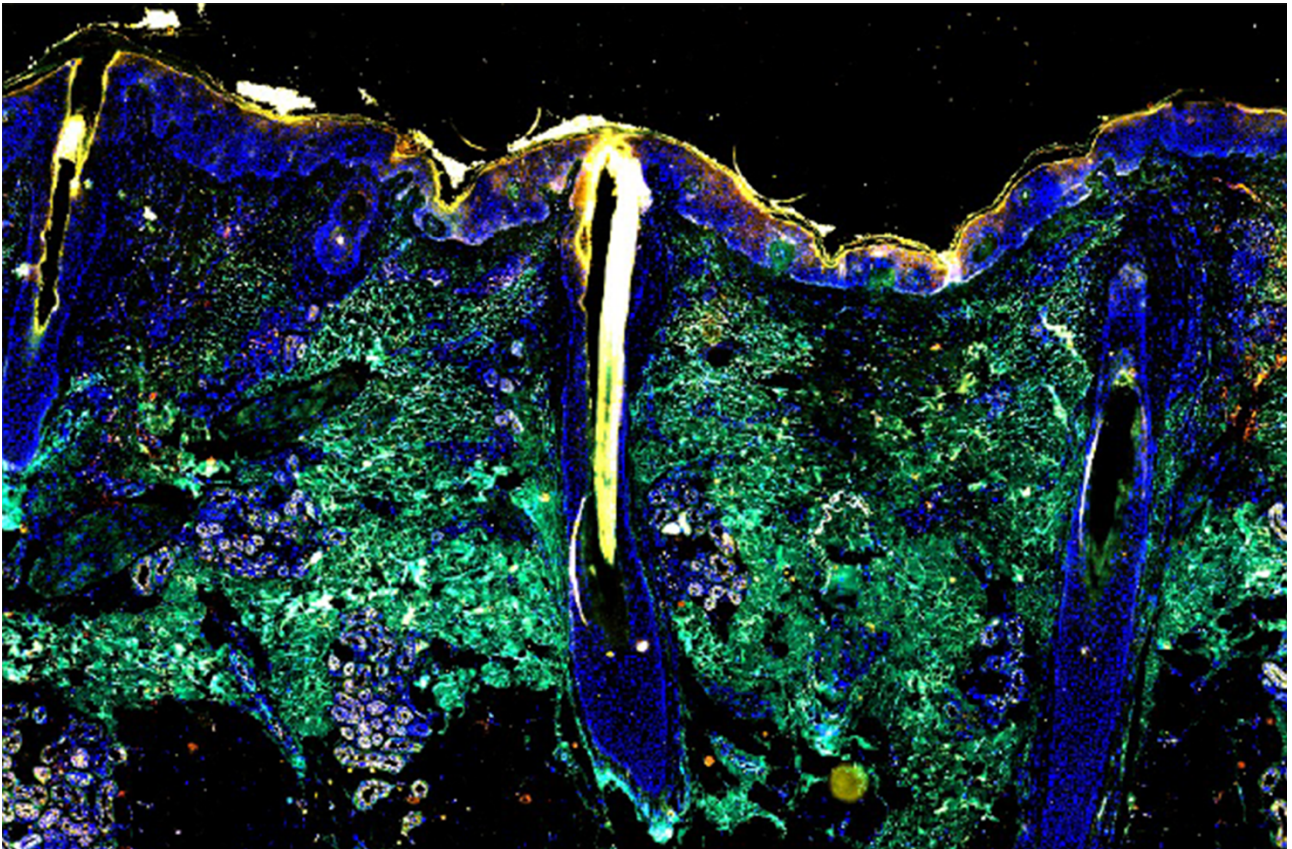


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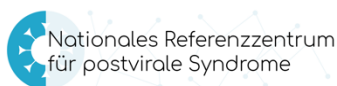
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Abstract Number: 5

Abstract Title: Monoclonal antibodies against L2 and chimeric virus-like particle vaccines cross-protect against genus beta human papillomaviruses (HPV) implicated in skin cancer development

Authors:

Huber B¹, Schüchner S², Mohr K², Ogris E², Kirnbauer R¹

¹Medical University of Vienna, Dept. of Dermatology, ²Medical University of Vienna, Max Perutz Labs

Abstract:

Certain cutaneous genus beta HPV types (β HPV) have been implicated in the development of non-melanoma skin cancer in immunosuppressed patients. Licensed multivalent HPV vaccines based on Virus-like Particles (VLP) assembled from major capsid protein L1 are highly immunogenic but do not target any β HPV types.

One strategy to develop a broad-spectrum β HPV vaccine is based upon the highly conserved N-terminus of the minor structural protein L2. To identify cross-neutralization epitopes, we employed an innovative sequential immunization strategy and generated monoclonal antibodies (mAbs) against L2 of five β HPV.

Four distinct mAbs were obtained that neutralized several of the 8 β HPV types tested (5/8/20/24/38/76/92/96) in vitro, and by passive transfer protected mice in vivo against 2 or all three β HPV types tested. Following epitope mapping, chimeric HPV16 VLP were designed that present novel β HPV5 L2 (cross-)neutralization epitopes repetitively spaced on the L1-VLP surface, to increase immunogenicity.

Five chimeric proteins were generated and VLP assembly examined by electron microscopy and ELISA. Induction of (cross-)neutralizing antibodies was assessed in mice and rabbits, and a murine genital model was used to analyze in vivo protection against challenge with β HPV.

In mouse immunizations, 4/5 chimeric VLP-induced sera broadly cross-neutralized all 8 tested β HPV and oncogenic mucosal HPV16 in vitro. In rabbit immunizations, 4/5 chimeric VLP induced sera that cross-neutralized several tested β HPV types as well as HPV16. By passive serum transfer, 2/4 chimeric VLP-raised antisera conferred partial protection against β HPV5, and 3/3 tested chimeric VLP-raised sera partially cross-protected against β HPV24. To circumvent protective antibody dilution in the blood circulation after passive transfer, active immunization with each chimeric VLP provided protection against β HPV5 challenge. In addition, immunization with two tested chimeric VLP provided either complete or partial protection against β HPV38 or 76.

Novel β HPV-targeting chimeric VLP vaccine candidates elicit broad-spectrum immunity and protection against potentially oncogenic β HPV.

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Abstract Number: 6

Abstract Title: Broad-Spectrum HPV Protection Via Recombinant Measles Virus Vectors

Authors:

Sanchez Jimenez A¹, Lange M², Potzmann E¹, Ebenig A², Huber B¹, Mühlebach M², Kirnbauer R¹

¹Medical University Of Vienna, ²Paul-Ehrlich-Institut

Abstract:

Current multivalent HPV vaccines utilize L1-based virus-like particles (VLPs) to induce potent, type-restricted immunity against up to nine HPV types. However, broad protection against non-vaccine types remains challenging. To achieve broader coverage, we previously engineered RG1-VLP by incorporating the conserved cross-neutralizing HPV16 L2 RG1 epitope into the DE-loop of HPV16 L1, demonstrating protection against at least 22 mucosal HPV types in preclinical models and advancing to a Phase I trial.

Here, we used the Recombinant Measles Virus (rMeV) Moraten vaccine strain as a vehicle to express the HPV16-RG1 fusion protein, aiming for dual protection against multiple HPV types and measles. A codon-optimized ORF encoding the L1-RG1 fusion protein was inserted into an additional transcriptional unit of the MeV genome. New Zealand White (NZW) rabbits were immunized four times at 3-week intervals with the rMeV-RG1 candidate (n=3/group).

Measles-specific immunity was confirmed using ELISA and viral neutralization assays. RG1-specific antibodies were detected in peptide ELISAs with titers reaching up to 12,800. HPV16 neutralization and cross-neutralization against HPV31/59/5 were confirmed by PBNA and L2-based PBNA, respectively. Avidity ELISA and Surface Plasmon Resonance (SPR) demonstrated progressive antibody affinity maturation following booster immunizations. Crucially, passive transfer of rabbit sera to Balb/c mice conferred in vivo cross-protection against challenge with HPV16, 45, 39, and 59 pseudoviruses.

These data demonstrate the strong cross-neutralizing potential of the rMeV-RG1 candidate and its capacity to protect against in vivo challenge with at least four high-risk HPV types.

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Abstract Number: 7

Abstract Title: Metabolic profiling of immune cells using flow cytometry

Authors:

Aronis C¹, Tóth K¹, Thiel J¹, Lorenzetti R¹, **Villa M**¹

¹Medical University Of Graz

Abstract:

Nutrient sensing and metabolic reprogramming are key players in immune cell activation and function. The exploration of the metabolic needs of immune cells may provide new angles to understand and tackle human diseases.

We used spectral flow cytometry to integrate the staining of immunological markers for the discrimination of T cells, B cells and myeloid cells, and of nutrient transporters (CD71, CD98 and CD36) with dyes that report mitochondrial membrane potential, mass and reactive oxygen species content. We used this method to quantify proxies of cellular metabolic pathways in human, non-fixed, peripheral blood mononuclear cells (PBMC) and polymorphonuclear cells (PMN), with an eye to the diagnostic implementation of this method.

Antigen-experienced B cells showed elevated mitochondrial function and glycolytic predilection as compared to naïve B cells, a feature most evident in plasma cells. While naïve and memory subsets of T cells showed small metabolic differences, CD4+ T cells had elevated mitochondrial membrane potential as compared to CD8+ counterparts. Monocytes expressed high CD98 and CD36, the latter indicative of their metabolic preference to fatty acid utilization. Neutrophils and eosinophils showed low levels of CD71 and CD98, low levels of CD36, but sustained mitochondrial membrane potential, suggesting their reliance on mitochondrial metabolism.

Our spectral flow cytometry strategy probes the cellular metabolism of human blood immune cells faithfully, reproducing current knowledge about their metabolic status, as well as providing new insights. Our immunometabolic phenotyping strategy will aid the understanding on how cellular metabolism impinges on immune function in patients with inflammatory and autoimmune diseases.

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Abstract Number: 8

Abstract Title: Understanding the metabolic adaptations of immune cells to the microenvironment of the arthritic joint

Authors:

Aronis C¹, Tóth K¹, Lorenzetti R¹, Thiel J¹, Villa M¹

¹Division of Rheumatology and Immunology, Medical University of Graz

Abstract:

Background

Arthritides are inflammatory diseases affecting the joints. To drive tissue inflammation, immune cells must infiltrate the tissues after leaving the circulation. We hypothesize that immune cells infiltrating the joint respond to local tissue environment cues and reprogram their cellular metabolism in order to adapt and perform their effector functions. Studying how immune cells adapt their metabolism during their transition from blood to the arthritic joint can ultimately identify novel metabolic targets for therapeutic interventions.

Methods

Using spectral flow cytometry on matched peripheral blood mononuclear cells (PBMCs) and synovial tissue from osteoarthritis patients, we have integrated staining of surface lineage markers and nutrient transporters (CD36 for fatty acids, CD71 for transferrin, CD98 for amino acids) with fluorescent dyes reporting mitochondrial membrane potential (TMRM), mass (MitoTracker Green) and the intracellular reactive oxygen species content (CellROX). This strategy will be further used to analyze samples from patients affected by other inflammatory and autoimmune arthritides.

Results

Matched PBMC and synovium analysis revealed distinct metabolic states in tissue macrophages compared to their blood monocyte counterparts. Specifically, synovial macrophages demonstrated a drop in mitochondrial membrane potential, indicative of a potential mitochondrial dysfunction in response to the tissue environment, alongside differential expression of surface nutrient transporters when compared to monocytes.

Conclusion

Immune cells undergo marked metabolic reprogramming upon encountering the synovial microenvironment. Targeting these tissue-specific metabolic shifts offers a promising therapeutic strategy for inflammatory joint diseases. Our work on patients affected by osteoarthritis suggests an inflammatory component that is progressively being recognized. Ongoing work will validate whether metabolic pathways have therapeutic significance across in vitro and in vivo models using biochemical and functional assays.

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Abstract Number: 9

Abstract Title: Spatial organization of stromal cell subsets stratifies colorectal cancer patients and predicts clinical outcomes

Authors:

Frank M¹, Ghirardello G¹, Howie J¹, Braun N¹, Zirnbauer R², Stecher C¹, Gruener S¹, Regele H³, Barozzi I¹, Bergmann M², Laengle J², **Herndler-Brandstetter D¹**

¹Medical University of Vienna, Center for Cancer Research, ²Medical University of Vienna, Department of General Surgery, ³Medical University of Vienna, Department of Pathology

Tumor-associated stromal (TAS) cells within the tumor microenvironment (TME) exhibit marked transcriptional heterogeneity. However, the spatial organization of TAS subpopulations and their clinical relevance in human colorectal cancer (CRC) are incompletely understood. Using single-cell RNA sequencing (scRNA-seq) and multiplex imaging, we identified multiple TAS subpopulations with distinct intratumoral and peritumoral abundance, and found that CRC patients enriched in FAP+ TAS cells and CD73+ tumor cells had the lowest disease-free survival (DFS). NGFR+ stromal cells localized predominantly within tertiary lymphoid structures (TLS), which could be further classified into NGFR+ organized TLS, NGFR+ unorganized TLS and NGFR- TLS based on the spatial distribution of NGFR+ stromal cells. CRC patients enriched for NGFR+ organized TLS exhibited improved DFS. SCENIC analysis revealed HAND2, IKZF2 and SOX10 as transcriptional regulators of

human NGFR+ antigen-presenting TAS cells, and they frequently expressed enteric glial cell markers SOX10,

PLP1, CDH19 and NCAM1. In summary, our study demonstrates that the frequency and spatial distribution of TAS subpopulations, particularly NGFR+ TAS organization within TLS, varies between CRC patients and correlates with DFS and distinct changes in the TME.

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Abstract Number: 10

Abstract Title: Neutrophil-derived arginase 1 restrains macrophage-driven inflammation

Authors:

Ettel P¹, Wilson J¹, Saha P¹, Mazic M¹, Kopf A^{2,3}, Brazdilova K^{2,3}, Stary G^{2,3,4}, Melikhov I¹, Miller A¹, Jablonska J^{5,6}, Hoffmann M⁷, Schabbauer G⁸, Hengstschläger M¹, Weichhart T¹

¹ Medical University of Vienna, Institute of Medical Genetics, ²Medical University of Vienna, Department of Dermatology, ³CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences, ⁴Christian Doppler Laboratory for Chronic Inflammatory Skin Diseases, ⁵Department of Otorhinolaryngology, Head and Neck Surgery, University Hospital Essen, University of Duisburg-Essen, ⁶German Cancer Consortium (DKTK) partner site Düsseldorf/Essen, ⁷Institute for Systemic Inflammation Research, University of Lübeck, ⁸Medical University of Vienna, Institute for Vascular Biology

Abstract:

Introduction & Background

Macrophage-driven inflammation underlies many inflammatory diseases, yet the mechanisms that restrain macrophage activation within inflamed tissues remain poorly understood.

Methods

Using mouse models of foreign body granuloma formation and macrophage activation syndrome, we investigated the role of neutrophils in regulating macrophage-driven inflammation. Findings were complemented by analyses of human neutrophils and patient samples from individuals with sarcoidosis and macrophage activation syndrome.

Results

Neutrophils accumulated at sites of inflammation and metabolically restrained macrophage-driven pathology. Neutrophil depletion or genetic impairment exacerbated tissue pathology, whereas induced neutrophilia attenuated inflammatory damage. Tissue-infiltrating neutrophils acquired an alternatively polarized state characterized by high arginase 1 expression, regulated by an IL4R α –STAT3–NOX2 signaling axis. Functionally, these polarized neutrophils depleted extracellular arginine in an arginase 1-dependent manner, thereby limiting macrophage effector programs. Human neutrophils exhibited conserved regulation of arginase activity, and alternatively polarized neutrophils were detected in patients with sarcoidosis and macrophage activation syndrome.

Conclusion

These findings identify an arginine-dependent metabolic mechanism through which alternatively polarized neutrophils restrain macrophage-driven inflammation and reveal a previously unrecognized immune-regulatory role for these cells in chronic inflammatory disease.

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Abstract Number: 11

Abstract Title: Deletion of tumor necrosis factor in mice leads to altered macrophage iron homeostasis and promotion of *Salmonella enterica* serovar Typhimurium multiplication

Authors:

Brigo N¹, Pfeifhofer-Obermair C¹, Grubwieser P^{1,2}, Engl S¹, Seifert M¹, Hilbe R¹, Bumann D³, Schleicher U⁴, Bogdan C⁴, Weiss G¹

¹Department of Internal Medicine II, Medical University of Innsbruck, Anichstrasse 35, ²Institute for Hygiene and Medical Microbiology, Medical University Innsbruck, ³Biozentrum, University of Basel,

⁴Mikrobiologisches Institut - Klinische Mikrobiologie, Immunologie und Hygiene, Universitätsklinikum Erlangen and Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg

Abstract:

Background: Tumour necrosis factor alpha (TNF) is crucial for controlling intracellular bacterial infections and regulates cellular iron homeostasis by modulating the iron storage protein ferritin (FTH), thereby affecting cellular iron levels. This impacts intracellular multiplication of siderophilic bacteria like *Salmonella enterica* serovar Typhimurium (S.tm), influencing infection control.

Methods: We investigated the impact of TNF on the control of S.tm infection in vivo and employing bone marrow-derived macrophages (BMDM) from TNF-deficient (TNF^{-/-}) and C57BL/6 wild-type mice. Mechanistic pathways including systemic and cellular iron homeostasis, immune response and pathogen multiplication/bacterial iron acquisition were studied. Additionally, we assessed the effects of pharmacological iron modulation on disease outcomes and analysed alterations of iron homeostasis in rheumatoid arthritis patients receiving anti-TNF therapy.

Results: Compared to wild-type BMDMs, TNF^{-/-} BMDMs showed significantly reduced S.tm killing capacity, associated with reduced expression of the iron exporter ferroportin (FPN-1), increased FTH, expanded intracellular iron levels and diminished anti-microbial immune responses (iNOS, NO, IL-1b). TNF^{-/-} mice showed accelerated mortality and higher bacterial burden, alongside splenic and hepatic iron retention, facilitating bacterial access to iron as confirmed by employing iron-sensitive fluorescence plasmids in the bacterial strain. Systemically, TNF deletion increased IL-6 formation, which induced hepcidin formation in the liver, subsequently targeting and degrading FPN-1 and blocking iron export. Consistently, rheumatoid arthritis patients receiving anti-TNF treatment displayed increased hepcidin and serum iron levels three months post-treatment. Of note, treatment of murine TNF^{-/-} BMDM with the iron chelator desferasirox (DFX) which reduces intracellular iron levels, improved control of *Salmonella* infection and increased anti-microbial immune effector pathways.

Conclusion: TNF deletion alters iron metabolism, leading to macrophage iron retention through hepcidin-mediated blockade of iron export. This creates a favourable environment for *Salmonella* proliferation and compromises host anti-microbial defences, highlighting the critical role of TNF in linking iron homeostasis to infection control.

Abstract Number: 12

Abstract Title: T-cell PKM2 as a novel therapeutic target in multiple sclerosis

Authors:

Ellmeier E¹, Schnabl A¹, Meissel J¹, Stracke A¹, Rittchen S¹, Stöger L¹, Passegger C¹, Schwarzl L¹, Tafrali C², Demjaha R², Martinez-Serrat M², Kaiser T^{1,2}, Zeiler L^{1,2}, Seifried K^{1,2}, Topler A¹, Klemen I¹, Heschl B², Damulina A², Runtsch M³, Fessler J¹, Hofer E^{2,4}, Khalil M^{2,5}, Angiari S^{1,5,6}

¹Division of Pathophysiology and Immunology, Otto Loewi Research Center, Medical University of Graz, ²Department of Neurology, Medical University of Graz, ³Division of Oncology, Medical University of Graz, ⁴Institute for Medical Informatics, Statistics and Documentation, Medical University of Graz, ⁵BioTechMed-Graz, ⁶Research Unit Sex and Gender in Disease Pathophysiology, Medical University of Graz

Abstract:

Background: Pyruvate kinase M2 (PKM2) is an enzyme with moonlighting activities that controls murine T cell pro-inflammatory potential in a mouse model of multiple sclerosis (MS). However, no study analysed in detail the expression of PKM2 in human T cell subsets, and whether targeting PKM2 may limit the inflammatory potential of T cells from patients with MS is unknown.

Methods: In this observational, case control study we evaluated the expression of PKM2 in circulating T cells of healthy control individuals (HCs) and patients with MS, as well as its isomerisation in peripheral blood mononuclear cells (PBMCs) from HCs and patients. In parallel, we analysed the impact of targeting PKM2 on the inflammatory profile of T cells from HCs and individuals with MS.

Results: Circulating effector and memory T cells express higher PKM2 levels compared to naïve T cells, and PKM2 expression in such T cell subsets may correlate with age and disease duration in individuals with MS. Among effector/memory T cells, the Th17/Tc17 subsets display the highest PKM2 expression. Additionally, we observed a preferential inhibition of interferon-gamma (IFN- γ), interleukin-5 (IL-5), IL-13, and IL-17 production by MS T cells upon PKM2 pharmacological targeting. Finally, we found that PBMCs from patients with MS have a higher percentage of PKM2 monomer compared to PBMCs from HCs, supporting heightened PKM2 moonlighting activity.

Conclusion: Our data suggest that PKM2 may represent a therapeutic target to limit T cell-driven inflammation in MS and potentially other human autoimmune diseases.

Targeting pyruvate kinase M2 (PKM2) reduces T cell pathogenicity in multiple sclerosis

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Abstract Number: 13

Abstract Title: $\gamma\delta$ T-lymphocytes reciprocally interact with human periodontal soft tissue derived MSCs

Authors:

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¹Medical University Of Vienna, ²Al-Ahliyya Amman University

Abstract:

Background: Human periodontal soft tissue-derived mesenchymal stromal cells (hPST-MSCs) are crucial mediators of tissue homeostasis by influencing cells of the innate and adaptive immune system in a predominantly immunosuppressive style. This reciprocal interaction is executed via soluble (indoleamine-2,3-dioxygenase-1 (IDO-1), and prostaglandin E2 (PGE2)) and membrane-bound (programmed cell death-ligand 1 (PD-L1)) immunomediators which are triggered by the local immune cell-dependent production of cytokines (interferon (IFN)- γ and tumor necrosis factor (TNF)- α).

Human $\gamma\delta$ T-lymphocytes are unconventional T-lymphocytes bridging innate and adaptive immunity. Despite studies on their role in murine models of periodontitis, data on their role in human oral tissues is lacking and their interaction with hPST-MSCs unexplored.

Methods: We investigated key players within the reciprocal interaction of $\gamma\delta$ T-lymphocytes and hPST-MSCs in vitro.

Paracrine and cell-to-cell contact-dependent interactions were investigated by comparing direct and indirect co-cultures of allogenic $\gamma\delta$ T-lymphocytes with primary hPST-MSCs in the presence or absence of pharmacological inhibitors of immunomediators. Viability and proliferation of $\gamma\delta$ T-lymphocytes were assessed via flow cytometry, metabolic activity of hPST-MSCs by Resazurin assay and immunomediator gene expression by RT-qPCR. Supernatants were analyzed regarding IDO activity and cytokine levels by photometric analysis and multiplex assay.

Results: The immunomodulatory activity of hPST-MSCs significantly reduced $\gamma\delta$ T-lymphocyte proliferation in indirect co-cultures. hPST-MSCs showed a significant upregulation of PD-L1, cyclooxygenase-2 and IDO-1 expression, resulting in increased IDO activity. Upon pharmacological inhibition of IDO, proliferation was restored almost entirely, identifying IDO as the main immunomediator. This cascade was triggered by TNF- α and IFN- γ production of the $\gamma\delta$ T-lymphocytes. Additionally, hPST-MSCs were highly susceptible to $\gamma\delta$ T-lymphocyte induced cell death, however, only in direct co-culture setting.

Conclusion: These results demonstrate a strong multifactorial reciprocal interaction between hPST-MSCs and $\gamma\delta$ T-lymphocytes, thereby opening up questions on the role of $\gamma\delta$ T-lymphocytes in the context of periodontal diseases, such as periodontitis.

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Abstract Number: 14

Abstract Title: Defining and characterizing bona fide senescent CD8⁺ T cell populations in health and disease

Authors:

Pangrazzi L¹, Pehl P¹, Hoffmann L¹, Walser L, Cavinato M¹, Weinberger B¹

¹Institute for Biomedical Aging Research, University of Innsbruck

Abstract:

Cellular senescence represents a crucial contributor to the age-associated decline in immune function, including within the CD8⁺ T cell compartment. This study aimed to define and characterize candidate bona fide senescent CD8⁺ T cell populations, which have previously been identified using different combinations of markers, including CD27, CD28, CCR7, CD45RA, and CD57. We specifically examined the relationships between senescence-associated markers, mitochondrial parameters, and other immune-cell features across CD8⁺ T cell subsets and donor age groups.

Peripheral blood samples from healthy donors of different ages and from patients with rheumatoid arthritis (RA) were analysed for senescence and differentiation markers, pro-inflammatory cytokines, effector molecules, mitochondrial fitness, oxidative stress, apoptosis, and proliferative capacity. Unsupervised hierarchical clustering was used to identify distinct molecular patterns, and RNA sequencing was performed on sorted cell populations.

Among the phenotypes analysed, CD27⁻CD45RA⁺ cells displayed the strongest overall senescence signature, including elevated p21 and SA-β-gal expression, metabolic dysfunction with altered lipid profiles, and impaired mitochondrial function. This phenotype was further refined by the CD27⁻CD28⁻CCR7⁻CD57⁺CD45RA⁺ population, which most consistently combined terminal differentiation with senescence-associated features. Particularly in older donors, these cells showed reduced DNA-damage-induced apoptosis, impaired DNA-damage responses, and diminished proliferative capacity. RA patients exhibited differences in the expression of several senescence-associated features, consistent with an accentuated or disease-modulated senescent phenotype. Finally, treatment of old mice (> 18 months) with the senolytic cocktail fisetin and quercetin reduced SA-β-gal levels in total CD8⁺ T cells and in CD8⁺CD44⁺ memory CD8⁺ T cells.

Taken together, our findings identify bona fide senescent CD8⁺ T cell populations that may be further altered or exacerbated in RA. They also provide preliminary evidence that fisetin and quercetin can target senescent CD8⁺ T cells in aged mice, supporting further investigation of senolytic strategies for immune rejuvenation.

Abstract Number: 15

Abstract Title: Do Allergen immunotherapy-induced allergen-specific serum IgA antibodies exhibit blocking activity?

