World Immune RegulationMeeting XIX

12 - 15 March 2025 | Davos, Switzerland



Final Program and Abstracts

SIAF

WIR

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Welcome to the

19th World Immune Regulation Meeting

Great to have you here!

WIR

#WIRM



Welcome Message from the Chairman & Co-Chairs

Dear WIRM Friends and Colleagues,

A full scientific program: On behalf of the Swiss Institute of Allergy and Asthma Research (SIAF), University of Zurich, it is a great pleasure to welcome you to the World Immune Regulation Meeting XIX on „Immune Activation, Effector Functions and Immune Tolerance with a special focus on Allergy and Autoimmunity". As it is becoming a tradition, the contribution of the participants to the development of the program by sending us their suggestions, has been essential to achieve our goal. This year we have 48 plenary talks. 72 abstracts will be presented in 12 workshops and 65 abstracts in 10 poster sessions. As every year, workshop presentations will be additionally displayed in the poster sessions to facilitate further discussions.

Meet the experts:
The traditional "Meet the Expert Session" enables open discussions with world's top scientific figures on scientific achievements and career development. Our expert to meet the participants this year is Prof. Hans Clevers. He is Professor in Molecular Genetics from the University of Utrecht in the Netherlands and the Head of Pharma Research and Early Development (pRED) at Roche since 2022. The format is designed to facilitate informal discussions, allowing participants to present their questions and gain new insights. Another tradition of WIRMs, the "Special Lecture" of this year will be given by Prof. Dr. Jacob de Boer, one of the pioneers of environmental hazards of microplastic and research, from the Vrije University Amsterdam in the Netherlands. He will talk about "The size and Extension of the Plastic Pollution: Human Health vs Environment".

Special thanks to the sponsors: If you have ever organized such meetings, you know very well that it is impossible to organize a successful meeting without the help of sponsors. Our sponsors are listed on page 5 of this program book. Please visit their booths from the first day on and use the opportunity to discuss new developments with the experts of the company sponsors during the long working hours of WIRM from 08:30 until 23:00. In addition, we would like to thank our main sponsor journals, Nature Immunology, Nature Reviews Immunology, Science Translational Medicine, Allergy and Swiss Young Immunologists Society for contributing to the program and providing best presentation awards. Wel also thank BioLegend for the generous support for the workshop prizes and the gala dinner. We are proud to give 25 travel grants this year. Thanks very much for the generous support of the European Federation of Immunological Societies and Swiss Society for Allergology and Immunology for the travel grants.

Social events and activities: As at other WIRMs, we will come together for dip & discuss poster sessions with dinner and drinks providing a relaxing and stimulatory atmosphere for scientific exchange for young researchers to meet senior scientists. Lunch breaks will allow to digest attended symposia, while enjoying winter sports and landscape. The Gala Dinner will be on Saturday, on the 15 March 2025, in the Main Hall together with the band „The BPM". Previous Gala Dinner participants know very well that we will have hours of dance with great professional musicians.

Davos is a winter sports paradise for snowboard and skiing enthusiasts from all over the world. The region provides 57 mountain transport facilities and around 300 km of well-prepared slopes. In addition, cross country skiing, ice sports, wonderful hiking routes through the beautiful countryside are all possibilities offered to you in Davos. For the participants, who are not skiing, we particularly suggest the hiking route „Hohe Promenade" or a tour around the Davos lake. The east side of the walking path in the forest is amazing and full of squirrels. They will wake up with a little bit of sunshine and say hello to you. In addition, you can visit the Kirchner Museum, Medicine Museum, Wintersports Museum and Local History Museum. Being inspired by the Davos Spirit is an essential motto of WIRM, which is "work very hard together with harmony, openly discuss with transparency, come together socially and scientifically to improve the state of the World in your area. We would like to inform you that the inspiration of Davos has been confirmed about a century ago when Sir Arthur Conan Doyle wrote some Sherlock Holmes stories, Robert Louis Stevenson wrote „Treasure Island", Thomas Mann wrote „Magic Mountain" and later Erich von Däniken wrote „Chariots of the Gods" in Davos. Albert Einstein was a fan of Davos and has organized several meeting in our city. Davos is hosting of many worldwide front research institutions in their area, the AO Research Institute, Institute for Snow and Avalanche Research, Christine Kühne Center for Allergy Research and Education, Global Risk Forum, Physical Meteorological Observatory and our SIAF that have contributed several thousands of articles, several hundreds of inventions, several hundreds of PhD titles and habilitations, and more than 100'000 citations.

Teamwork, success and continuation: The organizing committee promises to present you a great scientific program, a surprising social program and a warm smile. We would like to acknowledge the enormous enthusiasm of SIAF group leaders Mübeccel Akdis, Christoph Messner, Katja Baerenfaller, and Claudio Rhyner, congress organizer Anja Schultz, abstract manager Laura Bürgi, SIAF head of administration Regina Maier, WIRM IT managers Claudio Rhyner and Patrick Westermann, WIRM technology manager Costel Agache, all of the other SIAF co-workers and "Davos Congress", who have worked during the past year to ensure that our meeting has an exceptional impact on all who attend.

With best wishes for WIRM XIX and many future WIRMs.

Cezmi A. Akdis
Chair WIRM

Milena Sokolowska
Co-Chair WIRM

Willem van de Veen
Co-Chair WIRM

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Air Davos, Davos Congress, Eau-là-là, Kirchner Museum, Lufthansa Group, OMPharma, Paarsenn Sports, Swiss Society for Allergology and Immunology (SSAI), Swiss Young Immunologists Societiy (SYIS), Weber Bäckerei-Konditorei, Zeiss

Best Presentation Award
Nature Reviews Immunology, Nature Immunology, Science Translational Medicine, Allergy, Swiss Young Immunologists Societiy (SYIS)

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SYIS Swiss Young Immunologists Society

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ZEISS

SSAI Société Suisse d'Allergologie et d'Immunologie

Weber Bäckerei - Konditorei Restaurant-Café-Bar DAVOS

Poster Prize Sponsors & Media Partners

Allergy European Journal of Allergy and Clinical Immunology | EAACI

nature reviews immunology

nature immunology

SYIS Swiss Young Immunologists Society

Science Translational Medicine AAAS

Meeting Information

Admission to Sessions
Admission to the sessions is reserved for meeting registrants and registered members of the press only. Guests and non-registered exhibitors will not be admitted to any scientific session.

Award Ceremonies
Thursday, 13 March 2025	17:15 *(Room: Davos 1)*
Friday, 14 March 2025	17:00 *(Room: Davos 1)*
Saturday, 15 March 2025	12:00 *(Room: Davos 1)*
Saturday, 15 March 2025	15:00 *(Workshop rooms)*

Best Workshop Presentation Award
BioLegend Best Presentation Awards will be distributed to the best presenter of each of the 12 workshops to be selected by the chair persons.

Children and Guests
We kindly ask delegates to refrain from taking children, spouses or guests to any educational session. Registered accompanying persons are welcome to visit the booth area and poster sessions. Children under the age of 18 are not allowed.

Social Events
The combination of idyllic alpine landscape, urban atmosphere and the wide range of service, infrastructure, fine food and activities is unique. Please visit us at the registration desk to get interesting information about possible activities in Davos.

Jobcenter www.wirm.ch
You will have ideal opportunities to apply for open positions or to find highly motivated fellows. The entire service is free of charge. If you would like to advertise your job offer, please submit your advertisement as PDF file to wirminfo@wirm.ch.
If you are looking for an open position, browse our job offers at www.wirm.ch/jobcenter.html.
If you would like to reserve a room for an interview, please ask our staff at the registration desk.

Lost and Found
Should you have lost something, please contact the registration desk.

Meeting Room Policy
No video and audio equipment, cameras or any other type of recording device will be allowed during all scientific sessions.



No Smoking
Smoking is prohibited in the entire Congress Center and during all sessions and events.

Poster Presenter Information
Poster presenters are asked to mount their posters until 10:00 on the presenting day and to remove the posters until 23:00 the same evening. Adhesive stripes will be available at the registration desk. A poster overview, including poster presenter, poster number, session and room can be found on the last pages of this book.

Poster Walk Information
In order to increase scientific discussions, a poster walk will take place at the beginning of each poster session.
Selected chair persons and poster presenters will meet in front of the first poster of their session at 20:00. Each poster should be explained within two minutes by the poster presenter, followed by one minute discussion.
There won't be a poster walk for the workshop posters.

Best Presentation Awards
Best Presentation Awards (for Posters) will be sponsored by Nature reviews immunology, Nature immunology, Swiss Young Immunologists Society, Science Translational Medicine and Allergy. The prizes will be one year free subscription to one of the journals and the SYIS CHF 150.-.
The winners will be selected by the chair persons according to the scientific quality and announced during the award ceremonies.
Thanks to the sponsors:

Registration Desk

If you have questions concerning WIRM, our registration team will be happy to help you at the registration desk:

Opening hours:

Tuesday, 11 March 2025	15:00 - 20:00
Wednesday, 12 March 2025	07:30 - 19:00
Thursday, 13 March 2025	08:00 - 19:00
Friday, 14 March 2025	08:00 - 19:00
Saturday, 15 March 2025	08:00 - 16:00

Speaker's Ready Room

The speaker's ready room (*Room: Dischma*) serves for the speakers to check their presentations and make final changes.

Speaker's Presentation Upload

All speakers are kindly asked to bring their presentation on a memory stick to the "Presentation Upload Desk" until 19:00h the evening before their talk or at the latest 30 minutes before their talk.
Opening hours: daily 08:00 – 19:00

Travel Grants

10 travel grants of CHF 300.- are sponsored by WIRM.

10 travel grants of EUR 500.- are sponsored by the European Federation of Immunological Societies (EFIS) and the European Journal of Immunology (EJI).

5 travel grants of CHF 500.- are sponsored by the Swiss Society of Allergology and Immunology (SSAI)

Société Suisse d'Allergologie et d'Immunologie
Schweizerische Gesellschaft für Allergologie und Immunologie
Swiss Society for Allergology and Immunology

WIRM Gala Dinner

Dinner & Dance Gala Night with the band "thebpm".

Saturday, 15 March 2025
19:30 at the Plenary Hall "*Davos 1*" of the Davos Congress Center.
After the last talk of the scientific program on Saturday, 15 March 2025, the plenary hall will change into a ballroom for our Dinner & Dance Gala Night. A delicious menu will be served followed by live music. Another great opportunity to meet the experts, colleagues and to have fun.

Feel free to register for this entertaining evening at the registration desk until Friday, 14 March 2025, 12:00 noon.

This evening is sponsored by BioLegend.

WLAN

Free WLAN will be provided in the premises of the Congress Center.

Network: Davos Congress

Help the climate

Each time we take a flight, drive a car or heat our homes, CO2 is added into the atmosphere. Take the opportunity to reduce CO2, visit www.climatecare.org or websites of similar organizations. Reduce your personal CO2 emission and pay your CO2 offsets.

What to do in Davos

Premium Card



One card, many benefits

Anyone who spends at least one night in a commercially rented establishment such as a hotel, holiday apartment or group accommodation in Davos Klosters will receive the new Davos Klosters Premium Card. This guest card offers numerous advantages and discounts during your stay.

Outdoor Activities

Ski & Snowboard

Are you a peak performer? Then the days on the magical mountains of Davos Klosters will be over all too soon for you. Because you can choose between 2 snow sports resorts here: The Jakobshorn and the Parsenn/Gotschna resort.

Snow Sports Schools

Regardless of whether you are a beginner or an advanced skier, snowboarder or cross-country skier, the numerous snow sports training centres in Davos Klosters offer the best trained instructors, who will ensure that you are safe, successful and having fun in snow.

Cross-Country Skiing

Every year, the world's elite cross-country skiers gather at the starting line to compete in the prestigious Davos Nordic. The renowned FIS racing tracks in Flüelatal, where top athletes like Dario Cologna have battled for World Cup points, offer an exceptional challenge. Beyond the competition, enthusiasts can explore the scenic tributary valleys and carve their own path through breathtaking winter landscapes. For those who can't get enough, the night cross-country ski run provides an unforgettable experience. Best of all—cross-country skiing in Davos is completely free! free!

Ice Sports

Davos Klosters is an ice sports Eldorado – for active participants and spectators alike. This is guaranteed by Europe's largest natural ice rink in Davos, as well as further ice rinks across the entire region, which can be used for ice skating, speed skating, playing ice hockey, curling and Bavarian curling.
In addition to this, with the Vaillant Arena Davos also boasts one of the most stunning ice hockey stadia anywhere, with the Hockey Club Davos (HCD) one of the most popular ice hockey clubs in Switzerland, and with the Spengler Cup the most richly traditional ice hockey tournament in the world.

Winter Walks

Do you like to stand with both feet on firm ground? Then we recommend to you our winter footpaths in Davos (111km). You can take an easy stroll or a pacey walk along these snow-cleared footpaths through the snowy landscape.

Playing ice mini golf by Lake Davos

Grab a hockey stick and puck and step onto the ice—not for a game of hockey, but for a round of ice mini-golf! This unique family-friendly sport offers a fun and exciting challenge. Try it for yourself on the 18-hole ice mini-golf course and enjoy an introduction from an expert.
Location: Arkadenplatz, Davos Platzwinter.

Transportation

Rhaetian Railway

Unlimited travel in 2nd class on the line Klosters Dorf – Davos – Filisur with cour guest card

Local bus Davos

Unlimited travel on the local bus lines (except buses to all side valleys (Dischma, Sertig, Clavadel, Monstein, Wiesen)

Reduced Ski Rental

Paarsenn Sports, which is located right next to the Parsenn Cable Car Station in Davos Dorf an at the train station Davos Platz, offer to all WIRM participants, speakers, exhibitor staff and registered accompanying persons a reduction for the renting and storage of wintersports equipment.

Paragliding

Fulfil the human dream of flying: As a passenger of a tandem pilot, you will safely float amidst the mountains of Davos Klosters.

Indoor Activities - Sport

Tennis, Squash, Badminton, Climbing

The Färbi sports hall in Davos offers:

- 4 indoor tennis courts (Reboundace surface)
- 5 outdoor tennis courts (sand courts)
- 2 squash courts
- 2 badminton courts
- Climbing wall
- Sports restaurant
- Tennis school (individual lessons, group courses and competition training dipl. trainer STV)
- Bar & club room with television room
- Sports shop & relaxation service
- Changing facilities & showers

Davos Fitness

The modern fitness center in the heart of Davos. It offers endurance training, strength training, group fitness and medical massages. Check it out: davosfitness.ch.

Wellness and Water Park Eau-Là-Là

Thanks to the "eau-là-là" fun pool, the Davos indoor swimming pool is a year-round oasis for big and small water sports-lovers, pleasure-seekers and the health conscious alike.

Indoor Activities - Entertainment

BierVision Monstein
In 2001, in Monstein, the highest brewery in Switzerland and the first demonstration brewery in the Canton Grisons, went into production. It is housed in the former village dairy, a building that was erected 100 years ago. BierVision Monstein AG uses crystal clear spring water, Swiss hops and aromatic malt to brew Monstein beer specialities in accordance with a richly traditional recipe. Monstein is a picturesque hamlet located 1625 metres above sea level. The typical Walser houses and stilts lend the village with its two churches and two guest houses an unforgettable charm.
Every Friday from 16-19 unguided tours and cosy get-togethers with the brewer, ideally suited for individual guests.

Adventure Room - do you manage to get out?
(Promenade 106, 7270 Davos Platz)
Fascinating real life game in Davos! Imprisoned in mysterious rooms! Will you be able to escape, before the countdown runs out? Experience a unique adventure! The group of players will be locked up: the adventure room is completely their own, uncovering hiding places and secrete doors and find the meaning behind mysterious objects, devices, to get the clues to escape, before the countdown runs out!

Indoor Activities – Art & Culture

Kirchner Museum
(Ernst Ludwig Kirchner Platz, 7270 Davos Platz, Tue–Sun 11-18, CHF 15.- instead of CHF 20.- with reduction voucher)
Ernst Ludwig Kirchner, a leading figure of German Expressionism, lived in Davos from 1918 until his passing. His groundbreaking work played a pivotal role in shaping the movement. Established in 1992, the Kirchner Museum Davos houses the world's most extensive collection of his masterpieces, offering a profound insight into his artistic legacy.
Current exhibition:
Rediscovered and reunited: Kirchners frames and paintings.
Guided tours: Sunday & Tuesday, at 16:00, in German, Audio guides in E, F, I and G, CHF 5.- plus entry fee per person.





Museum of local history
(Museumstrasse 1, 7260 Davos Dorf, Sun-Wed 15-17, CHF 10.-, 20% reduction with Premium Card)
The museum of local history in Davos endeavours to convey a living image of history, early everyday life, traditions and crafts from Davos. The rich collection of objects and documents is presented in the large Jenatschhaus. As an old patrician house and historic building, it also tells many stories itself.

Wintersport Museum
(Promenade 43, 7270 Davos Platz, Tue&Thu 16:30-18:30, free admission, donations are welcome)
The museum is perfectly suited for exhibiting the rich collection of valuable winter sports equipment and documents from the foundation of the family of Jürg Kaufmann, Davos due to its central location. In the winter sports museum, visitors can view impressive exhibits (sledges, bob sleighs, skis, skates, curling equipment, etc.) from the beginning of winter sports right through to the present day.

Museum of medicine
(Promenade 43, 7270 Davos Platz, Tue&Thu 17-19h, free admission)
The foundation for the documentation of medical scientific development in Davos has set itself the objective of collecting and recording devices, x-ray images and files that document the activities of the physicians and researchers in Davos. The collection at the museum of medicine in Davos is an expansion and addition to the documentation library. It is accessible to all persons interested in historical, social, scientific and medicinal information for study purposes.

