties
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Presenter	Miggitsch, C.

The bone marrow (BM) is a primary lymphoid organ of the human immune system where T and B cell precursors are generated and antigen-experienced adaptive cells are maintained. The BM has proven to be a major reservoir of resting memory T cells and long-lived plasma cells, capable of providing protection against recurrent infections. The survival and maintenance of these cells is mediated by cytokine and chemokine producing stromal cells and myeloid cell types, forming specific areas known as BM niches. However, no information is yet available on the production of memory T cell survival factors by BM fat tissue and the interaction with adaptive immune cells in the BM.

Using microarrays, we show that bone marrow fat significantly differs from subcutaneous fat regarding specific gene expression profiles including inflammatory responses. Reduced expression levels of the adipocyte-specific genes may suggest that the BM is an immune regulatory organ. Higher expression of the effector/memory T cell survival factors IL-7 and IL-15 were found in BM compared to subcutaneous adipocytes. The expression of the pro-inflammatory molecules TNFα and IL-6, which contribute to the low-grade inflammatory background known as “inflamm-aging” observed in elderly persons, was also higher in BM fat.

With our data, we can show that the unique phenotype of BM adipocytes expressing pro-inflammatory cytokines may have a negative effect on long-lived plasma cells while maintaining effector/memory T cells.

Abstract Title	Active transport of iron-flavonoid complexes by the major allergen bet v 1 leads to enhanced activation of the aryl hydrocarbon receptor
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Presenter	Regner, A.

Our *in silico* calculations predicted that the major allergen from birch, Bet v 1, has lipocalin-like function and is able to bind iron via high-affinity-iron-chelators called siderophores. Only when loaded with iron it was *in vivo* able to prevent to the development of IgE and allergic sensitization. Here we analysed *in vitro* the iron-binding capacity of Bet v 1, using flavonoids (catechol-type-siderophores). Furthermore, we determined the bioactive function of these iron-chelators focusing on the aryl-hydrocarbon-receptor (AhR). UV/VIS-spectra of three major flavonoids (Quercetin, Catechin, Epi-Catechin) in the presence or absence of allergens and iron were analyzed. Using the reporter cell line AZ-AhR activation of the AhR-pathway was determined by measuring luciferase activity. Presence of iron was measured with Calcein. All three tested flavonoids served as ligands for Bet v 1 regardless of the presence or absence of iron. Binding of these flavonoids alone or in complex with iron to Bet v 1 significantly enhanced AhR-activation in a concentration-dependent manner indicating active shuttling of flavonoids into the intracellular compartment. Moreover, iron transport into cells was confirmed by Calcein measurements. Flavonoids act as siderophores and bind to Bet v 1. Only the loaded form of Bet v 1 significantly stimulated AhR-activation via active transport of these flavonoids and iron into the cell, thereby enabling an immune-suppressive stimulus. The ligands of allergens may thereby be decisive for the subsequent immune response promoting tolerance.

The study was supported by the Austrian Science Fund FWF, grant SFB F4606-B28 to EJJ.

EJJ, LFP and FRW are inventors of EP2894478, owned by Biomedical International R+D GmbH, Vienna, Austria. The other authors declare no conflicts of interests.

Abstract Title	Mouse chow composition impacts on immune response and food allergy development in experimental models
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Presenter	Samadi, N.

Our diet is known to substantially influence the immune response not only by support of mucosal barriers, but also via direct impact on immune cell. Thus, it was of great interest to compare the influence of two mouse chows with substantial differences in micro-, macronutrient, lipid and vitamin content on the food allergic response in our previously established mouse model.
As the two mouse chows of interest, we used the feed previously used in animal facilities at the Medical university of Vienna (soy + low fatty acid (FA) feed) and compared it to the mouse chow in current use (soy free + high FA feed) in an established protocol of oral immunizations using Ovalbumin (OVA) as a model allergen under concomitant gastric acid suppression.
In the animals receiving soy + low FA feed, significantly more OVA-specific IgE, IgG1, IgG2a antibodies were detected compared to the animals receiving soy free + high FA feed. Moreover, food allergy was evidenced only in mice sensitized under soy + low FA feed by a drop of body temperature. In contrast, mice on soy free + high FA feed had significantly higher IL-10 levels and were protected from food allergy development.
In conclusion, soy + low FA feed was auxiliary during sensitizations, while soy free + high FA feed supported oral tolerance development and food allergy prevention.