Authors:

Repiská K¹, Wozniak-Knopp G², Möbs C³, Pfützner W³, Bohle B¹

¹Institute of Pathophysiology and Allergy Research, Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, ²Institute of Molecular Biotechnology, Department of Biotechnology, University of Natural Resources and Life Sciences (BOKU), ³Clinical & Experimental Allergology, Department of Dermatology and Allergology, Philipps-Universität Marburg

Abstract:

Background

Allergen immunotherapy (AIT) induces allergen-specific antibodies, including IgA. Some AIT-induced antibodies can block allergen-induced IgE-mediated effector cell activation, a key mechanism for the development of immune tolerance in treated patients. However, whether IgA exerts blocking activity and whether this differs between subcutaneous (SCIT) and sublingual immunotherapy (SLIT) is debated. We compared the allergen-specific blocking activity of IgA in the course of SCIT and SLIT.

Methods

Major birch pollen allergen (Betv1)-specific IgA levels were quantified by ELISA in serum samples collected from patients receiving either birch pollen SCIT (n=8) or SLIT (n=7) after 6, 12, 18, and 24 months of therapy. A Bet v 1-specific monoclonal antibody was generated as IgG1 and IgA variant. Patient sera were depleted of IgG by Protein G beads. IgE-blocking activity was evaluated in basophil activation tests. Sera were incubated with Betv1-coupled NHS sepharose beads, and low-affinity IgA was negatively selected and quantified.

Results

Betv1-specific IgA levels increased to comparable levels in both treatment groups, however, peaked at month 24 during SCIT and at month 6 during SLIT. High-affinity monoclonal IgG1 and IgA demonstrated similar IgE-blocking activity. Despite a general low blocking activity of IgG-depleted sera, IgA-mediated blocking was higher in SLIT. A high proportion of SCIT-induced Betv1-specific IgA was of low affinity.

Conclusion

SCIT and SLIT induced comparable levels of allergen-specific IgA, albeit with different kinetics. The comparable blocking activity of IgA and IgG1 rules out an influence of the antibody subclass on the protective effect. Nevertheless, serum IgA, particularly following SCIT, shows limited protective function, potentially due to low concentrations and affinity.

Abstract Number: 16

Abstract Title: Time-resolved immune dynamics in rheumatoid arthritis under methotrexate therapy

Authors:

Preglej T¹, Tosevska A¹, Brinkmann M¹, Schatzlmaier P^{2,3}, Schmidt F⁴, Korzhenevich J⁴, Simader E¹, Sieghart D¹, Hofer P⁵, Krausgruber T^{6,7}, Dobnikar L⁶, Bock C^{6,7}, Karonitsch T¹, Kain R⁵, Stockinger H², Smolen J¹, Ellmeier W⁸, Padyukov L^{9,10}, Rizzi M^{4,11,12,13}, Aletaha D¹, Göschl L¹, Bonelli M¹

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Abstract:

Background: Methotrexate (MTX) remains the first-line treatment for rheumatoid arthritis (RA), although the mechanisms underlying its therapeutic effects are not fully understood. In particular, longitudinal cellular and molecular changes associated with MTX response have not been comprehensively characterized. We aimed to investigate early immune alterations following MTX initiation and identify features associated with treatment response.

Methods: In a prospective longitudinal study, newly diagnosed RA patients starting MTX underwent serial peripheral blood profiling. High-dimensional immunophenotyping and single-cell RNA sequencing were performed on PBMCs from six patients at baseline and during treatment. Functional in vitro assays assessed the direct effects of MTX on B cell differentiation. Findings were further evaluated in an independent cohort of 22 RA patients stratified according to clinical response and compared with external transcriptomic datasets.

Results: MTX treatment was associated with substantial immune changes detectable within three weeks of therapy initiation, preceding clinical improvement. Among the earliest alterations were changes in naïve and memory lymphocyte compartments, with particularly pronounced reductions of T follicular helper (Tfh) cells and plasmablasts in patients achieving a clinical response. These changes were not observed to the same extent in non-responders and were supported by independent datasets. In vitro experiments demonstrated that MTX directly interferes with plasmablast differentiation. Single-cell transcriptomic analyses further identified regulatory pathways and candidate molecular hubs associated with MTX exposure. An interactive single-cell browser was established to facilitate exploration and validation of the identified molecular signatures.

Conclusion: MTX induces rapid and coordinated cellular and molecular changes in the immune system, detectable well before clinical response. Early alterations in Tfh cells and plasmablasts may

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represent promising biomarkers for MTX treatment response and provide insights into its immunomodulatory mode of action.

(Preglej et al., ARD, 2026)

Abstract Number: 17

Abstract Title: Hymenoptera stings are causing more severe anaphylactic reactions than food or other allergen sources

Authors:

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Abstract:

Background: Anaphylaxis is the most severe IgE-mediated allergy. Food, hymenoptera insect stings, drugs and, rarely, inhalative and other allergens such as latex are known triggers. We were interested in whether specific allergen groups cause more severe reactions and looked for risk factors.

Methods: 357 patients presenting with a history of anaphylaxis in the Floridsdorf Allergy Center were included. We retrospectively analyzed previously unpublished parts of a historic patient cohort from 2018. At that time, the repertoire for commercially available skin prick test solutions was much wider than nowadays and more allergens could be tested. The database contained skin prick tests, in the case of drugs additional intradermal tests, clinical records, total and specific IgE, and serum tryptase to identify the eliciting triggers. Anaphylaxis was graded according to Mueller HL (Pediatrics. 1977;59(5):773–7.). Statistics were calculated using RStudio 2026.07.1.

Results: There were 198 (55.5%) females, and the patients were 38.7±21.6 years old. The triggers were: insects 162 (43.3%), foods 156 (41.7%), drugs 34 (39.1%), and 22 cases (5.9%) of other allergen sources including inhalant allergens or latex; 24 patients suffered from anaphylaxis from more than one triggering group. Proportionally, grade IV anaphylaxis was most often caused by insects 41 (25.3%), followed by drugs 4 (11.8%), food 6 (3.8%) and none in the other allergen groups. In general, higher age (>60 years) was a risk factor for grade IV reactions (24/52=46.2%). In food allergy, however, the situation was reversed and the youngest patients (<10 years) had the most anaphylactic reactions by far (45/156=28.8%). Confirming previous reports, in grade IV anaphylaxis, basal serum tryptase was elevated compared with grade I-III (mean: 8.41 vs. 4.51 kU/L) and total IgE behaved in a reverse way (median: 83.8 vs. 103.0 kU/l).

Conclusion: Insects are the most dangerous allergens amongst all causes of anaphylaxis.

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Abstract Number: 18

Abstract Title: Harnessing myeloid cell-based therapy for modulation of anti-tumor immunity in tumor-draining lymph nodes

Authors:

Elaslan F¹, Dobinger L¹, Ascic E¹, Maier B¹

¹CeMM

Abstract:

Tumor-draining lymph nodes (TDLN) are critical sites of immune activation against tumor antigens. Yet, they are often reprogrammed into immunosuppressive niches, resulting in dysfunctional T cell priming. In this project, our key goal is to improve T cell immunity within TDLN by using genetically engineered myeloid cells (GEMys).

Prior studies have used GEMys expressing immunostimulatory cytokines to target the tumor microenvironment, successfully reprogramming immunosuppressive niches. In contrast, we will leverage GEMys for tissue-specific targeting of TDLN. By using GEMys as a platform for LN-targeted therapy, we aim to reverse immunosuppression and boost anti-tumor T cell responses within the TDLN, leading to systemic and durable anti-tumor immunity.

To achieve our goal, we are focusing on three key aims: (1) induce GEMys migration to TDLN by CCR7 chemokine receptor expression; (2) deliver immunostimulatory cytokines to enhance anti-tumor immunity in TDLN; and (3) explore mechanisms of successful T cell activation in the TDLN upon immunostimulatory cargo delivery by GEMys.

We have already successfully introduced the lymph node-specific homing receptor CCR7 in GEMys and confirmed that CCR7-expressing GEMys preferentially migrate into TDLN in recipient mice in vivo. In addition, we characterized their persistence over time and their phenotype in the TDLN, confirming sustained presence of GEMys. We have further confirmed that CCR7-expressing GEMys can efficiently secrete IL-12 in TDLN in vivo, causing strong T cell activation, thus validating our approach. We are currently prioritizing IL-15, which promotes CD8⁺ T and NK cell survival, proliferation, and cytotoxicity, and IL-7, which supports naïve/progenitor-like and memory T-cell responses. We are currently testing TDLN-targeting GEMys secreting both cytokines in a lung adenocarcinoma model to compare anti-tumor immunity induced by different cytokines in the TDLN and establish TDLN as promising immunotherapy targets.

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Abstract Number: 19

Abstract Title: Fibroblastic reticular cells modulate immune architecture in tumor-draining lymph nodes

Authors:

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Abstract:

Anti-tumor immunity depends on effective T cell priming in tumor-draining lymph nodes (TDLN), where dendritic cells present tumor antigens within a highly organized microenvironment maintained by fibroblastic reticular cells (FRCs). FRCs produce chemokine gradients that guide immune cell positioning, provide trophic signals that sustain dendritic cell homeostasis, and construct the reticular network along which T cells scan for cognate antigen. While tumor-driven changes in TDLN immune populations are intensively studied, the stromal compartment has remained largely inaccessible. FRCs are rare, mechanosensitive, and poorly captured by conventional dissociation-based approaches. Spatial transcriptomics overcomes these limitations by resolving FRC identity and gene expression in situ, preserving the spatial context essential for understanding how stromal architecture shapes immune function. Here, we used high-resolution spatial transcriptomics to map FRC remodeling in cervical lymph nodes from naive and orthotopic MOSC2 oral carcinoma-bearing mice. We identified four spatially and transcriptionally distinct FRC populations, all undergoing coordinated reprogramming in TDLN. A central feature was pan-FRC upregulation of secreted Wnt antagonists and loss of Wnt pathway targets, indicating widespread stromal Wnt suppression. This was accompanied by withdrawal of trophic immune factors and remodeling of the extracellular matrix. Ongoing work is investigating whether analogous stromal reprogramming occurs in lymph nodes under distinct inflammatory conditions, including aging, and defining the mechanisms by which FRC reprogramming shapes anti-tumor immune responses. Our findings position the FRC network not as a passive scaffold but as an active driver of TDLN immune remodeling, opening new avenues for therapeutic modulation of lymph node function in cancer.

Abstract Number: 20

Abstract Title: Exploiting metabolic vulnerabilities in pediatric leukemia with MR1-restricted T cells

Authors:

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Abstract:

Background. Pediatric leukemias exhibit a low mutational burden, limiting neoantigen generation and reducing tumor visibility to conventional, peptide-specific T cells – highlighting the need for alternative, HLA-independent immunotherapeutic strategies. Metabolite-reactive, MR1-restricted T cells offer such an approach. Unlike conventional T cells, they recognize small molecules via the monomorphic molecule MR1, which traffics to the cell surface only upon ligand binding. We hypothesize that malignant transformation and therapy-induced cellular stress – particularly replication stress and DNA damage response pathways – generate tumor-associated metabolites that can influence MR1 antigen presentation, making leukemic cells detectable by MR1-restricted T cells in an HLA-independent manner.

Methods. As a first step, we characterized basal MR1 surface expression by flow cytometry across a panel of AML/myeloid, T-ALL/lymphoid, and B-cell lymphoma cell lines. In parallel, we are screening a drug collection targeting DNA replication and the DNA damage response across multiple timepoints, to identify compounds able to modulate MR1 surface expression and potentially alter the MR1-presented metabolite repertoire.

Results. MR1 expression differed consistently by lineage with myeloid cell lines showing the highest expression, while T-ALL and B-lymphoma lines expressed MR1 at levels close to background. Within our ongoing drug screens, preliminary data show a time-dependent upregulation of MR1 following treatment with selected DNA-damaging agents, providing initial evidence that cellular stress may modulate the MR1 pathway.

Conclusion. These findings establish a lineage-resolved baseline and nominate candidate drugs for further investigation. Paired metabolomics profiling across treatment timepoints, compared to untreated controls, will next identify which metabolites accumulate and may contribute to MR1 ligand presentation. Compounds combining direct leukemia cytotoxicity with enhanced antigen presentation could integrate conventional chemotherapy with metabolite-based immunotherapy, supporting a donor-unrestricted strategy for pediatric leukemia and, potentially, other malignancies.

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Abstract Number: 21

Abstract Title: The CARGONAUT antigen delivery platform as a novel targeted cancer immunotherapy

Authors:

Klein-Eberl* K¹, Mühlgabner* V¹, Le Heron* A¹, Pichler J¹, Wilkinson J¹, Ebinger M¹, Eizinger B¹, Casari G¹, Fischl W¹, Gorki A¹

¹YGION Biomedical GmbH, ²*contributed equally

Abstract:

YGION develops personalized neoepitope immunotherapies, combining its neoepitope prediction pipeline (YGNITETM) with an immunostimulatory antigen delivery platform (CARGONAUTTM) to directly target neoepitopes at antigen-presenting cells (APCs) to promote neoantigen-specific immune responses.

To show targeting of APCs, in vitro binding and uptake assays using CARGONAUT (CGN) coupled to fluorescently labelled peptides demonstrate its CD32-specificity in cell lines and peripheral blood mononuclear cells. Part of the CGN is the intrinsic adjuvant CpG that allows for superior pro-inflammatory responses in CD32-positive cells compared to free CpG. CGN-delivered peptides, derived from viral or tumor antigens, are efficiently cross-presented by different types of APCs to effector T cells, including CRISPR-engineered and endogenous T cells with model antigen-specificity. In vivo studies, using a mouse-adapted version of the CGN, show that CGN-coupled peptides induce a superior T cell response and anti-tumor immunity compared to peptides alone in a murine syngeneic tumor model.

Taken together, our preclinical data demonstrate that the CGN represents a targeted antigen delivery system with high potency to induce antigen presentation, including cross-presentation of MHC I peptides, in vitro and in vivo. First insights into the immunogenicity of CGN-delivered neoepitope immunotherapies (YG-01), combining both MHC I and MHC II-restricted peptides, in humans will be assessed within the approved Phase I dose-escalation study in glioblastoma patients.

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Abstract Number: 22

Abstract Title: COVID-19 lung imprinting and consequences for disease development

Authors:

Brösamlen J¹, Jose Geetha Aarathy R², Hladik A¹, Chen B¹, Chen H¹, Meng F¹, Shen J¹, Lakovits K¹, Pinter F¹, Pimenov L¹, Fokina A¹, Radhouani M¹, Farhat A¹, Oberndorfer F³, Ponweiser E⁴, Knapp S¹, Haschemi A⁴, Krausgruber T^{5,6}, Fortelny N², Starkl P¹

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Abstract:

The COVID-19 pandemic, caused by SARS-CoV-2, represents the first global infectious disease crisis of the 21st century. Increasing evidence suggests that SARS-CoV-2 infection can induce persistent alterations in the pulmonary immune environment that may influence responses to subsequent respiratory challenges. Here, we investigated the long-term consequences of SARS-CoV-2 infection for the cellular and functional state of the lung and determined how prior infection affects pulmonary responses to heterologous inflammatory triggers. Using a mouse model of COVID-19 (mCOVID-19), we characterized the kinetics of pulmonary inflammation to define a time point of recovery. At this stage, we comprehensively characterized the pulmonary imprint left by the SARS-CoV-2 infection at the cellular, transcriptional, epigenetic, and functional levels. Single-cell transcriptomic analyses revealed persistent alterations in alveolar macrophages and endothelial cells, while chromatin accessibility profiling by ATAC-sequencing identified altered epigenetic states in alveolar macrophages and epithelial cells. Recovered animals also displayed persistent alterations in pulmonary physiology upon stress, indicating that the consequences of prior infection extended beyond molecular and cellular changes. We next investigated the consequences of whether this pulmonary imprint influenced responses to heterologous respiratory challenges. Following infection with *Streptococcus pneumoniae*, recovered mice exhibited reduced neutrophil recruitment to the bronchoalveolar space and increased bacterial dissemination to the spleen, suggesting impaired pulmonary antimicrobial defense. In contrast, prior mCOVID-19 was associated with an attenuated pulmonary immune response upon induction of secondary allergic airway inflammation. Together, these findings demonstrate that SARS-CoV-2 infection leaves a persistent molecular, epigenetic, and functional imprint on the lung that remains detectable after apparent recovery. This inflammatory memory alters the response to subsequent respiratory challenges in a context-dependent manner, impairing antibacterial host defense while attenuating allergic airway inflammation. Our findings identify infection-induced pulmonary imprinting as a potential mechanism linking previous SARS-CoV-2 infection to altered susceptibility and disease outcomes upon subsequent respiratory challenges.

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Abstract Number: 23

Abstract Title: From Bet v 1 Recognition to Targeted Allergy Intervention: Generation of Bet v 1-specific Nanobody-IgG1 Fc fusion

Authors:

Izewski V¹, Aderhold W^{1,3}, Drescher A², Menzel S³, Bublin M¹, Flicker S¹

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Abstract:

Introduction: More than 70% of birch pollen-allergic individuals develop birch pollen-related food allergy. Specific immunotherapy using birch pollen or the major birch pollen allergen, Bet v 1 provides only modest therapeutic benefit for associated food allergies.

Objective: The need to identify strategies targeting secondary food allergies motivated us to generate and evaluate Bet v 1-specific nanobody-human IgG1 Fc fusion (Nb-hIgG1) formats as potential treatment approach.

Methods: Bet v 1-specific Nb (Nb32) and Nb-hIgG1 (Nb32-hIgG1) were generated and expressed in HEK293-6e cells. Both formats were analyzed for their cross-reactivity to Bet v 1-related allergens (ELISA) and affinity to Bet v 1 (SPR). Their efficacy to inhibit patients' IgE binding to Bet v 1 was investigated (ELISA).

Results: Nb32-IgG1 bound to Bet v 1 and other related airborne allergens, as well as to associated food allergens. Nb32-hIgG1 demonstrated a more pronounced capacity to diminish IgE binding to Bet v 1 in comparison to Nb32. Nb32-hIgG1 displayed slow dissociation rates alongside a remarkable level of complex stability with Bet v 1.

Conclusion: The generation of Bet v 1-specific Nb-hIgG1, characterized by its bivalent nature, resulted in the observation of high-affinity binding to Bet v 1. The results obtained demonstrated that Nb-hIgG1 exhibited a greater capacity to inhibit the IgE-allergen interaction in comparison to Nb monomers. Subsequent steps will include Nb-hIgG1 investigation for its affinity and its protective ability to block basophil activation to cross-reactive pollen and pollen-associated food allergens.

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Abstract Number: 24

Abstract Title: CDK6 Restrains NK Cell Cytotoxicity and Is Therapeutically Reversed by CDK4/6 Inhibition

Authors:

Huszarek S¹, Klein K¹, List J¹, Harm T¹, Borojevic A¹, Chen G², Garcia-Beltran W², Sexl V³, Gotthardt D¹

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Abstract:

Natural killer (NK) cell-based immunotherapies are actively being explored for cancer treatment; however, their efficacy is limited by functional impairment within immunosuppressive tumor microenvironments and heterogeneous patient responses. Novel strategies to enhance NK-cell cytotoxicity are therefore urgently needed. Cyclin-dependent kinases 4 and 6 (CDK4/6), key regulators of G1-S cell cycle progression, are clinically targeted by inhibitors such as Palbociclib, used in cancer therapy. While the immunomodulatory effects of CDK4/6 inhibition on T cells are well studied, their impact on NK-cell function remains unclear.

Here, we investigated the role of CDK4/6 inhibition and loss in regulating NK-cell effector function. In-vitro cytotoxicity assays demonstrated that treatment with three distinct CDK4/6 inhibitors significantly enhances NK cell-mediated killing, with this increased cytotoxicity persisting overtime. Gene set enrichment analysis of treated human NK-cell lines revealed consistent upregulation of the NK cell-mediated cytotoxicity pathway, further validated at protein levels.

Using NK cells isolated from wildtype (WT), CDK4-deficient, and CDK6-deficient mice, we further dissected the individual contributions of CDK4 and CDK6. Loss of CDK6 - but not CDK4 - was essential for enhanced NK-cell cytotoxicity. Importantly, Palbociclib-treated anti-CD19 CAR-NK92 cells exhibited enhanced killing of target cells. In-vivo, CDK6-deficient mice displayed reduced tumor burden following B16F10 or EO771 tumor challenge. Notably, adoptive transfer of Palbociclib-treated NK92 cells in NSGhIL15 mice enhanced tumor control, highlighting the therapeutic promise of CDK4/6-modulated NK-cell therapy.

Our findings identify CDK6 as a critical negative regulator of NK-cell cytotoxicity and highlight CDK4/6 inhibition as a promising strategy to potentiate NK cell-based cancer immunotherapies.

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Abstract Number: 26

Abstract Title: Non-canonical STAT1-S727 phosphorylation in NK cells following target cell stimulation

Authors:

Rauscher A¹, Kiss K¹, Schindler N¹, Stofner S², Vlasitz L¹, David F¹, Putz E¹

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Abstract:

Natural killer (NK) cells are a crucial component of the innate immune system, responsible for detecting and eliminating infected or malignant cells through signals from activating and inhibiting surface receptors. Their activation and functions are regulated by intracellular signaling pathways that integrate cytokine signals, receptor engagement, and microenvironmental cues. Signal transducer and activator of transcription 1 (STAT1) is a signaling protein and transcription factor involved in innate and adaptive immune responses. Upon canonical type I interferon stimulation, STAT1 is phosphorylated by Janus kinases (JAKs) at tyrosine 701 (Y701), promoting STAT1 dimerization and nuclear translocation. Phosphorylation at serine 727 (S727) further enhances STAT1 transcriptional activity.

Importantly, our previous findings demonstrated that STAT1-S727A knock-in NK cells, in which phosphorylation at S727 is prevented, exhibit enhanced cytotoxicity, indicating that STAT1-S727 phosphorylation can function as a negative regulator of NK cell activity. This prompted us to investigate the pathway responsible for S727 phosphorylation in NK cells.

In this project, we identified a non-canonical mode of STAT1 activation following target cell stimulation, characterized by STAT1-S727 phosphorylation in the absence of JAK-dependent Y701 phosphorylation and subsequent STAT1 translocation. We investigated potential receptors and kinases involved in this pathway, with the activating NK cell receptor NKp46 emerging as an upstream regulator. Furthermore, the serine/threonine kinase STK38 was found to associate with STAT1 upon target cell stimulation, suggesting its potential involvement in regulating STAT1-S727 phosphorylation.

Together, these findings provide evidence for a previously uncharacterized mode of STAT1 activation in NK cells and suggest a signaling cascade involving NKp46 and STK38. Further characterization of this pathway will provide new insights into NK cell activity and STAT1 signaling beyond its canonical JAK-dependent activation. Given the enhanced cytotoxicity observed in STAT1-S727A NK cells, targeting the pathway responsible for STAT1-S727 phosphorylation may represent a potential strategy to enhance NK cell effector functions.

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Abstract Number: 27

Abstract Title: Characterizing the role of LGALS3BP and LGALS3 in tumor immune evasion

Authors:

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Abstract:

The immune system plays a critical role in shaping tumor development. Natural killer (NK) cells are key mediators of antitumor immune surveillance and can directly recognize and eliminate transformed cells. Previous studies demonstrated that NK cells contribute to all phases of tumor immunoediting, highlighting their ability not only to eliminate tumor cells but also to shape tumor cell plasticity and thereby promoting immune resistance and escape. To investigate mechanisms underlying this adaptation, long-term co-culture experiments of NK cells with leukemic cells were performed. Among the proteins upregulated in tumor cells following prolonged NK-cell exposure, Galectin-3-binding protein (LGALS3BP) and Galectin-3 (LGALS3) were identified. Both proteins have been reported to be upregulated across multiple cancer types and are generally associated with poor prognosis.

Functional characterization of LGALS3BP-overexpressing tumor cells revealed increased tumor-NK cell conjugation but reduced NK cell-mediated cytotoxicity, suggesting that LGALS3BP may impair effective NK-cell responses despite promoting physical tumor-NK cell interactions. These findings led us to hypothesize that LGALS3BP contributes to tumor cell adaptation and immune evasion by engaging inhibitory receptors on NK cells, particularly Siglec -7/-9. To test this hypothesis, we will investigate the interaction between LGALS3BP and these inhibitory receptors and determine how this axis affects NK-cell activation and cytotoxicity. In parallel, we will characterize the contribution of LGALS3, the binding partner of LGALS3BP, to this phenotype.

Together, this work aims to define how NK cell-tumor cell interactions drive phenotypic adaptation of tumor cells and identify LGALS3BP as a potential mediator of NK-cell resistance during tumor immunoediting.

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Abstract Number: 28

Abstract Title: Mature Dendritic Cells Suppress Tenocyte and Fibroblast Function via Type I Interferon Signaling

Authors:

Rodriguez Monje S¹, Pinnarò V¹, König S¹, Lamot N¹, Elbe-Bürger A¹, Ciardulli M², Della Porta G², Stöckl J¹

¹Medical University of Vienna, ²University of Salerno

Abstract:

Dendritic cells (DCs) play a critical role in modulating immune responses and tissue homeostasis. While immature DCs have been shown to enhance cell proliferation, the function of mature DCs (mDCs) in connective tissue biology remains less well understood. Here, we report that mDCs exert a potent inhibitory effect on tenocytes (TCs) and fibroblasts (FBs), suppressing both cell proliferation and type I collagen production. Using in vitro co-culture and supernatant transfer experiments, we demonstrate that this suppression is primarily mediated by soluble factors. Further mechanistic analysis revealed that type I interferons (IFN- α , IFN- β , IFN- ω), produced by mDCs upon LPS-induced maturation, are key mediators of these effects. Neutralization of the type I IFN signaling pathway restored both proliferation and collagen synthesis in TCs and FBs, confirming the central role of IFN signaling. Our findings suggest that mDCs may contribute to impaired tissue regeneration in inflammatory tendon pathologies.