Where to eat & drink in Davos

These are just a few recommended restaurants/bars, which are located in a walking distance from the Congress Centre.

Gastronomy

Café Weber
(opposite of Parsenn valley station at Promenade 148 daily from 6:00-20:00)
Bakery, snacks, lunch menus, dinner, coffee and cakes.

Restaurant Stau
(15 minutes walk from Congress Center at Promenade 45, daily 9:30-22:00)
Authentic kitchen, lunch menus, fresh patisserie, baguettes.

da Elio
(opposite of Congress Centre at Promenade 95, daily 10-14:00 & 17:00-22:00)
Good tasting italian food, Pizza, seasonal specialities.

Extrablatt
(right next to Congress Centre at Promenade 90, Tue-Sat 11:30–14:00, 18:00-22:00)
Fresh-market experience rotisserie, house-made pasta and light daily menus.

Kaffeeklatsch
(15 minutes walk from Congress Centre at Promenade 38, daily 07:30-19:00)
A definite must for coffeelovers. Homemade hot and cold food specialties created from fresh regional products.

Lokal
(5 minutes walk from Congress Centre at Promenade 100, Wed-Sun 12:00-23:00)
Local and homemade dishes and drinks, vegetarian and vegan options.

Pulsa Restaurant @ Hotel Grischa
(20 minutes walk from Congress Centre, opposite of train station Davos Platz, daily lunch 11:30-14:00h and dinner 18-22:00h)
A relaxed bistro. The concept is simple and the atmosphere easy and cozy. Modern, creative, seasonal and an uncomplicated personal service. Sushi specialities are served from Fri-Tue.

Sessions @ Hard Rock Hotel Davos
(10 minutes walk from Congress Centre at Tobelmuehlestrasse 2, daily 12:00-14:00 and 18:00-22:00) - Snacks, burgers, soups & salads, vegetarian & vegan food

Nightlife - Bars & Clubs

Chämi Bar
(5 minutes walk from Congress Centre at Promenade 83, Tue-Sun 18:00-late)
Wide range of drinks, small menu, special choice of whisky.

Ex Bar
(10 minutes walk from Congress Centre at Promenade 63, Mon-Sat from 17:00–late)
The (in)famous place to be in the heart of Davos. Try the chicken wings at 4 in the morning after a hard party night.

Ochsen 2 Bar
(10 minutes walk from Congress Centre at Talstrasse 12, Mon-Sat 17:00-open end)
How about a cold beer, a glass of wine or a fruity drink? Whether for an aperitif or a nightcap - stop by.

Parsenn Gada
(15 minutes walk from Congress Centre at Promenade 154, opposite of the Parsenn valley station, Wed- Sun 15:00-22:00)
The bar directly opposite of the Parsenn cable car station. Warm food, snacks and drinks.

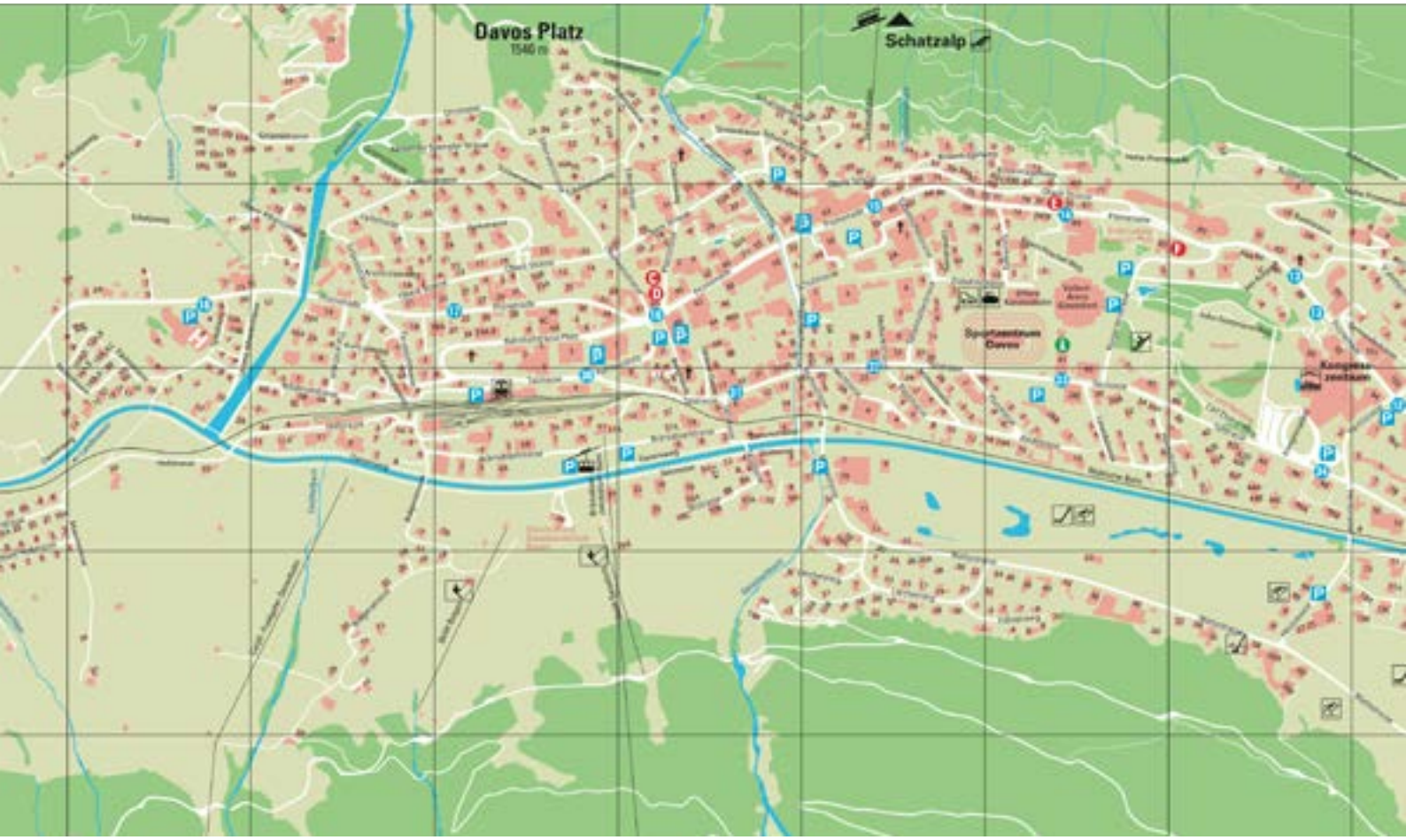
Piano Bar Tonic @ Hotel Europe
(10 minutes walk from Congress Centre, in the Hotel Europe at Promenade 63, Tue-Sat from 21:00-3:00)
Timeless and elegant. Daily Piano live music.

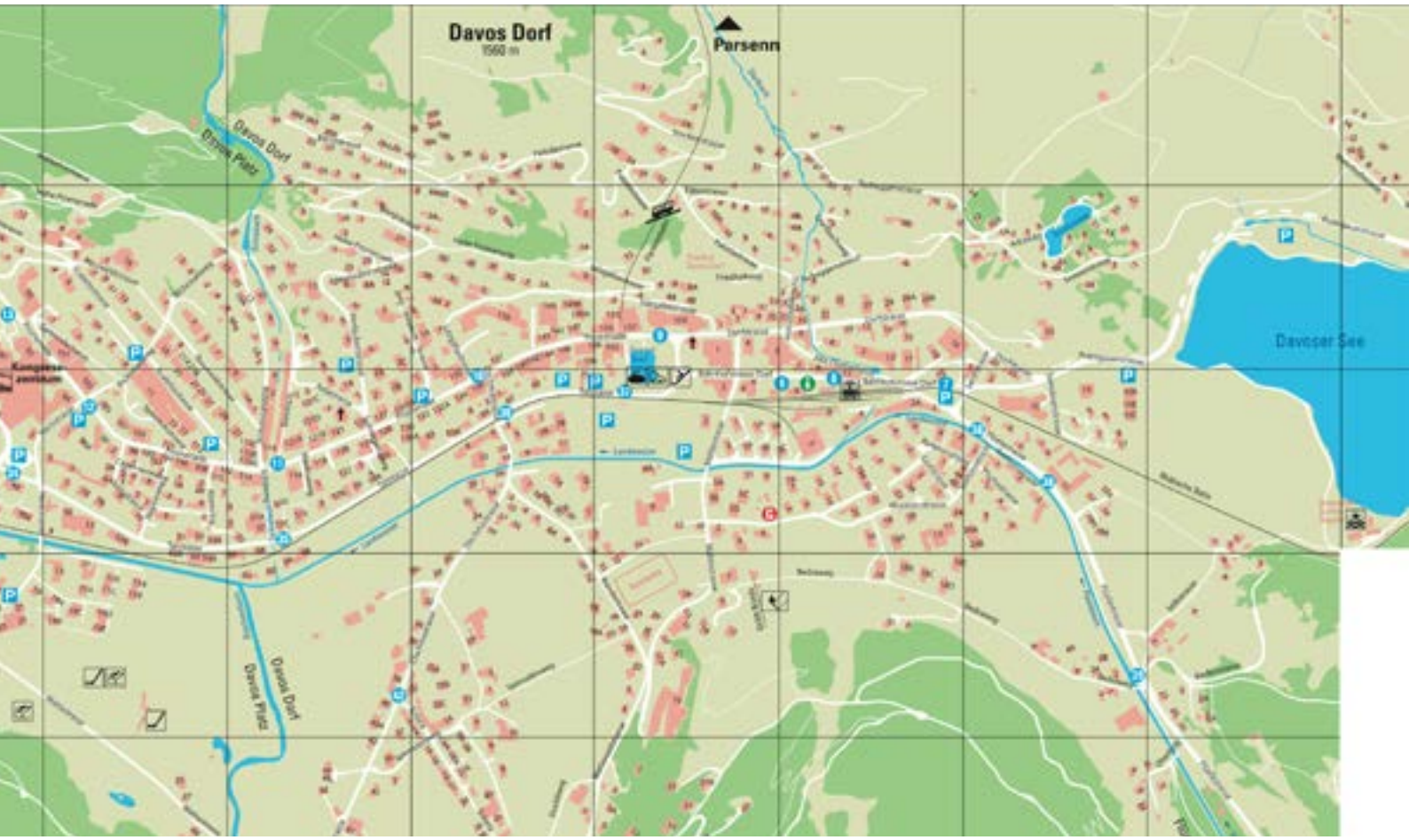
Pulsa Bar & Lounge @ Hotel Grischa
(20 minutes walk from Congress Centre, opposite of train station Davos Platz, daily 15:00-22:00)
Cozy lounge with fireplace. Modern bar for a coffee in the morning or to enjoy the evening.