Supported in part by a research grant of Nordmark Arzneimittel GmbH & Co. KG, Uetersen, Germany, by the Austrian Science Fund grant KLI248 and by the global research budget of the Medical University of Vienna (all to EU).
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Abstract Title	Molecular analysis of the guanine nucleotide exchange factor Rin-like in T follicular helper cell development and function
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Presenter	Sandner, L.

The differentiation of peripheral naïve CD4+ T-cells into effector T helper (Th) subsets upon activation by antigen presenting cells (APCs) has to be tightly regulated to enable an effective T-cell-mediated adaptive immune response. Molecular switches called GTPases which are controlled by guanine nucleotide exchange factors (GEF) and GTPase-activating proteins (GAP) participate in T cell activation.

We recently identified a novel member of the Rin family, designated Rin-like (Rinl) and showed that Rinl functions as a GEF for the Rab5 subfamily of GTPases. By generating Rinl-deficient mice, we have obtained evidence that Rinl modulates the development of follicular helper T- cells (Tfh) in vivo and *in vitro*. Tfh are essential for the development of germinal center B-cells and high-affinity antibody- producing B-cells in humans and mice.

As Rin and Rab proteins were mainly known to mediate intracellular protein trafficking, these findings unravel novel important functions for Rin proteins. We further aim to study the role of Rinl in the generation and function of Tfh in more detail and we expect that our studies will reveal how Rinl regulates Tfh development and function.

Supported by FWF

Abstract Title	The tissue-specific nature of cytotoxic T lymphocyte-driven viral evolution
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Presenter	Smyth, M.

Cytotoxic T lymphocytes (CTLs) represent key immune effectors of the host response against chronic viruses. Viruses can evade the selective pressure exerted by CTLs through escape mutations in viral T cell epitopes. This mechanism of immune escape is common to both chronic viral infections and malignant tumours.
Due to the fact that each tissue has distinct biological, chemical and biophysical properties, and that tissue-specific viral populations have been characterised both in clinical and experimental settings, we propose that CTL selection pressure acts in a tissue-specific manner. In order to investigate tissue-specific impact of CTL selection pressure and the emergence of CTL escape mutations, we employ the systemic chronic infection model of lymphocytic choriomeningitis virus (LCMV). We used T cell receptor transgenic mice and viral escape mutants to modulate the selection pressure on the immunodominant GP_{33-41} CTL epitope. Thereby, we expect to elucidate understand how CTL selective pressure shapes tissue-specific viral populations. We expect fundamental insights into the evolutionary dynamics of T cells and pathogens which could also be applicable to cancer immunotherapy.

Supported by a DOC fellowship of the Austrian Academy of Sciences

Abstract Title	Characterization of the affinity of Mal d 1-specific antibodies induced by sublingual immunotherapy with recombinant Bet v 1 or Mal d 1
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Presenter	Strobl, M.R.

High structural similarity between the major birch pollen allergen Betv1 and the major apple allergen Mald1 results in immunological cross-reactivity, causing food allergy in up to 70% of birch pollen-allergic individuals. Betv1-sensitized individuals with birch pollen-related apple allergy (BPRAA) were treated with sublingual immunotherapy (SLIT) using recombinant (r)Betv1, rMald1 or placebo for 16 weeks within the framework of a single center, double-blind, placebo-controlled study to investigate the effect of SLIT on BPRAA. Significant clinical improvements to apple were recorded in the rMald1-treated group, in contrast to patients who were administered rBetv1 or placebo. One immune mechanism underlying successful SLIT is the induction of allergen specific IgG4 antibodies which may block the formation of IgE-allergen complexes and thereby hamper allergic responses. Notably, rMald1-specific IgG4 antibodies were found in post-SLIT sera of both verum groups, however, only those induced by SLIT with rMald1 showed IgE-blocking capacity. We hypothesize that rMald1-specific IgG4 antibodies induced by SLIT with rMald1 have a higher affinity to the apple allergen than those induced by SLIT with rBetv1. We will analyze and compare the binding characteristics of rMald1-specific antibodies in post-SLIT sera of both patient groups by surface plasmon resonance. Subsequently, we will correlate possible differences with clinical efficacy of SLIT. Thereby, we will gain a deeper understanding of the SLIT-induced antibody response and mechanism of tolerance induction in BPRAA.