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Abstract Number: 29

Abstract Title: CRISPR/Cas9 based in vivo screening to identify novel regulators controlling the effector-like exhausted T cell differentiation

Authors:

Rohrmeier S¹, Zhang J¹, Waldheer M¹, Furlano P¹, Medina R¹, Schäfer M², Zuber J², Sakaguchi S¹

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Abstract:

During chronic viral infections and cancer, cytotoxic CD8 T cells adopt a functionally attenuated state known as T cell exhaustion. Exhausted CD8⁺ T cells (Tex cells) are subdivided into several functionally distinct subsets. Among these, effector-like Tex cells (Texeff-like cells) retain a certain degree of cytotoxic capacity, and their differentiation from the progenitor subset (Texprog cells) is therefore of particular therapeutic relevance. Recently, we demonstrated that histone deacetylase 1 (HDAC1) promotes the generation of Texeff-like cells during chronic viral infection, by priming the expression of effector-like signature genes in Texprog cells. However, it remains unknown whether, and which, HDAC1-primed genes direct cell fate specification toward the Texeff-like subset. In this study, we will conduct an in vivo CRISPR screening to examine the function of HDAC1-primed genes in Tex cells and thereby aim to identify novel molecules controlling the generation of Texeff-like subset. By combining sets of transcriptome and genome-wide chromatin accessibility analysis of HDAC1-sufficient and deficient Tex subsets, we have narrowed down candidate genes for screening into 138 genes, and a pooled sgRNA library targeting these genes will be transduced into CD8 T cells and assessed for their role in Texeff-like cell differentiation upon chronic viral infection. Following identification and validation of candidate regulators, molecular mechanisms by which they control the generation of Texeff-like cells will be further investigated. Our study will thereby potentially reveal novel therapeutic avenues for immunotherapy of patients with cancer and chronic infections.

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Abstract Number: 30

Abstract Title: An in vitro model for studying pathogenic Th2 differentiation, function, and therapeutic response

Authors:

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¹Institute of Immunology, Medical University of Vienna, ²Department of Applied Life Sciences/Bioengineering/Bioinformatics, FH Campus Wien, ³Department of Obstetrics and Gynecology, Division of Obstetrics and Feto-Maternal Medicine, Medical University of Vienna

Abstract:

Background

Pathogenic Th2 cells (pTh2) are key drivers of allergic diseases, including allergic asthma. Chronic antigen exposure, co-stimulatory signals, and the cytokine milieu in the tissues promote their differentiation. As a result, Th2 cells undergo changes in their chromatin architecture and metabolism, driving pathogenic effector function through upregulated expression of IL-5 and IL-13. These type 2 cytokines further induce features of allergic lung inflammation, such as eosinophil expansion and airway hyperresponsiveness.

Methods

Studying human pTh2 cells in detail is challenging, primarily due to their low abundance in the peripheral blood of allergic patients. Therefore, we established an in vitro differentiation protocol for generating pTh2 cells from human naïve CD4⁺ T cells, considering the inflammatory conditions present in the lungs of allergic patients and a recently developed mouse pTh2 differentiation protocol.

Results

Optimized conditions were tested, and cells were characterized extracellularly and intracellularly by spectral flow cytometry. The differentiated cells closely resembled the extracellular phenotype, cytokine profile (IL-5⁺/IL-13⁺), and key transcriptional signature of pathogenic Th2 cells found in allergic patients, as described in the literature, and murine pTh2 cells.

Conclusion

Our in vitro model provides the basis for further studies to investigate transcriptional and epigenetic regulations as well as specific signaling pathways induced in these cells.

Abstract Number: 31

Abstract Title: Mechanisms and functions of type 2 immunity against enteropathogenic bacteria

Authors:

Chen B¹, Brösamlen J¹, Meng F¹, Shen J¹, Hladik A¹, Schneider F¹, Chen H¹, Radhouani M¹, Zelger P¹, Vervaeke A¹, Lakovits K¹, Chakrabarty A², Campbell C^{2,3}, Knapp S¹, Starkl P¹

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Abstract:

Allergies are driven by misdirected type 2 immune responses and today represent a global health problem. Bacterial infections have been suggested as risk factors for food allergy development. Experimental studies have shown that infection with *Citrobacter rodentium* (CR), a murine bacterial pathogen related to enteropathogenic *Escherichia coli*, can enhance allergic sensitization against dietary antigens. However, the molecular mechanisms that fuel gastrointestinal antibacterial type 2 immunity and the potential physiologic functions of this response remain unclear. To determine the molecular mechanisms and the potential biological functions of type 2 immunity against enteropathogenic bacteria in the gastrointestinal tract, we established and applied a mouse model of CR infection and performed immunophenotyping throughout initiation, peak and resolution of inflammation. In accordance with the literature, the colon was the primary site of inflammation, characterized by epithelial hyperplasia and mucus expulsion. In addition to typical antibacterial neutrophil as well as TH1, and TH17 responses, CR infection also induced a pronounced type 2 immune response. Two weeks after infection, we observed increased number of TH2 cells, together with elevated IL13 and IL33 mRNA expression in the colon. Importantly, the infection was associated with increased total IgE and CR-specific IgG1 antibody levels, indicating a humoral type 2 immune response. Comparative analysis of wild-type and systemic cytokine-deficient mice revealed that IL-25 deficiency broadly reduced CR-specific IgG1, IgA, IgG2b, and IgG2c antibody levels, whereas IL-4 deficiency selectively decreased IgE and IgG1. Beyond regulating humoral immunity, we found evidence for physiologic effects of type 2 immunity on the infection course. IL-4 deficiency resulted in delayed recovery of body weight and disrupted colonic mucus expulsion, whereas IL-13 deficiency led to delayed body weight recovery and impaired bacterial clearance. Together, these findings demonstrate key features of type 2 immunity during CR infection and highlight the distinct functions of IL-4, IL-13 and IL-25 in antibacterial antibody production and host-pathogen interaction.

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Abstract Number: 32

Abstract Title: Human keratinocytes and fibroblasts coordinate early cutaneous innate defenses against *Candida auris*

Authors:

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Abstract:

Candida auris is an emerging fungal pathogen with a remarkable ability to persist on human skin, but how structural skin cells respond to colonization is unclear. We used ex vivo human skin models, together with primary keratinocytes and fibroblasts, to characterize epithelial and stromal responses to *C. auris* compared with responses to *C. albicans*. *C. auris* formed biofilms and induced a wound-model-dependent pattern of cytokine secretion dominated by IL-1 β and IL-6, yet caused minimal epithelial damage and modest reductions in leukocyte viability. RNA sequencing revealed complementary but cell-type-specific responses. Keratinocytes and fibroblasts both amplified a proinflammatory IL-6/CXCL8 response, whereas keratinocytes additionally upregulated antimicrobial genes such as RNASE7, TSLP, DEFB103A (encoding human β -defensin 3), and the neutrophil-recruiting chemokines CXCL2 and CXCL3. Fibroblasts further induced CCL28, supporting T-cell recruitment, alongside transcriptional programs associated with tissue remodeling. Recombinant RNase 7 and short-form TSLP directly inhibited *C. auris* growth in vitro in a dose-dependent manner. Together, these findings identify keratinocytes as epithelial sentinels that integrate inflammatory and antimicrobial defenses against skin-tropic *C. auris* and suggest that fibroblast-driven cytokine amplification and, especially, antimicrobial peptides from within the skin barrier may provide therapeutic targets to limit *C. auris* skin colonization.

(Seiser et al., Journal of Investigative Dermatology, 2026)

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 33

Abstract Title: Exhaustion-poised CD8+ T cells as driver of infection-associated cachexia

Authors:

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Abstract:

Background: Cachexia is characterized by involuntary body weight loss with muscle and/or adipose tissue wasting, commonly observed in cancer and chronic infections. While excessive inflammation is a central feature, the contribution of the immune system remains poorly understood. CD8+ T cells are pivotal for host defense against cancer and viral infections, and emerging evidence suggests they contribute to cachexia across disease etiologies.

Methods: We investigated the contribution of CD8+ T cells in the infection-associated cachexia model of lymphocytic choriomeningitis virus (LCMV) using adoptive transfer of CD8+ T cell subsets, single-cell RNA sequencing (scRNAseq), and systemic immunometabolic phenotyping.

Results: Adoptive transfer of CD8+ T cells from cachectic mice revealed that these cells were both required and sufficient to induce cachexia. Using T cell transgenics and scRNAseq, we generated an atlas of virus-specific and bystander CD8+ T cells across tissues associated with cachexia. Cachexia was associated with a diverging CD8+ T cell response with regards to T cell exhaustion and bystander activation. We found that viral persistence and induction of an exhaustion T cell trajectory induce systemic wasting including sarcopenia. Modulating the CD8+ T cell exhaustion trajectory through decreasing antigenic burden or ablation of Tox, a key exhaustion regulator, reduced or accelerated muscle wasting, respectively.

Conclusion: Our data indicate that an exhaustion-poised CD8+ T cell subset has a causative role in the development of infection-associated cachexia. Ongoing studies aim to define the contribution of distinct CD8+ T cell subsets, identify cachexia-inducing effector mechanisms and translating them to human cancer patients.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 34

Abstract Title: TRPM7 Mg²⁺ channel fuels glycolytic and mitochondrial metabolism in T cells

Authors:

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Abstract:

Magnesium is indispensable for mammalian cells. Mg²⁺ counterbalances phosphometabolites and stabilizes enzymatic reactions, shaping cell proliferation and signaling. Cellular metabolism is critically dependent on Mg²⁺, aiding ATP synthesis during glycolysis, the citric acid cycle and the electron transport chain. Consequently, the regulation of ionic fluxes across cellular membranes is crucial for cellular homeostasis.

TRPM7 was identified as main ion channel conducting Mg²⁺ into mammalian cells. Its lack is embryonically lethal to mice. We recently attributed TRPM7 to main T-cell functions including activation and differentiation. T cells rely on a timely and orchestrated metabolic machinery to drive bioenergetic decisions, utilizing both glycolytic and oxidative conversions. We here show that T cells are critically dependent on TRPM7-mediated Mg²⁺ influx for their metabolic function. We apply tailored metabolic flux, metabolomics, transmission electron microscopy, electrophysiology and immunology methods to study primary human T cells and CRISPR-Cas9-edited Jurkat T cells upon TRPM7 perturbation. Our preliminary results indicate that lack or pharmacological blockade of TRPM7 disrupts glycolytic and oxidative flux in T cells, amenable to Mg²⁺ rescue. Consequently, mitochondrial morphology is altered in TRPM7-deficient cells. In summary, TRPM7 Mg²⁺ channel fuels metabolic conversions and shapes mitochondrial homeostasis in and, possibly, beyond T cells.

Abstract Number 35

Abstract Title: STRA6 regulates subepithelial dome fibroblast homeostasis to control adaptive responses in Peyer's patches

Authors:

Yilmaz Y¹, Mössl H¹, Draganic D¹, Belyus C¹, Zhang R², Grimsholm O², Ghyselinck N³, Ludewig B⁴, Sitnik K¹

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Abstract:

STRA6 is a highly conserved vertebrate receptor for retinol-binding protein 4, which uniquely couples cellular uptake of vitamin A with activation of JAK/STAT signalling. Putative immunological functions of STRA6 remain unknown. Here, we uncover that STRA6 is constitutively expressed by fibroblastic reticular cells (FRCs) located in B-cell occupied areas in human tonsils and murine Peyer's patches (PPs), the latter being the main inductive site for mucosal IgA production. Using FRC-specific Stra6-knockout mice, we show that STRA6 mainly supports the homeostasis of Tnfsf11+Glycam1+ FRCs located at the PP subepithelial dome-B cell follicle border, in which it upregulates expression of the insulin-like growth factor (IGF) sequestering agent, IGFBP6. We further demonstrate that FRC-specific Stra6 ablation leads to perturbations in constitutively-driven adaptive responses in PPs, characterized by an elevated frequency of T follicular helper 17 cells and a more diverse clonal repertoire of class-switched germinal center (GC) B cells. The IgA- and IgG1-positive GC B cells that developed in the absence of FRC-specific Stra6 expression featured fewer somatic hypermutations and longer complementarity-determining region 3 sequences, indicative of reduced selection pressure. Given that IGF signaling has been implicated in upregulating the T follicular helper-like gene expression signature in T helper 17 cells, ongoing experiments aim to establish whether the observed immune phenotype results from diminished IGF sequestration by IGFBP6. In addition, we are currently assessing the impact of FRC-specific Stra6 deletion on the quantity and quality of intestinal IgA production. Our results uncover a previously unrecognized role for STRA6 in adaptive immune regulation.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 36

Abstract Title: Knock, Knock, It's AM O'Clock

Authors:

Meng F¹, Shen J¹, Pimenov-Reifeltshammer L¹, Fokina A¹, Lakovits K¹, Hladik A¹, Brösamlen J¹, Chen B¹, Jeyasankar S¹, Farhat A¹, Deckert F¹, Knapp S¹, Gawish R¹

¹Medical University Of Vienna

Abstract:

Background

Circadian rhythms coordinate physiological and immune processes across the day through systemic signals and tissue-specific peripheral clocks. In the lung, this temporal organisation may influence how immune cells respond to respiratory pathogens. Alveolar macrophages (AMs) are long-lived tissue-resident sentinels that maintain pulmonary homeostasis and initiate early immune responses, yet how their temporal state contributes to time-of-day-dependent susceptibility to infection remains incompletely understood.

Methods

We performed single-cell RNA sequencing of naïve mouse lungs collected at Zeitgeber time 0 (ZT0) and ZT12, and of lungs two days after SARS-CoV-2 infection initiated at ZT0 or ZT12. To assess the functional contribution of the myeloid clock in vivo, wild-type and myeloid-specific Bmal1-deficient mice were infected at both time points and monitored for disease severity, lung pathology, immune-cell infiltration and inflammatory mediators.

Results

At baseline, AMs showed relatively limited time-of-day-dependent transcriptional differences, mainly involving core clock and glucocorticoid-responsive genes. Following infection, this divergence was markedly amplified, with 1,509 differentially expressed genes between ZT0- and ZT12-infected AMs. ZT0 AMs showed enhanced lipid-anabolic, LXR-associated, ER/secretory and inflammasome-related programmes, whereas ZT12 AMs displayed stronger inhibitory and survival-associated signatures. In vivo, infection timing markedly influenced disease trajectory: ZT0 infection caused earlier and more pronounced body-weight loss, whereas ZT12 infection was associated with more severe late-stage disease and greater histopathological lung injury. Myeloid-specific Bmal1 deletion attenuated these time-of-day-dependent differences in disease severity and altered the temporal pattern of inflammatory mediators, including IL-6, GM-CSF and TNF- α .

Conclusion

SARS-CoV-2 infection unmasks pronounced time-of-day-dependent differences in AM state and disease outcome. Myeloid BMAL1 contributes to this temporal regulation, identifying alveolar macrophages as a key time-sensitive component of pulmonary immunity.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 37

Abstract Title: PR-10 cross-reactivity and identification of natural Altered-Peptide-Ligands (APL) in birch pollen allergy

Authors:

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Abstract:

Background

Sensitization to birch (*Betula verrucosa*) pollen is one of the main causes of pollinosis in the Northern hemisphere. Bet v 1 represents the major allergen, to which over 95% of birch pollen allergic patients are sensitized. The peptide Bet v 1₁₄₂₋₁₅₃ had previously been identified as the immunodominant T-cell epitope in birch pollen allergic individuals. In this study, we investigated how TCR signaling shapes the differentiation of allergen-specific CD4⁺ T cells, using a recently developed Bet v 1 TCR+HLA-DR7⁺ transgenic (tg) humanized mouse model. Furthermore, we aimed to identify natural altered peptide ligands (APLs) derived from Bet v 1-homologous PR-10 peptides.

Methods

We established a flow cytometry-based competitive binding assay with HLA-DR7⁺ K562 cells to assess the relative binding capacity of 26 Bet v 1₁₄₂₋₁₅₃-homologs derived from PR-10 proteins of pollen, fruit, vegetables and nuts. The peptides were also tested for their potency to activate Bet v 1₁₄₂₋₁₅₃-specific T cells of TCR+HLA-DR7⁺ tg mice, and cytokines in cell culture supernatants were analyzed, revealing their cross-reactive and immunomodulatory potential.

Results

While the general peptide binding data correlated with the T cell stimulation potential, some peptides showed interesting exceptions from that rule. Thus, peptides could be classified as agonists, partial agonists and antagonists. Partial agonists seem to be of particular interest, because they may preferentially induce IL-10 secretion and thus foster immunoregulatory responses.

Conclusion

We identified several agonists, partial agonists and antagonists among the 26 Bet v 1- cross-reactive PR-10 peptides derived from different tree, nut, and fruit allergens. These natural altered peptide ligands may provide valuable insights for the development of prophylactic and therapeutic strategies for birch pollen allergy.

Abstract Number: 38

Abstract Title: TIGIT as an NK-cell immune checkpoint in calreticulin-mutated myeloproliferative neoplasms

Authors:

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Abstract:

Background

Myeloproliferative neoplasms (MPNs) are chronic diseases characterized by an excessive production of myeloid blood cells. Janus kinase (JAK) 2 V617F is the most common mutation in MPNs but a substantial proportion of patients harbour calreticulin (CALR) mutations - an attractive target for emerging immunotherapies. Natural killer (NK) cells have a central role in the elimination of malignant cells, but NK cells of MPN patients have reduced activity. Thus, reactivating their function might improve the disease outcome. Here, we aim to uncover the impact of CALR mutation on NK-cell function.

Methods

NK cells from CALR-mutant mice were analysed using flow cytometry. Bone marrow cells were transplanted into immunodeficient mice followed by in vivo treatment with TIGIT blocking antibody. NK cells were sorted from peripheral blood mononuclear cells from healthy donors and MPN patients and subjected to transcriptomic analysis followed by flow cytometric validation, while patients' plasma was subjected to proteomic analysis.

Results

We demonstrate that NK cells from a CALR-mutant mouse model exhibit normal maturation but enhanced degranulation. Consistently, NK cells from CALR-mutant patients exhibit preserved degranulation ability, exceeding that observed in JAK2-mutant patients. Notably, NK cells from CALR-, but not JAK2-mutant patients express high levels of the immune checkpoint TIGIT, while CD34⁺ cells from MPN patients express elevated levels of the TIGIT ligand CD112. Proteomic analysis identified S100 family proteins as enriched in the plasma of CALR-mutant patients. Exposure of healthy donor NK cells to S100 proteins partially recapitulates the TIGIT phenotype, suggesting their contribution to TIGIT upregulation. Importantly, TIGIT blockade results in reduced platelet numbers in a transplant mouse model.

Conclusion

These findings suggest that NK cells in CALR-mutant MPNs are activated but functionally constrained when encountering TIGIT ligand-expressing target cells, providing a strong rationale for exploring TIGIT blockade to restore NK-cell immunity in this disease subset.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 39

Abstract Title: Metabolic regulation of Th9 cells

Authors:

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¹Medical University Of Graz, ²Massachusetts General Hospital

Abstract:

T helper 9 (Th9) cells, characterized by their production of Interleukin-9 (IL-9), exert dual roles in immunity by promoting antitumor responses while contributing to allergic and autoimmune inflammation. Although their differentiation is driven by defined cytokines and transcription factors, the metabolic cues governing Th9 programming remain to be elucidated. Polyamines, small cationic metabolites essential for cell growth and survival, have recently emerged as important modulators of immune cell function.

Here, we investigated how inhibition of polyamine synthesis by difluoromethylornithine (DFMO), an irreversible inhibitor of ornithine decarboxylase, influence Th9 differentiation and function. For this purpose, naïve CD4⁺ T cells from murine splenocytes were polarized into Th9, Th2 and Treg lineage in the presence or absence of DFMO. Analysis of bulk RNA-sequencing and flowcytometry revealed an increase in the expression of IL-9 following DFMO treatment. Additionally, the analysis revealed altered expression of several other enzymes involved in polyamine metabolism, further supporting the effect of the treatment on the intrinsic polyamine machinery. Pathway analyses indicated a broad transcriptional reprogramming in T cell subsets treated with DFMO and suppression of apoptotic pathways, suggesting altered metabolic and survival mechanisms. To extend these findings in vivo, we aim to characterize Th9 cells and its contribution to the pathogenesis of inflammatory disease models.

Together, our data identify polyamine metabolism as a critical regulator of Th9 differentiation and function. By disrupting polyamine synthesis, DFMO amplifies IL-9 expression and enforces Th9-associated transcriptional circuits across multiple CD4⁺ T cell subsets. Therefore, targeting this pathway may open new avenues for modulating Th9-driven immune response in cancer and autoimmunity.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 40

Abstract Title: Triple-Negative Breast Tumours Induce Functional Impairment of Peripheral Natural Killer Cells

Authors:

Harm T¹, Eder T², Schmiedhofer C¹, Klein K², Grebien F², Gotthardt D², Vallet S¹, Stoiber D¹, Witalisz-Siepracka A¹

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Abstract:

Breast cancer is the most common cancer diagnosed in women worldwide. 15-20% of breast tumours are classified as triple-negative (TNBC), an aggressive subtype with higher rates of metastasis. Metastases are the main cause of patient death, constituting an unmet medical need for novel therapeutic approaches.

Natural killer (NK) cells are able to limit distant metastases by eliminating tumour cells in the blood stream. However, NK-cell function is often suppressed by the cancer microenvironment. Thus, the aim of this project is to analyse changes in peripheral NK cells during metastatic TNBC progression to find novel therapeutic targets.

Publicly available scRNAseq data of human PBMCs from healthy donors and TNBC patients was analysed with focus on NK cells. Blood NK cells from primary TNBC tumour-bearing mice and healthy controls were subjected to scRNAseq. Identified targets and NK-cell functionality were validated ex vivo and in vitro using a co-cultivation system of NK and TNBC cells.

Analysis of publicly available scRNAseq data of human PBMCs identified an enrichment of distinct NK-cell clusters at the primary-tumour stage in TNBC patients compared to healthy donors. To get deeper mechanistic insights, we performed scRNAseq of peripheral NK cells from a TNBC mouse model at the pre-metastatic stage. Mouse scRNAseq showed enrichment of NK cells with an activated signature but downregulation of degranulation-related genes in primary tumour-bearing mice, which was confirmed by ex vivo analysis. Impaired NK cells were characterized by elevated Ly6C expression. In vitro co-cultivation also resulted in accumulation of dysfunctional, Ly6Chigh NK cells.

Ly6C is a potential new biomarker for peripheral NK cell dysfunction at the pre-metastatic stage of TNBC, a time point where improvement of NK cell function could limit metastasis formation. The mechanism of Ly6C induction and potential parallels to human NK cells might lead to the discovery of novel targetable molecules.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 41

Abstract Title: Elucidating Signaling Endotypes in Rheumatoid Arthritis to Predict Therapy Responses

Authors:

Sun Y¹, Dreö B¹, Lackner A², Handl D², Bosch P², Husic R², Villa M², Thiel J², Stradner M², Fessler J¹

¹Division Of Immunology, Medical University Of Graz, ²Division of Rheumatology and Immunology, Medical University of Graz

Abstract:

Background :

Approximately 40% of patients with rheumatoid arthritis (RA) do not achieve low disease activity or remission to currently available bDMARDs and tsDMARDs. We aimed to identify candidate biomarkers associated with treatment response and assess their potential utility for treatment stratification.

Method:

RA patients who were scheduled to switch to a new therapeutic regimen, with an inclusion criterion of a Clinical Disease Activity Index (CDAI) ≥ 10 , were included. Peripheral blood samples were collected prior to drug administration on the day of treatment switch and three months later. Flow cytometry was performed to assess the activation levels of key phosphorylated molecules in the JAK-STAT and NF- κ B signaling pathways within immune cell subsets. Combined with patients' clinical data, a comprehensive stratification analysis was conducted.

Results:

A total of 30 RA patients were enrolled and at present, 23 patients have finished the follow up. Among patients with available treatment-response data, 14 were classified as responders and nine as non-responders on whether the CDAI <10 . Baseline immune cell frequencies and pSTAT1/3/5/6 expression levels across immune cell subsets showed substantial inter-individual heterogeneity, without clear patterns distinguishing responders from non-responders. Drug-stratified analyses were preliminary because of the limited sample sizes within individual treatment groups. Abatacept (ABA) was the only subgroup with sufficient numbers of both responders and non-responders for exploratory statistical comparisons (4 responders vs 6 non-responders). Among 23 immune cell-frequency parameters, switched-memory B cells showed the most pronounced difference, with lower frequencies in responders than in non-responders. Analysis of pSTAT signaling identified higher pSTAT5 levels in CD4-CD8-/NKT-like cells in ABA responders, while basophil pSTAT1 tended to be lower.

Conclusion:

The data suggest that analysis of active signalling pathways in immune cells potentially represents a viable tool to assess drug-specific treatment responses. However, more data are needed to draw a definite conclusion.

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Abstract Number: 42

Abstract Title: Evaluating the role of the coenzyme A synthesis pathway in human T cells

Authors:

Meissel J¹, Passegger C¹, Ellmeier E¹, Schnabl A¹, Stracke A¹, Angiari S¹

¹Medical University Of Graz, Division Pathophysiology And Immunology, Otto Loewi Reserach Center

Abstract:

Background. Immune cells control the generation and strength of immune responses by rewiring their intracellular metabolic profile. The coenzyme A (CoA) synthesis pathway has recently emerged as a key regulator of T cell functionality in models of cancer and autoimmunity. In particular, we recently demonstrated that encephalitogenic T cells mediating the development of experimental autoimmune encephalomyelitis, the mouse model of multiple sclerosis, display a break in the CoA synthesis pathway. Notably, CoA fueling in encephalitogenic T cells limited their pathogenicity and EAE development. Nonetheless, the importance of such a pathway in human T cells is currently unknown.

Methods. We investigated the expression of the enzymes of the CoA synthesis pathway in human T cell subsets, at day 0 (naïve T cells) and at different time points of activation and polarization in vitro. In parallel, we evaluated the effect of several CoA precursors on T cell subset polarization.

Results. Our preliminary results showed a strong down-regulation of the enzyme CoA synthase (COASY) upon T cells activation in vitro, while the expression of the other enzymes of the pathway was differentially modulated in the different subsets. This was independent from polarization, as COASY was downregulated in all the subsets analyzed (T helper 1 [Th1], Th17, Th2 and regulatory T cells [Tregs]). However, CoA fueling in polarizing T cells selectively inhibited the polarization of human Th1 and Th17 cells, without impacting Th2 and Treg subsets. Finally, among the tested CoA precursors, pure CoA had the strongest impact on Th1 and Th17 polarization, while vitamin B5 and pantethine only partially recapitulated this effect.