Map

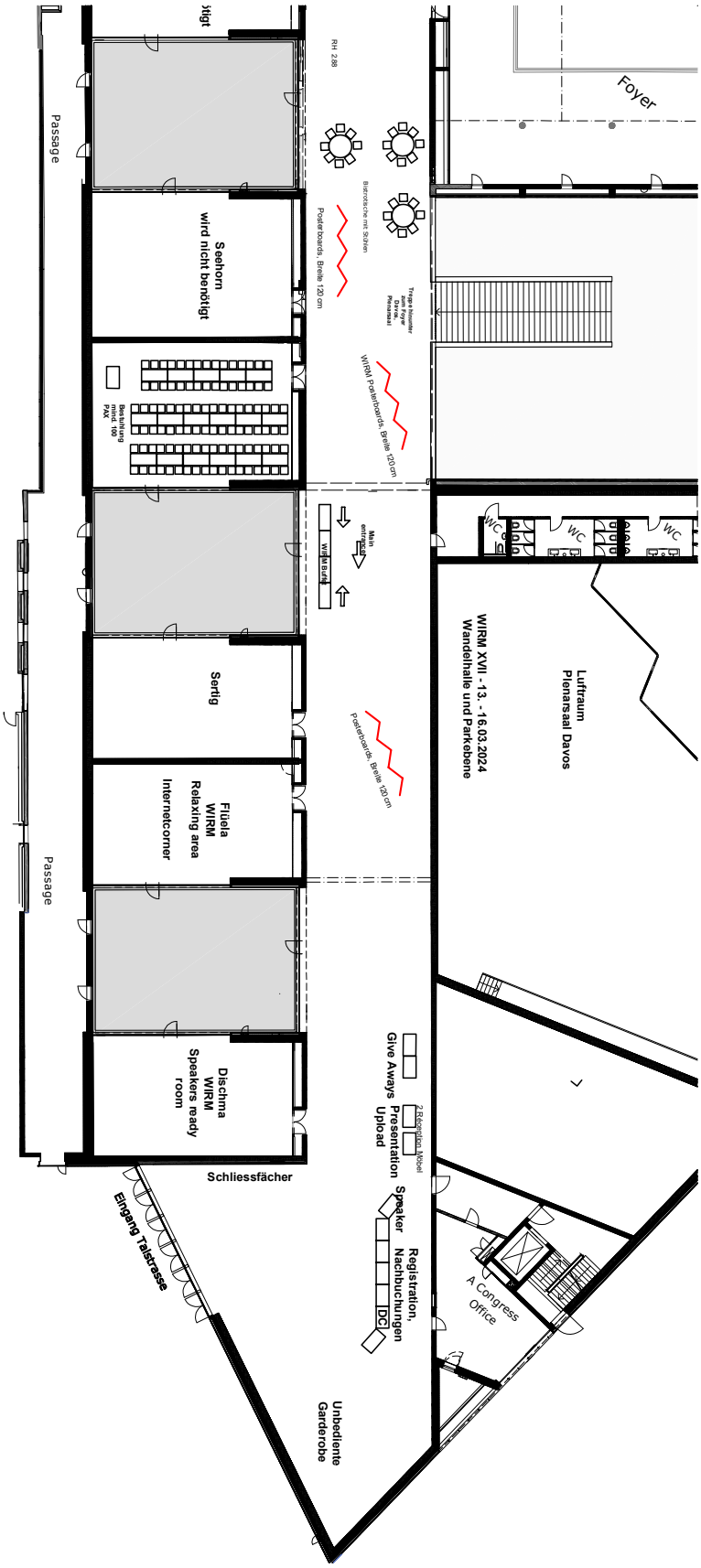
Davos Platz & Davos Dorf





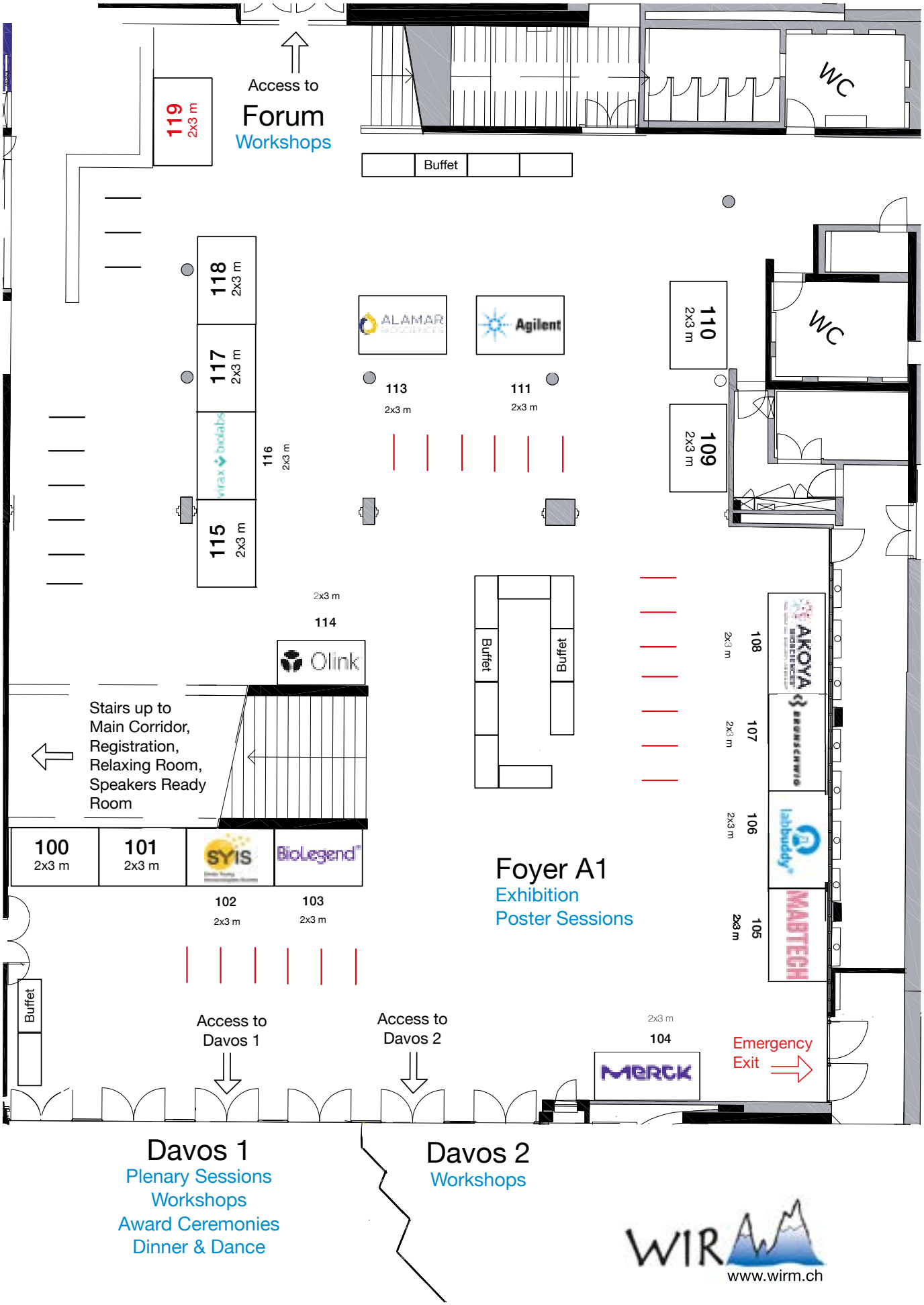
Map

Level: Main Corridor



Map

Level: Foyer A1



www.wirm.ch

Main Program 1. Day - Wednesday, 12 March 2025 - Room: Davos 1

Session 1		**Immune Homeostasis and Novel Cell Therapies**
		Chairs: Cezmi A. Akdis, Onur Boyman
08:30 - 09:00	S01	**Alexandre Harari** Tumour-infiltrating lymphocyte (TIL)-adoptive cell therapy
09:00 - 09:30	S02	**Isabelle Arnold** Eosinophils in homeostasis and disease
09:30 - 09:45	S03	**Irina Iten** The transcriptional regulator IkappaBzeta controls the effector functions of group 2 innate lymphoid cells
09:45 - 10:00	S04	**Richard Iten** Next-Generation CAR-T mediated B cell depletion therapy for sustained remission in severe refractory SLE and other autoimmune diseases
10:00 - 10:30		*Coffee break and time to visit the booths of our exhibitors*
Session 2		**Neuroimmune Regulation**
		Chairs: Mübeccel Akdis, Steve Pascolo
10:30 - 11:00	S05	**Nicolas Gaudenzio** Neuroimmunology of the skin
11:00 - 11:30	S06	**Daniela Latorre** Acute and prolonged impact of epidermal CD8+ memory T cells
11:30 - 11:45	S07	**Charlotte Menne Bonefeld** Rejuvenation of the germinal center reaction and affinity maturation following depletion of T follicular helper cells
11:45 - 12:00	S08	**Maria Escribese** Differential Immune metabolism linked to mAB treatment in allergic asthma
12:00 - 15:30		*Lunch break*
15:30 - 16:30		**Workshops 1 - 3** *(please see workshop program)*
16:30 - 17:00		*Coffee break and time to visit the booths of our exhibitors*
17:00 - 17:15		**Cezmi A. Akdis** Opening Address
Session 3		**Epithelial Barriers, Microbiome and Immune System Interactions**
		Chairs: Ismail Ogulur, Liam O`Mahony
17:15 - 17:45	S09	**Tomasz Wypych** Harnessing bile acids to ameliorate lung inflammation
17:45 - 18:15	S10	**Benjamin Marsland** Defining the factors driving mucosal healing
18:15 - 18:30	S11	**Duygu Yazici** Common food emulsifiers impair epithelial barrier integrity and trigger pro-inflammatory responses
18:30 - 18:45	S12	**Daniel Regan-Komito** Delineating molecular and microbial signatures across disease severity in Inflammatory Bowel Disease in adult treatment naive patients through single-cell transcriptomic and microbiome profiling
18:45 - 19:00		**Statthalterin und Landrätin Davos - Valérie Favre Accola** Welcome Address by the City Major of Davos
19:00 - 22:00		*Dip & Discuss Dinner Buffet*
20:00		**Poster Sessions 1 - 3**, Room: Foyer A1 *(please see poster program)* **Poster presentations of workshops 1 - 3**, Room: Main Corridor

Main Program 2. Day - Thursday, 13 March 2025 - Room: Davos 1

Session 4		**Novel Aspects of Innate and Adaptive Immune Responses**
		Chairs: Christoph Messner, Maria Jose Torres
08:30 - 09:00	S13	**Florent Ginhoux** Heterogenity of Resident Tissue Macrophages
09:00 - 09:30	S14	**Christoph Hess** Increasing CAR T cell persistence instructed by basic immuno-metabolic principles
09:30 - 09:45	S15	**Femke Broere** Harnessing Tolerogenic Dendritic Cells for Antigen-Specific Immune Modulation in Rheumatoid Arthritis: Findings from the TOLERANT Trial
09:45 - 10:00	S16	**Alexander Eggel** High-affinity omalizumab variants with optimized disruptive efficacy rapidly desensitize allergic effector cells in vivo
10:00 - 10:30		*Coffee break and time to visit the booths of our exhibitors*
Session 5		**Immunomodulation of Chronic Inflammation**
		Chairs: Christoph Hess, Ibon Eguiluz
10:30 - 11:00	S17	**Mohamed Shamji** Biomarker and adaptive trial driven approaches: Innovation in allergen immunotherapy
11:00 - 11:30	S18	**Jamie Orengo** Novel strategies for modulating type 2 immunity
11:30 - 11:45	S19	**Alba Angelina Querencias** Peanut allergoids conjugated to mannan as novel candidates for allergen-specific immunotherapy: unraveling their immunological mode of action
11:45 - 12:00	S20	**Liam O'Mahony** Impact of microbial metabolism on mucosal immune responses
12:00- 14:45		*Lunch break*
14:45 - 15:45		Workshops 4 - 6 *(please see workshop program)*
15:45 - 16:15		*Coffee break and time to visit the booths of our exhibitors*
16:15 - 17:15		Special Lecture **Jacob de Boer** The size and Extension of the Plastic Pollution: Human Health vs Environment
17:15 - 17:25		Award Ceremony for poster & workshop prizes of day 1
Session 6		**Immunometabolism**
		Chairs: Milena Sokolowska, Maria Escribese
17:30 - 18:00	S21	**Jeffrey Rathmell** Fever and immunometabolism of T cells
18:00 - 18:30	S22	**Dirk Brenner** cROSsing barriers: Metabolism meets T cell function
18:30 - 18:450	S23	**Urszula Radzikowska** Immunometabolism of Airway Epithelium in Asthma and Viral Infection
18:45 - 19:00	S24	**Marcela Hortova Kohoutkova** Sepsis-associated immunosuppression: long-term effects on pediatric innate immune cells and their immunometabolic status
18:45 - 22:00		*Dip & Discuss Dinner Buffet*
20:00		Poster Sessions 4 - 6, Room: Foyer A1 *(please see poster program)* **Poster presentations of workshops 4 - 6**, Room: Main Corridor

Main Program 3. Day - Friday, 14 March 2025 - Room: Davos 1

Session 7 — **Trained Immunity and Adaptive Immune Responses**

Chairs: Willem van de Veen, Hans Jürgen Hoffmann

08:30 - 09:00 S25 **Cezmi A. Akdis**
Epithelial Barrier Theory and Molecular Mechanisms of Tissue Injury in Allergic and Autoimmune Diseases

09:00 - 09:30 S26 **Julia Merkenschlager**
Optimising antibody affinity maturation; how to win big without losing it all

09:30 - 09:45 S27 **Oscar Palomares**
The regulation of immune response and inflammation by cannabinoids and their receptors

09:45 - 10:00 S28 **Simon Barry**
Using multi omics to discover drivers of seroconversion to Islet Autoimmunity using the ENDIA longitudinal Type 1 diabetes cohort

10:00 - 10:30 *Coffee break and time to visit the booths of our exhibitors*

Session 8 — **Regeneration and Tissue Responses**

Chairs: Matthias Zilbauer, Jiu-Yao Wang

10:30 - 11:00 S29 **Christoph Schneider**
Cytokine-mediated epithelium – immune cell crosstalk

11:00 - 11:30 S30 **Roger Geiger**
Decoding T Cell Cytotoxicity via Single-Cell CRISPR Screens in Droplets

11:30 - 11:45 S31 **Burkhard Ludewig**
Fibroblastic reticular cells generate protective intratumoral T cell environments in lung cancer

11:45 - 12:00 S32 **Nora Barrett**
Tuft Cells Shape Airway Remodeling By Eliciting OXGR1- and SOX9-Dependent Stem Cell Programs

12:15 - 13:30 Alamar Biosciences Lunch Symposium *(Room: Schwarzhorn, Lunch bags provided)*
Huseyn Babayev
Dynamic Changes in Plasma Biomarkers in Air Pollution Exposure and Immunotherapy Cohorts

13:30 - 14:30 *Lunch break*

14:30 - 15:30 Workshops 7 - 9 *(please see workshop program)*

15:30 - 16:00 *Coffee break and time to visit the booths of our exhibitors*

16:00 - 17:00 Meet the expert
Hans Clevers
Lessons learned: exploring the immune system and beyond

17:00 - 17:10 Award Ceremony for poster & workshop prizes of day 2

Session 9 — **Organoids in Inflammation and Tissue Barriers**

Chairs: Christoph Schneider, Jin-Ah Park

17:15 - 17:45 S33 **Matthias Zilbauer**
Intestinal organoids as translational tools in inflammatory bowel diseases

17:45 - 18:15 S34 **Hans Clevers**
Organoids to model human disease

18:15 - 18:30 S35 **Christian Schwartz**
Obesity impairs skin barrier function and facilitates allergic sensitisation

18:30 - 18:45 S36 **Silvio Brugger**
Commensal-pathogen interactions as a source for microbiota-targeted treatments

18:45 - 22:00 *Dip & Discuss Dinner Buffet*

20:00 Poster Sessions 7 - 10, Room: Foyer A1 *(please see poster program)*
Poster presentations of workshops 7 - 12, Room: Main Corridor

Main Program 4. Day - Saturday, 15 March 2025 - Room: Davos 1

Session 10		**Advanced Immune Profiling and Personalized Medicine**
		Chairs: Katja Bärenfaller, Paul Klenerman
08:30 - 09:00	S37	**Thomas Vogl** High-dimensional profiling of the antibody repertoire in gastrointestinal inflammatory diseases
09:00 - 09:30	S38	**Eran Segal** Personalized medicine based on deep human phenotyping
09:30 - 09:45	S39	**Pei-Chi Chen** Anti-Nucleocapsid Antibodies of SARS-Cov2 as Predictors of Post-Acute Sequelae of COVID-19 (PSAC) Severity in Pediatric Patients: Insights from the DISCOVER Cohort in Taiwan
09:45 - 10:00	S40	**Ismail Ogulur** Circulatory microinflammation and its association with serum antibody epitope repertoires by PhIP-sequencingt
10:00 - 10:30		*Coffee break and time to visit the booths of our exhibitors*
Session 11		**Autoimmunity and Autoinflammation**
		Chairs: Jürgen Schwarze, Richard Siegel
10:30 - 11:00	S41	**Luke O'Neill** A break in mitochondrial endosymbiosis as a basis for inflammatory diseases
11:00 - 11:30	S42	**Eicke Latz** Inflammatory responses to pyroptosis
11:30 - 11:45	S43	**Douglas Nixon** Single Nucleotide Variations in Human Endogenous Retroviral Sequences can affect peptide presentation by HLA-B27: Implications for Viral Mimicry and Ankylosing Spondylitis
11:45 - 12:00	S44	**Jens Geginat** Single-Cell RNA and TCR sequencing suggests a key role for tissue-infiltrating EOMES+Tr1-like cells and their circulating precursors in autoimmune diseases
12:00 - 12:10		Award Ceremony for poster & workshop prizes of day 3
12:15 - 14:00		*Lunch break*
14:00 - 15:00 subsequently		Workshops 10 - 12 *(please see workshop program)* Award Ceremony for workshop prizes of day 4 *(will be given directly in the workshop rooms by the chairpersons)*
15:00 - 15:30		*Coffee break and time to visit the booths of our exhibitors*
Session 12		**Allergic Diseases and Type II Immunity**
		Chairs: Claudio Rhyner, Luke O'Neill
15:30 - 16:00	S45	**Clare Lloyd** Stromal -immune interactions drive asthma pathology in children and adultsy
16:00 - 16:30	S46	**Milena Sokolowska** Metabolic Regulation of Human Th2 Cells in Health and Disease
16:30 - 16:45	S47	**James King** Airway Inflammation Drives Resting to Inflammatory Transition of Lung Eosinophils
16:45 - 17:00	S48	**Katja Baerenfaller** Targeted Proteomics Reveals the Action Site of Tralokinumab in Atopic Dermatitis: The Skin
17:00 - 17:10		**Milena Sokolowska & Willem van de Veen** Closing Address
19:30		**Dinner & Dance Gala Night** *(Ticket are available at the registration desk until Friday, 15 March 2024 at 12:00 lunch time)*

Workshop Program 1. Day - Wednesday, 12 March 2025

Workshop 1 — Muscosal tolerance and intestinal homeostasis

Room: Davos 1

Chairs: Benjamin Marsland, Tomasz Wypych

15:30 - 15:40 WS01 **Jan Fric**
Sepsis induced tissue specific dysregulation analysed through model of 3D iPSCs derived organoids

15:40 - 15:50 WS02 **Sena Ardicli**
Micro- and nanoplastics with diverse sizes and chemical structures compromise barrier integrity, cause extensive epithelial cell injury, and induce oxidative and endoplasmic reticulum stress

15:50 - 16:00 WS03 **Marit Zuurveld**
LPS presence promotes, but is not required for, an ovalbumin induced type 2 mucosal immune response in vitro

16:00 - 16:10 WS04 **Angelina De Martin**
IL-33-mediated fibroblast-myeloid cell crosstalk controls intestinal granuloma formation

16:10 - 16:20 WS05 **Can Zeyneloglu**
Food emulsifier polysorbate 80 causes gut barrier distruption and inflammation

16:20 - 16:30 WS06 **Severine Navarro**
Hookworms shape tolerogenic dendritic cell function via metabolic reprogramming

Workshop 2 — B cell subsets and immune regulation

Room: Davos 2

Chairs: Ganesh Phad, Alexander Eggel

15:30 - 15:40 WS07 **Eva Conde Garcia**
IL-33 expands plasma cells, disrupts germinal centers, and increases autoantibody production

15:40 - 15:50 WS08 **Juan Felipe Lopez**
The role of IgD in the development of natural and induced tolerance to allergens

15:50 - 165:00 WS09 **Josue Enriquez**
B cell and Antibody Response to Influenza Vaccination with Thermally Denatured Hemagglutinin

16:00 - 16:10 WS10 **Ozge Ardicli**
Impact of Surfactants in Oral Care Products on Epithelial Cell Activation and Barrier Dysfunction in Eosinophilic Esophagitis

16:10 - 16:20 WS11 **Paul Engeroff**
On the role of Interleukin-1 in regulating allergic B cell responses

16:20 - 16:30 WS12 **Ningxuan Cui**
PDL1-expressing macrophages infiltrate diffuse large B cell lymphoma and promote lymphoma growth in a MCY-driven experimental mode

Workshop 3 — T cells and innate lymphoid cells

Room: Forum

Chairs: Daniela Latorre, Mirjam Schenk

15:30 - 15:40 WS13 **Lisa-Marie Graf**
Impact of cDC2s on ILC2s and eosinophilia in allergic bronchopulmonary aspergillosis

15:40 - 15:50 WS14 **Juan Carlos López-Rodriguez**
Unraveling the Role of Mucosal-Associated Invariant T Cells (MAITs) in Type 2 Inflammation induced by alarmins

15:50 - 16:00 WS15 **Melanie Grusdat-Pozdeev**
Glutathione regulates natural killer cell immunity and mediates tumor control

16:00 - 16:10 WS16 **Jens Geginat**
The human bone marrow may offer and Il-15-dependent survival niche for EOMES(+) Tr1-like cells

16:10 - 16:20 WS17 **Fabian Guendel**
ILC3s are Required for Intestinal Adaptation to Fasting and Feeding

16:20 - 16:30 WS18 **Swetlana Urban**
Influence of serotonin-signaling on maturation and cytokine production of dendritic cells in comparison with BPE and influence on T cell priming

20:00 **Poster presentations of workshops 1 - 3,** Room: Main Corridor

Workshop Program 2. Day - Thursday, 13 March 2025

Workshop 4 **Immune response to tumors**

Room: Davos 1 *Chairs: Preben Boysen, Burkhard Ludewig*

14:45 - 14:55 WS19 **Klaus Seuwen**
Deletion of the proton-sensing receptor GPR4 reduces tumor progression in mouse models of colon cancer

14:55 - 15:05 WS20 **Yun-Tsan Chang**
MHC-I upregulation safeguards neoplastic T cells in the skin against NK cell-mediated eradication in mycosis fungoides

15:05 - 15:15 WS21 **Arnau Solé Casaramona**
Preclinical Potential of Gamma Delta T Cells with Novel Nanoparticles for Antigen-Directed Immunotherapy in Triple-Negative Breast Cancer

15:15 - 15:25 WS22 **Mirjam Schenk**
Agonistic GITR treatment enhances antitumor immune responses and suppresses tumor progression in pancreatic ductal adenocarcinoma

15:25 - 15:35 WS23 **Chrysa Papadopoulou**
Accessory lymph nodes support local control of tumor growth

15:35 - 15:45 WS24 **Simon Barry**
Path to the clinic: design, validation and manufacture of an Igr5-targeting CAR-T against colorectal cancer

Workshop 5 **Epithelial barrier and microbiome**

Room: Davos 2 *Chairs: Ganesh Namasivayam, Nicolas Gaudenzio*

14:45 - 14:55 WS25 **Burcu Tepekule Müller**
The ontogeny of immune tolerance: a model of early-life secretory IgA - gut microbiome interactions

14:55 - 15:05 WS26 **Magdalena Wolska**
Microbiota-derived metabolite improves lung inflammation by modulating metabolism of alveolar macrophages

15:05 - 15:15 WS27 **Paolo D'Avino**
The effects of IL-4, IL-13, and IL-22 in epithelial barrier dysfunction and skin Inflammation

15:15 - 15:25 WS28 **Anita Kral**
Aspergillus and Beta-glucan sensing by basal progenitor cells reprograms airway epithelial differentiation

15:15 - 15:25 WS29 **Yagiz Pat**
Anti-inflammatory functions of indole-3-propionic acid

15:35 - 15:45 WS30 **Pilar Rodríguez Viso**
Microbiota-derived bile acids attenuate lung inflammation: Evidence from mouse models and human-derived lung organoids