Supported by FWF, W1212 and SFBF4610

Abstract Title	Anti-apoptotic regulator Bcl-2 is upregulated in graft-versus-host disease
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Presenter	Strobl, J.

Graft-versus-Host Disease (GvHD) remains a major cause of mortality after allogeneic hematopoietic stem cell transplantation with 30-80% of graft recipients developing acute or chronic GvHD. Recently, a small molecule inhibitor of Bcl-2, an anti-apoptotic protein highly expressed in barrier tissues and activated immune cells, was approved for treatment of chronic lymphocytic leukemia. To test Bcl-2 as a potential pro-inflammatory target in treatment of GvHD, we performed RT-PCR, flow cytometry and tissue immunofluorescence in human blood, lung, gut and skin samples of 90 patients with previously untreated acute or chronic GvHD.

While Bcl-2 RNA and protein levels were not elevated in overall leukocytes, pathogenic cell subsets including monocytes, CD8+ T lymphocytes and NKT cells showed significantly higher expression of Bcl-2 in peripheral blood of GvHD patients as compared to healthy controls. These results could be recapitulated in tissue samples, where cytotoxic lymphocytes (T, B, NK, NKT) were numerically expanded and expressed Bcl-2 in acute and chronic GvHD skin lesions. Notably, non-pathogenic cell types such as keratinocytes did not exhibit increased Bcl-2 expression compared to control samples from healthy donors.

We could show exclusive upregulation of Bcl-2 in GvHD-mediating cell types in peripheral blood and tissue samples affected by GVHD. Thus, Bcl-2 inhibition may present a novel and highly needed targeted therapy in treatment of acute and chronic GvHD.

Supported by a DOCmed fellowship of the Austrian Academy of Sciences

Abstract Title	Molecular Analysis of the Guanine Nucleotide Exchange Factor Rin-Like in Development and Differentiation of Follicular T Helper Cells
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Presenter	Tscharntke, R.

Rin-like (Rinl) was first identified as interaction partner of the muscle-specific receptor tyrosine kinase MuSK. Previous studies characterized Rinl as member of the Ras-interaction/interference (Rin) protein family and revealed its function as guanidine exchange factor (GEF) for members of the Rab5 GTPase subfamily. Rab GTPases regulate membrane trafficking including vesicle function and movement by acting as molecular switches. Their conformational change is catalysed by GEFs. Upon Rinl overexpression an increased fluid-phase uptake and EGFR endocytosis implicated Rinl as regulator of Rab5-dependent endocytic processes. Recent studies have linked Rab GTPases with the formation and sustainment of the immunological synapse in T cells. To determine Rinl function *in vivo* a knock-out (KO) mouse line was generated. While Rinl-KO mice represent with normal development and fertility, they show enhanced inflammatory responses upon immunization with an increase in the number of T follicular helper (Tfh) cells, a T cell subset essential for the development of germinal centre B cells and high-affinity antibody-producing B cells in humans and mice. The aim of this thesis is to investigate the role of Rinl in the regulation of Tfh development and function. Therefor it is necessary to understand which molecular mechanisms are regulated by Rinl in T cells. We want to study Rab5-GTPase family members in T cells with emphasis on Rab5a and Rab22a activity as well as potential alterations of the endocytic processes in the T cell receptor/CD28 signalling pathway. Further a proteomics approach will be used to identify Rinl interaction partners.

Supported by FWF Project P30885-B30

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