Conclusions. These preliminary data support our previous results suggesting a break in the CoA synthesis pathway in activated T cells, but also suggest a differential role for CoA and its synthesis pathway in different human T cell subsets.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 43

Abstract Title: Temporal dynamics of Rinl interactions during T cell activation in vitro and in vivo

Authors:

Gaur A¹, Dickinson K², Alteneder M¹, Herbst R², Boucheron N¹

¹Medical University of Vienna, Institute For Immunology, ²Medical university of Vienna, Institute of specific prophylaxis and tropical medicine

Abstract:

Background

T cell activation and differentiation into different subsets requires coordinated signalling downstream of the T cell receptor and co-stimulatory receptors particularly CD28. These signalling events are tightly regulated by intracellular trafficking, yet the molecular mechanisms connecting receptor trafficking to T cell activation and differentiation remains poorly understood. Rin like (Rinl), a guanine nucleotide exchange factor, has been identified as a negative regulator of T follicular helper (Tfh) cell differentiation. However, the molecular interaction network of Rinl and how it changes during T cell activation remains unknown.

Methods

We are using TurboID-based proximity labelling to characterise the Rinl interactome during T cell activation. Rinl TurboID is expressed together with a GFP reporter, allowing identification of transduced cells and biotin-dependent labelling of proximal proteins. The system is optimised in primary murine CD4⁺ T cell cultures and being extended in vivo using bone marrow chimera mice. Biotinylated proteins will be enriched by streptavidin pulldown and identified by mass spectrometry. In parallel, Kinase activity profiling will compare activation induced signalling changes in Rinl wildtype and Rinl knockout mice.

Results

We established Rinl TurboID expression in primary murine T cells and optimised conditions for detecting biotin dependent protein labelling. In vivo labelling and kinase profiling are currently being established.

Conclusion

This approach will identify activation dependent Rinl-associated protein networks and signalling pathways, extending our understanding on how Rinl connects intracellular trafficking with T cell activation and differentiation. Protein networks will be established during an in vivo immune response upon immunization. This approach will establish a novel methodology to map protein networks directly in vivo and under physiologically relevant conditions.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 44

Abstract Title: Exploring the metabolic crosstalk between immune and stromal cells in the arthritic synovium

Authors:

Tóth K¹, Aronis C¹, Lorenzetti R¹, Thiel J¹, Villa M¹

¹Medical University of Graz

Abstract:

Joint inflammation is a common hallmark of arthritic disorders, such as osteoarthritis (OA) and rheumatoid arthritis (RA), despite their distinct pathogenesis. Arthritis manifests in the synovial membrane (synovium) of joints caused by infiltrating immune cells, sustained by resident macrophages and fibroblasts. Cell activation and effector mechanisms have a high energy demand that requires metabolic rewiring. Although different cell types might have different metabolic needs, they may also influence the metabolism of one another within the same tissue microenvironment, where nutrient availability is limited. By investigating metabolic crosstalk among synovial cells, we aim to identify cell-specific vulnerabilities and metabolic pathways that might serve as novel therapeutic targets to reduce inflammation.

Using spectral flow cytometry and a combination of mitochondrial dyes and staining of surface nutrient transporters, we found significant differences in metabolic activity among OA synovial fibroblasts (FLSs), macrophages (MΦs) and endothelial cells (ECs). Our data suggest that FLSs rely mostly on oxidative phosphorylation (OXPHOS), MΦs sustain energy production through OXPHOS and amino acid uptake, while ECs appear to be less metabolically active. A publicly available single cell RNA sequencing dataset (Zhang et al., 2023) was re-analysed using the METAFlex package (Huang et al., 2023) to infer metabolic reaction activity from gene expression levels of the associated enzymes and connect this data to metabolite usage by solving flux balance analysis. This approach helped to identify candidate metabolites and metabolic pathways preferentially used by our target cells. Bulk RNA sequencing of sorted target populations is expected to further validate these findings with improved sequencing depths and gene coverage. In vitro validation is ongoing, including cell competition and nutrient supplementation/deprivation assays in 2D and 3D models, with cellular proliferation and effector functions being monitored.

Overall, our findings suggest promising targets for nutrient partitioning among synovial cells, which may offer novel therapeutic avenues for arthritic disorders.

Abstract Number: 45

Abstract Title: Development of an Fc engineered anti-KIT antibody to deplete neoplastic mast cells in mastocytosis

Authors:

Worrall W¹, Andrieux L¹, Sehran N¹, Kamphuis J¹, Hateb C¹, Lose A¹, Karrich J¹, Abdullah N¹, Battut L¹, Labit E¹, El Samrout C¹, Axisa P¹, Dewitte H², David A³, Mbida E², Mougél A¹, Pecalvel C¹, Maure E¹, Apoil P^{1,4}, Lobjois L¹, Coco-Viloin M⁵, Livideanu C⁵, Guilleminault L^{1,6}, Liblau R^{1,7}, Gaudenzio N^{1,3}, Reber L¹

¹Toulouse Institute for Infectious and Inflammatory Diseases, ²argenx, ³Genoskin SAS, ⁴Institut Fédératif de Biologie, ⁵CERAMAST, Dermatology Department, ⁶Pôle des Voies Respiratoires, Service de Pneumo-allergologie, ⁷Department of Immunology, Toulouse University Hospitals

Abstract:

Background:

The stem cell factor receptor (KIT) is essential for the maturation, growth and survival of mast cells (MCs) in tissue. Somatic KIT gain-of-function mutations drive advanced mastocytosis, a rare hematologic malignancy marked by massive mast cell accumulation and dysregulated activation in multiple organs. Two “Fc silent” anti-KIT monoclonal antibodies (mAbs), Barzolvolimab® and Briquilimab®, can reduce MC numbers in the skin, yet whether such agents can target mutant KIT and provide therapeutic benefit in mastocytosis is unknown.

Methods:

ACK2, an anti-mKIT mAb clone that blocks KIT signalling, was used as a surrogate for Barzolvolimab®. This anti-mKIT was engineered in three formats: Fc silent, wild-type (WT), and Fc enhanced. 30µg of these mAbs were administered subcutaneously twice to C57BL/6 or KIT^{ΔK512I} mice (containing a constitutively active KIT receptor). The anti-hKIT mAb, Barzolvolimab® was produced in different Fc formats. Subsequently, the mAbs were tested in two humanized mouse models: (1) CD34+ engrafted NSG-SGM3-IL15 mice and (2) ROSA^{ΔKIT} D816V engrafted NSG mice, with two 30µg subcutaneous injections. Genoskin® human skin explants were treated with 50µg anti-hKIT mAbs. MCs were quantified via flow cytometry, histochemistry, or immunofluorescence.

Results:

An Fc enhanced anti-mKIT mAb is most efficient at depleting healthy and malignant MCs compared to other mAb formats in numerous tissues in mice and protects against anaphylaxis. The anti-hKIT Fc enhanced antibody can also deplete healthy and malignant human MCs containing KIT gain-of-function mutations in humanized mice, increasing survival in the model of mastocytosis (ROSA^{ΔKIT} D816V engrafted NSG mice). MCs were rapidly depleted in human skin explant by Fc enhanced format of anti-hKIT.

Conclusion:

Collectively, our findings highlight how Fc enhancement of anti-KIT antibodies not only reshapes MC-targeted strategies but also provides a framework for designing tailored effector functions in antibody therapeutics in the field of KIT-dependent haematological diseases, such as mastocytosis.

Abstract Number: 46

Abstract Title: Evaluating Mitochondrial DNA Copy Number as a biomarker in Multiple Sclerosis

Authors:

Ivic I¹, Granig M^{2,3}, Martinez-Serrat M^{2,3}, Tafrali C^{2,3}, Rados M¹, Demjaha R^{2,3}, Haindl M², Helmlinger B^{2,4}, Hofer E⁵, Heschl B², Damulina A^{2,3}, Platos E², Liutkevych K², Pinter D^{2,4}, Ropele S², Enzinger C², Windpassinger C⁶, Khalil M^{2,3}, Fessler J¹

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Abstract:

Background

Multiple sclerosis (MS) is a chronic inflammatory, demyelinating, and neurodegenerative disease of the central nervous system. Its pathogenesis is multifactorial, involving a complex combination of genetic, epigenetic, and environmental factors. Mitochondrial DNA copy number (mtDNA-CN) is commonly used as a biomarker of mitochondrial dysfunction. In MS, lower peripheral blood mtDNA-CN has been associated with longer disease duration (DD) and may reflect disease progression. Longitudinal changes in mtDNA-CN and their association with brain atrophy in people with MS (pwMS) remain unclear and are investigated in this study.

Methods

123 pwMS (median age 32.6, IQR: 26.7 - 37.8; 59.4% female) and 47 healthy controls (HC; median age 31.33, IQR: 25.2-39.1; 72.3% female) were included. Among pwMS, the median disease duration was 3.1 years (IQR: 1.0–7.9) and the median expanded disability status scale (EDSS) score was 1.0 (IQR: 0.0–2.0). Follow-up blood samples were available for 60 pwMS after a median of 2.1 (IQR: 1,3-3,3) years. Peripheral blood mtDNA-CN was measured using quantitative real-time PCR, while annualized brain volume changes were determined from 3-T MRI scans using SIENA.

Results

PwMS showed significantly lower mtDNA-CN levels than HC ($p < 0.05$). mtDNA-CN was unrelated to baseline variables such as age, sex, annualized relapse rate, DD and EDSS. The subgroup analysis showed that lower mtDNA-CN at baseline correlated with greater brain atrophy during the follow-up period (Spearman's $\rho = 0.348$, $p < 0.05$), however no significant longitudinal change was observed in mtDNA-CN.

Conclusion

These findings confirm reduced mtDNA-CN in pwMS and suggest its potential as a biomarker for the rate of brain atrophy.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 47

Abstract Title: In-vitro Investigation of the Effects of Low-Level-Laser Irradiation on Immune and Endothelial Cells as a Potential Future Treatment for Post-COVID Fatigue

Authors:

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Abstract:

Background: Post-Acute Infection Syndromes (PAIS), such as Post-COVID Syndrome (PCS), represent a growing public health challenge, with no causative treatment currently available. Evidence points towards altered immune activation, mitochondrial dysfunction and vascular dysregulation as key drivers for persistent fatigue and post-exertional malaise (PEM). This study aims to develop an endothelial 2D co-culture cell model simulating the clinical application of low-level laser therapy (LLLT) delivered via Haemo-Laser® device to investigate pathomechanisms and potential treatment strategies for PCS fatigue.

Methods: PBMCs from 10 healthy donors were cultured on a HUVEC monolayer to simulate vascular immune interactions. Using a standardized adapter for LLLT developed with Heltschl GmbH. The co-culture was irradiated with 404 nm or 660 nm (10 min or 20 min, once daily, for 3 days). Trans-endothelial electrical resistance (TEER), ATP production and mitochondrial function, mtDNA production as well as immune-metabolic mRNA and cytokine levels were measured.

Results: Both wavelengths significantly increased TEER after 10 min of irradiation, suggesting enhanced endothelial integrity. ATP levels were elevated in PBMC lysates following LLLT at 404 nm, an effect not observed in HUVEC lysates. mtDNA levels were significantly increased in HUVECs after 10 min LLLT with both wavelengths. LLLT at 404 nm maintained this effect after 20 min, whereas after 20 min LLLT at 660 nm led to a reduction. RT-qPCR revealed a modulation of IRF1 and IRF3 in HUVECs, alongside a significant upregulation of ATP synthase following 20 min of LLLT with both wavelengths.

Conclusion: Our preliminary results suggest wavelength- and duration-dependent effects of LLLT on endothelial integrity, mitochondrial activity and immune-metabolic mRNA levels. LLLT at 404 nm may attenuated oxidative stress in PBMCs, while LLLT at 660 nm modulates the oxidative stress response in HUVECs. Future work will extend this model to analyse samples from PAIS patients to validate our observations.

Abstract Number: 48

Abstract Title: Functional Profiling of Allergen Epitopes Using T-Cell Receptor Reporter Cell Lines

Authors:

Brod L¹, Leitner J², Steinberger P², Bohle B¹

¹Institute For Pathophysiology And Allergy Research, ²Institute for Immunology
Functional Profiling of Allergen Epitopes Using T-Cell Receptor Reporter Cell Lines

Abstract:

Background

An exacerbated type-2 response underlies the induction and maintenance of IgE-mediated allergies. Consequently, allergen immunotherapy aims to modulate the allergen-specific T cell response. To this end, allergen vaccines should contain the relevant T cell epitopes of an allergen. Unfortunately, in vitro cultured primary T cell clones from allergic individuals are unsuitable for the screening of allergen vaccines due to their limited lifespan and functional variability. Our goal is to generate stable Jurkat reporter cell lines that express the allergen-specific T-cell receptors (TCR) of such clones. Our toolbox shall include TCR specific for the most frequently recognized epitopes of the major birch pollen allergen Bet v 1.

Methods

Bet v 1-specific T cell lines generated from 90 birch pollen-allergic individuals were mapped for epitope recognition with a panel of fifty 12mer peptides representing the complete amino acid (aa) sequence of the allergen. T cell clones were expanded from birch pollen-allergic individuals. Their TCRs were sequenced, cloned into vectors, and virally transduced into Jurkat E6.1 cells harbouring an NFkB::eGFP reporter construct. EBV-transformed autologous B cells were incubated with allergen for 24 hours and then added to transduced Jurkat cells. After 24 hours, reporter gene expression was analysed by flow cytometry. (1,2)

Results

Five peptides induced proliferation in more than 20% of the T cell lines. A TCR specific for an epitope located within aa 55-66, and a TCR specific for the immunodominant epitope located within aa 142-153 and recognized by 55% of the T cell lines, were successfully transduced in Jurkat cells. Both reporter cell lines reacted with recombinant and natural Bet v 1, but differed significantly in their dose-response profiles, indicating differences in the TCR affinity.

Conclusion

The first two functional reporter cell lines of our toolbox for the screening of the T-cell activating characteristics of novel allergy vaccines were successfully established.

1 Jutz et al., J Immunol Methods, 2016;430:10–20., 2 Leitner et al., Biochem Pharmacol, 2026;249:11787.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 49

Abstract Title: A reporter platform to evaluate inhibitors targeting the SIRPalpha-CD47 axis

Authors:

Gumpelmair S¹, Leitner J¹, Tobias J², Libisch M³, Edthofer K³, Wiedermann-Schmidt U², Steinberger P¹

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Abstract:

CD47, which is broadly expressed on healthy cells but also on tumor cells, acts as a “do not eat me signal” by engaging the inhibitory receptor SIRP-alpha on myeloid cells. The CD47-SIRP-alpha axis is a promising therapeutic target to enhance anti-cancer immunity, especially in the context of immune evasion. Numerous CD47 and SIRP-alpha antibodies targeting this important immune checkpoint are in development, among which some are currently being evaluated in advanced clinical studies. However, there are few reports where such immune checkpoint inhibitors have been assessed and compared in functional assays. One ongoing concern of targeting CD47 is hemagglutination due to expression of CD47 on erythrocytes. So, the newer antibodies aim to reduce hemagglutination while sustaining efficient blocking or targeting of SIRP-alpha with antagonistic antibodies instead of CD47.

Here we describe the development of a functional cellular reporter assay for the evaluation of immune checkpoint inhibitors targeting the CD47-SIRP-alpha axis. Biosimilars of the CD47 antibodies Magrolimab, Lemzoparlimab, Urabrelimab, and Lingufalimab were evaluated in our reporter assay and in a hemagglutination assay. Due to the broad expression of CD47, off-target binding and low efficiency of CD47 antibodies are issues that need to be addressed. Targeting SIRP-alpha instead could prove advantageous in this regard. We used reporter cells expressing two common SIRP-alpha variants to evaluate the blocking capacity of SIRP-alpha antibodies Anzurstobart and Epacmarstobart.

Our data show that the efficacy of the tested antibodies varies greatly and highlight the importance of reductionist cellular assays to evaluate and compare antibodies or small molecule inhibitors targeting the CD47-SIRP-alpha axis.

Abstract Number: 50

Abstract Title: Role of glycans in post-acute infection syndromes

Authors:

Ret D^{1,2}, García de Otazo Hernández D^{1,2}, Sabatino G¹, Maliqi C^{1,2}, Sgarz P¹, Gentile A², Rohrhofer J², Keppler S³, Untersmayr E²

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²Institute of Pathophysiology and Allergy Research, Medical University of Vienna, ³Division of Rheumatology and Clinical Immunology, Medical University Graz

Abstract:

Background

Glycomics represents the molecular language of cells, based on sugar structures encoded on proteins, lipids and tissues. Various diseases are characterized by altered glycans structure due to different mechanisms. This study aims to investigate alterations in glycan profiles in the peripheral blood of post-infectious Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) patients, long covid patient compared to healthy controls.

Methods

Peripheral blood samples were collected from healthy controls, long Covid patients, post infectious ME/CFS patients and covid recovered patient. Total and free serum sialic acid was quantified via HPLC-FL. Serum N-Glycan profiles were analyzed by MALDI mass spectrometry. IgG antibodies were purified, and their N-glycosylation pattern were analyzed after fluorescent derivatization using HPLC.

Results

A significant increase in free serum sialic acid was observed in the long covid and ME/CFS group compared to the healthy control. Analysis of IgG glycosylation in the ME/CFS and Long COVID groups compared with healthy controls, suggestive of ongoing neuraminidase activity and latent pathogenic processes. Plasma protein N-glycans showed minimal change, implicating cellular or tissue sources source of the free sialic acid. IgG glycosylation showed increased sialylation with reduced agalactosylated forms, a profile compatible with diminished Fc receptor engagement and potential immunosuppression

Conclusion

Free sialic acid can be a useful biomarker for determination of the severity and to monitor interventions in PAIS diseases. Finding the tissue or cells where the sialic acid is released (source of the free sialic acid) will help the future understanding of the pathology. Antibody glycosylation in ME/CFS and long covid patients show an abnormally high anti-inflammatory signature suggesting a downregulation of the immune system.

Funding

This research received funding from the WWTF project Understanding ME/CFS – ME-CFS24-016.

Abstract Number: 51

Abstract Title: STK38(L) Deletion alters Natural Killer Cell Immunity

Authors:

David F¹, Stofner S², Baik H², Schindler N¹, Kiss K¹, Rauscher A¹, Buri M^{1,2}, Borojević A^{1,3}, List J³, Gotthardt D³, Putz E¹

¹Institute Of Pharmacology, Center For Physiology And Pharmacology, ²STK38(L) Deletion alters Natural Killer Cell Immunity, ³Institute of Pharmacology and Toxicology, University of Veterinary Medicine

Abstract:

Natural killer (NK) cells are innate lymphocytes that recognize and eliminate virus-infected and transformed cells through the integration of signals from germline-encoded activating and inhibitory receptors. Enhancing NK cell effector function is a major goal of NK cell-based cancer immunotherapy. Serine/threonine kinase 38 (STK38) and STK38-like (STK38L) are highly expressed in peripheral lymphocytes and have been implicated in regulating immune cell migration and cytokine production. However, their role in NK cell immunity remains unknown. Here, we investigated whether STK38(L) regulates cellular and functional processes in NK cells.

To this end, we analyzed NK cells from Stk38(l)-deficient mice and generated human STK38-deficient NK-92 cells. Flow cytometric analysis revealed that Stk38 deficiency in mice was associated with a more mature and activated NK cell phenotype in multiple organs. Consistent with this phenotype, bulk RNA sequencing demonstrated an enhanced activation signature in STK38-deficient NK cells, which was accompanied by increased protein expression of IFN- γ , TNF- α , and perforin. Functional analyses further showed enhanced cytotoxicity of both murine and human STK38-deficient NK cells in vitro. Finally, the enhanced effector function of Stk38-deficient NK cells translated into improved antitumor responses in vivo.

To investigate the underlying molecular mechanism, we examined the potential link between STK38 and STAT1, which were previously shown to interact at the immunological synapse following tumor cell stimulation. Proximity ligation assays confirmed an interaction between STK38 and STAT1 in activated human NK cells, while in vitro kinase assays demonstrated that STK38 is able to phosphorylate STAT1-S727, suggesting that STK38 may regulate NK cell function through STAT1-S727 phosphorylation, which is known to inhibit NK cell effector functions.

Together, our findings demonstrate that STK38 deficiency promotes NK cell maturation and enhances their effector and antitumor activity, identifying STK38 as a potential therapeutic target for improving NK cell-based cancer immunotherapy.

Abstract Number: 52

Abstract Title: Obesity-associated hormonal changes transiently enhance natural and vaccine-specific IgG production, while metabolic inflammation impairs vaccine-induced B memory cells and repertoire maturation

Authors:

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¹Institute of Specific Prophylaxis and Tropical Medicine, Center of Pathophysiology, Infectiology and Immunology, Medical University of Vienna, ²Department of Laboratory Medicine, Medical University of Vienna, ³Institute of Artificial Intelligence, Center for Medical Data Science, Medical University of Vienna, ⁴Center for Public Health, Medical University of Vienna

Abstract:

Obesity (BMI >30) is associated with metabolic systemic low-grade inflammation, leading to immune dysfunction and increased susceptibility to infections. Here, the influence of obesity-related metabolic, hormonal and inflammatory factors on innate Abs (against oxidation-specific epitopes [OSE]) and Ag-specific vaccine responses were investigated in a booster study with tick-borne encephalitis (TBE) vaccine. Metabolic/hormonal profiles, innate OSE-Abs, and humoral/cellular vaccine-specific responses, as well as B-cell-receptor repertoire (BCR) were analyzed in obese (n=37) and normal-weight (n=36) adults.

Obese subjects had reduced OSE-specific IgM levels pre-booster, while IgG were similar to controls. Obese responded to booster-vaccination with more rapid increase of TBE-specific Abs (1wk to 4wks post-booster), but this was followed by faster decline (4wks to 6mo), both in correlation with BMI and metabolic parameters. Highest fold-increase of TBE-specific Abs and also induction of OSE-specific IgG (after 4wks) was observed in obese males, and associated with reduced testosterone and increased B-cell-activating factors. Regarding cellular responses, obese vaccinees of both sexes showed more (naïve) B-cells pre-booster, but lacked progression to B-memory phenotype thereafter. BCR-sequencing of switched B-memory cells before and 1wk post-booster revealed more different clones of similar size in obese compared to normal-weight controls. After vaccination, obese showed less changes in CDR3/N2 regions, and reduced class switch to IgG clones.

Taken together, the altered metabolic and hormonal state in obese subjects, especially males, accelerated formation of both innate and vaccine-specific Abs. Faster loss of TBE-specific Ab was sex-independent but inflammation-associated with impaired induction of B-memory cells. Reduced CDR3/N2 remodeling and IgG isotype-switch after booster in obese suggest limited germinal center activity in presence of chronic metabolic inflammation, favoring short-lived extrafollicular responses with limited formation of long-lived B memory cells and repertoire diversification. More frequent/different infections in obese might lead to presence of more different switched B-memory cell clones.

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Abstract Number: 53

Abstract Title: Immunological Biomarkers for Rapid Diagnosis of Infective Endocarditis

Authors:

Wrighton S¹, Saleh R², Tobudic S³, Kussmann M³, Schubert L³, Wolner L², Gangl C⁴, Winkler S³, Zuckermann A², Pickl W^{1,5}, Aliabadi-Zuckermann A²

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Abstract:

Background: Infective endocarditis (IE) poses significant diagnostic challenges due to heterogeneous clinical presentations and high rates of culture-negative disease, often exceeding 30–50% of cases. Reliance on traditional blood cultures frequently delays definitive diagnosis and targeted antimicrobial therapy. To address this critical unmet need, this project will investigate peripheral and local immunomodulatory changes to discover novel, highly sensitive immunological biomarkers for IE diagnosis.

Methods: We have established high-dimensional flow cytometry panels to systematically profile peripheral blood monocyte, dendritic cell, natural killer cell, and neutrophil subpopulations. By evaluating activation markers, maturity gradients, and subpopulation expansion, we aim to define circulating cellular profiles specific to IE compared to non-endocarditis bacteremia and healthy controls. Concurrently, to unravel the local pathogenic niche, we will enzymatically digest surgically resected valvular vegetations and subject them to single-cell RNA sequencing.

Results: Preliminary analyses revealed limited overall immune modulation, with selective expansion of a circulating monocyte subpopulation previously associated with sepsis. Furthermore, vegetation dissociation can be efficiently achieved on ice to prevent nonspecific immune cell activation.

Conclusion: By combining tissue-infiltrating immune signatures with altered circulating immune subsets, this study will identify key surface proteins and transcriptional biomarkers that reflect active endocardial infection. Ultimately, this work aims to translate localized immune responses into a peripheral blood diagnostic marker panel, providing a rapid, culture-independent method to improve early detection, guide clinical management, and reduce mortality in culture-negative endocarditis.

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Abstract Number: 54

Abstract Title: Histone Deacetylases 1 and 2 Regulate Intestinal T Cell Subsets and are Essential for Th1/Th17 Immunity against *Citrobacter rodentium*

Authors:

Huu Tran P¹, **de Freitas e Silva R**¹, F. F. Hansel Fröse A¹, Madern M^{1,9}, Waldherr M^{1,4}, Preglej T^{1,2}, Niederreiter B², Lassnig C^{3,10}, Da Silva Miranda S³, Högl S⁵, Krausgruber T^{6,7}, Bock C^{6,7}, Starkl P⁸, Knapp S⁸, Strobl B³, Bonelli M², Ellmeier W¹

¹Medical University of Vienna, Center for Pathophysiology, Infectiology and Immunology, Division of Immunobiology, Institute of Immunology, ²Medical University of Vienna, Vienna, Austria, Department of Internal Medicine III, Division of Rheumatology, ³University of Veterinary Medicine Vienna, Centre of Biological Sciences, ⁴University of Applied Sciences Campus Vienna, Department of Applied Life Sciences, ⁵University of Veterinary Medicine Vienna, Unit of Laboratory Animal Pathology, ⁶CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences, ⁷Medical University of Vienna, Center for Medical Data Science, Institute of Artificial Intelligence, ⁸Medical University of Vienna, Department of Medicine I, Research Division of Infection Biology, ⁹Medical University of Vienna, Center for Medical Data Science, Institute of Clinical Biometrics, ¹⁰Vetbiomodels, University of Veterinary Medicine Vienna

Abstract:

The gastrointestinal tract contains conventional CD4⁺ and CD8 $\alpha\beta$ ⁺ T cells as well as unconventional TCR $\alpha\beta$ ⁺ subsets. Among these, CD4⁺CD8 $\alpha\alpha$ ⁺ lymphocytes possess cytotoxic activity and are termed CD4 cytotoxic T lymphocytes (CTLs). To define regulatory mechanisms underlying intestinal T cell heterogeneity and function, we investigated the role of the epigenetic regulators HDAC1 and HDAC2 in small intestinal intraepithelial lymphocytes (SI-IEL), lamina propria (SI-LP), and colonic T cells using mice lacking both Hdac1 alleles and one Hdac2 allele (HDAC1cKO-HDAC2HET). Single-cell RNA-sequencing showed that SI-IEL transcriptional programs were more dependent on HDAC1-HDAC2 than those of other intestinal T cells at steady state. HDAC1cKO-HDAC2HET SI-IELs exhibited expansion of RUNX3^{high} CD4⁺CD8 $\alpha\beta$ ^{low} subsets, including populations with CD4-associated transcriptional features. Across intestinal tissues, HDAC1cKO-HDAC2HET CD4-lineage cells displayed enhanced CTL signatures but reduced IL-17A expression in the colon. During *Citrobacter rodentium* infection, HDAC1cKO-HDAC2HET mice failed to express protective Th1/Th17 responses but generated CD4 CTLs. Thus, HDAC1-HDAC2 restrain CD4 CTL differentiation and maintain intestinal T cell homeostasis and effector function during bacterial infection.