Workshop 6 **Immune metabolism**

Room: Forum *Chairs: Julia Merkenschlager, Dirk Brenner*

14:45 - 14:55 WS31 **Zoltán Griger**
Disease Activity-Dependent Siglec-1 Expression on Monocyte Subsets of Patients with Idiopathic Inflammatory Myopathies

14:55 - 15:05 WS32 **Nadine Cadosch**
Pericardial lymphoid clusters control cardiopathogenic T-cell activation and differentiation during autoimmune myocarditis

15:05 - 15:15 WS33 **Naomi Benne**
Autoantigen-Dexamethasone Conjugate-Loaded Liposomes Halt Arthritis Development in Mice

15:15 - 15:25 WS34 **Lenka Sukenikova**
Investigating autoreactive T cells in IgLON5-antibody associated encephalopathy

15:25 - 15:35 WS35 **Milad Ameri**
Cellular and Molecular Immunoprofiling of Lupus Panniculitis: Elucidating the Roles of Cytotoxic T Cells, B Cells, and Complement Activation

15:35 - 15:45 WS36 **Marie Tauber**
Chronic hand eczema revealed as a Type 2 Disease: Evidences from Clinical Trial and Molecular Profiling

17:15 - 17:25 **Award Ceremony for workshop prizes of workshops 1 - 3,** Room: Davos 1

20:00 **Poster presentations of workshops 4 - 6,** Room: Main Corridor

Workshop Program 3. Day - Friday, 14 March 2025

Workshop 7 — Novel diagnosis methods, treatments and drugs

Room: Davos 1 — *Chairs: Jan Fric, Jamie Orengo*

14:30 - 14:40 WS37 **Hans Jürgen Hoffmann**
Fast, pre-seasonal Intralymphatic Immunotherapy for grass pollen allergy reduces the symptom and medication score

14:40 - 14:50 WS38 **Ibon Eguiluz Gracia**
Investigation of the effect of the nasal allergen challenge on the volatile organic compounds in exhaled breath of patients with allergic phenotypes of rhinitis

14:50 - 15:00 WS39 **Basak Corak**
Establishing Genetically Modified Alveolar Macrophages as Versatile Cell Therapy Against Pulmonary Diseases

15:00 - 15:10 WS40 **Elisabeth De Leeuw**
Early life RSV infection as a preventable risk factor for asthma

15:10 - 15:20 WS41 **Jannes Gavel**
PAPER TCR transgenic CD4+ T cells reveal the requirement for papain's enzymatic activity in the induction of Th2 responses

15:20 - 15:30 WS42 **Margarida Viola**
Gut-derived microbial metabolite P-cresol sulfate modulates chemokine production in nasal and bronchial epithelial cells in vitro

Workshop 8 — Metabolism and immunity

Room: Davos 2 — *Chairs: Jeffrey Rathmell, Eicke Latz*

14:30 - 14:40 WS43 **María Isabel Delgado Dolset**
Comprehensive multi-omics analysis reveals the immunomodulatory role of platelet content in healthy subjects

14:40 - 14:50 WS44 **Inés Jardon Parages**
Innate Immune Memory and Metabolic Reprogramming in the Lower Airway Epithelium of Patients with Allergic Asthma

14:50 - 15:00 WS45 **Jackie Bader**
Obesity reprograms bone marrow derived macrophages to promote anti-tumor immunity

15:00 - 15:10 WS46 **Lin Cheng**
The molecular and metabolic mechanisms of TCR-independent activation of human CD8+ effector memory T cells

15:10 - 15:20 WS47 **Leticia Martin-Cruz**
Thymic stromal lymphopoietin (TSLP) imprints a metabolic and epigenetic reprogramming in human CD1c+ myeloid dendritic cells promoting Th2 polarization

15:20 - 15:30 WS48 **Christoph Wilhelm**
ACC1 regulates adipose type 2 innate lymphoid cell differentiation to maintain metabolic health

Workshop 9 — Innate immune response

Room: Forum — *Chairs: Antonios Kolios, Isabelle Arnold*

14:30 - 14:40 WS49 **Annika Eggestein**
Exposure of nasal epithelial cells with pollen aerosols and coronaviruses in a near-physiological in vitro model

14:40 - 14:50 WS50 **Jiu-Yao Wang**
Reprogramming lipid-laden foamy macrophages and exosomes production in lung inflammatory diseases

14:50 - 15:00 WS51 **Elena Barletta**
Effect of Physical Exercise on the Immune System: Proteomic Profiling Reveals Endotype Variations Associated with Activity Level and Intensity in Athletes

15:00 - 15:10 WS52 **Laura Fisch**
Lymphocyte-derived IFN-γ primes alveolar macrophages for ZBP1-mediated death during influenza infection

15:10 - 15:20 WS53 **Cassandra Harapas**
Alternative splicing of Nod-like receptor (NLR) isoforms

15:20 - 15:30 WS54 **Ahmad Luqman-Fatah**
A network of interferon-stimulated genes regulates human LINE-1 retrotransposition

17:00 - 17:10 **Award Ceremony for workshop prizes of workshops 4 - 6,** Room: Davos 1

20:00 **Poster presentations of workshops 7 - 12,** Room: Main Corridor

Workshop Program 4. Day - Saturday, 15 March 2025

Workshop 10 **Infections, pathogenesis and immune responses**

Room: Davos 1 *Chairs: Oscar Palomares, Pierre-Yves Mantel*

14:00 - 14:10 WS55 **David Funda**
Benefitial effects of gluten-free diet in the chonic model of MPTP-induced alpha-synucleinopathy (Parkinson´s disease) in C57Bl/6 mice

14:10 - 14:20 WS56 **Barbora Drabonova**
Gluten-free diet reduces severity of DSS-induced colitis in BALB/c mice

14:20 - 14:30 WS57 **Claudia Beerweiler**
Asthma-protective in vitro farm-dust stimulation modulates dendritic cell co-inhibition and co-stimulation in childhood asthmatics

14:30 - 14:40 WS58 **Hannah Devotta**
Revisiting the Hygiene Hypothesis – Impact of Siblings on Early Life Microbiome Composition and Metabolism

14:40 - 14:50 WS59 **Preben Boysen**
A rodent model to explore the impact of farm-like environmental conditions on gut barrier, immune regulation and disease outcomes

14:50 - 15:00 WS60 **Weronika Barcik**
The role of bacteria-derived histamina in allergy-associated airway diseases

Workshop 11 **Type II inflammation**

Room: Davos 2 *Chairs: Clare Lloyd, Simon Barry*

14:00 - 14:10 WS61 **Régis Joulia**
Single-cell spatial transcriptomics reveals the mucosal landscape at the airway wall in health and asthma

14:10 - 14:20 WS62 **Caroline Kliem**
Novel cytokine pattern associated with severe childhood asthma

14:20 - 14:30 WS63 **Antonios Kolios**
Fast itch relief during dupilumab predicts clinical efficacy in bullous pemphigoid

14:30 - 14:40 WS64 **Nuria Contreras**
Metabolomic and Proteomic Profiling of Severe Olive-Allergic Patients Treated with Dupilumab

14:40 - 14:50 WS65 **Daniel Crepaz**
Eosinophils control intestinal commensalism to sustain homeostasis

14:50 - 15:00 WS66 **Hassan Melhem**
Unveiling GPR35 as a Metabolic Hub in Eosinophilic Esophagitis: Connecting 8-methoxykynurenate, Macrophages, and Epithelial Dysfunction

Workshop 12 **T and B cell memory and immune regulation**

Room: Forum *Chairs: Peter Ernst, Cevdet Ozdemir*

14:00 - 14:10 WS67 **Boran Li**
Arginase 1 and 2 as regulators of the B cell responsee

14:10 - 14:20 WS68 **DiyaaElDin Ashour**
Tracking antigen specific T cell responses during myocardial aging

14:20 - 14:30 WS69 **Abhijeet Kulkarni**
Ineffective L-phenylalanine metabolism aids pro-inflammatory Th2 phenotype in severe allergy

14:30 - 14:40 WS70 **Adrian Ilich**
Proteomic and Transcriptomic Insights into Diet-Induced Modulation of Neonatal T Cell DevelopmentV

14:40 - 14:50 WS71 **Kristin Weinstein**
A dys-regulatory T-cell? Defects in CD8+ T-cell suppression by Foxp3-dE2 regulatory T-cells

14:50 - 15:00 WS72 **Anna Rizakou**
Characterization of ADRB1-specific CD4+ T cells in patients with myocardial infarction

12:00 - 12:15 **Award Ceremony for workshop prizes of workshops 7 - 9** Room: Davos 1

Award Ceremony for workshop prizes of workshops 10 - 12 *(will be given directly after the workshops by the chairpersons)*

Poster Program 1. Day - Wednesday, 12 March 2025

Poster Session 1 — Epithelial barrier I

20:00, Room: Foyer A1

Chairs: Paola Martinez Murillo, Yagiz Pat

P01	**Magdalena Paplińska-Goryca**	The effect of PM2.5 and microplastic fibres in model of chronic epithelial injury
P02	**Ismail Ogulur**	Mechanisms of gut barrier dysfunction: Effects of detergents and food additives on epithelial integrity
P03	**Krzysztof Krawczyk**	The halophilic archaea, Halorhabdus rudnickae, positively enhance the barrier integrity of the human epithelial cell line Calu-3
P04	**Xiangting Bu**	Inflammation infiltration weakens innate defense against air pollutants in nasal mucosa
P05	**Sena Ardicli**	Human PBMC can be used as a surrogate to demonstrate the molecular actions of innovative bone materials promoting bone formation while minimizing inflammatory responsess
P06	**Sara Trzos**	Swainsonine protects human thyrocytes from Fas-induced apoptosis: in vitro study on Nthy-ori 3-1 cell lines
P07	**Huseyn Babayev**	Circulating inflammatory responses to air pollution exposure
P08	**Huseyn Babayev**	Targeted proteomics reveals distinct circulating inflammation and inflammatory subgroups in healthy individuals

Poster Session 2 — Regulatory and effector T cell subsets and cytokines: from bench to bedside

20:00, Room: Foyer A1

Chairs: Charlotte Bonefeld, Maria Asuncion Garcia Sanchez

P09	**Nigel McCracken**	Evaluation of T cell dysfunction in post acute infection syndromes
P10	**Pia Fehrenbach**	Alterations in innate and adaptive immune cells among patients with surgical site infections in the spine
P11	**Alice Wiedmann**	Nuclear receptor LRH-1 regulates early T cell development in mice
P12	**Marko Hasiuk**	Tmem127 regulates the T cell proteome and homeostatic Interleukin-7 signaling
P13	**Ya-Ting Chuang**	Elucidating the Roles of ETS-1 and GATA-3 in iNKT Cell Differentiation and Effector Lineage Specification
P14	**Margaret Clark**	Seasonal variation in sunlight is associated with differences in levels of T regulatory and T-helper 17 cells in girls and women
P15	**Anders Funch**	CD8+ Skin-Resident Memory T Cells Require TCR Signaling for their Persistence in a Mouse Model of Allergic Contact Dermatitis

Poster Session 3 — Immune response in tumors and chronic inflammation

20:00, Room: Foyer A1

Chairs: Klaus Seuwen, Anders Funch

P16	**Oltin-Tiberiu Pop**	Cancer immunoediting in melanoma patients from early stage to advanced disease
P17	**Yun-Tsan Chang**	TRBC1: A Key Indicator of T Helper Cell Clonality in Skin Tissues
P18	**Yun-Tsan Chang**	Multi-omics cytokine screening reveals immunosuppressive microenvironment in cutaneous T-cell lymphoma
P19	**Yun-Tsan Chang**	Multi-Harmonic Imaging-Based Automated Recognition of Cutaneous T-Cell Lymphoma
P20	**Veszelka Medea**	Anti-inflammatory Effect of a Natural Polyphenol, Resveratrol in TNBS-Induced Rat Model of Colitis: the Role of TNFRs
P21	**Nikoletta Almasi**	Acute Inflammation-Induced Barrier Dysfunction in a Rat Model of IBD: a Focus on the Gut-Brain Axis

20:00 **Poster presentations of workshops 1 - 3,** Room: Main Corridor

Poster Program 2. Day - Thursday, 13 March 2025

Poster Session 4 — Allergy and Autoimmunity

20:00, Room: Foyer A1

Chairs: Femke Broere, Juan Felipe Lopez

P22	**Mel Diedro**	IL4-Ralpha and IFN-gamma opposing signals modulate neutrophils effector functions
P23	**Máté Manczinger**	HLA-II peptide-binding diversity shapes humoral immune responses and infection risk
P24	**Dagmar Duijzer**	Development of a robust methodology for blood-based biomarker discovery in patients with eosinophilic esophagitis
P25	**E Da Choi**	Basophils in skin-mediated sensitization to allergic lung Inflammation
P26	**Milad Ameri**	Deciphering Immune endotypes within Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndromey
P27	**Danielle Fehr**	No Grass Pollen Allergy in sub-Saharan Africa? Analysis of Sensitization Patterns to Pollen in Swiss & sub-Saharan African Atopic Dermatitis Patients
P28	**Sarang Chafle**	Insights into active and spontaneously resolved atopic dermatitis: Meta-analysis of tissue-resident cells from public dataset

Poster Session 5 — Epithelial barrier II

20:00, Room: Foyer A1

Chairs: Duygu Yazici, Juan Carlos Lopez Rodriguez

P29	**Bingjie Zhao**	Monosodium glutamate affects cellular stress, protein folding defect, mitochondrial dysfunction and cell death in intestinal epithelial cells
P30	**Bingjie Zhao**	Detrimental effects of tooth paste ingredients sodium dodecyl sulfate and cocamidopropyl betaine on oral and fecal microbiome balance
P31	**Paulina Misiukiewicz-Stepien**	The effect of PM2.5 and microplastic on cell injury in lipopolysaccharide stimulated bronchial epithelial cells
P32	**Lihong Chang**	Micro- and nano-polystyrene impair epithelial barrier integrity
P33	**Marlinde Waardenburg**	IL4 and IL13 induce an atopic dermatitis-like phenotype in N/TERT-2G human epidermal equivalents in vitro
P34	**Manru Li**	Sodium dodecyl sulfate impairs the skin epithelial barrier by inducing oxidative stress in human skin
P35	**Maria Asuncion Garcia Sanchez**	Common non-nutritive sweeteners disrupt the gut barrier and cause inflammation via multiple mechanisms of cellular stress in vitro
P36	**Xiaoqing Liu**	Wildfire smoke causes cytotoxicity and activates the AhR pathway on airway epithelial cells

Poster Session 6 — B cell subsets, cytokines and antibody production

20:00, Room: Foyer A1

Chairs: Ozge Ardicli, Thomas Vogl

P37	**Minglin Yang**	The role of differential expression of HR1 and HR2 on B cell subsets and their functions
P38	**Celia Makowiec**	An emerging dual role for ProtA in EBV infected B cells
P39	**Stephan Schneider**	Investigation of allergen specific B cells
P40	**Johanna Siegel**	Antibody responses to myocardial antigens released in the context of a myocardial infarction
P41	**Hang Du**	Exploring the Role of Type II Cytokines in Alarmin Receptor Regulation in B Cells
P42	**Leon ten Hoopen**	Characterization of the Memory B Cell Response to Bee Venom Phospholipase A2 in Novice Beekeepers

20:00 **Poster presentations of workshops 4 - 6,** Room: Main Corridor

Poster Program 3. Day - Friday, 14 March 2025

Poster Session 7 — **Immune response to viruses**

20:00, Room: Foyer A1 — *Chairs: Severine Navarro, Pei-Chi Chen*

P43	**Tanja Karl**	Unraveling the Complexities of SARS-CoV-2 Antibody Responses: Towards Optimized Vaccination Approaches
P44	**Lu Yao**	Microbial-Derived Tryptophan Metabolites Selectively Influence Cytokine Secretion, Proliferation and Differentiation of Polarized Human Lymphocytes
P45	**Nitish Sahani**	Proteomic Analysis of Extracellular Vesicle Cargo in COVID-19 Patients During Acute and Post-Acute Phase Infectionl
P46	**Tanzeela Hanif**	Bocavirus and/or rhinovirus infection and tonsillar immune responses

Poster Session 8 — **Metabolism**

20:00, Room: Foyer A1 — *Chairs: Marcela Hortova Kohoutkova, Urszula Radzikowska*

P47	**Piotr Szatkowski**	Characteristic of 15-LOX and 5-LOX oxo-metabolites with Lund-Mackay score in aspirin-exacerbated respiratory disease
P48	**Jacqueline Ratter-Rieck**	Metabolic phenotypes in type 2 diabetes shape immunometabolic signatures of circulating CD4+ T cells
P49	**Alaa Sherri**	Towards new biomarkers in psoriatic arthritis
P50	**Cheryl Brown**	A novel role in Treg for the transcription factor JAZF1, which orchestrates a transcriptional programme to help maintain Treg lineage fidelity and metabolic homeostasis
P51	**Simon Barry**	Investigating GAD65-CAR Tregs as a Novel Therapy for Type 1 Diabetes

Poster Session 9 — **Novel diagnosis methods, treatments and drugs**

20:00, Room: Foyer A1 — *Chairs: Douglas Nixon, Sena Ardicli*

P52	**Ibon Eguiluz Gracia**	Microneedle-based delivery of ovalbumin-loaded mesoporous silica nanoparticles for allergen-specific immunotherapy
P53	**Nicolo Marchi**	Development of a Novel Platform for Engineered Extracellular Vesicles in Targeted Immunomodulation
P54	**Anna Ehlers**	Monovalent binding of synthetic high affinity Siglec-9 ligands: A potential candidate for allergy immunotherapy?
P55	**Jasmijn Burgelman**	Defining a new role for Charcot-Leyden crystals in Type 2 immunity and airway obstruction
P56	**Huseyn Babayev**	Dynamic changes in plasma biomarkers following oral immunotherapy in multifood allergic patients
P57	**Hadja Safiat Simboro**	Extracellular Vesicles for Drug Delivery
P58	**Cezar-Fabian Moise**	Protein Expression Dynamics in Female Elite Athletes: Insights into Training, Recovery, Performance, and Menstrual Cycle Impact
P59	**Eveline de Geus**	Development of a non-invasive method to collect immune mediators from skin

Poster Session 10 — **Innate immune response**

20:00, Room: Foyer A1 — *Chairs: Irina Iten, Christian Schwartz*

P60	**Katarina Kouter**	Genetic factors of the complement system and suicidality
P61	**Andrian Fratea**	Transcriptional profiling of immune cells reveals a role for IFN-gamma/CXCL9/CXCL10 pathway in sepsis patients with exaggerated inflammation
P62	**Daniel Simpson**	Obesity-linked Sphingomyelin d18:1/14:0 (S14) agonises TLR4 in human macrophages
P63	**Selket Delafontaine**	Life-threatening CMV encephalitis and RSV infection caused by a TLR3 mutation in twin girls
P64	**Markus Kleinewietfeld**	Beyond bacteria: A novel look at the gut mycobiome's role in Multiple Sclerosis
P65	**Szilvia Agnes Toeroek**	Lawesson's reagent ameliorates inflammation via the modulation of inflammatory cytokines and NET formation in TNBS-induced rat colitis

20:00 **Poster presentations of workshops 7 - 12,** Room: Main Corridor



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Speakers Abstracts

S01 Tumour-infiltrating lymphocyte (TIL)-adoptive cell therapy

Alexandre Harari
Ludwig Institute for Cancer Research Lausanne, Lausanne University Hospital (CHUV) and University of Lausanne (UNIL)

Adoptive cell therapy (ACT) using in vitro expanded tumor-infiltrating lymphocytes (TILs) has demonstrated significant efficacy in advanced melanoma and is being tested in other cancer types. Although potentially curative in patients who achieve a complete response, the inconsistency of clinical responses to TIL-ACT across patients stresses the need to discern the mechanisms driving therapeutic success. Limitations to therapeutic efficacy have been attributed to date to the scarcity of tumor-specific T cells in tumors of origin, the terminal differentiation of TILs in cell products or the lack of cell persistence following ACT. Although the absolute frequency of cells recognizing mutational neoantigens is on average low in TIL products, the tumor mutational burden as well as the frequency of neoantigen-specific clones in TIL infusion products have also been correlated with TIL-ACT efficacy. However, correlates of efficacy remain mostly unknown. In particular, the profiles, specificity and dynamics of tumor-specific clonotypes associated with clinical response to TIL-ACT remain unclear. In a phase I clinical trial (NCT03475134), we tracked T-cell dynamics in 13 melanoma patients. Using state-of-the-art single-cell sequencing technologies, we tracked TIL clonotypes across treatment phases. Results revealed that patients with clinical responses had baseline tumors enriched in tumor-reactive TILs and that tumor-reactive TILs were more effectively mobilized upon in vitro expansion. In contrast, non-responders' ACT products were mostly composed of blood-borne clonotypes. Furthermore, the study showed that TIL-ACT drove important cell reprogramming. This work not only enhances our understanding of T-cell mobilization during therapy but also provides vital insights for improving patient selection and optimizing next-generation therapies.

S02 Eosinophils in homeostasis and disease

Isabelle Arnold
Institute of Experimental Immunology, University of Zürich, Zürich, Switzerland

Eosinophils are bone marrow-derived granulocytes best known for their effector functions in parasitic infections or allergen challenge. They are also increasingly recognized as important modulators of immune, metabolic and tissue morphogenetic processes. The largest population of eosinophils resides in the lamina propria of the gastrointestinal tract under homeostatic conditions, with their numbers significantly increasing during inflammation, such as in inflammatory bowel diseases. Despite their abundance, the functions of eosinophils in intestinal homeostatic and inflammatory processes are still not fully understood. Here we show that the eosinophil lineage comprises highly heterogeneous populations, whose activities are instructed by the surrounding tissue environment. Their ability to integrate microbial and environmental signals results in remarkable functional plasticity, supporting intestinal homeostasis, immune regulation, and host defense. Using a combination of single-cell transcriptomics, patient cohorts and experimental models of colitis, cancer and bacterial infections, we explore the mechanisms of eosinophil activities at mucosal sites, their interactions with adjacent immune and non-immune cells, as well as their crosstalk with the indigenous microbiota.

S03 The transcriptional regulator IkappaBzeta controls the effector functions of group 2 innate lymphoid cells

Irina Iten[1], Ivan Berest[1], Nikolaos D. Sidiropoulos[1,2], Xiaogang Feng[2], Gariné Magarditchian[1], Laura Fisch[1], Daniela Kramer[3], Christoph Schneider[2], Manfred Kopf[1]
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2Institute of Physiology; University of Zurich, Switzerland

ILC2s are sentinel cells that ensure tissue homeostasis and engage in the immune response to helminths by secreting type 2 cytokines. Here, we show that IkappaBzeta, an atypical member of the IkappaB family, controls basal IL-5 production by ILC2s and governs their effector program during helminth infection and asthma. Peripheral ILC2s express IkappaBzeta at steady state, which is further induced upon stimulation with IL-33 or IL-25 in an NF-kappaB- and STAT3/5-dependent manner. Upon activation, IkappaBzeta refines chromatin accessibility at regulatory elements of effector cytokine loci and thereby licenses transcription. Due to reduced type 2 cytokine secretion and impaired proliferative capacity of ILC2s, mice with IkappaBzeta-deficient ILC2 show delayed clearance of the hookworm Nippostrongylus brasiliensis and reduced papain-induced airway inflammation. Taken together, our study highlights the central role of IkappaBzeta in orchestrating the ILC2 effector program in different tissues in health and disease

S04 Next-Generation CAR-T mediated B cell depletion therapy for sustained remission in severe refractory SLE and other autoimmune diseases

Thomas Calzascia[1], Isabelle Isnardi[1], Dexiu Bu[1], Alexandre Avrameas[1], Stephen Oliver[1], Carole Sips[1], Josefina Cortés Hernández[2,3], Pere Barba[3,4], Mònica Linares Alberich[5], Nan Shen[6], Ozana Fischer[1], Beata Kovacs[1], David Pearson[1], Chih-Yung Sean Lee[1], Tamas Shisha[1], Peter Gergely[1], Elodie Riquet[1], Vanessa Cornacchione[1], Jennifer Brogdon[1], Gerhard Krönke[7], Georg Schett[7], Elisabetta Traggiai[1], and Richard Siege[1]
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Systemic lupus erythematosus (SLE) is characterized by autoreactive B cells and expansion of circulating plasmablasts. Despite the putative pathogenic role of B cells in SLE, efficacy of the B cell depleting anti-CD20 monoclonal antibody (mAb) rituximab in RCT's has been limited. Improved efficacy has been demonstrated with Ianalumab (VAY736), an afucosylated mAb targeting the BAFF receptor (BAFFR) that depletes B cells and plasmablasts and blocks BAFF:BAFFR mediated survival signals, with 48% more subjects reaching SRI-4 compared to placebo after 28 weeks. Yet the proportion of patients reaching LLDAS low disease activity status with ianalumab was lower, 26% vs. 9% with placebo. Recent case series have shown that CD19-directed chimeric antigen receptor T cell (CAR-T cell) therapies can induce durable clinical remission in severe refractory SLE (srSLE). High-dimensional profiling of the antibody 'autoreactome' from these patients revealed reversion to a profile more similar to healthy controls. We initiated an open-label, single-arm, multi-center phase I/II study to assess the safety, efficacy and cellular kinetics of rapcabtagene autoleucel (YTB323), a novel, rapidly manufactured autologous CD19-directed CAR-T cell therapy that has shown preserved T cell stemness and efficacy comparable to 1st generation CD19-CART in hematological malignancies, in srSLE (NCT05798117). In the first 11 patients treated with YTB323 at a single dose of 12.5x106 cells, we observed rapid CAR-T expansion and B cell depletion for a minimum of 60 days. Low-grade CRS was observed in 6 patients that resolved upon treatment. Immune cell-associated neurotoxicity syndrome (ICANS) (grade 2) was observed in 1 patient. Initial efficacy was demonstrated by rapid improvement in SLE Disease Activity Index 2000 (SLEDAI-2K), Physician's Global Assessment (PhGA) and relevant disease biomarkers. These results supported initiation of larger randomized controlled studies to assess the efficacy and safety of YTB323 as a one-time therapy to induce long-term remission in four autoimmune rheumatic diseases.

S05 Neuroimmunology of the skin

Nicolas Gaudenzio
1Toulouse Institute for Infectious and Inflammatory Diseases (Infinity) INSERM UMR-CNRS UMR University Toulouse III, France
2Genoskin SAS, Toulouse, France

Mast cells (MCs) are emerging as central players in the complex dialogue between the nervous and immune systems, shaping both homeostasis and disease. From allergic skin inflammation to prenatal stress-induced eczema, our research reveals how MCs act as key sensors and effectors of environmental and physiological cues. We demonstrate that allergens, such as house dust mites, directly activate sensory neurons, triggering MC degranulation and initiating allergic inflammation. Beyond allergies, MCs exhibit remarkable tissue specificity, with distinct populations in connective and mucosal tissues, orchestrating local immune responses. Importantly, we uncover a prenatal origin of eczema, where maternal stress alters fetal MC and neuronal development, leading toearly-life susceptibility to skin inflammation. These findings redefine MCs as active mediators of neuroimmune circuits, bridging environmental exposures with immune programming. Understanding these mechanisms opens new avenues for therapeutic interventions in allergic diseases, neuroimmune disorders, and stress-induced inflammatory conditions.

S06 Dissecting autoreactive T cell immunity in human neurological disorders

Daniela Latorre[1,2]
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2Insititute of Microbiology, ETH Zurich, Switzerland

Understanding the immune mechanisms underlying neurological disorders in humans remains a significant challenge. In our research, we integrate in vitro T cell screenings, single-cell cloning, T cell receptor sequencing and computational tools to identify and characterize autoreactive T cells in patients with neurological disorders affecting the central or peripheral nervous systems. This talk will highlight our recent findings on autoreactive T cell immunity in patients with acute inflammatory demyelinating neuropathies, particularly Guillain-Barré Syndrome, as well as new data demonstrating their presence in the chronic disease subtype. Additionally, I will discuss emerging evidence of cross-reactive T cell immunity, which may underlie the strong association between preceding microbial infections and disease onset.

S07 Acute and prolonged impact of epidermal CD8+ memory T cells

Anders Funch, Helen Vaher, Carsten Geisler, Charlotte Menné Bonefeld

The LEO Foundation Skin Immunology Research Center, Department of Immunology and Microbiology, Faculty of Health and Medical Sciences, University of Copenhagen; Copenhagen, Denmark
Epidermal-resident CD8+ memory T (TRM) cells are formed locally in the epidermis upon exposure of the skin to antigens. They can respond rapidly following re-exposure of the skin to the given antigen. However, whether the response induced by CD8+ TRM cells is similar or differs from the response induced by circulation CD8+ memory T cells and whether CD8+ TRM cells have a prolonged impact on the epidermis are not known. Using mouse models for allergic contact dermatits, we confirmed that CD8+ TRM cells induce a much faster response compared to circulating CD8+ memory T cells following re-exposure of the skin to the given antigen. Furthermore, we show that the faster response is mediated by a massive CD8+ TRM cell-induced infiltration of neutrophils to the epidermis, which is not seen in the response mediated by circulating CD8+ memory T cells. The correlation between the fast, local response to antigen, presence of epidermal CD8+ TRM cells and recruitment of neutrophils was confirmed in humans allergic to nickel. In addition, we found that epidermal CD8+ TRM cells induce a local, prolonged down-regulation of various skin barrier molecules, including keratin 5 and keratin 14. Taken together, we found that epidermal CD8+ TRM cells alter the acute response induced in the skin following re-exposure to a given antigen and that they have a prolonged impact on the skin barrier.

S08 Differential Immune metabolism linked to mAB treatment in allergic asthma

Contreras N.[1,2], Delgado-Dolset M.I.[1,2], Fernández P.[1], Carrillo T.[4], Blanco C.[5], Villaseñor A.[2], López-Rodríguez J.C.[1], Ruiz-León B.[3], Barber D.[1], Maria Escribese[1]
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Las Palmas de Gran Canaria, Spain
5Servicio de Alergia, Hospital Universitario de La Princesa, Instituto De Investigacion Sanitaria Princesa (IIS-Princesa), Madrid, Spain
Background: Asthma prevalence has progressively increased during the last decades, and 5-10% of total asthmatic patients develop a severe phenotype entailing increased hospitalizations and frequent exacerbations. In this sense, biologics emerged as potential adjuvant therapies for treating severe asthma by targeting inflammatory T2-modulators at different levels of the signalling cascade. However, how these biological treatments affect the immune and metabolic profiles remains unknown. Methods: This study includes three cohorts of severe allergic asthmatic patients (GINA 4-5) treated with specific biological monoclonal antibodies (moAb) for a 6-month follow up. Cohort 1: olive-allergic patients (n=12) sensitized to the minor allergen Ole e 7. Cohorts 2 and 3: house dust mites (HDM) allergic patients treated with Mepolizumab (n=36) and Omalizumab (n=20). Treatment monitoring was performed by analysing serum samples using a targeted metabolomic methodology previously developed by our group (Obeso D, et al. 2019) through liquid chromatography coupled to a triple quadrupole tandem mass spectrometry (LC-QqQ-MS), and targeted proteomic approach (Olink®Target 48 Cytokine panel). In addition, clinical variables such as FEV1, ACT, the number of severe exacerbations, hospitalizations and blood eosinophils were included in the analysis. Results: The analysis revealed that Dupilumab treatment induced significant changes in the metabolomic (e.g. decrease fatty acids) and proteomic (e.g. increase IL-4 and CCL2) profile of these patients after 6 months. On the other hand, Mepolizumab induced different changes in the metabolomic (e.g. fatty acids, and sphingolipids) and proteomic (e.g. TNF-α and CCL11) profiles, as well as Omalizumab (e.g. S1P, TNFSF10 and OLR1). Conclusions: Our results demonstrate that Dupilumab, Mepolizumab and Omalizumab, trigger differential metabolic pathways and promote unique immune responses that might explain their clinical effects and provide new insights to provide evidence-based use of these moAb therapeutic approaches.

S09 Harnessing bile acids to ameliorate lung inflammation

Pilar Rodriguez-Viso[1*], Magdalena Wolska[1*], Edyta Bulanda[1], Anna Świątkowska[1], Magdalena Lebiedzińska[2], Mariusz Więckowski[2], Aleksandra Cabaj[3], Bartosz Wojtaś[3], Tomasz Wypych[1*]
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Bile acids are emerging as potent immunomodulators in the gut, primarily affecting CD4+ T cell differentiation and dendritic cell function. Clinical data collected during the COVID-19 pandemic revealed the association between reduced levels of fecal secondary bile acids and mortality due to respiratory failure, suggesting that bile acids might also function outside the intestines. Despite this, it remains unknown if a causative relationship can be confirmed experimentally, which bile acid species are implicated, and what downstream mechanisms are relevant. Here, using mouse models of airway inflammation, we identified the causative link between a microbiota-dependent bile acid, named here "the metabolite X" due to a pending patent application, and the protection against lung immunopathology. Next, we pointed to the Sphingosine-1-phosphate receptor 2 (S1PR2)-dependent metabolic rewiring of alveolar macrophages as a key mechanism of action. Together, our results identify a microbiota-dependent bile acid capable of ameliorating lung inflammation via previously undescribed mechanisms.

S10 Defining the factors driving mucosal healing

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Department of Immunology, School of Translational Medicine, Monash University, Melbourne, Australia
Achieving mucosal healing without relying on immunosuppression is the ultimate therapeutic goal in inflammatory bowel disease (IBD). Yet the current medical mainstay of IBD almost exclusively relies on the suppression of the immune system, often leading to adverse effects. Exclusive enteral nutrition (EEN) is the only non-pharmacological short-term therapy with strong evidence of safety and efficacy in not only inducing clinical remission but also promoting mucosal healing through underlying mechanisms that are however poorly defined. Herein we employed a clinical EEN as a dietary model to identify the molecular and cellular mechanisms of mucosal healing. EEN restored damaged epithelial barriers without altering levels of inflammation and immune cells, highlighting a direct effect on intestinal epithelial cells. This repair process was dependent on the optimal dietary energy derived from EEN's highly digestible macronutrients, such as simple carbohydrates. EEN-mediated mucosal healing during tissue repair was associated with the restoration of normal mitochondrial phenotypes in epithelial cells. Single-cell RNA sequencing (scRNA-seq) of epithelial cells further revealed that recovered, sub-type- and location-specific enterocytes adopted distinct transcriptional programs during tissue repair. Thus, optimising dietary energy derived from simple macronutrients is crucial for achieving mucosal healing without immunosuppression.