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Abstract Number: 55

Abstract Title: AI-based approach to evaluate high-dimensional datasets for patient stratification in ME/CFS

Authors:

Aigner B¹, Rohrhofer J¹, Milicic M¹, Schulz C², Untersmayr E¹

¹Institute For Pathophysiology And Allergy Research, ²Institute for Informatics

Abstract:

Background

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a multi-systemic disease characterized by severe fatigue, post-exertional malaise, and various systemic symptoms. A major challenge in managing ME/CFS is the lack of objective biological markers for diagnosis, which leads to prolonged diagnostic delays for patients. To address this issue, we implemented an unsupervised machine-learning approach for patient stratification, to achieve faster, more accurate diagnosis and targeted therapeutic strategies.

Methods

In collaboration with ME/CFS patients, a questionnaire was developed to collect information on potential causes of the disease, lifestyle factors, symptoms, and disease progression. The data are analyzed using unsupervised machine-learning for cluster analysis and responses are mapped onto numerical scale values ranging from 0 to 10. Distance functions determine pattern similarities to establish overall data distances. These form a proximity matrix that algorithmically clusters related datasets.

Results

Responses from 687 patients were analyzed to identify patterns and subgroups. Patients can be stratified into distinct groups based on shared characteristics, and patterns within the heterogeneous ME/CFS population. The questionnaire also generated clinically relevant insights that contributed to the development of a treatment guideline for ME/CFS.

Conclusion

The study demonstrates the potential of machine-learning assisted analysis to identify clinically meaningful subgroups within heterogeneous patient populations. The alpha version of this questionnaire serves as starting point for an EC-funded Horizon Europe project, which will recruit approximately 2000 patients across Europe. A refined beta version will be analyzed using graph-based clustering combined with supervised machine-learning to improve patient stratification. This approach may support faster diagnosis and definition of targeted therapy.

Abstract Number: 56

Abstract Title: The impact of mast cell activation on epithelial and endothelial barrier dysregulation in post-acute infection syndromes

Authors:

Milicic M¹, Rohrhofer J¹, Piatek K¹, Milanovic K¹, Wolflehner V¹, Schweighardt J¹, Koidl L¹, Pipper C², Augustin M³, Stingl M⁴, Komenda-Lett M⁵, Ferlitsch M^{6,7}, Ruhr-Udilova N⁶, Trauner M⁶, Starkl P⁸, Westermeyer F², Untersmayr E¹

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Abstract:

Background

Enhanced mast cell activation (MCA) is increasingly recognized in Post-acute Infection Syndromes (PAIS), affecting 25% of an Austrian Myalgic-Encephalomyelitis / Chronic Fatigue Syndrome (ME/CFS) cohort (n=383). Since MCA and ME/CFS share symptoms, and factors like coagulation dysregulation and blood-brain barrier disruption contribute to disease, we propose mast cells at epithelial and endothelial barriers act as early responders to infection.

Methods

PBMCs and plasma from 76 participants (Post-COVID ME/CFS-phenotype, n=20; EBV-triggered ME/CFS, n=16; convalescent COVID, n=20; healthy controls, n=20) were analyzed. Endothelial (HUVEC) and epithelial (CaCo2) barriers were co-cultured with patient PBMCs; integrity was assessed by TEER and RT-qPCR. Arginine metabolites were quantified by UHPLC-MS/MS. Mast cell activation tests (LAD2 cells stimulated with plasma) evaluated degranulation (β -hexosaminidase, tryptase, flow cytometry: CD63, CD117, CD107a, MRGPRX2). Human intestinal biopsies were stained for EBV and mast cell markers assessing virus-host interactions.

Results

Patient PBMC co-culture reduced HUVEC TEER values and cell junction mRNA indicating impaired integrity and altered CaCo2 arginine metabolites. LAD2 cells stimulated with PCS-fatigue plasma showed distinct degranulation patterns versus convalescent controls. CD63 expression increased with degranulation, being lowest in healthy controls. Intestinal biopsies revealed tryptase/EBV double-positive mucosal cells.

Conclusion

Enhanced MCA contributes to barrier dysfunction in post-viral ME/CFS via long-term immune priming. Distinct degranulation signatures and tryptase/EBV double-positive cells warrant investigating EBV-related MCA. These findings support MAT-based diagnostics and mast cell-stabilizing therapies to restore barrier integrity in ME/CFS.

Abstract Number: 57

Abstract Title: Targeting the catalytic activity of HDAC1 in T-cells protects mice against experimental autoimmune encephalomyelitis

Authors:

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Abstract:

Histone deacetylases (HDACs) are key epigenetic regulators controlling T-cell-mediated immunity. T-cell-specific deletion of Hdac1 (HDAC1cKO) protects mice against experimental autoimmune encephalomyelitis (EAE), a preclinical model of multiple sclerosis (MS). Some HDACs have non-enzymatic functions in addition to their catalytic activity, thus knockout of HDAC protein expression does not mimic HDAC isoform selective pharmacological inhibitor treatment. Therefore, whether inhibiting HDAC1 enzymatic activity and thus mimicking HDAC1 inhibitor treatment is sufficient to block EAE induction remains unclear. We generated a novel mouse strain expressing catalytically inactive HDAC1 (HDAC1Off) in HDAC1cKO CD4+T-cells to mimic selective inhibition of HDAC1 enzymatic activity in vivo. Control mice expressed wildtype HDAC1 in HDAC1cKO CD4+T-cells (HDAC1On).

HDAC1Off mice exhibited normal T-cell homeostasis. HDAC1Off and HDAC1On forms were comparably expressed in CD4+T cells, equally-well incorporated into co-repressor complexes, with similar interactomes. As expected, deacetylase activity was markedly reduced in HDAC1Off CD4+T-cells. HDAC1Off mice were fully protected from EAE, exhibiting a significant reduction in leukocyte infiltration into the CNS, and a profound decrease in pathogenic CD4+T-cells. HDAC1Off CD4+T-cells expressed lower levels of proinflammatory cytokines, indicating impaired T-cell effector function. Transcriptomic analysis uncovered a broad downregulation of gene pathways governing T-cell activation, inflammatory response, and T-cell migration, supporting functional impairment of HDAC1Off T-cells driving autoimmune inflammation. Our study demonstrates that inhibiting the catalytic activity of HDAC1 in T-cells is sufficient to achieve a clinical benefit in EAE development. This raises the translational perspective that targeting HDAC1 enzymatic activity might represent a promising therapeutic strategy in treating human T-cell mediated autoimmune diseases.

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Abstract Number: 58

Abstract Title: Benchmarking Tools for the Event-Level Detection of Alternative Splicing from Short-Read Data

Authors:

Waldherr M^{1,2}, Ellmeier W¹, Graf A²

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Abstract:

Background:

Alternative splicing (AS) is a key post-transcriptional mechanism that contributes to the diversification of transcripts and proteins by generating multiple mRNA isoforms from a single gene. AS has been observed to impact a significant proportion of multi-exonic genes, operating within a context-dependent manner and contributing to a variety of outcomes, including alterations in protein function, RNA localization, or degradation. However, comprehensive data about AS patterns in immune cells, particularly T cells, remain scarce.

Methods:

RNA-seq has facilitated large-scale transcriptome analysis, yet AS isoforms are often underexplored due to analytical challenges. Computational tools are therefore essential for transcriptome-wide AS detection, with event-based approaches generally outperforming isoform-based methods. However, reliable detection remains difficult with short-read sequencing, leading to high false-positive rates. Existing benchmarking studies are limited by inconsistent evaluation criteria, tool selection, and dataset variability.

Results:

Here, we present a systematic evaluation of AS detection tools using both simulated and real RNA-seq data. From 66 identified tools, 14 were selected through a rigorous multi-step filtering process. Performance was assessed primarily using precision and recall, prioritizing precision to minimize false positives. Additional metrics included inter-tool agreement. Results were integrated into a comprehensive framework that also considers usability factors such as installation and documentation quality.

Conclusion:

This benchmark provides the community with an evidence-based guide for selecting optimal AS detection workflows and highlights opportunities to improve the accuracy of AS analysis in RNA-seq studies. Based on these findings, the most promising set of tools will be employed to address the role of AS in different Th subsets.

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Abstract Number: 59

Abstract Title: High-Salt Conditions Modulate T Cell Activation through Multiple Distinct Signaling Pathways

Authors:

Schmetterer K¹, Weiss S², Hutter S¹, Krampert L², Frey T¹, Schmidt R¹, Gerner C³, Jantsch J^{2,4}

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Abstract:

Background

Elevated tissue sodium concentrations occur in inflammatory microenvironments and modulate immune responses. However, their broader effects on T cell activation and the underlying molecular mechanisms remain incompletely understood. We investigated conserved effects of high-salt (HS) conditions on human and murine T cells.

Methods

Primary human and murine CD4⁺ and CD8⁺ T cells were stimulated with anti-CD3/anti-CD28 under normal-salt or HS conditions (+40 mM NaCl). Proliferation, differentiation, cytokine production, and cytotoxicity were assessed. Human spleen-derived immune organoids were used to investigate follicular helper T cell (Tfh) responses. Phosphoproteomics, bulk RNA sequencing, signaling analyses, pharmacological inhibition, and CRISPR/Cas9-mediated knockout identified molecular mediators.

Results

HS delayed cell cycle entry and reduced early proliferation and CD69 expression, while enhancing IL-2 and IFN- γ production, CD40L and granzyme B expression, and cytotoxic activity. These effects were broadly conserved across species and T cell subsets. HS promoted acquisition of memory phenotypes and enhanced Th1, Th9, Th22, and Tfh differentiation. In immune organoids, HS increased Tfh frequencies, IL-21 production, plasmablast formation, and antigen-specific IgG responses. PD-1 and LAG-3 were selectively upregulated, and increased cytotoxicity was reversed against PD-L1-expressing targets. Mechanistically, HS attenuated calcium–NFAT1/2 signaling and NEK2 induction, implicating this axis in reduced proliferation. RSK2 mediated enhanced effector function, whereas CLK1 inhibition partially counteracted differentiation changes. HIF-1 α contributed to phenotypic remodeling, including LAG-3 induction, without mediating memory differentiation.

Conclusion

HS microenvironments selectively reshape T cell responses, uncoupling early proliferation from enhanced differentiation and effector function while increasing susceptibility to inhibitory signaling. Distinct molecular pathways regulate these outcomes, extending the mechanistic framework beyond canonical NFAT5/SGK1 signaling and identifying potential targets for modulating T cell responses.

Abstract Number: 60

Abstract Title: Influence of age on functional and structural changes in experimental glomerulonephritis

Authors:

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Abstract:

Background: Immune-mediated glomerulonephritis is characterized by glomerular damage and albuminuria, and can present as rapidly progressive glomerulonephritis (RPGN), particularly in older age. Glomerulonephritis is studied primarily in young mice, although the disease frequently occurs in older individuals whose kidneys are already marked by nephrosclerosis and vascular rarefaction. The aim of this study is to investigate whether aging leads to an altered renal response in nephrotoxic serum nephritis (NTSN), a murine model of immune complex glomerulonephritis that recapitulates key features of human RPGN.

Methods: NTSN was induced in young (8-12 weeks) and aged (90 weeks) mice and compared with age-matched healthy control groups. Urine samples were collected on days 7 and 14 after disease induction to determine the albumin-to-creatinine ratio (UACR). On day 14, inguinal lymph nodes were harvested for immunophenotyping using flow cytometry. One kidney was cleared using the ECI-based EMOVI protocol, antibody-stained, and imaged using light-sheet microscopy for three-dimensional volumetric analysis. The contralateral kidney was evaluated following Periodic acid-Schiff (PAS) staining.

Results: Albuminuria was significantly decreased in aged nephritic mice. Consistent with this finding, histopathological analysis demonstrated significantly less glomerular damage in the aged nephritic group compared with the young nephritic group.

CD4⁺ T-cell numbers were decreased in draining lymph nodes of aged NTSN mice compared to young NTSN mice, while regulatory T-cells and CD8⁺ T-cell numbers were comparable between age groups. Although CD4⁺ proliferation was reduced in healthy aged mice, NTSN induction resulted in a comparable increase in CD4⁺ T-cell proliferation in both age groups.

Conclusion: Aging significantly attenuated the NTSN phenotype, highlighting the importance of age as a consideration when translating findings from the experimental model to the human setting. Ongoing structural analyses will investigate how age-related alterations in renal architecture and immune responses influence NTSN pathology.

Abstract Number: 61

Abstract Title: Co-expression of IL-12 on allergen-laden VNPs enhances their Th1 priming activity and reduces Th2 immune responses in a preclinical humanized mouse model of mugwort allergy

Authors:

Kratzer B¹, Hofer S¹, Tauber P¹, Trapin D¹, Schaar M¹, Sehgal A¹, Hofer G², Keller W², Gadermaier G³, Pickl W^{1,4}

¹Medical University Of Vienna, Center for Pathophysiology, Infectiology and Immunology, Institute of Immunology, ²University of Graz, Division of Structural Biology, BioTechMed, Institute of Molecular Biosciences, ³Paris Lodron University Salzburg, Department of Biosciences and Medical Biology, ⁴Karl Landsteiner University of Health Sciences

Abstract:

Background: Shielding an allergen safely inside of virus-like nanoparticles (VNP) can be used for the tolerogenic delivery of allergens due to preservation of their allergen-specific T-cell activation capacity in the absence of sensitization. We have investigated whether the additional surface decoration with the Th1 inducing cytokine IL-12 would improve the immunomodulatory properties of VNP in a humanized mouse model of mugwort allergy.

Methods: N-terminal fusion of the allergen to the viral matrix protein M₁p15 of MoMLV results in shielded expression, while for the surface decoration of VNPs a single-chain mIL-12 was C-terminally fused to the minimal CD16b GPI-anchor acceptor sequence. The immunomodulatory capacity of IL-12+VNP were analyzed thoroughly in vitro and in vivo in a humanized mouse model of mugwort allergy

Results: Allergen-expressing IL-12+VNP significantly increased IFN- γ production, moderately increased IL-10 production but reduced IL-4, IL-5, IL-13 and IL-17A production and cellular proliferation in splenocyte cultures of allergen-specific mice compared to allergen-only control VNPs. IL-12+VNP were able to differentiate naïve allergen-specific T cells in the presence of bone marrow-derived dendritic cells into T-bet+IFN- γ +CD4⁺ Th1 cells, comparable to classical Th1 polarization, which remained stable after secondary allergen stimulation. The co-incubation of IL-12+VNP with pre-polarized Th2-cells in the presence of irradiated splenocytes as antigen-presenting cells lead to re-expression of IFN- γ . In vivo, intratracheal application of VNPs confirmed the safety of application to the airways since no overshooting IFN- γ responses were induced. The prophylactic, intranasal treatment with IL-12-decorated allergen-laden VNP seven days before exposure of humanized allergy mice to allergen aerosol reduced the expansion of IL-4⁺ and IL-13⁺ CD4⁺ T cells compared to treatment with control VNP expressing an inactive form of IL-12.

Conclusion: Application of allergen-laden IL-12+VNP leads to improved Th1-priming and reduced Th2 expansion and may thus prove useful for the prophylactic and therapeutic treatment of allergies in the future.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 62

Abstract Title: INK4a and ARF in NK-cell senescence and leukemia

Authors:

Borojević A¹, List J¹, Kudweis P¹, Huszarek S¹, Gotthardt D¹

¹University Of Veterinary Medicine, Vienna

Abstract:

Natural Killer (NK) cells are effector lymphocytes controlling tumors and microbial infections. Age-related NK-cell dysfunction contributes to a reduced host defense with accumulating age, called immunosenescence. Senescence is a physiological event limiting the proliferation of damaged cells, thereby functioning as a barrier to malignant transformation. We have limited knowledge of senescence and neoplastic drivers in NK cells and how it progresses to an aggressive NK-cell leukemia. New pre-clinical mouse models of NK-cell leukemia are required to develop novel therapeutic approaches.

We have established an NK-cell senescence model and could show that senescent NK cells upregulate p16INK4a and p19ARF and that loss of the Ink4a/Arf locus allows leukemic transformation of NK cells. Transplantation of Ink4a/Arf KO NK cells into immunocompromised mice leads to the development of NK-cell leukemia.

We propose that INK4a and ARF have pivotal roles in NK-cell senescence and postulate that the development of NK-cell leukemia is only promoted when both p16INK4a and p14/19ARF are lost concurrently, allowing for the accumulation of additional mutations in NK cells. This study aims to explore the individual functions of p16INK4a and p19ARF, as well as their cooperative roles, in i) NK-cell senescence both in vitro and in vivo in mice, ii) NK-cell transformation, and iii) validation of the role of INK4a and ARF in human NK-cell senescence.

Additionally, we seek to establish a senescence signature for mouse NK cells to precisely define and characterize senescent mouse NK cells, and to identify pathways implicated in NK-cell senescence.

We will use NK-cell in vitro cultures and genetically modified mouse models, aging experiments, flow cytometry, CRISPR-Cas9-mediated manipulation of NK cells and multiplex arrays to study NK-cell senescence and leukemia development. Given the challenges posed by NK-cell malignancies, our project could establish a pre-clinical NK-cell leukemia mouse model, providing crucial resources for screening new therapies.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 63

Abstract Title: CRISPR-screening to identify a novel epigenetic regulator for exhausted T cell differentiation

Authors:

Zhang J¹, Sakaguchi S¹

¹Division of Immunobiology, Institute of Immunology, Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna

Abstract:

Persistent antigen exposure during chronic viral infection drives CD8 T cells into an exhausted state characterized by progressive functional impairment and the establishment of distinct differentiation states. Although epigenetic remodeling is a key feature of T cell exhaustion, the regulators controlling the differentiation and maintenance of exhausted CD8 T cell subsets remain incompletely understood.

To systematically identify epigenetic regulators of exhausted T cell differentiation, we performed an in vivo CRISPR-Cas9 screen using antigen-specific CD8 T cells in the lymphocytic choriomeningitis virus Clone 13 (LCMV Cl13) model of chronic infection. Different exhausted CD8 T cell populations were analyzed by next-generation sequencing and compared with the original CRISPR library to identify candidate regulators of exhausted T cell differentiation.

Our screen identified several candidate epigenetic regulators potentially involved in exhausted CD8 T cell differentiation. We are currently investigating the roles of these candidates in the differentiation of exhausted CD8 T cells during chronic viral infection. We will present our recent progress on the functional characterization of these candidates in exhausted T cell differentiation.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 64

Abstract Title: Developed for SARS-CoV-2 - Ready for the next viral threat: A rapidly adaptable antibody-dependent cell mediated cytotoxicity (ADCC) assay

Authors:

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Abstract:

Background: Antibody dependent cellular cytotoxicity (ADCC) plays a key role in antiviral immunity, including that against SARS-CoV-2. However, robust and reproducible in vitro systems for assessing ADCC remain scarce.

Methods: Herein, we developed a NK-92 cell line stably expressing the high-affinity variant F158V of CD16a and either IL-2 or IL-15 to enable high-levels of ADCC and cytokine-independent proliferation of NK effector cells. Target cells were generated using HEK-293T and NIH-3T3 cells expressing GPI-anchored SARS-CoV-2 antigens. NK cell lines were characterized for CD16 expression, binding of heat-aggregated IgG, elaboration of distinct cytokine profiles, and cytotoxic activity.

Results: Both NK cell lines expressed high levels of transgenic (tg) CD16 and secreted high levels of tg cytokines, but only IL-2-transduced cells showed strong binding of heat-aggregated IgG and efficient ADCC function. NIH-3T3 compared to HEK-293T cells were considered to be better suitable as target cells, expressing GPI-anchored SARS-CoV-2 receptor-binding domains (RBDs), because they underwent less frequent non-specific killing. The ADCC assay was benchmarked and optimized using a SARS-CoV-2 specific monoclonal antibody and then used to test the activity of sera obtained from 26 convalescent individuals at 10 weeks and 10 months after SARS-CoV-2 infection. The stretch of the SD1 domain encoded by amino acids 519 - 571 turned out to be the most important ADCC target. The resulting interindividual variations in ADCC levels may be attributable to differences in epitope specificity and/or the underlying IgG subclasses.

Conclusion: We have established a reproducible and rapidly adaptable ADCC assay system using SARS-CoV-2 antigens as the model. The developed platform enables direct functional antibody analysis and provides a valuable tool for investigating antiviral immune responses and vaccine-induced immunity. The ease with which the test system can be adapted, will help us to quickly and efficiently overcome the challenges posed by dangerous human pathogens in the future.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 65

Abstract Title: Premature immunosenescence is linked to distinct immunologic, metabolic and proteomic signatures in healthy individuals

Authors:

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Abstract:

Background

Immunosenescence is described as one of the main contributors to the aging phenotype and is associated with poor vaccination responses and a lack of disease protection. However, immunosenescence is still very poorly defined and our understanding of what factors drive or contribute to it are not well understood.

Methods

We conducted a study on 120 healthy subjects (age range 18-80 years) to discover biological and immunological aging signatures. Analyses included collecting the subject's demographic and medical history, as well as extensive peripheral T cell phenotyping and biological aging marker analysis. Subsequently, we performed metabolic and proteomic phenotyping using multi-omic approaches.

Results

Unsupervised clustering identified a specific subgroup of young healthy individuals (<40 years) that display a prematurely aged immune system, with reduced frequency of naïve T-cells, recent thymic emigrants (RTEs) as well as a reduced number of T cell receptor excision circles (TRECs) compared to healthy subjects of the same age. Based on these findings we started defining molecular senescence traits that set this pre-matured aging endotype apart from both young and old healthy individuals. Firstly, we found that pre-maturely individuals displayed additional alterations on the cellular level, for instance higher frequencies of Th2 and Th17 cells. Secondly, initial analyses indicate that these individuals show distinct metabolic and proteomic phenotypes. We identified 42 differentially abundant serum metabolites in our study cohort, including heightened concentrations of glutamine, iso/-leucine and valine in the pre-maturely aged subjects. Thirdly, we detected increased prevalence of serum chemokines in this group associated with cell movement and inflammaging. Notably, these differences occur independent of age, sex, chronic infections or lifestyle of the study participants.

Conclusion

Here we were able to identify a pre-matured immune-aging phenotype in a subgroup of young, healthy individuals. Subsequent studies will further elucidate the impact of accelerated immunosenescence in healthy individuals.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 66

Abstract Title: Naïve T-cells of individuals with strong T-cell reactivity after vaccination show a distinct epigenetic signature

Authors:

Dreo B¹, Sallegger C², Hodl-Kühnast I², Raicht A³, Schwinger W⁴, Schlenke P³, Thiel J², Holasek S¹, Lackner S¹, Madi A⁵, Inbal K⁵, Bock C⁶, Stradner M², Fessler J¹

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Abstract:

Background

T-cell immunity is a crucial part of fighting infections. However, identifying and predicting cell-mediated responses that correlate with vaccination efficacy is still challenging. We set out to investigate how environmental factors impact T-cell immunogenicity after vaccination.

Methods

Whole blood collection from healthy subjects was performed 21-28 days after receiving the second dose of COVID-19 vaccine. Isolated PBMCs were treated with Sars-Cov 2 Spike protein to evaluate T-cell reactivity after vaccination using flow cytometry. Furthermore, an extensive work-up of samples collected pre-vaccination was performed, including T-cell phenotyping, T-cell receptor excision circles (TREC) quantification and ATAC-Sequencing. Additionally, participants were asked to fill out the Vienna Food Record (VFR) to monitor their nutrient intake.

Results

Based on CD4+ and CD8+ T-cells reactivity to produce pro-inflammatory cytokines and activation markers in vitro we were able to identify healthy subjects with a strong and poor T-cell response respectively. Focusing on epigenome changes linked to strong T-cell reactivity, we identified a total of 888 upregulated and 950 downregulated differentially accessible regions in naïve CD4+ and CD8+ T-cells. Additionally, we found an association between strong T-cell reactivity post vaccination and higher binding intensities of transcription factors that help control cell development and secretion of pro-inflammatory cytokines in naïve T-cells prior to vaccination. Moreover, we detected higher TREC numbers in T-cells of healthy subject with strong T-cell reactivity, indicating higher thymic output in these subjects. Lastly, evaluation of the VFR revealed that healthy participants with poor T-cell reactivity reported a higher intake of foods containing omega-3/-6 fatty acids and polyunsaturated fatty acids (PUFAs), indicating that specific metabolites could have the capacity to adjust immune cell responsiveness during an infection.

Conclusion

Our study reveals a multifactorial network that yields the ability to shape vaccine-dependent immunogenicity. Further research is required to elucidate the underlying mechanisms in greater detail.

Abstract Number: 67

Abstract Title: Mitochondrial oxidative stress promotes an IL-4-producing phenotype in human T cells

Authors:

Frey T¹, Schaffer K¹, Lampl A¹, Hutter S¹, Hollenstein M¹, Schmidt R¹, **Schmetterer K¹**

¹Department of Laboratory Medicine, Medical University Of Vienna

Abstract:

Introduction: Reactive oxygen species (ROS) are important regulators of intracellular signaling and T cell effector functions. Mitochondria represent a major cellular source of ROS. However, the impact of mitochondrial oxidative stress on human T cell cytokine responses remains incompletely understood.

Objective: This study aimed to investigate how mitochondrial oxidative stress influences human T cell effector functions and IL-4 production and whether the resulting cytokine environment promotes Th2 polarization relevant to allergic sensitization.

Methods: Primary human CD4⁺ and CD8⁺ T cells were activated in the presence of Mitoquinone mesylate (MitoQ). CRISPR/Cas9-mediated knockout of Superoxide Dismutase 1 (SOD1) was performed. T cell effector functions were assessed by flow cytometry, multiplex ELISA, RNA sequencing, and qPCR. The role of mitochondrial ROS in IL-4 regulation was further investigated using the ROS scavenger MitoTEMPO and the complex III inhibitor Antimycin A.

Results: MitoQ broadly suppressed T cell effector functions, including proliferation and multiple cytokines, while IL-4 showed a distinct response with initial suppression followed by marked induction at later time points. This effect was observed at both protein and transcriptional level and was recapitulated in SOD1-deficient T cells, supporting a direct link between mitochondrial oxidative stress and IL-4 induction. Treatment with Antimycin A also enhanced IL-4 expression, whereas the mitochondrial ROS scavenger MitoTEMPO partially reversed the MitoQ-mediated increase. Importantly, supernatants from MitoQ-treated T cells promoted pronounced Th2 polarization of naïve CD4⁺ T cells, characterized by increased GATA3 expression and higher frequencies of IL-4⁺ and IL-13⁺ cells, indicating the generation of a Th2-polarizing cytokine environment potentially relevant to allergic sensitization.

Conclusion: Our findings demonstrate that mitochondrial oxidative stress induces a distinct IL-4-producing phenotype in human T cells. These data suggest that mitochondrial redox dysregulation may promote a Th2-polarizing environment and thereby contribute to allergic sensitization.

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Abstract Number: 68

Abstract Title: Macrophage phenylalanine metabolism restrains Th17 driven inflammation

Authors:

Saha P¹, Holl V¹, Khan M¹, Jankowski C¹, Melikhov I¹, Murray P², Miller A¹, Boucheron N¹, Weichhart T¹

¹Medical University of Vienna, ²Max Planck Institute of Biochemistry

Abstract:

Macrophages are central organizers of inflammation, yet how their metabolic activity influences adaptive immune responses remains incompletely understood. While intracellular metabolic rewiring of macrophages has been widely studied, the functional role of metabolites released by macrophages is largely unknown. Here, we identify a previously unrecognized macrophage metabolite that directly regulates T cell-driven inflammation.

Using untargeted liquid chromatography-mass spectrometry, we profiled metabolites released by classically activated macrophages and identified L-phenyl lactic acid (PLA) as one of the most significantly secreted metabolites. Mechanistically, PLA production required the phenylalanine degrading enzyme IL4-induced gene 1 (IL4i1) and lactate dehydrogenase indicating that macrophages convert phenylalanine via phenylpyruvic acid into PLA. To investigate a potential immunoregulatory role of PLA, we cultured mouse splenic naïve CD4⁺ T cells under Th17-polarizing conditions. Addition of PLA strongly reduced IL-17A production. Transcriptomic analysis revealed negative enrichment of glycolytic pathway in the presence of PLA, consistent with a functional suppression of the TH17 cells. We next investigated whether this metabolite regulates inflammation *in vivo*. In the imiquimod-induced IL-17-driven acute skin inflammatory psoriasis model, PLA administration reduced the frequency of CD4⁺IL17A⁺ T cells and markedly attenuated disease severity. In contrast, IL4i1-deficient mice that are unable to produce PLA, developed significantly exacerbated inflammation compared to wild type controls.

Together, our study identifies PLA as a macrophage-derived immunoregulatory metabolite that links phenylalanine metabolism to adaptive immune control. This work reveals a metabolic communication pathway through which macrophages restrain TH17-driven inflammation.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 69

Abstract Title: Dissecting fibroblast reprogramming and inflammatory circuits in acute cutaneous graft-versus-host disease

Authors:

Gail L^{1,2}, Deckert F^{1,2}, Heinzl L¹, Holzer E¹, Kopf A^{1,2}, Kleissl L^{1,2}, Brazdilova K^{1,2}, Strobl J¹, Rabitsch W³, Stry G^{1,2,4}

¹Department of Dermatology, Medical University of Vienna, ²CeMM Research Center for Molecular Medicine, ³Department of Medicine I, Medical University of Vienna, ⁴Christian Doppler Laboratory for Chronic Inflammatory Skin Diseases

Abstract:

Allogeneic hematopoietic stem cell transplantation (HSCT) is a curative therapy for leukemia and other hematologic disorders, but many HSCT patients develop graft-versus-host disease (GVHD). GVHD manifests in acute and chronic forms, each driven by distinct pathogenic mechanisms. The skin is a major target organ of both forms, and the development of sclerosis in chronic GVHD indicates a key pathogenic role for fibroblast in chronic GVHD. Additionally, inflammatory and neoplastic skin lesions across different diseases harbor distinct fibroblasts subsets implicated in driving local immune responses. However, the role of fibroblasts in acute GVHD (aGVHD) remains poorly defined, and a systematic analysis of fibroblast heterogeneity in aGVHD lesions is lacking.

Here, we investigate aGVHD-specific fibroblast states and map fibroblast-immune cell niches in aGVHD lesions to evaluate their therapeutic potential. We combine single-cell RNA sequencing, spatial transcriptomics, immunofluorescence validation, and CRISPR-knockout co-culture models for mechanistic investigation.

Integration of single-cell transcriptomic profiles of fibroblasts from acute GVHD skin lesions with a reference human skin fibroblast atlas, we identified cell states shared with healthy skin and lesional skin of other inflammatory skin diseases. Fibroblasts in aGVHD displayed a pro-inflammatory phenotype characterized by interferon-response (STAT1, CXCL9, CXCL10) and allograft-rejection signatures, while downregulating tissue remodeling programs, including extracellular matrix genes (ELN, SPARC) and HOX genes. Importantly, genes related to FRC-like fibroblasts (CCL19, CD74) were upregulated in GVHD. Our preliminary data indicates a potential role for fibroblasts in amplifying inflammatory circuits during aGVHD.

Spatial mapping and functional validation of fibroblast subsets of interest will further define their role in tissue pathology and help to identify novel biomarkers, putative targets and therapeutic avenues to prevent or mitigate aGVHD.

Abstract Number: 70

Abstract Title: Structural Modeling and Mutational Analysis of Bet v 1-Induced Antibodies Reveals Key Residues Governing Cross-Reactivity with Mal d 1

Authors:

Zhang R¹, Bohle B¹, Hambrecht B¹, Grimsholm O¹

¹Medical University Of Vienna Institute for Pathophysiology and Allergy Research

Abstract:

Background

IgE-mediated allergies such as pollen allergies are on the rise globally. Birch pollen allergy is frequently associated with food allergy due to cross-reactive immune responses between the major birch pollen allergen Bet v 1 and homologous food allergens such as Mal d 1 from apple. Molecular docking is a powerful modelling method to predict antibody-antigen complexes. In this study, we investigated the structural basis of the antibody recognition and cross-reactivity by combining antibody structural modeling, molecular docking, and mutational analysis.

Methods

The paired antibody sequence of a monoclonal antibody (BIP1) obtained from mice immunized with birch pollen extract was used to reconstruct the three-dimensional structures of the antibody variable fragments (Fv) of both heavy and light chain with IgFold. The modeled Fv structure was then subjected to molecular docking simulations with the previously characterised Mal d 1 epitope to predict allergen–antibody binding. To further define the residues critical for binding, multiple mutation-based approaches were applied to the antibody sequences, and their effects on antibody–allergen interactions were assessed computationally.

Results

Our analysis identified several amino acid positions and specific residues with major contributions to the binding affinity and stability of the antibody–Mal d 1 complex. Instead of highly investigated heavy chain complementarity-determining regions (CDRs), amino acids lying in light chain CDRs, especially W206 and Y208 in the L-CDR3, play an important role in binding with Mal d 1. Our results also indicate that these two amino acids are from the germline sequence and not due to somatic hypermutation.

Conclusion

Our research provides an in silico approach from antibody Fv structure prediction, modeling allergen-antibody binding, to the identification of key residues for binding. This structural framework can potentially contribute to the future design of targeted interventions to block IgE-mediated responses.

Abstract Number: 71

Abstract Title: Atypical Chemokine Receptor 4 ameliorates Experimental Glomerulonephritis

Authors:

Leitinger D¹, Russo S², Klötzer K¹, Göhring S¹, Schabhüttl C¹, Hub E², Gutjahr J³, Samus M², Kirsch A¹, Eller P⁴, Rosenkranz A¹, Eller K¹, Rot A², Artinger K¹

¹Division of Nephrology, Department of Internal Medicine, Medical University of Graz, ²Centre for Microvascular Research, William Harvey Research Institute, Faculty of Medicine and Dentistry, Queen Mary University of London, ³Institute of Cell Biology and Immunology Thurgau (BITG) at the University of Konstanz, ⁴Intensive Care Unit, Department of Internal Medicine, Medical University of Graz

Abstract:

Background: The Atypical Chemokine Receptor 4 (ACKR4) binds chemokines without triggering G-protein-mediated signaling. Although well characterized in lymphoid organs, its functional significance and expression pattern in solid organs such as the kidney remain poorly defined. We aimed to investigate the expression of ACKR4 in the murine kidney and its contribution to the pathogenesis of experimental nephrotoxic serum nephritis (NTSN).

Methods: NTSN was induced in ACKR4^{+/+} (wild type), ACKR4^{eGFPKI/eGFPKI} (ACKR4-deficient), and ACKR4^{+/eGFPKI} reporter mice, and the disease phenotype was evaluated at days 3, 7 and 14 after induction of NTSN. Expression of ACKR4 in the murine kidney and numbers of podocytes and glomeruli were assessed using confocal and light sheet microscopy after whole tissue clearing.

Results: ACKR4 expression in the kidneys was restricted to a discrete population of glomerular parietal epithelial cells (PECs) with potential regenerative capacity, localized at the glomerular vascular pole. ACKR4 expression was reduced particularly in severely sclerotic glomeruli after NTSN induction. Although numbers of podocytes and glomeruli were comparable in healthy ACKR4-deficient and -sufficient mice, ACKR4 deficiency significantly aggravated parameters of NTSN, including albuminuria and histopathology. Total numbers of kidney-infiltrating immune cells were comparable between the two groups 14 days after NTSN induction; however, numbers of kidney-infiltrating dendritic cells were significantly higher at days 3 and 7 in ACKR4-deficient mice. There was no difference in the immune cell composition in the draining lymph node. Interestingly, healthy and nephritic ACKR4-deficient mice further exhibited significantly higher systolic blood pressure compared with ACKR4 wild-type mice.

Conclusion: ACKR4 is expressed in murine glomeruli by a subset of PECs close to the glomerular vascular pole. The aggravated NTSN phenotype in ACKR4-deficient mice indicates a new regulatory role of ACKR4 in the kidney, limiting the development of nephritis.

Abstract Number: 72

Abstract Title: Tissue Distribution of Type-2 Memory B Cell Subsets in Allergic and Non-Allergic Individuals

Authors:

Petsiou D¹, Stanek V¹, Brückl C¹, Zghaebi M¹, Tu A¹, Schmetterer K², Frey T², Lampl A², Benazzo A³, Aigner C³, Berlakovich G⁴, Wekerle T⁴, Breiteneder H⁵, Schneider S¹, Eckl-dorna J¹

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Abstract:

Background: Type-2-polarized memory B cells (MBCs), characterized by high expression of interleukin-4 receptor α chain (IL-4R α) and CD23, are attracting growing interest within the field of human type-2 immunity. However, current data originate primarily from mouse models and human PBMCs. Here, we aimed to identify and compare Type-2 MBC subsets across human peripheral blood and lymphoid tissues, including the spleen and lymph nodes adjacent to the respiratory tract (RT).

Methods: Fifteen samples were collected from allergic and non-allergic human donors including peripheral blood (n=6), the spleen (n=6), and RT-lymph nodes (n=3). Single-cell suspensions were immunophenotyped ex vivo by flow cytometry to quantify non-switched (CD27+/IgD+) and switched (CD27+/IgD-) type-2 memory B cell subsets (CD19+CD23+IL-4R α +). Additionally, primary splenocytes from different allergic and non-allergic human donors (n=3) were cultured in vitro under allergen-specific (Bet v 1) and type-2-polarizing (IL-4 + CD40-L) conditions to assess subset expansion.

Results: Ex vivo profiling revealed that while type 2 memory B cells can be detected across peripheral blood and lymphoid organs, their frequencies show a distinct upward trend in lymph nodes, particularly within the switched memory subset. Moreover, consistent with established models of peripheral B cell recall, in vitro stimulation of primary splenocytes with Bet v 1 and type-2-polarizing conditions induced an expansion of both type 2 switched and non-switched memory B cells compared to control samples.

Conclusion: Our findings demonstrate that human lymph nodes harbor an enriched pool of type 2 switched memory B cells compared to peripheral blood and spleen, highlighting distinct anatomical heterogeneity across human lymphoid niches. Further investigations are to be performed to shed more light on the dynamics of type 2 B cell recall within human lymphoid tissues.

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Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 73

Abstract Title: Nasal allergen provocation triggers B-cell activating factor (BAFF) and adaptive immune pathways in birch pollen allergic individuals

Authors:

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Abstract:

Background: The rising global prevalence of allergic rhinitis and associated type 2 inflammatory conditions has prompted a critical re-evaluation of mucosal immunity. The epithelial barrier hypothesis provides a crucial framework for understanding the rising prevalence of allergic diseases due to the disruption of the epithelial barrier followed by local dysbiosis and chronic inflammation. Local tissue-resident B-cell responses in the nasal mucosa are still poorly understood. **Methods:** Therefore, we conducted a nasal provocation study with birch pollen extract in allergic and healthy individuals, collecting nasal scrapings at 0, 15, 30, 60, and 120 minutes for RNA sequencing, while simultaneously quantifying cytokines in nasal secretions via ELISA.

Results: We could demonstrate that the B-cell activating factor (BAFF), a cytokine crucial for B-cell maturation and survival, was elevated in allergic patients. BAFF mRNA levels were induced upon provocation, and this coincided with an upregulation of monocyte-specific genes. Using publicly available data we confirmed that BAFF is mainly produced by monocytes and dendritic cells in the nasal mucosa. Next, we identified differentially expressed genes (DEGs) in allergic patients by comparing baseline to immediate (15 and 30 mins) and to early (60 and 120 mins) timepoints. We observed a greater number of DEGs (266 in total) between the baseline and immediate timepoints. Subsequent pathway analysis indicated the induction of several B-cell-specific pathways including B-cell proliferation. Simultaneously, we also detected an early increase in tissue-resident plasma-cell signatures, which was significant in the immediate timepoints (FDR = 0.031), and a similar early increase in tissue-resident memory B-cell signatures in allergic patients, although the latter did not reach statistical significance.

Conclusion: Together, our data suggest that tissue-resident immune memory cells in the nasal mucosa are rapidly activated upon allergen re-stimulation.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 74

Abstract Title: Characterizing ME/CFS in Clinical Practice: Insights from an Unselected Austrian Cohort

Authors:

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¹Medical University Of Vienna, Center for Pathophysiology, Infectiology and Immunology, Institute of Pathophysiology and Allergy Research

Abstract:

Background

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS; ICD-10: G93.3) is a chronic multisystem disorder characterized by post-exertional malaise (PEM) and substantial functional impairment. To date, ME/CFS is clinically diagnosed based on established international consensus criteria. Diseases with similar symptom presentation need to be evaluated and excluded, even though presence of PEM is an exclusive feature of ME/CFS. Objective biomarkers that could facilitate diagnosis and improve disease characterization are yet to be identified.

Methods

As part of the establishment of Austria's first ME/CFS biobank, validated questionnaires (inter alia FUNCAP-55, Bell score, KLOK score, COMPASS-31) and clinical measures were evaluated in patients with ME/CFS and healthy controls. Associations between disease severity, handgrip strength, and changes in blood lactate levels, pulse and blood pressure before and after a standing test were assessed and statistically evaluated.

Results

Correlations were observed between FUNCAP-55, handgrip strength, the change in blood lactate levels following the standing test, a COMPASS-31-based dysautonomia score, and the Bell score, which reflects disease severity.

Conclusion

Our findings support the potential of handgrip strength measurement as an objective, accessible measure for the characterization of ME/CFS and are consistent with previous reports. The observed associations between clinical severity, muscle strength, lactate response, and autonomic dysfunction warrant further investigation in larger, longitudinal cohorts to determine their diagnostic and prognostic value.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 75

Abstract Title: Palmitic Acid Alters the Immunoregulatory Function of Human Periodontal Ligament Mesenchymal Stromal Cells

Authors:

Qinawi H^{1,2}, Demidova A³, Lorenz A¹, Behm C¹, Andrukhov O¹

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³Department of Natural Sciences and Sustainable Resources, University of Natural Resources and Life Sciences

Abstract:

Background: Human periodontal ligament mesenchymal stromal cells (hPDL-MSCs) support periodontal tissue regeneration and regulate local immune responses. Palmitic acid (PA), a saturated fatty acid elevated in obesity and type 2 diabetes mellitus, can induce metabolic and inflammatory stress in stromal cells and may therefore influence hPDL-MSC immunomodulatory function. This study investigated the effects of PA on the inflammatory and immunoregulatory properties of hPDL-MSCs.

Methods: hPDL-MSCs from healthy donors were exposed to PA (10-500 μ M). Metabolic activity and cell death were assessed using MTT and Live/Dead assays. hPDL-MSCs were stimulated with IFN- γ , IL-1 β , TNF- α , or Toll-like receptor (TLR) agonists with and without PA. Expression of IDO1, CD274, PTGS2, IL6, CXCL8, CCL2, TLR2, and TLR4 was quantified by RT qPCR; IDO1 and surface PD-L1 were analyzed by flow cytometry, and IL-6 and IL-8 secretion by ELISA. The effect of PA-treated hPDL-MSCs on CD4+ T-cell proliferation was evaluated in an indirect co-culture model.

Results: PA reduced hPDL-MSC metabolic activity in a concentration-dependent manner and increased cell death at higher concentrations. 200 μ M of PA was selected because it induced measurable metabolic stress while preserving cell viability. PA reduced cytokine-induced IDO1 gene and protein expression, particularly after IL-1 β and TNF- α stimulation, and decreased surface PD-L1 expression across all cytokine conditions tested. In contrast, PA increased PTGS2 expression and enhanced IL-6 and IL-8 responses to several TLR agonists. PA-treated hPDL-MSCs showed a reduced capacity to suppress CD4+ T-cell proliferation in unstimulated, IL-1 β stimulated, and TNF- α -stimulated co cultures.

Conclusion: PA alters the balance between inflammatory and immunoregulatory functions in hPDL-MSCs. Under the conditions tested, PA enhanced inflammatory cytokine responses while reducing immunoregulatory features, including IDO1 and surface PD-L1 expression and suppression of CD4+ T-cell proliferation. These findings suggest that lipid associated metabolic stress may impair hPDL-MSC-mediated immune regulation in the diabetic periodontal microenvironment.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 76

Abstract Title: Orthodontic Forces Modulate hPDL-MSC Immunoregulatory Effects on Macrophages During Aseptic Inflammation

Authors:

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Abstract:

Orthodontic tooth movement (OTM) involves mechanical forces that trigger an aseptic inflammatory response in the periodontium, marked by upregulation of pro-inflammatory cytokines interleukin (IL)-1 β and tumor necrosis factor (TNF)- α and macrophage recruitment. Human periodontal ligament-derived mesenchymal stromal cells (hPDL-MSCs) play a pivotal role in periodontal tissue homeostasis and in regulating immune cells, including macrophage polarization modulation and immunosuppression via modulating the expression of immunoregulatory mediators such as indoleamine 2,3-dioxygenase 1 (IDO-1). However, how orthodontic forces affect these immunomodulatory functions under inflammatory conditions remains unclear. We therefore investigated how static tensile strain (STS) affects hPDL-MSC-mediated regulation of pro-inflammatory (M1) and anti-inflammatory (M2) macrophages under cytokine microenvironments.

Primary hPDL-MSCs were subjected to 12% STS. To mimic aseptic inflammatory conditions, cells were stimulated with IL-1 β or TNF- α in the presence or absence of STS for 3,6,24h. IDO-1 expression was measured by qPCR and flow cytometry. Conditioned medium (CM) from hPDL-MSCs was applied to macrophages to assess M1/M2 polarization (CD80, CD206) and cytokine secretion after 48h. IDO-1 was pharmacologically inhibited during STS.

STS-CM induced time- and cytokine-dependent changes in macrophage polarization, increasing CD80⁺ macrophages following IL-1 β and TNF- α stimulation and producing more variable effects on CD206⁺ macrophages. M1-associated secretion showed increased TARC and reduced IP-10 after IL-1 β stimulation, whereas TNF- α primarily reduced arginase, while M2-associated cytokine secretion remained largely unchanged apart from alterations in IP-10. IL-1 β and TNF- α significantly reduced IDO-1 expression at gene and protein levels after 6h. Pharmacological IDO-1 inhibition further reduced CD80 expression under untreated and IL-1 β conditions, but had no significant effect following TNF- α stimulation and did not alter CD206⁺ macrophage polarization.

Overall, these findings suggest that STS modulates hPDL-MSC-mediated macrophage responses in a time- and cytokine-dependent manner, with IDO-1 contributing mainly to pro-inflammatory CD80⁺ macrophage regulation, highlighting a mechanism by which orthodontic forces shape local inflammatory dynamics during OTM.

Abstract Number: 77

Abstract Title: Hypoxia and dimethyloxalylglycine differentially modulate inflammatory licensing and immunoregulatory mediators in human gingiva-derived mesenchymal stromal cells

Authors:

Schwarz K¹, Kompaneets I¹, Dankovych Y¹, Bećirović M¹, Mišek O¹, Janjić K², Behm C¹, Andrukhov O¹

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Abstract:

Background: Human gingiva-derived mesenchymal stromal cells (hG-MSCs) encounter hypoxia and inflammatory cytokines within oral tissues. Although hG-MSCs can regulate immune responses, it remains unclear how low oxygen tension and hypoxia-inducible factor (HIF) pathway activation affect their inflammatory licensing. We investigated the effects of hypoxia and the HIF-stabilizing agent dimethyloxalylglycine (DMOG) on immune mediator profiles in resting and cytokine-primed hG-MSCs.

Methods: Primary hG-MSCs from six healthy donors were cultured for 24 h under normoxia (21% O₂), hypoxia (<1% O₂), or with DMOG (300 µM). Simultaneously, cells were maintained under basal conditions or stimulated with interferon-γ (IFN-γ), tumor necrosis factor-α (TNF-α), or interleukin-1β (IL-1β). Metabolic activity and viability were assessed using MTT and live/dead assays. Gene expression of VEGFA, SLC2A1, CA9, CXCL8, PTGS2, CD274, and IDO1 was quantified by qPCR. IL-8 and prostaglandin E₂ (PGE₂) secretion were determined by ELISA, and PD-L1 and IDO-1 protein expression by flow cytometry.

Results: Hypoxia and DMOG activated hypoxia-responsive signalling in hG-MSCs, indicated by increased VEGFA, SLC2A1, and CA9 expression across basal and inflammatory conditions. Although both treatments lowered metabolic activity, viability was largely retained. Hypoxia and DMOG produced cytokine-specific immune mediator patterns. In basal, IFN-γ- and TNF-α-exposed hG-MSCs, both interventions enhanced the CXCL8/IL-8 axis. After IL-1β priming, hypoxia lowered CXCL8 expression without significantly affecting IL-8 release, whereas DMOG increased IL-8 secretion despite unchanged CXCL8 expression. Hypoxia reduced IL-1β-induced PTGS2 expression, while DMOG increased PTGS2 expression and, depending on cytokine context, PGE₂ release. Hypoxia and DMOG downregulated CD274 and IDO1 expression, broadly supported by reduced PD-L1 and IDO-1 protein levels.

Conclusion: Hypoxia and DMOG differentially reprogram hG-MSC immune mediator profiles rather than uniformly enhancing immunosuppressive immune mediator expression. Tissue oxygenation and cytokine context may therefore determine the immune phenotype of hG-MSCs.

Abstract Number: 78

Abstract Title: Pre-transplant Expansion of Activated CD25⁺ and Exhausted TIGIT⁺ Cytotoxic T Lymphocytes and NK Cells as convergent Predictors of Acute Kidney Transplant Rejection

Authors:

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Abstract:

Background: Acute rejection (AR) remains a key driver of allograft loss after kidney transplantation. We tested whether distinct pre-transplant lymphocyte signatures of effector activation and exhaustion independently predict AR.

Methods: Matched cohort analysis of 12 AR patients (median time to T cell mediated rejection 10 days) and 12 rejection-free controls, with 9 healthy donors as reference. Pre-transplant PBMCs were immunophenotyped by 11-colour flow cytometry. Predictive performance was assessed by ROC and Kaplan–Meier analysis. Intra-graft single-cell RNA sequencing (GSE189536; 11 biopsies, 3.583 CD8⁺ T cells) was analysed by Leiden clustering and pseudobulk Spearman correlation with Banff scores.

Results: Activated CD25⁺FoxP3⁻ CTL were expanded in future rejectors (57.8% vs. 30.9%, $p = 0.0015$). Exhausted TIGIT⁺ effector memory CD8⁺ T cells (25.2% vs. 10.9%, $p = 0.022$) and TIGIT⁺ NK cells (22.8% vs. 11.3%, $p = 0.003$) were elevated. ROC analysis identified CD25⁺ CTL as the strongest individual predictor (AUC 0.89), followed by TIGIT⁺ NK cells (AUC 0.86) and TIGIT⁺ effector memory CD8⁺ T cells (AUC 0.78). Kaplan–Meier analysis confirmed shorter rejection-free survival with high pre-transplant CD25⁺FoxP3⁻ CTL, TIGIT⁺ NK cells and TIGIT⁺ effector memory CD8⁺ T cells (log-rank $p < 0.01$ in all). Intra-graft transcriptomics identified three exhausted CD8⁺ subpopulations enriched in rejection biopsies; pseudobulk TIGIT expression in CTLs correlated with tubulitis ($p = 0.671$, $p = 0.024$) and interstitial inflammation ($p = 0.714$, $p = 0.014$) Banff scores.