S11 Common food emulsifiers impair epithelial barrier integrity and trigger pro-inflammatory responses

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The barrier function of the epithelia is crucial for maintaining homeostasis. Environmental exposures may alter the epithelial barrier integrity and influence the development of diseases. We hypothesized that emulsifiers introduced to processed foods after 2000s damage the epithelial barriers and play a role in increased prevalence of food allergy and anaphylaxis. We investigated the effects of two commonly used food emulsifiers, soy lecithin (SoyLec) and diacetyl tartaric acid ester of mono- and diglycerides (DATEM) on epithelial cells at consumer-relevant doses in vitro and in vivo using transepithelial-electrical resistance (TER), RNA-seq, and targeted proteomics. SoyLec and DATEM elicited a dose- and time-dependent decrease in TER. RNA-seq analysis indicated SoyLec upregulated the pathways of TNF signaling, unfolded protein response, and apoptosis. DATEM showed increased cell death, ER stress and response to lipids. SoyLec induced the production of proinflammatory cytokines (IL-6, IL-18) as well as alarmins (TSLP, IL-33). DATEM induced the production alarmins and proinflammatory and cell death-related proteins such as TSLP, CASP8, IL-18, and DDX58. For the in vivo experiments, emulsifiers were administered to mice once a week for 6 weeks. Both emulsifiers showed increased production of proinflammatory cytokines and chemokines (IL1□, IL3, IL6, TNF, CCL4) in serum samples. SoyLec-treated colon samples showed increased production of IL33 together with TNF, CCL17, and CCL11. Interestingly, SoyLec induced downregulation of keratinocyte differentiation in esophagus tissue significantly while pro-inflammatory pathways were upregulated. In conclusion, the present study provides direct evidence on the detrimental effects of food emulsifiers on esophagus and gastrointestinal epithelial integrity, due to extensive inflammation, endoplasmic reticulum stress, and alarmin release.

S12 Delineating molecular and microbial signatures across disease severity in Inflammatory Bowel Disease in adult treatment naive patients through single-cell transcriptomic and microbiome profiling.

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Background: Inflammatory Bowel Disease (IBD) is a group of chronic inflammatory conditions with complex etiology involving genetic, immune, microbiome, and environmental factors. This study aims to elucidate the cellular and microbial landscape of adult treatment-naive IBD patients to identify potential disease mechanisms and therapeutic targets, presenting one of the largest single-clinic, IBD single-cell datasets to date.Methods: Tissue biopsies were collected from inflamed and non-inflamed regions of the colon in UC patients and colon + ileum in CD patients. Using 10x Genomics single-cell RNA sequencing (scRNA-seq), we analyzed 1.4 million cells from 68 treatment-naive IBD patients (38 CD, 30 UC) and 70 symptomatic healthy controls. Shotgun metagenomic sequencing was performed on 36 IBD patients with matched scRNA-seq data to explore host-microbe interactions, and a further 49 patients with paired clinical data. Results: Our analysis revealed distinct cellular populations and gene expression profiles between IBD patients and healthy controls along the disease severity axis. Specific immune cell subsets were significantly expanded in IBD patients, with inflammatory monocytes particularly prominent in those with higher disease severity, exhibiting upregulated expression of pro-inflammatory cytokines and chemokines. Additionally, a shift from IgA to IgG antibody-producing cells was observed along the disease severity axis, indicating a dysregulated immune response associated with disease progression. Fecal microbial community typing revealed two clusters defined by low or high abundance of Bacteroidetes phylum taxa. Integration of clinical metadata and transcriptional profiles indicated that Bacteroidetes-high UC patients displayed lower levels of inflammation and up-regulation of interferon signaling in B cells and myeloid cells. Conclusion: This comprehensive profiling of adult treatment-naive IBD patients provides a deeper understanding of the underlying disease pathology at the time of presentation along the axis of disease severity. This study expands the dynamic range of IBD patient profiling and may inform future therapeutic strategies.

S13 Heterogenity of Resident Tissue Macrophages

Florent Ginhoux
Fondation Gustave Roussy, Villejuif, France
Macrophages have a broad spectrum of immune- and non-immune-related tissue-supporting activities. The roots of this heterogeneity and versatility are only beginning to be understood. Here, we propose a conceptual framework for considering macrophage heterogeneity that organizes the factors shaping their identity within four cardinal points: (1) ontogeny and the view that adult macrophage populations comprise a defined mixture of cells that arise from either embryonic precursors or adult monocytes; (2) local factors unique to the niche of residence, evolving during development and aging; (3) inflammation status; and (4) the cumulative effect of time spent in a specific tissue that contributes to the resilient adaptation of macrophages to their dynamic environment. We will especially discuss how to transpose these concepts to disease to better understand macrophage heterogeneity.

S14 Increasing CAR T cell persistence instructed by basic immuno-metabolic principles

Christoph Hess
University of Basel (CH) and University of Cambridge (UK)
Insufficient persistence of CAR T cells represents a major hurdle both when treating cancer as well as auto-immunity. In my talk, I will propose a pseudo-metabolic intervention with potential to increase CAR T cell persistence, and describe the molecular logic underpinning our reasoning.

S15 Harnessing Tolerogenic Dendritic Cells for Antigen-Specific Immune Modulation in Rheumatoid Arthritis: Findings from the TOLERANT Trial

Arie Jan Stoppelenburg[1,2], Naomi Benne[2], Gerty Schreibelt[3], Paco Welsing[1], Laureen Lammers[4], Anna de Goede[5], Tjitske Duiveman-de Boer[3], Willem van Eden[2,6], Paul Leufkens[6], I Jolanda M de Vries[3], Jacob M van Laar[1]*, Femke Broere[2]*
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6Trajectum Pharma B.V., Utrecht, The Netherlands
*Contributed equally
Current treatments for rheumatoid arthritis primarily rely on immunosuppression, which carries significant long-term risks and fails to address the underlying immune dysregulation. The TOLERANT trial investigates the safety, feasibility, and immunological effects of a novel autologous tolerogenic dendritic cell (tolDC) therapy loaded with the heat shock protein 70-derived peptide B29 (tolDC-B29) for inducing antigen-specific tolerance. This phase I/II open-label dose-escalation trial enrolled nine patients in remission under stable immunosuppressive therapy. Patients received two intranodal tolDC-B29 injections across escalating doses. The treatment was well-tolerated, with no serious adverse events reported, confirming the safety and feasibility of this novel cell product and administration route. Immunological monitoring revealed key changes, including a decreased abundance of T follicular helper, alongside an increased interleukin-10 to interleukin-17 ratio following the second injection in a portion of the patients. Furthermore, ex vivo stimulation assays demonstrated increased T cell activation to B29 peptide single-peptide T cell responses, providing evidence of antigen-specific immune modulation induced by tolDC therapy. These findings provide encouraging evidence supporting the safety and feasibility of tolDC therapy in RA, alongside preliminary insights into its immunological effects. While further studies are needed to validate these findings and assess clinical efficacy, this approach holds promise as a potential step towards more targeted and durable treatments for RA.

S16 High-affinity omalizumab variants with optimized disruptive efficacy rapidly desensitize allergic effector cells in vivo

Daniel Brigger[1,2,†], Pascal Guntern[1,2,†], Luke F. Pennington[3], Robin van Brummelen[1,2], Theodore S. Jardetzky[4]and Alexander Eggel[2,3]
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† These authors contributed equally to this work.
Omalizumab, a therapeutic monoclonal anti-immunoglobulin E (IgE) antibody, has been successfully used in the treatment of multiple allergic conditions. Its moderate affinity for IgE, however, necessitates frequent dosing over prolonged time periods. We have previously demonstrated that the ability of omalizumab to actively dissociate IgE:FcepsilonIRalpha complexes is weak. In this study we generated and characterized two new high-affinity omalizumab variants with improved disruptive efficacy, which could potentially optimize current treatment strategies. We compared binding characteristics and treatment efficacy of the two new anti-IgE antibodies C03-H1L2 and C03-H2L2 with omalizumab. Surface plasmon resonance was used to measure binding kinetics and stoichiometry was assessed by size exclusion chromatography. In vitro assays were employed to evaluate receptor inhibition profiles, disruptive efficacy and anaphylactogenicity. Overall, in vivo efficacy was explored using a passive systemic anaphylaxis mouse model. The new omalizumab variants demonstrated high-affinity binding to human IgE with a ~10-fold improvement over omalizumab. While immune complex formation and receptor inhibition profiles remained similar, the high-affinity variants exhibited significantly improved disruptive efficacy. Both new C03 antibodies removed IgE from its high-affinity receptor FcepsilonIRalpha on allergic effector cells with faster kinetics than omalizumab without inducing spontaneous activation of the cells. In the systemic anaphylaxis mouse model, C03-H1L2 and C03-H2L2 reached complete desensitization within 36 hours of single dose application. Both C03 antibodies showed improved affinity, similar receptor inhibition profiles, and greater disruptive efficacy compared to omalizumab. While both new anti-IgE candidates feature favourable properties for clinical development our findings further underscore their potential as optimized therapeutic option for the treatment of various allergic disorders.

S17 Biomarker and adaptive trial driven approaches: Innovation in allergen immunotherapy

Mohamed Shamji
National Heart and Lung Institute, Imperial College London
Allergen immunotherapy (AIT) is a disease-modifying treatment aimed at inducing long-term immune tolerance to allergens. Traditional AIT has limitations such as long treatment durations and risks of adverse reactions. Biomarker-driven approaches and adaptive trial designs offer innovative solutions to enhance safety, efficacy, and patient stratification. Adaptive trials allow the use of real-time data analysis to modify trial parameters such as dosages, patient selection and treatment duration, allowing a more flexible approach to obtaining a successful outcome and reducing cost. Here, we will discuss the application of biomarker driven approaches and adaptive trial design in the context of allergic rhinitis (grass pollen) and food allergy (peanut).

S18 Novel Strategies To Modulate Type 2 immunity

Jamie Orengo
Regeneron Pharmaceuticals, Tarrytown, USA
Biologics targeting classical type 2 (T2) cytokines IL-4, IL-5, and IL-

13, as well as the proinflammatory cytokine, IL-33, have emerged as promising therapies for moderate-to-severe asthma. However, the mechanisms by which these therapeutics modulate airway inflammation and remodeling, and their comparative effects, are not well-understood. To address these gaps, we evaluated transcriptional, cellular and pathophysiological processes driven by IL-4/ IL-13 and IL-33 using human innate cells in vitro, mouse models of house dust mite (HDM)-induced airway inflammation and a Bronchial Allergen Challenge (BAC) in HDM-sensitized individuals with mild asthma. Global transcriptomic analysis of human mast cells and eosinophils stimulated with IL-4, IL-13, and IL-33 revealed that IL-33 induced significantly more gene expression changes than IL-4 and IL-13, with notable distinctions in their respective gene expression profiles. In contrast to immune cells, lung structural cells primarily responded to IL-4 and IL-13 and, to a much lesser extent, to IL-33. In an HDM mouse model with a dominant T2 lung inflammation, blockade of either IL-4Ralpha (with dupilumab) or IL-33 (with itepekimab) led to a marked reduction in inflammatory mediators of asthma, including lung eosinophils, T2 cytokines, chemokines and mucus plugging. Some of these findings were mirrored in human studies, where blocking IL-33 or IL-4Ralpha reduced biomarkers of T2 airway inflammation in individuals with mild persistent asthma following BAC. Interestingly, in an HDM mouse model with mixed airway inflammation and remodeling, IL33 blockade reduced both T2 and T1/T17 lung inflammation and markers of fibrosis. Taken together, these data highlight key common and unique mechanisms of IL-4/IL-13 and IL33 in driving inflammation and tissue remodeling in asthma.

S19 Peanut allergoids conjugated to mannan as novel candidates for allergen-specific immunotherapy: unraveling their immunological mode of action

Alba Angelina Querencias[1], Sofía Sirvent[1], Natalia Cuervo[1], Mario Pérez-Diego[1], Carmen Sevilla-Ortega[1], Beatriz Marcos[1], Eva Abel-Fernández[2], Salvador Iborra[2], José Luis Subiza[2]and Oscar Palomares[1]

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Food allergy is a worldwide health problem of increasing prevalence. Although increasing research focuses on the study of allergen-specific immunotherapy (AIT) for food allergies, only an oral immunotherapy product for peanut allergy has been approved by FDA. Glutaraldehyde-polymerized grass pollen allergoids coupled to mannan have shown efficacy and safety in phase II and III clinical trials for pollen allergy. Here, we investigate the capacity of peanut allergoids conjugated to mannan (PM) to regulate human dendritic cells (DCs) function and its potential therapeutic effect in mouse models of peanut allergy. Human monocyte-derived DCs (hmoDCs) were stimulated with native (N), glutaraldehyde-polymerized (P) or PM peanut extracts, and cell surface markers, cytokine production, metabolic changes, and allogenic co-cultures with naïve CD4+T cells were analyzed. The in vivo potential therapeutic capacity of PM was determined by analyzing humoral responses, the induction of blocking antibodies, and the induction of regulatory T cells (Tregs). PM significantly increases the expression of PD-L1 and CD83, the production of IL-6 and IL-10 in hmoDCs and their capacity to polarize FOXP3+Tregs compared to N or P. Metabolic assays demonstrated that PM induces a metabolic rewiring towards glycolysis, which is essential for the PM-induced phenotype and function in hmoDCs. In vivo, PM displays slightly higher hypoallergenic features than P. In addition, PM-immunized mice show lower levels of total and peanut-specific IgE and high levels of peanut specific-IgG2a and FOXP3+Tregs than N- or P-immunized mice. The antibodies generated after immunization of mice with PM inhibit the binding of serum IgE from peanut allergic patients to native peanut extracts. In conclusion, peanut allergoid-mannan conjugates are hypoallergenic conjugates with tolerogenic capacity able to enhance the generation of functional FOXP3+Tregs and induce blocking antibodies, thus positioning this preparation as a potential suitable novel AIT vaccine candidate for peanut allergy.

S20 Impact of microbial metabolism on mucosal immune responses

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Human mucosal surfaces and body cavities harbour diverse communities of commensal microbes that play essential roles in regulation of host metabolic responses, epithelial barrier function, immune education, and immune regulation. Microbial-derived factors are integral components of immune and metabolic functions required for host health and survival. These host effects are partially induced by activation of host pattern recognition receptors to microbial-derived danger signals, but increasingly the role of bacterial metabolites in shaping host immune function is being recognized. Immunoregulatory bacterial metabolites can trigger host G protein-coupled receptors (GPCRs), aryl hydrocarbon receptors (AhRs), nuclear hormone receptors such as the farnesoid X receptor, or can directly modulate gene expression through epigenetic mechanisms. Importantly, many immunoregulatory bacterial metabolites are generated from dietary ingredients (e.g. fiber, tryptophan), linking diet and lifestyle to immune health via microbial mechanisms. Recent changes in dietary habits and microbiota composition have resulted in reduced levels of immune regulatory metabolites that are expected and evolutionarily hardwired into immune cell development and decision-making processes. The lack of immune regulatory molecules, potentially coupled with excess proinflammatory mediators, results in a hypersensitive immune system that reacts inappropriately to non-pathogenic stimuli and does not respond effectively to infection but is associated with a poorly regulated immune system that contributes to increased risk of inflammatory disease throughout the lifespan.

S21 Fever and Immunometabolism of T cells

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T cells in tumors and other inflamed tissues accumulate signs of stress and mitochondrial damage that affect cell metabolism but remain poorly understood. The metabolism of T cells and other immune cells is dynamically regulated and influences biosynthesis, signaling, and cell fate. We have shown that CD4 T cell subsets are metabolically distinct and that each requires a specific metabolic program for their function. Temperature is a microenvironmental variable that changes with body location, fever, and inflammation. While heat is well-known to influence activities of enzymes and complex structures, the impact of fever or locally increased temperatures on T cell metabolism and function are uncertain. We tested the effects of elevated temperatures found that T cells become more pro-inflammatory but begin to experience stress that may shape immunity. Effector CD4 T cells of all subsets tested had increased proliferation and cytokine secretion. While Treg also had increased proliferation, they had reduced ability to suppress. Interestingly, Th1 cells selectively showed mitochondrial stress, with many cells experiencing mitochondrial dysfunction, reactive oxygen species, and DNA damage that Th17 and Treg did not experience. This ultimately led to p53 and STING activation to enhance both inflammation and apoptosis. Mechanistically, our data point to mitochondrial electron transport complex 1 (ETC1) as sensitive to elevated temperatures and Th1 as selectively dependent on this complex. Together, these data show that physiologic heat is pro-inflammatory and that Th1 cells selectively develop mitochondrial stress with ETC1 as a potential thermosensitive modulator of mitochondrial metabolism. This heat sensitive ETC1 mitochondrial stress pathway may have broad implications in fever and inflamed tissues.

S22 cROSsing barriers: Metabolism meets T cell function

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The intestinal tract generates significant reactive oxygen species (ROS), but the role of T cell antioxidant mechanisms in maintaining intestinal homeostasis is poorly understood. We used T cell-specific ablation of the catalytic subunit of glutamate cysteine ligase (Gclc), which impaired glutathione (GSH) production, crucially reducing IL-22 production by Th17 cells in the lamina propria, which is critical for gut protection. Under steady-state conditions, Gclc deficiency did not alter cytokine secretion; however, C. rodentium infection induced increased ROS and disrupted mitochondrial function and TFAM-driven mitochondrial gene expression, resulting in decreased cellular ATP. These changes impaired the PI3K/AKT/mTOR pathway, reducing phosphorylation of 4E-BP1 and consequently limiting IL-22 translation.