Conclusion: Pre-transplant CD25⁺ activated CTL and exhausted TIGIT⁺ effector memory CD8⁺ T cells and NK cells are independent pre-transplant predictors of early acute rejection after kidney transplantation, corroborated by intra-graft enrichment of exhausted CD8⁺ T cell subpopulations in correlation to inflammation severity.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 79

Abstract Title: IgE Induction in the Gut Aggravates Liver Disease in an FcεRIα-Mediated Manner

Authors:

Baranovskyi T¹, Dragana R¹, Höbinger C¹, Duckova T¹, Schabbauer G², Schwarz M³, Hofer B³, Simbrunner B³, Reiberger T³, Starkl P⁴, Hendrikx T¹

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Abstract:

Despite the well-established role of IgE in allergic disorders, the mechanisms underlying its elevation during liver disease in non-atopic patients and its involvement in disease progression remain unclear. We profiled serum IgE titers across liver diseases of diverse etiologies and corresponding mouse models, identifying the strongest induction in patients and mice with alcohol-related liver disease (ALD), which were subsequently used for mechanistic studies. In murine ALD, CD4⁺ T cell depletion, as well as impaired IL-4 signaling (IL4Rα^{-/-}, IL4^{-/-}), abrogated IgE elevation. Serum IgE from ethanol-fed mice bound dietary antigens, and these mice mounted antigen-specific responses to ovalbumin introduced into the diet, suggesting that IgE induction occurs in the gut. Consistently, markedly elevated IgE levels were detected in the cecum, alongside increased frequencies of IgE⁺ B cells and enhanced εGLT in mesenteric lymph nodes. Furthermore, microbiome depletion using non-absorbable antibiotics reduced IgE levels. Importantly, mice lacking hepatic IL-33 (IL33fl/flAlbCre⁺) exhibited lower serum IgE following ethanol exposure, linking epithelial stress signals to downstream type 2 immunity. Ethanol-fed mice also showed elevated hepatic MCPT8 and histamine, but not MCPT1, together with higher frequencies of circulating basophils. Functionally, both genetic IgE deficiency and therapeutic IgE blockade prevented ethanol-induced steatohepatitis. Consistently, FcεRIα-deficient mice displayed attenuated liver injury and inflammation, accompanied by reduced hepatic histamine. In ALD patients, serum IgE correlated with plasma histamine and disease severity, while single-nucleus RNA-sequencing data revealed increased hepatic IL33 expression compared with healthy controls. Circulating basophil frequencies were also higher in ALD than in non-ALD patients. Collectively, these findings define an IL-33-Th2-IgE-FcεRIα axis as a key mediator of gut-liver crosstalk and highlight it as a potential therapeutic target in liver disease.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 80

Abstract Title: Inflammatory Environments Regulate Vitamin D₃ Metabolism in Periodontal Ligament MSCs

Authors:

Hilberath S¹, Liepert M¹, Otterbein C¹, Behm C¹, Andrukhov O¹

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Abstract:

Vitamin D₃ is a fat-soluble secosteroid hormone essential for bone metabolism, immune modulation, and inflammation control. Therefore, its status substantially influences oral health and disease. In human periodontal ligament-mesenchymal stromal cells (hPDL-MSCs), the enzymes CYP27B1 and CYP24A1 govern the intracellular balance of active 1,25(OH)₂D₃ and its inactive metabolites. We investigated how these enzymes and vitamin D-related signaling are regulated in hPDL-MSCs by various modulators, including pro-and anti-inflammatory cytokines, hormones, and growth factors.

hPDL-MSCs isolated from extracted third molars were treated for 48 hours with 25(OH)D₃ or 1,25(OH)₂D₃ in combination with potential modulators of vitamin D₃ metabolism and inflammatory cytokines. Subsequently, gene and protein expression of key vitamin D-metabolic enzymes and receptors were quantified.

Classical endocrine regulators of renal vitamin D₃ metabolism, such as fibroblast growth factor 23 (FGF-23), 17β-estradiol (E2), parathyroid hormone (PTH), and insulin-like growth factor-1 (IGF-1), exerted only minor effects on vitamin D-related gene expression in hPDL MSCs. In contrast, pro-inflammatory cytokines such as interferon-γ (IFN-γ), tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), as well as the anti-inflammatory cytokine transforming growth factor-β (TGF-β) modulated vitamin D₃ metabolism. Notably, TNF-α, IL-1β, and TGF-β increased CYP27B1 expression, an effect partially attenuated by co-treatment with both vitamin D₃ metabolites. In general, vitamin D₃ treatment upregulated CYP24A1 expression, which was partially suppressed by pro-inflammatory cytokines. In contrast, TGF-β acted synergistically with vitamin D₃ to further induce CYP24A1. TGF-β also increased vitamin D receptor (VDR) expression, while vitamin D₃ partially counteracted this effect. Pro-inflammatory cytokines produced the opposite pattern on VDR expression, particularly in combination with 1,25(OH)₂D₃.

The regulation of vitamin D₃ metabolism in hPDL-MSCs differs markedly from that in the kidney and is predominantly influenced by the inflammatory microenvironment. These findings highlight the importance of local immune conditions in modulating vitamin D₃ activity in periodontal tissues.

Abstract Number: 81

Abstract Title: Kupffer cell activation critically shapes systemic immunity to infection

Authors:

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Abstract:

Kupffer cells (KCs), the resident macrophages of the liver, are strategically positioned in the hepatic sinusoids to detect and eliminate invading microbes. Although these cells have been proposed to serve as critical barriers preventing the systemic spread of bacteria, how KCs respond to infection and contribute to microbe clearance remains poorly understood. Here, we demonstrated that resident KCs are temporally activated following infection and that this activated state plays a critical role in shaping systemic responses to infection. The precise responses elicited by KCs were, however, context dependent. KC-specific deletion of the negative regulator of NFκB signaling, A20, amplified KC activation and led to an acute, lethal inflammatory response to soluble LPS, mediated by TNF/RIPK3. In contrast, enhancing KC activation during infection with live *Salmonella* resulted in rapid bacterial elimination through upregulation of a NOS/ROS-dependent anti-bacterial programme. These findings establish KC activation as an important context-dependent regulator of systemic immune responses to infection and highlight the potential of modulating macrophage activation to shape host immunity across different inflammatory contexts.

Abstract Number: 82

Abstract Title: Lineage-Resolved Multi-Omics Profiling Reveals Protein Acetylation as a Major Regulatory Layer in T Helper Cells

Authors:

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T helper (Th) cell fates is orchestrated by layers of epigenetic, transcriptional, and post-translational control. It is known that histone acetyltransferases (HATs) and deacetylases (HDACs) modulate the epigenome by reversible histone lysine acetylation, however their broad impact on non-histone proteins in Th cells still needs further investigation. Here, we present a comprehensive multi-omics atlas mapping chromatin accessibility, transcriptome, proteome, acetylproteome, and phosphoproteome across Th1, Th2, Th17, and iTreg cells. We reveal that non-histone acetylation competes with phosphorylation in terms of scale and predominantly targets cytosolic and mitochondrial proteins. Additionally, we identified shared and subset-specific acetylation and phosphorylation profiles, which indicates that lineage-specific acetyl-proteoforms could fine-tune context-dependent effector functions. Importantly, acetylation and phosphorylation networks converged in shared master transcription factor regulators such as transcription factors of the STAT family, BACH2 and IKZF3, highlighting a coordinated post-translational control of Th cells. Collectively, we show that non-histone protein acetylation is a major regulatory layer governing Th cell identity and function. Additionally, to further elucidate the epigenetic and non-histone role of HDAC1, a driver of T cell autoimmunity, we integrated multi-omics profiles across WT and HDAC1-deficient Th cell subsets. The absence of HDAC1 did not hinder minimally affected lineage differentiation and chromatin accessibility but broadly rewired the transcriptome, proteome and the phosphoproteome, further regulating conserved acetylation signatures across Th lineages. Finally, we have developed the T Cell Explorer, an integrative and interactive multi-omics resource of T cells. Our resource features AlphaFold3 protein structure integration, chromatin accessibility tracks, gene expression, protein abundance, and structural 3D PTM profiles in T cells, collectively tailored to hypothesis generation and data exploration. The integrative resource will be available at tcellexplorer.org.

Annual Conference 2026

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Abstract Number: 83

Abstract Title: Spatial immunophenotyping of human MPOX lesions reveals keratinocyte-CXCR3-driven pDC recruitment and localized epidermal viral containment

Authors:

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Abstract:

Mpox emerged as a global health threat in 2022, with sporadic outbreaks continuing in Europe. Despite its ongoing relevance, the immune mechanisms underlying human Monkeypox virus (MPXV) clearance and elicited strong and durable antiviral immunity are still under studied. Here, we apply state-of-the-art single-cell transcriptomics, T-cell receptor sequencing, and spatial profiling of matched lesional skin and blood of n=5 patients presenting with acute mpox infection. Mpox lesions exhibited a structurally segregated immune infiltration characterized by enrichment of plasmacytoid dendritic cells (pDCs) and B cells in the epidermis and inflammatory macrophages and newly recruited circulating T cells in the dermis. We observed keratinocytes (KCs) expression of CXCL10 and CXCL9 with concomitant co-localization of CXCR3+ pDCs into the epidermis surrounding MPXV infected KCs. Concomitantly, dermal immune and stromal cells reorganized into lymphoid niches supporting chemokine-guided positioning, antigen presentation, and Innate-adaptive immune crosstalk. Clonal tracking revealed extensive coupling between blood and skin T cell compartments, with influx of polyclonal circulating central memory T cells into the dermis. Together, MPXV remains spatially contained in the epidermis by IFN α /b-producing-KCs, trafficking pDCs and B cells, while the dermal compartment integrates systemic antiviral responses. A deeper understanding of these tissue-specific immune programs may inform strategies to elicit robust and long-lasting protective immunity not only against MPXV but also across a broader spectrum of skin-tropic viral infections, with potential implications for vaccine design and immunotherapeutic approaches targeting barrier tissues.

Abstract Number: 84

Abstract Title: A fibroblast-immune niche sustains granulomatous inflammation in humans and collapses upon targeted therapy

Authors:

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Abstract:

Background

Sarcoidosis is a granulomatous inflammatory disease characterized by persistent immune activation and organized tissue lesions. We previously showed that mTOR inhibition induces sustained remission in cutaneous sarcoidosis. Here, we used therapeutic mTOR inhibition as a longitudinal in vivo perturbation to investigate the cellular and spatial mechanisms underlying granuloma persistence and resolution.

Methods

Lesional and non-lesional skin biopsies obtained longitudinally during mTOR inhibition were analyzed by single-cell RNA sequencing. Downstream analysis included scVI integration, differential gene expression, and compositional analysis. Spatial organization and cellular phenotypes were further assessed by immunofluorescence. Primary human dermal fibroblasts isolated from healthy individuals and patients with sarcoidosis were stimulated with sarcoidosis-related cytokines in vitro and subjected to transcriptomic profiling using Smart-seq2.

Results

Our analyses identified spatial tissue organization as a key determinant of granuloma persistence. T cell-derived cytokines reprogram fibroblasts into inflammatory niche organizers, which promote monocyte recruitment through chemerin signaling and sustain granuloma architecture. Therapeutic mTOR inhibition disrupted this stromal-immune circuit by reducing both chemerin secretion by fibroblasts and inflammatory cytokine production by T cells. This was accompanied by coordinated loss of granuloma-associated macrophage, T cell, and fibroblast states and restoration of tissue homeostasis. Signatures of the major cellular components of this circuit were also enriched in other granulomatous disorders such as granuloma annulare and tuberculosis, suggesting broader relevance of the identified mechanisms.

Conclusions

Our findings define a pathogenic T cell-fibroblast-macrophage circuit that maintains spatially organized granulomatous inflammation. Therapeutic mTOR inhibition disrupts this loop and promotes dissolution of granuloma architecture and restoration of tissue homeostasis, highlighting stromal-immune interactions as potential therapeutic targets in granulomatous disease.

Abstract Number: 85

Abstract Title: Targeting histone acetylation as novel therapeutic strategy for rheumatoid arthritis

Authors:

Brinkmann M¹, Tosevska A¹, Corgos M¹, Luckerbauer B¹, Hermann L¹, Rautner J¹, Emilius L¹, Acosta M¹, Heinz L¹, Hayer S¹, Simader E¹, Sieghart D¹, Krausgruber T^{3,4}, Bock C^{3,4}, Ellmeier W², Göschl L¹, Aletaha D¹, Preglej T¹, Bonelli M¹

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Abstract:

Background: Rheumatoid arthritis (RA) is an autoimmune disease, characterized by persistent immune dysregulation driving chronic inflammation and progressive joint destruction. Despite advances in immune-modulating therapies, many patients remain refractory, highlighting the need for strategies targeting molecular programs underlying persistent disease. We hypothesized that epigenetic compounds could target pathogenic immune cell programs and provide novel therapeutic opportunities in RA.

Methods: Peripheral blood mononuclear cells from RA patients were treated with 26 epigenetic compounds, followed by bulk RNA sequencing to identify drugs targeting RA-associated gene programs. Candidate compounds were characterized by spectral flow cytometry, single-cell RNA sequencing, and ATAC sequencing. Effects on osteoclastogenesis were assessed using an in-vitro M-CSF/RANKL differentiation system. A bromodomain and extraterminal (BET) protein inhibitor was therapeutically evaluated in a murine collagen-induced arthritis (CIA) model.

Results: Epigenetic drug screening identified compounds targeting histone acetylation as modulators of RA-associated inflammatory programs, with monocytes emerging as major responder cells. Multi-omics characterization revealed a candidate BET inhibitor that selectively altered abundance of intermediate monocytes, associated with inflammation in RA. It further targeted disease-relevant transcriptional pathways in myeloid cells, including NF- κ B-associated inflammatory pathways and osteoclast differentiation programs, without altering global chromatin accessibility. Consistently, the BET inhibitor reduced osteoclast differentiation in-vitro. Therapeutic treatment in the CIA model significantly reduced disease severity and was associated with decreased myeloid cell infiltration, joint inflammation, and bone erosion.

Conclusion: Our findings identify a candidate BET inhibitor as a selective epigenetic modulator of pathogenic myeloid cell programs in RA. By targeting NF- κ B-driven inflammation and osteoclast differentiation without globally reprogramming chromatin, the BET inhibitor reduced both inflammatory and destructive manifestations of experimental arthritis. Together, our data identify a promising candidate for clinical evaluation and help close a critical gap in the translation of epigenetic therapies for RA.

Abstract Number: 87

Abstract Title: Maternal Immune Activation (MIA): The impact of maternal lung infection on offspring immunity

Authors:

Shen J¹, Fokina A¹, Pimenov L¹, Farhat A^{1,2}, Dekert F^{1,2}, Radhouani M^{1,2}, Brösamlen J¹, Meng F¹, Chen B¹, Hladik A¹, Lakovits K¹, Gawish R¹, Knapp S¹

¹Medical University Of Vienna, ²CeMM

Abstract:

Background: Early immune developmental periods are critical for establishing long-term immune homeostasis. Maternal immune activation (MIA), triggered by maternal infection or immune stimulation, can disrupt offspring development and has been associated with increased risk of neurodevelopmental disorders and asthma. However, little is known about how maternal inflammatory signals influence the trajectory of immune maturation in the offspring. This study investigates the effects and mechanisms of SARS-CoV-2-induced MIA on offspring lung immunity, fetal immune imprinting, and susceptibility to lung disease in mice.

Methods: The MIA model was established where pregnant mice were intranasally inoculated with mouse-adapted SARS-CoV-2 on embryonic day 14.5. Offspring were analyzed across early postnatal development and adulthood. Lung immune cell profiles were assessed by FACS and scRNA-seq, together with inflammatory cytokines. *Streptococcus pneumoniae* was used in in vivo and in vitro infection and stimulation models to investigate the functional consequences of MIA. Paired scRNA-seq analyses of the placenta and fetal liver were performed to identify potential maternal-fetal communication pathways.

Results: MIA-exposed offspring displayed an early expansion of lung neutrophils and eosinophils during the first four weeks of life. Elevated neutrophil numbers persisted into adulthood and were accompanied by a lung environment characterized by increased inflammatory cytokines. Functionally, these offspring showed improved resistance to *Streptococcus pneumoniae* pneumonia, including enhanced survival and more efficient bacterial clearance. Both alveolar macrophages and lung epithelial cells from MIA-exposed offspring contributed to enhanced pro-inflammatory responses upon bacterial stimulation, potentially shaped by epigenetic modifications. Mechanistically, CellChat analysis of placenta and fetal liver scRNA-seq datasets identified ligand-receptor communication involving TNF, CCL, and CXCL pathways from placental macrophages to fetal liver compartments during MIA.

Conclusion: This work shows that maternal inflammation caused by acute SARS-CoV-2 infection during pregnancy can alter lung immune development and function in the offspring, thereby modifying susceptibility to lung disease.

Abstract Number: 88

Abstract Title: Spermidine supplementation increases autophagic flux and reduces ROS production in T-cells from spondyloarthritis patients

Authors:

Rados M¹, Javorova P², Lackner A², Müller A³, Pein L³, Krivitsch V¹, Dreö B², Thiel J², Stradner M², Hermann J², Madeo F³, Eisenberg T³, Fessler J¹

¹Department of Immunology and Pathophysiology, Medical University of Graz, ²Division of Rheumatology and Immunology, Medical University of Graz, ³Institute of Molecular Biosciences (IMB), University of Graz

Abstract:

Background: Dysregulation of the Th17/Treg axis is recognized as a central pathogenetic mechanism in axial spondyloarthritis (axSpA). Emerging evidence identifies the polyamine pathway as an important modulator of this immunological balance, with dietary supplementation of the polyamine spermidine demonstrating anti-inflammatory properties in various murine models.

Objective: This open-label pilot study aimed to investigate the effects of dietary spermidine supplementation on immune cell functionality in patients with active axSpA.

Methods: Twenty axSpA patients with active disease (BASDAI ≥ 4) received daily supplementation of 6 mg spermidine as a nutritional adjunct to conventional baseline therapy over a three-month period. Clinical examinations, standard laboratory assessments, and immunophenotypic characterizations were performed at baseline and following three months of intervention. Intracellular reactive oxygen species (ROS; CellROX staining) and autophagic flux (CytoID staining) in T-cell subsets were quantified via flow cytometry. A wheat germ extract-based preparation (CelVio Complex®) served as the spermidine source.

Results: Data analysis revealed a significant reduction in the disease activity score BASDAI following spermidine supplementation, whereas BASFI, CRP, and ESR remained unchanged. Immunophenotypic analysis demonstrated neither major changes in immune cell composition nor circulating cytokine concentrations. Notably, a substantial reduction in cellular oxidative stress was observed across CD4⁺ and CD8⁺ T-cell subsets. A significant enhancement of autophagic flux was detected in all analyzed T-cell populations. The induction of autophagy correlated positively with the reduction of cellular stress markers.

Conclusion: These data suggest that dietary spermidine enhances autophagy in T-cells, contributing to amelioration of oxidative cellular stress and potentially promoting disease amelioration in chronic inflammatory conditions. These findings support further controlled investigations into the therapeutic relevance of polyamine supplementation in axSpA.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 89

Abstract Title: Spatial transcriptomics of fixed drug eruption skin lesions reveals an IFN γ -driven keratinocyte-macrophage-T-cell circuit

Authors:

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Abstract:

Fixed drug eruption (FDE) is a cutaneous adverse drug reaction characterized by well-demarcated lesions that reappear at the exact same sites after re-exposure to the culprit drug. Here, we used the Xenium in situ assay on FFPE samples of two recurring FDE skin lesions and healthy control skin to characterize immune cell subsets and spatial patterns of gene expression in FDE.

We found that FDE lesions show compositional remodeling dominated by infiltrating T cell subsets, macrophages and activated fibroblasts. Specifically, CD8⁺ effector T cells, a large pool of conventional T cells and MHC II⁺ macrophages are enriched in FDE, most prominently in the papillary dermis. In the epidermis, CD8⁺ resident memory T cells (TRM) are highly enriched in FDE compared to healthy skin. Spatial profiling showed cytotoxic effector molecules such as granzymes, perforin, and IFN- γ expressed by epidermal TRMs and dermal CD8⁺ effector T cells. Comparing FDE and healthy skin, differentiated keratinocytes had the largest transcriptional shift, marked by an IFN- γ -response signature and upregulation of the chemokines CXCL9 and CXCL11. Activated fibroblasts also upregulated CXCL9. In addition, keratinocytes expressed TRM maintenance cues like IL 15, TGF β and CXCL16, supporting TRM persistence within the epidermis.

Our results suggest that in recurring FDE, CD8⁺ TRM execute keratinocyte killing via granzymes and IFN- γ , whereas dermal effector T cells amplify inflammation. Keratinocytes and MHC-II macrophages sense T cell-derived IFN γ , and upregulate antigen presentation machinery, acting as APCs for T cells. Keratinocytes and fibroblasts produce chemokines to recruit T cells and keratinocytes sustain the TRMs and maintain site-specificity. These novel spatial insights identify a keratinocyte-macrophage-T cell circuit with an IFN- γ -driven chemokine axis in FDE.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 90

Abstract Title: Decoding the pathogenic shift: pathogenic CD4+ T cell development in rheumatoid arthritis

Authors:

Hermann L¹, Preglej T¹, Tosevska A¹, Luckerbauer B¹, Mrak A¹, Acosta M¹, Göschl L¹, Niederreiter B¹, Shvets T¹, Aletaha D¹, Bonelli M¹

¹Medical University of Vienna, Department of Internal Medicine III, Division of Rheumatology

Abstract:

Background

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by persistent joint inflammation and progressive bone destruction. CD4+ T cells are key players in RA, promoting synovial inflammation. Despite their relevance in RA pathology, effective therapies targeting CD4+ T cells are limited, highlighting the need to identify novel T cell-based targets. We established an OVA-induced arthritis (OIA) mouse model which allows to track the development of pathogenic T cells in RA.

Using this model, we aim to characterize the transcriptional landscape of CD4+ cells with bulk and single-cell RNA sequencing, identify therapeutically relevant target genes through a pooled CRISPR knockout screen, and validate selected target genes via single-gene knockouts.

Methods

Naïve CD4+ T cells from wild-type OTII transgenic mice are transferred into RAG1- deficient recipients. Arthritis is induced by intra-articular injection of cationized OVA. Six days post induction, CD4+ T cells from spleen and knee are analyzed by flow cytometry and histological scoring of knees is performed. Single-cell and bulk RNA sequencing are used to characterize transcriptional landscapes of pathogenic CD4+ T cells.

Results

Flow cytometry analysis of the knee from OIA-induced mice showed influx of TNF- α and IFN- γ producing CD4+ T cells. Histological scoring revealed severe inflammation and joint erosion, closely resembling human RA. Differential expression analysis of CD4+ T cells from knee vs. spleen showed a distinct transcriptional profile of knee-infiltrating cells, associated with pathways linked to inflammation and autoimmunity. The knee-enriched genes include both classical RA-associated genes alongside novel genes warranting further investigation.

Outlook

These knee-enriched genes, form the basis of a target gene list for a CRISPR knockout screen. Retroviral transduction of CD4+ T cells will be employed to perform a pooled CRISPR knockout screen in the OIA model to select disease-driving target genes. Top hits will subsequently be validated via single-gene knockouts.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 91

Abstract Title: Prophylactic Extracorporeal Photopheresis Reprograms Peripheral Immunity After Lung Transplantation and Associates with Long-Term Graft Function

Authors:

Parsonidis P¹, Weijler A¹, Cho A^{1,2}, Muckenhuber M¹, Toifl S¹, Kainz V¹, Streissenberger N¹, Malzl D⁵, Derdak S³, Benazzo A⁴, Jaksch P⁴, Wekerle T¹

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²Department of Dermatology, Medical University of Vienna, ³Core Facilities, Medical University of Vienna, ⁴Department of Thoracic Surgery, Medical University of Vienna, ⁵CeMM Research Center for Molecular Medicine, Austrian Academy of Sciences

Abstract:

Background: Chronic lung allograft dysfunction (CLAD) remains the principal barrier to durable survival after lung transplantation. Extracorporeal photopheresis (ECP) is increasingly used as an adjunct preventive strategy, but its immune mechanisms are not fully defined.

Methods: Peripheral blood mononuclear cells from lung transplant recipients treated with prophylactic ECP plus standard immunosuppression alone (bulk RNA-seq: n=8; scRNA-seq: n=3). Samples were collected at transplantation baseline (T0) and three months post-transplantation (T3). We performed differential expression analysis, pathway enrichment (GSEA), transcription factor activity inference, cellular deconvolution, and single-cell sub-clustering, and related molecular features to longitudinal lung function (FEV1) over 36 months.

Results: Compared with controls, ECP-treated recipients showed a more focused bulk transcriptional shift from T0 to T3 (136 vs 439 differentially expressed genes). Enriched programs included oxidative phosphorylation and TNF α signaling via NF- κ B, with increased activity of myeloid-associated regulators (SPI1/PU.1, CEBPB, NFE2L2/Nrf2). Among inferred regulators, NFE2L2 activity showed the strongest association with FEV1 preservation at 36 months (Spearman ρ Rho=0.73). Single-cell profiling at T3 demonstrated expansion of classical monocytes and naïve B cells in the ECP group. ECP-associated monocyte signatures included CD83, NFKBIA, TNFAIP3, IER3, and ZFP36; pathway analyses supported increased TNF α /NF- κ B and IL-1 response programs with reciprocal reduction of type I IFN signaling. Sub-clustering identified two expanded classical monocyte states under ECP (immediate-early response and antigen-processing) and a distinct expanded naïve B-cell compartment.

Conclusions: Integrated bulk and single-cell analyses indicate that prophylactic ECP induces coordinated immune reprogramming after lung-transplantation, characterized by myeloid activation, NF- κ B/oxidative stress engagement, attenuation of type I IFN programs, and naïve B/cell expansion. Correlation of molecular features with better long-term lung function, provides potential mechanistic support for the clinical benefit of ECP.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 92

Abstract Title: Molecular control of regulatory T cells by nuclear factor interleukin-3 regulated

Authors:

Luckerbauer B¹, Tosevska A¹, Preglej T¹, Heinz L¹, Acosta M¹, Brinkmann M¹, Hermann L¹, Dellinger M¹, Emilius L¹, Lange J¹, Niederreiter B¹, Högl S², Ellmeier W³, Müller L¹, Aletaha D¹, Bonelli M¹

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Abstract:

Background: Regulatory T (Treg) cells maintain self-tolerance by suppressing immune responses. Loss of Treg function causes severe autoimmune diseases. Treg functional specification is regulated by T cell receptor signaling, cytokines and transcription factors (TFs). Beyond master regulator forkhead box 3 (Foxp3), Tregs must acquire additional TFs to adapt to inflammatory environments and tissues. The TF nuclear-factor interleukin 3 regulated (NFIL3) has been described as part of the Treg signature, although its contribution remains unclear. This study aims to define the role of NFIL3 for Treg regulation and function.

Methods: A double reporter mouse strain, in which expression of Foxp3 and NFIL3 can be determined via red fluorescence protein and green fluorescence protein, respectively, was used to isolate Foxp3⁺NFIL3^{high} and Foxp3⁺NFIL3^{low} Tregs. Bulk RNA-sequencing was performed to characterize transcriptional differences. Binding of NFIL3 to Treg signature genes was investigated by CUT&RUN sequencing. The functional capacity of NFIL3-expressing Tregs was assessed in in vitro suppression assays. A conditional knock-out (NFIL3^{fl/fl} Foxp3^{YFPcre}) model was used to investigate the role of NFIL3 in vivo under steady-state conditions and adoptive CD4⁺ T cell transfer colitis.

Results: Transcriptional analysis of NFIL3-expressing Tregs revealed an increased expression of Treg genes associated with high suppressive capacity such as IL10 with NFIL3 directly binding to the IL10 locus. In line with this, NFIL3-expressing Tregs showed superior suppressive capacity in vitro compared to NFIL3^{low} Tregs. Treg-specific deletion of NFIL3 resulted in intestinal inflammation under steady-state conditions. NFIL3-deficient Tregs also failed to adequately protect mice from weight loss and intestinal inflammation following CD4⁺ T cell transfer, indicating impaired Treg-mediated disease control.

Conclusion: Our findings identify NFIL3 as positive regulator of Treg suppressive function and demonstrate that its loss compromising Treg-mediated control of intestinal inflammation. NFIL3 may therefore represent a potential target for improving Treg function in cell-based therapies for autoimmune diseases.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 93

Abstract Title: Preserved suppressive function despite loss of Foxp3: insights into the identity of regulatory T cells

Authors:

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¹Medical University Vienna

Abstract:

Regulatory T (Treg) cells are essential for maintaining immune homeostasis. Classically, Treg identity is defined by the expression of forkhead box P3 (Foxp3). While continuous Foxp3 expression has been considered critical for Treg identity and function, the extent to which regulatory programs persists following Foxp3 loss remains incompletely understood. This study investigates the transcriptional and epigenetic consequences of Foxp3 loss in Treg cells during Th2-driven inflammation.

Loss of Foxp3 expression was induced in vitro-induced Tregs (iTregs) upon stimulation with IL-4. The transcriptional and functional properties of these ex-iTregs were compared to Foxp3-expressing iTregs and conventional Th2 cells using flow cytometry, RNA-sequencing, in vitro suppression assays and an in vivo model of adoptive CD4⁺ T cell transfer colitis. Epigenetic changes were assessed by ChIP-seq profiling of histone modifications. In vivo, Foxp3 fate-mapping was performed in an ovalbumin (OVA)-induced model of allergic lung inflammation. Foxp3⁺ and ex-Foxp3⁺ cells were isolated from inflamed lungs and analyzed by flow cytometry, bulk and single-cell RNA-sequencing.

Th2-associated inflammatory signals induced loss of Foxp3 expression in Treg cells both in vitro and in vivo. Despite Foxp3 loss, ex-iTregs retained substantial features of the canonical Treg transcriptional program and remained distinct from conventional Th2 cells. Importantly, ex-iTreg cells retained their suppressive capacity in vitro and in vivo. Upon OVA-induced lung inflammation, ex-Foxp3⁺ cells maintained the expression of characteristic Treg markers, including CTLA-4 and GITR. ChIP-sequencing revealed preservation of H3K27ac-associated regulatory regions at Treg-associated loci following Foxp3 loss, indicating persistence of active regulatory chromatin landscapes.

Our findings demonstrate that loss of active Foxp3 expression does not result in immediate loss of Treg identity or suppressive function. Persistence of regulatory transcriptional and epigenetic programs following Foxp3 loss provides insight into mechanisms underlying Treg lineage stability and has important implications for the identification and therapeutic application of Tregs.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 94

Abstract Title: Intramuscular Influenza Vaccination Enhances Salivary Virus Neutralization and Limits Airway Epithelial Damage

Authors:

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Abstract:

Background: Inactivated influenza vaccines primarily elicit systemic IgG responses, with comparatively weak induction of mucosal IgA. Whether intramuscular immunization improves virus neutralization at the upper airway and protects the epithelium remains incompletely defined.

Methods: We prospectively followed 51 adults, quantifying influenza A- and B-specific IgG and IgA, hemagglutination-inhibition (HAI) titers, and half-maximal neutralization titers (NT50) in serum and saliva collected before vaccination and one and three months afterward, against vaccine strains and tested clinical isolates. Donor-matched saliva and serum with low or high NT50 were then applied to the apical and basolateral compartments, respectively, of H1N1-infected primary human airway epithelial air-liquid-interface cultures.

Results: Serum IgG, IgA, HAI, and NT50 all rose significantly after vaccination and remained elevated at three months, whereas salivary IgA showed no significant increase and influenza-specific salivary IgG was detected in only a minority of participants. Salivary NT50 nonetheless increased against vaccine strains and tested clinical isolates. Among participants with measurable salivary IgA, titers correlated with H1N1 and influenza B neutralization but not H3N2, suggesting an antigen-dependent contribution of pre-existing salivary IgA. In airway cultures, high-NT50 serum and saliva partially preserved barrier integrity, reduced basolateral viral RNA roughly 40-fold, and limited infection to fewer, more superficial foci, although apical viral RNA remained comparably detectable across conditions.

Conclusion: Intramuscular influenza vaccination robustly strengthens systemic immunity and, despite only modest changes in salivary IgA, also enhances functional virus-neutralizing activity in saliva, indicating that mucosal protection is not fully captured by binding-antibody levels alone. Donor samples with high neutralizing titers restrict viral spread within airway epithelium and help preserve tissue barrier integrity, pointing to a functional link between systemic vaccine-induced immunity and protection at the respiratory mucosal surface.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 95

Abstract Title: NEK2 as a regulator of human T cell activation and proliferation

Authors:

Hutter S¹, Frey T¹, Lampl A¹, Schmidt R¹, Schmetterer K¹

¹Department of Laboratory Medicine, Medical University of Vienna

Abstract:

Clonal expansion is a hallmark of T cell activation and requires tight regulation of the cell cycle. While members of the NIMA-related kinase (NEK) family are well-established regulators of cell cycle progression, their functions in T cells remain largely unexplored. Here, we investigated the role of NEK2 in the activation and proliferation of primary human T cells.

We primarily used pharmacological inhibition of NEK2 in primary human T cells and assessed its effects on proliferation and activation-associated phenotypes after activation using anti-CD3/anti-CD28 coated microbeads. Additionally, NEK2 inhibition was investigated in a spleen organoid model of allogeneic stimulation. To complement pharmacological inhibition, NEK2 expression was modulated by overexpression and knockdown approaches.

Pharmacological inhibition of NEK2 markedly suppressed T cell proliferation. This proliferative defect could not be rescued by additional stimulation with IL-2, suggesting that NEK2 regulates processes that cannot be bypassed by enhanced cytokine signaling. Beyond its effect on proliferation, NEK2 inhibition altered the expression of activation-associated markers, including CD25 and LAG-3, indicating a broader role for NEK2 in shaping the T cell activation phenotype. In a spleen organoid model, NEK2 inhibition attenuated the response to allogeneic stimulation and was associated with reduced plasmablast formation and antibody production against the stimulant, indicating an immunomodulatory role of NEK2. NEK2 overexpression enhanced T cell proliferation, whereas NEK2 knockdown showed reduced proliferation, further supporting a functional role of NEK2 in T cell expansion.

Together, our findings identify NEK2 as a regulator of human T cell activation and proliferation, extending its function beyond its established role in cell cycle control. These results highlight NEK2 as a potential molecular target for modulating T cell responses and provide a basis for further investigation of its role in T cell differentiation and immune regulation.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 96

Abstract Title: Treg-effector imbalance at the scarring hair follicle

Authors:

Strobl K¹, Bauer T¹

¹Medical University Of Vienna

Abstract:

Regulatory T cells (Tregs) maintain immune balance in the skin and are preferentially located at hair follicles. Paradoxically, Tregs are increased in scarring alopecia (SA), yet their presence fails to prevent the severe inflammatory state and permanent hair loss.

We previously showed that disruption of the epidermal growth factor receptor (EGFR) in the hair follicle compromises follicular immune privilege, with interferon gamma-expressing natural killer and CD8⁺ T cells driving the chronic cascade that leads to scarring hair loss.

In this study, we follow the Treg compartment across disease progression. In EGFR^{DEgr2} mice, immunofluorescence staining showed increased Treg numbers compared with wild-type littermates from 1 month of age, whereas significant accumulation of CD4⁺ and CD8⁺ effector T cells occurred only at postnatal day 60 and 90, respectively, coinciding with the onset of visible hair loss. Tregs are thus recruited early but outpaced by effector cells when the follicle is destroyed.

In patients, immunofluorescence staining of biopsies from frontal fibrosing alopecia (FFA), lichen planopilaris and folliculitis decalvans (n > 6 per group, 18 patients), quantified for CD4⁺FOXP3⁺ Tregs and CD4⁺ and CD8⁺ effector T cells in the follicular area, revealed heterogeneous infiltration patterns without significant differences in overall T cell density. The CD8⁺ effector T cell to Treg ratio, however, was markedly higher in FFA, arguing for a subtype-specific failure to suppress cytotoxic responses rather than a general lack of Tregs.

Tregs are therefore present at the site and time of immune privilege breakdown, in mouse and in human disease, without preventing it. Whether they are quantitatively insufficient, intrinsically impaired or functionally overridden by effector activity remains open. Treg boosting and Treg depletion experiments in the model are ongoing and will be presented. Beyond SA, this addresses a general problem in chronic inflammatory skin disease, where Treg numbers alone do not predict control of inflammation.

Abstract Number: 97

Abstract Title: Synovial Cytokines Orchestrate Bi-directional FLS–Monocyte Crosstalk Driving Inflammatory Activation in Rheumatoid Arthritis

Authors:

Dellinger M¹, **Emilius L**¹, Sacnun J¹, Kugler M¹, Kartnig F¹, Simader E¹, Brinkmann M¹, Luckerbauer B¹, Preglej T¹, Acosta M¹, Pontarini E², Fossati-Jimack L², Rivellese F², Pitzalis C^{2,3}, Steiner G¹, Heinz L¹, Aletaha D¹, Tosevska A¹, Karonitsch T¹, Bonelli M¹

¹Medical University Of Vienna, ²Queen Mary University and The London School of Medicine and Dentistry, ³Humanitas University & IRCCS Humanitas Research Hospital

Abstract:

Background: Rheumatoid arthritis (RA) is an inflammatory disease, which is driven by fibroblast-like synoviocytes (FLS) and activated immune cells (ICs). Based on the degree of immune cell infiltration RA can be classified into pathotypes, in part reflecting treatment response. To understand molecular mechanisms underlying pathotype development, we aimed to investigate cytokine-mediated priming of FLS-IC interactions.

Methods: RA synovial tissues were stained for FLS and ICs using immunofluorescence. Interactions and activation/transcriptomic changes were analysed by autologous co-cultures of cytokine-stimulated human FLS and ICs facilitating high-content microscopy, spectral cytometry and RNA-seq. Integration with bulk and scRNA-seq data from synovial biopsies further characterised FLS-IC interaction.

Results: Immunofluorescence of RA synovial tissues identified distinct niches where IC subsets localised to FLS-rich sub-synovial regions, suggesting robust FLS-immune cell interactions in the inflamed synovium. Co-culture experiments with FLS and autologous PBMCs revealed cell type- and cytokine-specific interaction patterns, highlighting the role of the inflammatory milieu in shaping FLS-IC interactions. Cytokine-priming of FLS modulated the activation of IC subsets, with IFN γ potentiating and TGF β repressing interactions. RNA-seq analysis of FLS co-cultured monocytes revealed significant transcriptomic changes, with IFN γ -primed FLS inducing a pro-inflammatory M1-like monocyte phenotype. Compared to synovial biopsy-derived inflammatory monocytes, we found a specific enrichment in the M6 cluster of the AMP-RA2 dataset, i.e. elevated CXCL10 and STAT1 expression. Notably, the found signature was predominantly observed in RA patients with lympho-myeloid pathotype, indicating that interactions with IFN γ -stimulated FLS contribute to the emergence of pro-inflammatory monocytes and drive the development of this highly inflammatory pathotype. Furthermore, CellChat analysis revealed several adhesion molecules likely driving monocyte activation by IFN γ -primed FLS.

Conclusion: This research underscores the critical role of FLS in orchestrating monocyte activation during synovitis. It also highlights the significant impact of the synovial cytokine environment, particularly IFN γ , on FLS-IC interactions driving synovial pathotype progression.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 98

Abstract Title: Glucocorticoid receptor GILZ signaling in B cells modulates myocardial infarction-accelerated atherosclerosis

Authors:

Zupcic A¹, Smeets D¹, Dereli G¹, Juhasz V¹, Weber L¹, Pilz P¹, Anto Michel N², Horstmann H², Zenker M¹, Ondracek A¹, Wolf D³, Zirikli A², Kiss A¹, Binder C¹, Lang I¹, Tsiantoulas D¹

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Abstract:

Myocardial infarction (MI) accelerates atherosclerosis in non-culprit vessels, thereby increasing the risk of recurrent cardiovascular disease (CVD).

To elucidate the molecular mechanisms underlying MI-accelerated atherosclerosis, we performed single-cell RNA sequencing of splenic CD45⁺ cells from atherosclerotic Ldlr^{-/-} mice subjected to MI or sham surgery. We discovered a significant downregulation of the Glucocorticoid-Induced Leucine Zipper (GILZ) gene expression in mature B cells following MI. Given that GILZ is robustly induced by glucocorticoid signalling, we next investigated the effect of exogenous glucocorticoid administration using low-dose short-term dexamethasone treatment. Our data demonstrate that low-dose dexamethasone administration prevents the expansion of B cells and abrogates the acceleration of atherosclerosis upon MI.

Furthermore, preliminary studies showed that atherogenic Ldlr^{-/-} mice that harbour tamoxifen-inducible B cell-specific deletion of GILZ displayed marked acceleration of atherosclerosis after MI.

As GILZ is transcriptionally regulated by the glucocorticoid receptor (GR), we next investigated the contribution of B cell-intrinsic GR signalling to MI-accelerated atherosclerosis. Similar to GILZ deficiency, inducible B cell-specific GR deficiency aggravated atherosclerosis following MI, suggesting a protective role of the GR-GILZ signalling axis. Future studies will address the requirement of GILZ-GR signalling for the protective effect of dexamethasone in MI-accelerated atherosclerosis.

Collectively, our findings identify B-cell-intrinsic GILZ-GR signalling axis as a potential regulator of post-MI acceleration of atherosclerosis, revealing a previously unrecognized therapeutic avenue for secondary prevention of CVD.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 99

Abstract Title: Identifying novel epigenetic regulators of CD8+ T cell exhaustion in cancer using in vivo CRISPR screens

Authors:

Bozic H¹, Miyakoda E¹, Orbegozo R¹, Zhang J¹, Schäfer M², Zuber J², Sakaguchi S¹

¹Division of Immunology, Institute of Immunology, Center for Pathophysiology, Infectiology and Immunology, Medical University Of Vienna, ²Research Institute of molecular pathology (IMP), Vienna BioCenter (VBC)

Abstract:

Cancer immunotherapies aim to restore the function of exhausted CD8+ T cells and thereby enhance anti-tumor immunity. However, only a subset of exhausted T cells responds effectively to treatment. This limited responsiveness has been linked to epigenetic mechanisms that restrict T cell plasticity and maintain dysfunctional cell states. Identifying epigenetic regulators that can overcome these constraints may provide new opportunities to enhance therapeutic responses in cancer patients.

Based on this, we aim to identify novel epigenetic regulators controlling the subset differentiation of exhausted T cells. To this end, we will employ an in vivo CRISPR screening approach, which involves the adoptive transfer of genetically engineered tumour-specific CD8+ T cells into tumour-bearing mice. Based on the results of the screen, candidate genes will be studied in depth by generating single-gene knockout T cells in murine tumour models. Moreover, we will elucidate the transcriptional and epigenetic mechanisms by which candidate genes control T cell exhaustion by performing single-cell RNA sequencing and ATAC sequencing. The insights provided by this study will improve our understanding of molecular mechanisms underlying CD8+ T cell exhaustion and thereby present a strong foundation for the development of future cancer treatments.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 100

Abstract Title: Lymph-Directed Nutrition Alleviates Canine Atopic Dermatitis and Restores Iron-Immune Homeostasis

Authors:

Frizzo-Ramos C^{1,2}, Doulidis P², Burgener I², Horvath-Ungerböck C², Einspieler V², Weiser U², Panakova L², **Roth-Walter F¹**

¹Centre for Animal Nutrition and Welfare, University of Veterinary Medicine Vienna, ²Department for Companion Animals and Horses, Clinical Unit of Small Animals Internal Medicine, Dermatology, University of Veterinary Medicine Vienna,

Abstract:

Background:

Canine atopic dermatitis (CAD) is frequently associated with iron depletion and low-grade inflammation despite meat-based diets, suggesting impaired nutrient absorption or utilization. We evaluated whether a complementary food formulated for lymphatic nutrient delivery could improve CAD and associated hematological and immune parameters.

Methods:

In this 112-day, double-blind, randomized, placebo-controlled study, 38 dogs with CAD received 10 g/day of either an active food containing whey protein, vitamins, minerals, and antioxidants (n=19) or a hydrolyzed-food placebo (n=19), alongside standard care. Owners recorded weekly Pruritus Visual Analog Scale (PVAS) scores and medication use. Veterinarians assessed lesions monthly using CADESI-4. Blood parameters were measured at baseline and day 112. Treatment success required a ≥ 2 -point PVAS decrease and $\geq 50\%$ CADESI-4 reduction.

Results:

Compared with placebo, the active food significantly improved CADESI-4 (-55% versus $+26\%$; $p < 0.0003$) and PVAS (-1.8 versus -0.05 ; $p = 0.0074$) and reduced medication use. Treatment success was approximately threefold more frequent in the active group. Red blood cell counts, packed cell volume, and serum iron increased only with active supplementation, while ferritin was lower in placebo-treated dogs at study completion. Active supplementation was also associated with a higher abundance of naïve CD14⁺ monocytes. These findings suggest that improved iron availability and preservation of a less differentiated circulating monocyte compartment may accompany clinical improvement.

Conclusion:

Lymph-directed nutrient supplementation improved CAD severity, pruritus, medication requirements, iron status, and the circulating monocyte profile. The results support a link between micronutrient insufficiency, innate immune alterations, and CAD, warranting further mechanistic investigation.

Annual Conference 2026

Vienna, November 4-6, 2026



Abstract Number: 101

Abstract Title: Chitinase-Like Proteins as Critical Amplifiers of Fibroblast-ILC2 crosstalk driving type 2 immunity

Authors:

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Abstract:

In the lung, adventitial cuffs represent a critical site for the induction and maintenance of type 2 immune responses. In these fibroblast-rich regions, adventitial fibroblasts (AFs) provide essential survival and activation cues, including IL-33, that regulate the magnitude and persistence of lung-resident ILC2 responses. While the AF-ILC2 axis is well defined, its integration with bronchial epithelial cells (BECs) is unclear. Positioned adjacent to adventitial cuffs, BECs may shape local immunity through IL-13-responsive secretion of inflammatory mediators. Chitinase-like proteins (CLPs) are components of such type 2-activated epithelial programs associated with tissue repair and remodelling, with the capacity to reprogram lung niche communication. Using recombinant protein technology and newly generated CLP-deficient mice, we show that CLPs, including Ym2, are both necessary and sufficient to potentiate type 2 alarmin activity. Ym2 synergized with AF-derived IL-33 and ILC2-derived IL-13 in vitro and in vivo to enhance ILC2 expansion and cytokine production while inducing a proinflammatory and profibrotic program in fibroblasts. Through structure guided interaction modelling, competitive binding assays and in vivo blocking experiments, we identified RAGE as a functional receptor for murine Ym2. Importantly, the human ortholog YKL-40 mirrored these effects, amplifying IL-33- and IL-13-driven cytokine production in primary human ILC2s and fibroblasts. Together, these findings reposition CLPs as active amplifiers of type 2 inflammation, particularly in the context of tissue alarmins, and define a conserved epithelial-fibroblast-ILC2 signalling axis that controls the magnitude and persistence of type 2 airway responses.

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Vienna, November 4-6, 2026



Abstract Number: 102

Abstract Title: Bidirectional Relationship Between Iron Homeostasis and Macrophage Metabolic Plasticity During Inflammation

Authors:

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Abstract:

Background: Metabolic flexibility (MF) describes the ability of cells to dynamically adapt substrate utilization and energy production according to nutrient availability and bioenergetic demand (DOI: 10.1210/er.2017-00211). MF is particularly important for immune cells, supporting transitions between quiescence, activation, effector function, and resolution. Impaired MF may contribute to maladaptive metabolic states, oxidative stress, impaired immune surveillance, and chronic inflammation (DOI: 10.1038/s41392-024-01954-6). Macrophages are key regulators of inflammatory responses and can transition between distinct functional states, thereby contributing to either tissue pathology or repair. Inflammatory activation is associated with increased expression of CD71 (transferrin receptor 1), which mediates cellular iron uptake. Iron is an essential regulator of cellular metabolism and a critical cofactor for mitochondrial respiration, tricarboxylic acid cycle enzymes, and redox homeostasis. Our previous work demonstrated that both iron overload and iron deficiency impair mitochondrial function and increase reactive oxygen species (ROS) production (DOI: 10.1039/c7mt00177k; DOI: 10.1002/mds.27482). However, the role of iron availability in macrophage metabolic plasticity, and viceversa, remains poorly understood. Methods: We investigated the bidirectional relationship between iron availability and macrophage metabolic remodeling in human-derived and primary murine macrophages. Cells were polarized in vitro and exposed to different iron conditions. SCENITH was used to assess cell metabolic plasticity, Seahorse and Oxygraph-2k analyses were performed to characterized mitochondrial respiration, while live-cell fluorescence microscopy was used to monitor iron availability, mitochondrial morphology and function, and cellular responses to inflammatory and iron perturbations. Results: Preliminary data reveal that iron availability significantly influences macrophage metabolism, including mitochondrial dynamics. Conversely, macrophage polarization determines cellular iron handling, suggesting that iron metabolism and macrophage metabolic state are interconnected and potentially mutually regulatory. Conclusion: These findings identify iron as an important regulator of macrophage metabolic plasticity and highlight iron-dependent metabolic pathways as potential targets for modulating inflammatory and tumor-associated immune responses.

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Abstract Number: 103

Abstract Title: Modulation of human early B cell development by iberdomide-mediated degradation of Ikaros and Aiolos

Authors:

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Abstract:

Background

Immature B cells develop in the bone marrow (BM) from hematopoietic stem cells (HSCs). Ikaros and Aiolos, zinc-finger transcription factors, regulate the development by activating or repressing gene expression. In humans, mutations in IKZF1 (Ikaros) or IKZF3 (Aiolos), are associated with impaired B differentiation while high Ikaros/Aiolos expression are associated with systemic lupus erythematosus (SLE) and multiple myeloma (MM). Treatment with iberdomide to enhance degradation of Ikaros and Aiolos are used in MM patients and under consideration in SLE. Our objective is to investigate the effect of iberdomide on human early B cell development simulated in vitro.

Methods

In vitro cultures in presence/absence of iberdomide over 7 weeks based on cord blood (CB)-derived HSCs. Spectral cytometry (27-color panel) and scRNA-sequencing allowing the discrimination of all early B cell subpopulations and measurement of transcription factors essential for B lymphopoiesis.

Results

Iberdomide treatment enhanced the degradation of Ikaros/Aiolos in CB-derived culture. Addition of iberdomide impaired lymphoid specification indicated by increased frequency and total numbers of CD34+ progenitors, and decreased frequency of CD10+CD38+ lymphoid progenitors. Also, iberdomide delayed the commitment to the B cell lineage shown by decreased pre B and immature cell differentiation. The differentiation was altered in favor of dendritic cell differentiation. Targeting already committed B cell progenitors (by treating the culture with iberdomide from day 28 on), enhanced the proliferation and increased the total counts of CD10+CD38+ lymphoid-committed cells. It had no effect on the quantity of developing immature B cells, however, promoted receptor editing and potentially altered central tolerance.

Conclusion

Iberdomide impairs the specification to the lymphoid lineage and commitment to the B cell lineage by enhancing Ikaros' degradation. In committed early B cells, reduction of Ikaros and Aiolos protein levels by 50% allows the development of immature B cells however affects the quality of developing cells.

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Abstract Number: 104

Abstract Title: Early immunophenotypic changes preceding Sjögren's disease: longitudinal flow cytometry from the PreSStige cohort.

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Abstract:

Due to longstanding subclinical disease at diagnosis, immunological changes in the pathogenesis of early Sjögren's Disease (SjD) are not well elucidated. Detection of autoantibodies in SjD patients more than 15 years before diagnosis, alongside reports of dryness before measurable thresholds are reached, indicate that there is a detectable pathogenic pathway to SjD.

Here, we aim to uncover lymphocytic subset changes before diagnosis in order to understand what drives early stages of SjD. We utilise the PreSStige cohort which comprises of those at risk of SjD (SSA autoantibody positive) following patients annually until their diagnosis.

We analysed samples from PreSStige patients who have developed SjD (n=9, mean age 50 yrs, 8 female, 1 male) at time points including one year before (D-1) and at diagnosis (D), showing the time course leading to SjD. Flow cytometry of whole blood and PBMCs was utilised to assess changes in B and T cell populations which were compared to both healthy donors (SSA +/-) (C) and those with established SjD.

We found significant changes in both B and T cell compartments detectable before diagnosis, specifically, an increase in atypical CD21 low B cells (C = 1.82 ± 0.303 , D-1 = 3.84 ± 0.541 p=0.009*), and an increase in CD4+ T effector memory cells (C = 9.19 ± 1.54 , D-1 = 16.3 ± 1.44 p=0.004*). We also observed a trend in the depletion of the naïve T cell compartment, regardless of patient age (C = 10.3 ± 2.38 , D-1 = 4.92 ± 1.32 p=0.099*).

This preliminary data identified changes measurable at least one year before diagnosis in lymphocytic subsets known to be implemented established SjD. This study holds the possibility for the discovery for a sequence of events within the same patient uncovering potential mechanisms initiating disease.

*Median $\pm$ SEM, one way ANOVA followed by T-test.