S23 Immunometabolism of Airway Epithelium in Asthma and Viral Infection

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Rhinovirus (RV) infection of airway epithelial cells from patients with asthma results in an abnormal engagement of retinoic-acid inducible gene I (RIG-I) into RIG-I inflammasome formation, which subsequently delays RIG-I dependent interferon (IFN) type I/III responses and enhances proinflammatory signaling in asthma. The exacerbation-prone asthma has been linked with metabolic dysfunctions, however, the metabolic regulation of antiviral responses during those pathogenic viral infections in asthma is not well understood. Therefore, bronchial epithelium from patients with asthma and healthy controls upon in vitro and in vivo RV infection were used to analyze the metabolic regulation of RIG-I-dependent signaling. Bronchial epithelium of patients with asthma upon RV infection demonstrated increased glycolytic ATP and decreased mitochondrial ATP production, indicating, in contrast to healthy epithelium, continuous reliance on glycolysis for ATP production in asthma. We also observed a broad downregulation of mitochondrial proteins, related to the electron transport chain (ETC), TCA cycle, reactive oxygen species (ROS) removal, and mitochondrial structure in asthma. Importantly, this mitochondrial impairment in asthma persists after RV infection. Moreover, inhibition of ETC complex I with rotenone reduced IFNB and DDX58 (RIG-I) expression while increasing the release of mature IL-1β protein upon RV infection. Conversely, blocking glycolysis with 2-deoxy-D-glucose (2-DG) reduced both viral replication and IL-1β release, demonstrating a clear metabolic regulation of RIG-I-dependent proinflammatory/antiviral responses in bronchial epithelium. These in vitro mechanistic insights were further validated in vivo through transcriptomic analysis of bronchial brushings from RV-infected patients with asthma and healthy controls. In patients with asthma, the upregulated glycolysis-HIF1A pathway was associated with heightened inflammasome signaling and impaired viral clearance. In contrast, healthy controls showed downregulated OXPHOS, reduced type I/III IFN production, and efficient viral clearance. It might further influence epithelial response to subsequent infections with other respiratory viruses, such as SARS-CoV-2.

S24 Sepsis-associated immunosuppression: long-term effects on pediatric innate immune cells and their immunometabolic status.

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Sepsis is a heterogeneous syndrome with dynamic progression, yearly affecting 50 million people worldwide, where around 40% of patients are children under 5-year-old. Survivors frequently suffer with immunosuppression, which can persist many months after sepsis onset and impede the patient's full recovery. The exposure of myeloid cells to environmental stimuli such as invading pathogens or pathogen-originated ligands is followed by their activation leading to a metabolic switch associated with phenotypic changes. The metabolic switch is necessary to obtain sufficient energy and intermediate metabolites to execute the defending processes against invading stimuli. Detailed characterization of immune cells' immunometabolic status and phenotypic alterations together with patient clinical status represent possible approach how to depict the sepsis dynamics, especially with emphasis to the long-term consequences of sepsis in pediatric patients. Using state-of-the-art techniques – immunophenotypization and single-cell metabolic analysis 'SCENITH' we depicted specific sepsis-induced alterations in myeloid cells from blood of pediatric patients, collected within three time points. We found changes in monocytic subsets frequency and altered expression of HLA-DR, CD86, or CD36 together with specific cytokine pattern. We also revealed the metabolic alterations across all innate immune cells. All markers were correlated to the severity of sepsis (pSOFA score) to obtain comprehensive information associated also with the clinical picture of patients. We also evaluated the decline of quality of life of these patients using self-reporting SF-36 questionnaire. In summary, we showed a sepsis-induced changes in immunophenotype and immunometabolic profile of myeloid cells of pediatric patients within three timepoints with special emphasis to long-term immunosuppression ~ 6 months after sepsis onset indicating persisting changes in myeloid cell functionality. By further integration of all obtained data by machine learning we will evaluate the potential risk of severe complications' development and design timely treatment strategy to facilitate the patient full recovery.

S25 Epithelial Barrier Theory and Molecular Mechanisms of Tissue Injury in Allergic and Autoimmune Diseases

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Humans are exposed to a variety of toxins and chemicals every day. It is estimated that more than 350'000 new chemicals have been introduced to our lives after 1960s, mostly without any reasonable control of their health effects. There is a plethora of studies pointing to the rapid rise of exposure to many of these harmful substances during the last six decades with their implications on skin and mucosal epithelial barrier functions. According to the epithelial barrier theory (www.epithelialbarriertheory.com), exposure to many of these substances damages the epithelium on the surface of our skin, lungs and intestine. A defective epithelial barrier has been demonstrated in allergic and autoimmune conditions such as asthma, atopic dermatitis, allergic rhinitis, chronic rhinosinusitis, eosinophilic esophagitis, celiac disease, and inflammatory bowel disease. In addition, leakiness of the gut epithelium is also implicated in systemic autoimmune and metabolic conditions such as diabetes, obesity, multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, and autoimmune hepatitis. Finally, distant inflammatory responses due to a 'leaky gut barrier' and microbiome changes are suspected in Alzheimer's disease, Parkinson's disease, chronic depression and autism spectrum disorders. The "epithelial barrier theory" proposes that the rise in epithelial barrier damaging agents linked to industrialization, urbanization and modern life underlies the rise in allergic, autoimmune and other chronic conditions. After breaking of the epithelial barriers by various environmental agents and infections, microbiome which normally floats above the skin and mucosas goes deeper between and beneath the epithelial barrier. Microbial dysbiosis and decreased biodiversity develop following the colonization of opportunistic pathogens. An "epithelitis" with the release of alarmins and multiple chemokines initiates the immune response and inflammation inside and beneath the epithelium with the aim of "expulsion response" to deeper and dysbiotic microbiome and pollutants and toxic substances reaching to deeper tissues, because of epithelial barrier defects. Oxidative stress, endoplasmic reticulum stress and protein folding defects, mitochondrial stress, DNA repairy delay and failures, and innate immune response have been identified as key mechanisms of tissue injury and inflammation. Cells and cytokines leak to the circulation from the barrier defective tissues and cause inflammation in target tissues in distant organs as repeatedly demonstrated in diabetes, rheumatoid arthritis and multiple sclerosis experimental models and patients. Disturbed epithelial barrier healing capacity because of microbial dysbiosis, chronic tissue inflammation and epigenetic mechanisms lead to the chronicity of the disease.

S26 Optimising antibody affinity maturation; how to win big without losing it all

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Germinal centers (GCs) are specialized sites where B cells can enhance their antibody affinity through a process called affinity maturation. Within GCs, B cells with higher-affinity antibodies are selectively expanded, dividing at rates proportional to their affinity. This process is coupled with antibody gene mutagenesis, estimated to occur at a rate of 1 mutation per 1,000 base pairs per division. However, because these mutations are random, harmful mutations are more probably than beneficial ones. This risk is particularly significant for high-affinity B cells, which undergo more divisions, mutate more and as such might experience a decline in antibody quality rather than an increase. In this study, we tested a model suggesting that affinity maturation is optimized by reducing mutation rates within high-affinity B cells. Experiments in mice immunized with SARS-CoV-2 or a model antigen support this hypothesis. High-affinity GC B cells were found to lower their mutation rates by shortening the G1 phase of their cell

cycle, thereby minimizing mutation-inducing activity.

S27 The regulation of immune response and inflammation by cannabinoids and their receptors

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The endocannabinoid system (ECS) is a complex signalling network involved in different physiological processes. Alterations of the ECS are associated with several diseases such as cancer, autoimmunity, neurodegenerative disorders or allergy. Due to their anti-inflammatory and immunomodulatory properties, cannabinoids have been pointed out as potential suitable therapeutic tools for inflammatory immune-mediated diseases. The synthetic cannabinoid WIN55212-2 (a CB1 and CB2 agonist targeting also other alternative receptors) induce tolerogenic dendritic cells (DCs) able to polarize functional regulatory T cells (Treg) by mechanisms depending on autophagy and metabolic rewiring. The epithelial cells (ECs) barrier function in the airways, gut or skin is defective in allergic patients, favoring the penetration of exogenous substances and chronic inflammation. WIN55212-2 restores human rhinovirus 16 (HRV-16)-induced bronchial epithelial disruption and reduces IL-13-induced epithelial barrier damage in air-liquid interface (ALI)-cultures of primary human bronchial epithelial cells (HBECs) and bronchial epithelial spheroids, which is further confirmed in vivo in asthma mouse models. Mechanistically, WIN55212-2 impairs IL-13-induced ROS production in HBECs cells restoring the activity of protein tyrosine phosphatases, which in turns inhibits STAT6-mediated signaling pathways and asthma features. Collectively, our data indicate that the synthetic cannabinoid WIN55212-2 display anti-inflammatory properties and strength epithelial defenses, which might well pave the way for the development of future cannabinoid-based vaccines for the prevention and treatment of asthma and other chronic inflammatory airway diseases.

S28 Using multi omics to discover drivers of seroconversion to Islet Autoimmunity using the ENDIA longitudinal Type 1 diabetes cohort.

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The intersection of T1D genetic risk and environmental factors are known to drive islet autoimmunity, which occurs as a result of the breakdown of immunological tolerance. This is linked to loss of function of Regulatory T cells (Tregs), which prevent inappropriate immune attack on beta cells. We used a multi omics approach to comprehensively annotate the genetic and epigenetic changes in T cells from children at risk of T1D using 3D genomics (bulk and sc RNAseq and ATAC seq; HiC and enhancer annotation). Comparing T cells from individuals with and without islet autoimmunity and/or T1D identifies the specific genes that are linked to T1D risk for therapeutic targeting. We have applied this to three cohorts of T1D. We identified 675 loci in Treg that were differentially accessible in adolescent cases vs controls, and 352 genes that were differentially expressed in the same samples. From this we annotated 41 enhancers containing T1D snps linked to genes/pathways disrupted in T1D. We then applied single cell RNAseq to PBMC from child cases vs controls and of 3100 differentially expressed genes 105 were linked to known T1D risk, and ~30% of these overlapped with the bulk RNA seq data. This identifies epigenetic changes in T1D cases but does not separate cause from consequence of progression. Therefore, we analyzed longitudinal Treg and Tconv samples from cases and controls at 2 timepoints: prior to the onset of islet autoimmunity and at the first sample post seroconversion. Of 2200 differentially expressed genes we identified 63 genes in Treg pre seroconversion linked to T1D risk and 29 were also altered in Treg from clinical T1D. Analyzing samples spanning the natural history of T1D from birth until established disease will allow us to separate causal changes in the epigenome from consequences of the underlying pathology.

S29 Cytokine-mediated epithelium–immune cell crosstalk

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The tissue-immune cell interface plays a pivotal role in maintaining integrity and homeostasis at mucosal barrier sites, profoundly influencing organ physiology. However, much of this complex biology remains poorly understood due to historical immunological focus on lymphoid tissues. In my group, we hold a specific focus on investigating the crosstalk between innate tissue-resident immune cells and non-immune cells within their respective tissue niches, with a specific emphasis on the lung and the intestine. Our primary objectives revolve around comprehending how these interactions shape organ physiology during fetal development and contribute to tissue homeostasis and inflammatory processes in adulthood. To unravel the molecular and cellular mechanisms underlying this interplay, we focus on identifying critical cellular modules, studying them under both homeostatic and inflammatory conditions.

S30 Decoding T Cell Cytotoxicity via Single-Cell CRISPR Screens in Droplets

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In the first part of the presentation, I will present a microfluidics-based platform for two-cell type CRISPR screens. Cytotoxic CD8+ T cells (CTLs) are pivotal effectors in tumor elimination, yet a comprehensive understanding of the genes regulating their cytotoxicity against cancer cells has been technically challenging. We developed a droplet-based microfluidics CRISPR screening platform that enables high-throughput, single-cell interrogation of CTL function. Individual CTLs with genetic perturbations are encapsulated alongside target cancer cells in picoliter droplets, where killing activity is assessed. Droplets are then sorted based on cytotoxic outcomes, followed by retrieval and analysis of sgRNAs. This approach faithfully recapitulated known mechanisms of T cell cytotoxicity and uncovered novel regulators. In the second part of my presentation, I will briefly describe our efforts to use live bacteria to potentiate anti-tumor T cell responses. We found that oral administration of L-arginine increased the number of tumor-infiltrating T cells, acting synergistically with PD-L1 blockade to induce tumor regression. Due to practical limitations associated with high-dose L-arginine administration, we developed an engineered probiotic bacterium capable of converting ammonia—a common metabolic waste product in tumors—into L-arginine. This strategy demonstrated synergistic effects with PD-L1 blockade, leading to enhanced tumor clearance.

S31 Fibroblastic reticular cells generate protective intratumoral T cell environments in lung cancer

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Stringent control of T cell activity in the tumor microenvironment is essential for the generation of protective antitumor immunity. However, the identity, differentiation, and functions of the cells that create critical fibroblastic niches promoting tumor-infiltrating T cells remain elusive. Here, we show that CCL19-expressing fibroblastic reticular cells (FRCs) generate interconnected T cell environments (TEs) in human non-small cell lung cancer including tertiary lymphoid structures and T cell tracks. Analysis of the FRC-T cell interactome in TEs indicated molecular networks regulating niche-specific differentiation of CCL19-expressing fibroblasts and T cell activation pathways. Single cell transcriptomics and cell fate-mapping analyses in mice confirmed that FRCs in TEs originate from mural and adventitial progenitors. Ablation of intratumoral FRC precursors decreased antitumor T-cell activity, resulting in reduced tumor control during coronavirus vector-based immunotherapy. In sum, specialized FRC niches in the tumor microenvironment govern the quality and extent of antitumor T cell immunity.

S32 Tuft Cells Shape Airway Remodeling By Eliciting OXGR1- and SOX9-Dependent Stem Cell Programs

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Tissue-resident stem cells play an essential role in repairing barrier tissues subjected to frequent insults. However, the local cues that coordinate barrier repair are largely unknown. Here we identify that rare tuft epithelial cells sense barrier breakdown and signal to submucosal stem cells through the generation of cysteinyl leukotrienes (CysLTs) and activation of the CysLT receptor OXGR1. This results in mobilization of SOX9+ submucosal gland progenitors, poor repair of the surface airway epithelium, and durable features of airway remodeling including submucosal gland hyperplasia and collagen deposition. Remarkably, selective deletion of SOX9 from the airway stem compartment allows epithelial restoration and prevents tissue remodeling. These findings demonstrate a tuft cell-OXGR1- and SOX9- circuit that remodels the airway after injury and is detected in the human sinus mucosa.

S33 Intestinal Organoids as translational tools in Inflammatory Bowel Diseases (IBD)

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Inflammatory Bowel Diseases (IBD), including Crohn's disease and ulcerative colitis, are chronic inflammatory conditions of the gastrointestinal tract that present significant clinical challenges due to their relapsing nature and heterogeneity in response to treatment. Intestinal epithelial organoids (IEOs), derived from patient mucosa, offer a unique translational platform for studying epithelial cell function and developing novel therapeutic strategies. These patient-derived IEOs faithfully recapitulate the cellular diversity and function of the intestinal epithelium, providing an invaluable resource for personalized medicine. Our research focuses on leveraging genome-wide DNA methylation (DNAm) profiling to unravel key epigenetic mechanisms driving epithelial cell dysfunction in IBD. By analyzing over 300 IEOs from pediatric IBD patients and matched healthy controls, we have identified intestinal epithelial MHC-I as a novel mechanism in Crohn's disease. Importantly, our findings suggest that the intestinal epithelium acts as a non-classical antigen-presenting cell, contributing to chronic relapsing inflammation by actively participating in immune responses. This talk will highlight the potential of IEOs as a model for studying epithelial-immune interactions, identifying biomarkers, and developing new treatment strategies for IBD, emphasizing the role of DNAm in regulating these processes. Our discoveries offer new insights into the complex pathophysiology of IBD and open avenues for personalized therapeutic approaches targeting epithelial function in chronic intestinal inflammation.

S34 Organoids to model human disease

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The intestinal epithelium is the most rapidly self-renewing tissue in adult mammals. We originally found that Lgr5+ve crypt base columnar cells (CBC) generated all epithelial lineages throughout life, implying that they represent the stem cell of the small intestine and colon. Lgr5 was subsequently found by us to represent an exquisitely specific, yet 'generic' marker for active epithelial stem cells, including in hair follicles, kidney, liver, mammary gland, inner ear, tongue and stomach epithelium. Single sorted Lgr5+ve stem cells can initiate ever-expanding organoids in the lab. These organoids recapitulate key aspects of the organ from which the stem cells were taken. 3D organoids have been developed for the Lgr5+ve stem cells of human stomach, liver, pancreas, prostate, kidney, breast and many others. Using CRISPR/Cas9 technology, genes can be efficiently modified in these organoids . Organoid technology opens avenues for the study of development, physiology and disease, for drug development and for personalized medicine. In the long run, cultured mini-organs may replace transplant organs from donors and hold promise in gene therapy.

S35 Obesity impairs skin barrier function and facilitates allergic sensitisation

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Atopic dermatitis (AD) is a chronic inflammatory skin disease characterised by pruritus and a compromised skin barrier, often leading to heightened immune responses and increased susceptibility to allergens. Recent studies suggest a link between obesity and an increased risk of certain allergic diseases, including AD; however, the underlying mechanisms connecting obesity and AD remain poorly understood. We hypothesised that obesity compromises skin barrier integrity, facilitating allergen penetration and thus promotes allergic sensitisation. To explore this, we utilised a diet-induced obesity (DIO) mouse model to examine skin barrier integrity and immune responses in both steady-state and inflammatory conditions. Our results show that obesity significantly alters skin barrier physiology, as indicated by increased transepidermal water loss (TEWL) in obese animals compared to lean controls. Over time, we observed a decrease in key skin barrier proteins - preceding inflammation -, further indicating a loss of barrier integrity during obesity. On a cellular level, immune profiling revealed a shift towards a type 17 helper T-cell (Th17) response bias, although this shift did not coincide with an increase in cytokine production under steady-state conditions. Upon topical application of MC903, a vitamin D3 analogue used to induce AD-like inflammation, obese animals displayed increased ear swelling and more pronounced Th17-biased inflammation compared to lean counterparts. These findings suggest that obesity disrupts skin barrier integrity, potentially allowing greater allergen penetration and facilitating allergic sensitisation. The Th17-biased immune environment observed in the skin of obese animals may also predispose them to enhanced inflammatory responses upon allergen exposure. This study highlights a mechanism by which obesity-induced skin barrier dysfunction could contribute to the development of allergic conditions such as AD. Our results underscore the importance of skin barrier restoration and immune modulation as potential therapeutic strategies for individuals with obesity and atopic disorders.

S36 Commensal-pathogen interactions in the upper respiratory tract as a source for microbiota-targeted treatments

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Antibiotic resistance is challenging current treatments for pathogens like Staphylococcus aureus and Streptococcus pneumoniae, which mainly rely on antibacterials. An alternative approach is the artificial inoculation of commensal bacteria—probiotic treatment—supported by evidence of commensal-mediated pathogen inhibition in vitro and microbiota studies showing negative associations. To explore this strategy, we employed a well-established 3D organotypic human airway model that mimics a tissue-like environment during bacterial colonization. Our study demonstrates that colonization with the upper respiratory tract commensal Dolosigranulum pigrum significantly reduces the survival of S. aureus while preserving epithelial barrier integrity. This effect appears to be driven by a synergistic interaction with tissue-resident monocyte-derived cells as D. pigrum exposure improved the intracellular killing of S. aureus. D. pigrum colonization modulated cytokine response in the model. It increases IL-8 and IL-1β levels while reducing S. aureus-induced TNF-α and S100A8/A9. In experiments with human monocytes and GM-CSF macrophages, exposure to live D. pigrum before a S. aureus challenge enhanced IL-8 secretion and dampened TNF-α production. In contrast, heat-killed D. pigrum failed to exert these cytokine modulatory effects, underscoring the necessity of live bacteria for effective host interaction. A thorough understanding of these host-microbiota interactions will pave the way for microbiota-targeted treatments designed to prevent or treat infections with pathogens.

S37 High-dimensional profiling of the antibody repertoire in gastrointestinal inflammatory diseases

Thomas Vogl
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Our current conception of antibody repertoires is mostly based on DNA sequencing of the respective antibody genes (B cell receptors - BCRs), whereas the actual antigens recognized are vastly unknown. My lab strives to unravel the functional capacity of these enormous immune repertoires targeting microbes, and to shed light on their role in human health and diseases such as Crohn's and ulcerative colitis. We apply phage-display immunoprecipitation sequencing (PhIP-Seq) allowing to study human antibody repertories at unprecedented depth. We typically test for antibody binding against hundred thousands of antigens in hundreds to thousands of individuals. Here, I will give an overview of our work with collaborators in inflammatory bowel diseases, leveraging prediagnostic cohorts as well as complementary adaptive immune profiling methods.

S38 Personalized medicine based on deep human phenotyping

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Recent technological advances allow large cohorts of human individuals to be profiled, presenting many challenges and opportunities. I will present The Human Phenotype Project, a large-scale (>25,000 participants) deep-phenotype prospective longitudinal cohort and biobank that we established, aimed at identifying novel molecular markers with diagnostic, prognostic and therapeutic value, and at developing prediction models for disease onset and progression. Our deep profiling includes medical history, lifestyle and nutritional habits, vital signs, anthropometrics, blood tests, continuous glucose and sleep monitoring, and molecular profiling of the transcriptome, genetics, gut and oral microbiome, metabolome and immune system. Our analyses of this data provide novel insights into potential drivers of obesity, diabetes, and heart disease, and identify hundreds of novel markers at the microbiome, metabolite, and immune system level. Foundation AI models that we developed provide novel representations of the diverse modalities that we measured on the cohort and achieve state-of-the-art performance in predicting future onset of disease and trajectories of disease risk factors. Overall, our predictive models can be translated into personalized disease prevention and treatment plans, and to the development of new therapeutic modalities based on metabolites and the microbiome.

S39 Anti-Nucleocapsid Antibodies of SARS-Cov2 as Predictors of Post-Acute Sequelae of COVID-19 (PSAC) Severity in Pediatric Patients: Insights from the DISCOVER Cohort in Taiwan

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Post-acute sequelae of COVID-19 (PASC) pose challenges in pediatric care due to the lack of standardized diagnostics. This study explores clinical and immunological aspects of PASC in children, focusing on anti-nucleocapsid (anti-N) antibodies. The Diagnosis and Support for COVID Children to Enhance Recovery (DISCOVER) cohort, initiated in July 2022, enrolled pediatric patients with PASC in central Taiwan. A specialized PASC condition scale, covering cardiovascular, respiratory, gastrointestinal, musculoskeletal, and neuropsychiatric symptoms, was developed. Blood samples were analyzed for biomarkers, including IgG against SARS-CoV-2 antigens and nucleocapsid gene measurements. Among 92 participants, the mean PASC condition scale score was 33.48±23.89, with higher cardiovascular and respiratory scores. Positive correlations existed between PASC scores and monocytes (R^2=0.284, p<0.01), neutrophils (R^2=0.207, <0.05), and hsCRP (R^2=0.250, p=0.06). Negative correlations were found with eosinophils (R^2=-0.275, <0.01) and lymphocytes (R^2=-0.181, p=0.09). Virus persistence was minimal, yet anti-N IgG levels correlated positively with RDW (R^2=0.253, <0.05) and monocytes (R^2=0.230, <0.05) and negatively with MCV (R^2=-0.213, <0.05). ROC analysis identified anti-N IgG as a predictor for PASC severity, with an optimal cutoff value of 11. This study sheds light on PASC in children, highlighting the significance of anti-N IgG in assessing severity and serving as a potential early predictor. These insights contribute to post-COVID care strategies, especially in pediatrics, and pave the way for further research on the immunological aspects of PASC.

S40 Circulatory microinflammation and its association with serum antibody epitope repertoires by PhIP-sequencing

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Understanding the variations in inflammatory states among seemingly healthy individuals can provide important insights into predisposition to chronic diseases. We aimed to examine circulatory microinflammation in a group of healthy controls and evaluate its relationship with their serum antibody epitope repertoires. Targeted proteomics using the Olink® inflammation, immune response, metabolism, organ damage and cell regulation (total 451 proteins) panels and phage-immunoprecipitation sequencing (PhIP-seq) were performed on serum samples collected from healthy individuals (n = 105). Here we have profiled the serum antibody responses against 344,000 rationally selected peptide antigens derived from gut microbiota and pathogenic and probiotic bacteria. Our results revealed that the healthy cohort could be divided into three distinct subgroups based on the levels of inflammatory proteins: high-inflammatory, middle-inflammatory and low-inflammatory. When we compared healthy individuals with low-inflammatory and high inflammatory, eight protein clusters defined by spearman correlation matrix according to relative serum levels. When we look at the hazard ratios for each previously identified disease from the UK Biobank in relation to proteins associated with all-cause mortality, we observe that three clusters are formed, similar to previous findings. We observed differences in linear antibody responses between the groups. Interestingly, these strong responses against commensal bacteria were identified in healthy individuals with low circulatory microinflammation. These findings suggest that even within healthy individuals, there can be significant differences in baseline inflammation related proteins, potentially indicative of early and subclinical physiopathological disturbances. Although these individuals may not present any clinical symptoms currently, the sustained elevation of inflammation may predispose them to an increased susceptibility to chronic conditions in the future.

S41 A break in mitochondrial endosymbiosis as a basis for inflammatory diseases

Luke O`Neill
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Metabolic changes triggered during innate immunity have become a particular focus for researchers interested in inflammation, whilst cancer researchers have had a long standing interest in metabolic disturbance since the days of Warburg. Mitochondrial disturbance is a feature of inflammatory cells and we have been analysing the Krebs cycle intermediates succinate and fumarate, as well as the Krebs cycle-derived metabolite itaconate, in activated macrophages in response to signalling by Toll-like receptors. Itaconate derivatives are anti-inflammatory and have potential for the treatment of immune and inflammatory diseases. Fumarate is proving to be a very interesting metabolite. It is generated via repression of the enzyme FH and also induction of the argininosuccinate shunt. Fumarate suppresses IL10 production which in turn leads to increased TNF. The decrease in FH however also leads to mitochondrial disturbance, which involves release of double-stranded mitochondrial RNA. This is sensed by the RNA sensors RIG-I, MDA-5 and TLR-7 driving production of Type I Interferons. Metabolites like fumarate are therefore acting as signals and impacting on signalling pathways in unexpected ways. Overall evidence is growing that a break in mitochondrial endosymbiosis might be a reason for the increasing indicence of autoimmune and inflammatory diseases. These insights are providing a new view of metabolism in immunity and inflammation and might indicate new therapeutic approaches.

S42 Inflammatory responses to pyroptosis

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German Rheumatism Research Center, Berlin, Germany

Cell death is a pivotal event in immune responses, with profound implications for tissue homeostasis and inflammation. This talk will explore the mechanisms by which cell death is recognized by bystander cells and the immune system, with a particular focus on inflammasome activation and its downstream effects. Upon activation, inflammasomes induce pyroptotic cell death, leading to the release of various pro-inflammatory cytokines from the IL-1 family. These cytokines are processed by a variety of proteases and can act in both autocrine and paracrine manners, shaping the immune landscape. Recent studies have shown that inflammasome activity also triggers the rapid release of extracellular vesicles, which carry specific RNAs that influence bystander cells upon uptake. Additionally, inflammasomes can induce the release of metabolites, which are sensed by neighboring cells triggering various pathways promoting repair and inflammatory responses. This talk will provide an overview of these dynamic inter-

actions and highlight the spatial regulation of cytokine release and its implications for immune regulation and disease progression.

S43 Single Nucleotide Variations in Human Endogenous Retroviral Sequences can affect peptide presentation by HLA-B27: Implications for Viral Mimicry and Ankylosing Spondylitis

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The etiology of ankylosing spondylitis (AS), an autoimmune condition with a significant association with the HLA-B27 genotype, remains incompletely understood. We investigated a novel mechanism involving single nucleotide variations (SNVs) within human endogenous retroviral (HERV) gene sequences in the HLA-B27 genomic region and their potential impact on AS pathogenesis. Specifically, we explored how an SNV (rs13202464) alters the binding affinity of the HLA-B27 molecule to self and microbial peptides. Our study hypothesizes that this SNV-induced missense mutation (methionine to threonine) may lead to differential T cell selection during immune development, where HSV peptides that mimic self-proteins are insufficiently tolerated. We compared predicted peptide binding to HLA-B27 using predictive modeling utilizing the Immune Epitope Database suite, demonstrating decrease in binding affinity for peptides in HLA-B27-positive individuals carrying the variant by a ten-fold increase in the predicted ANN IC50 values. This potentially could initiate AS pathogenesis, through either altered thymic selection or triggering molecular mimicry through sequence similarity between HSV- and HERV-derived peptides. Our findings underscore the need for further investigation into the interplay between HERV sequences, viral mimicry, and immune tolerance to identify novel therapeutic strategies targeting AS at its genetic and immunological roots.

S44 Single-Cell RNA and TCR sequencing suggests a key role for tissue-infiltrating EOMES+Tr1-like cells and their circulating precursors in autoimmune diseases

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EOMES+ regulatory T-cells produce IL-10 (EOMES+Tr1-like cells) and are involved in several immune-mediated diseases. We analyzed single-cell RNA and TCR sequencing datasets of CD4+T-cells from patients with autoimmune diseases. Gene set enrichment analysis identified clusters of EOMES+Tr1-like cells in multiple sclerosis (MS) and in juvenile idiopathic arthritis (JIA). They were located in the vicinity of cytotoxic effector T-lymphocyte (CD4+CTL) clusters in the UMAPs, suggesting that these clusters may represent distantly related differentiation stages. EOMES+Tr1-like cells were enriched and clonally expanded in the cerebrospinal fluid (CSF) in MS and in the synovial fluid in JIA. In MS, an additional cytotoxic cluster of GzmK+CCR6+T-cells was identified. This cluster was neither enriched nor clonally expanded in the CSF, displayed a gene signature of pro-inflammatory Th1/17-cells and was located distantly from EOMES+Tr1-like. Unsupervised sub-clustering of Tr1-like cells identified IL7RhiGzmK+Th1-like cells that expressed memory-associated genes, in contrast to IL7RloTr1-like effector subclusters. Cells from the same clones showed interactions between these subclusters, with IL7RhTh1-like cells being predominantly present in the blood and L7RloTr1-like cells in the target tissue. Furthermore, IL7RloTr1-like effector cells separated into two major subclusters, suggesting divergent fates, sustained also by trajectory analysis: (CTLA4+Tr1-like cells, characterized by elevated expression of genes regulating IL-10 expression that represented a terminally differentiation stage and (CHI3L2+Tr1-like cells that expressed increased levels of cytotoxic mediators and that were predicted to differentiate further to effector CTLs. Collectively, these observations suggest a key role for EOMES+Tr1-cells and their recirculating precursors in autoimmune diseases. Furthermore, they suggest that some Tr1-like cells might be able to differentiate to conventional CTL, and thus to switch back from regulatory to effector functions.

S45 Stromal -immune interactions drive asthma pathology in children and adults

Clare Lloyd
NHLI, Imperial College London UK

Maintaining the balance between immune homeostasis and inappropriate immune activation and ensuing pathology is particularly complex at mucosal sites that are constantly exposed to potentially antigenic particles. The growth and maturity of the peripheral immune system and subsequent development of pulmonary immunity in early life is dictated by host, environmental and microbial factors. Dysregulation during the critical window of immune development in the postnatal years results in disease which impacts on life-long lung health. We have examined immune pathways in the respiratory tract during early life using samples from children and adults in combination with age-appropriate murine models of allergic inflammation. To gain insight into the mechanisms underlying airway remodelling we have applied single-cell spatial transcriptomics to map the airway wall landscape in health and during asthma. We identified proinflammatory cellular ecosystems, that exist within discrete spatial niches in healthy and asthma samples. These cellular hubs are characterised by a high level of chemokine and alarmin expression, along unique combinations of stromal cells. Investigation into the interactions between structural airway cells and the developing immune system has shown that the Type 2 immune pathways that are characteristic of asthma also contribute to tissue repair and remodelling in the lung. We have determined that the local environment provides directional cues that dictate the motility and function of immune cells within the lung, and this impacts the course and magnitude of local tissue inflammation. This presentation will focus on the cellular and molecular interactions that govern development of inflammation and remodelling in the lung following allergen exposure.

S46 Metabolic Regulation of Human Th2 Cells in Health and Disease

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Swiss Institute of Allergy and Asthma Research (SIAF), University of Zurich

CD4+ T helper 2 (Th2) cells play a central role in allergic inflammation and immunity to helminths, yet their metabolic regulation remains incompletely understood. Emerging evidence reveals that metabolic programming critically shapes Th2 cell function, proliferation, and differentiation. Distinct metabolic signatures of Th2 cells, including their enrichment in amino acid metabolism, have been recently identified. Specifically, L-phenylalanine emerges as a key regulator, enhancing glycolysis while limiting oxidative phosphorylation (OXPHOS) in memory and effector CD4+ T cells, including Th2 cells. Dysregulation of amino acid transport, particularly impaired LAT1-mediated uptake of L-phenylalanine, characterizes Th2 cells in allergic dseases, leading to increased intracellular processing and an expansion of pathogenic Th2 subsets. Beyond amino acid metabolism, Th2 cells display a reliance on glycolysis for effector function, while oxidative metabolism and lipid catabolism have been implicated in regulatory T cell (Treg) stability and immune tolerance. In allergy, metabolic rewiring of Th2 cells correlates with disease severity, suggesting that metabolic checkpoints, such as L-phenylalanine availability and utilization, could serve as potential therapeutic targets. Understanding the interplay between cellular metabolism and immune regulation provides new avenues for modulating Th2-driven pathologies.

S47 Airway Inflammation Drives Resting to Inflammatory Transition of Lung Eosinophils

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Eosinophils constitute a small population of resident immune cells in the lungs under homeostatic conditions. However, during airway inflammation, eosinophils are rapidly recruited to the lungs, contributing to tissue damage and exacerbating inflammation. Intriguingly, lung eosinophils have been divided into two distinct subsets: resident and inflammatory eosinophils population, the latter being abundant during airway inflammation. Whilst anti-IL-5 biologics have shown promise in selectively targeting inflammatory eosinophils to treat airway inflammation, studies suggest that all lung eosinophils depend on IL-5, questioning the true extent of eosinophil heterogeneity in the lung. Here, we aimed to dissect the heterogeneity of lung eosinophils using single-cell RNA sequencing (scRNA-seq), flow cytometry and immunofluorescent imaging. Our analysis identified five distinct eosinophil clusters within the lung, representing a continuum from a cyclic precursor state to an activated subset. Notably, we found no arrival of a new eosinophil populations during inflammation. Instead, inflammation prompted a shift of pre-existing eosinophils toward an activated state, suggesting that 'resting' eosinophils transition into an inflammatory phenotype rather than being replaced by newly recruited populations. Furthermore, both populations were spatially segregated, with resting eosinophils present in the lung parenchyma and inflammatory eosinophils localising to the airway epithelium. We further identified that inflammatory cues within the lung microenvironment drive the transition from resting to inflammatory eosinophils. Notably, IL-33, potentially derived from local epithelial niches, plays a key role in promoting the inflammatory eosinophil phenotype. The resting-to-inflammatory transition was further induced following in situ maturation in the lung microenvironment. Together, our findings

provide new insights into eosinophil dynamics, their spatially distinct niches, and their functional plasticity during lung inflammation, offering new avenues for developing targeted therapies to better manage eosinophil-driven lung diseases.

S48 Targeted Proteomics Reveals the Action Site of Tralokinumab in Atopic Dermatitis: The Skin

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Tralokinumab is a human monoclonal antibody that specifically targets interleukin-13 (IL-13), a key cytokine involved in the pathogenesis of atopic dermatitis (AD). It is administered subcutaneously into the thigh, with an initial 600 mg loading dose, followed by 300 mg every other week for 16 weeks. Several clinical studies, trials, and a meta-analysis have confirmed its efficacy in reducing disease severity and improving various clinical endpoints. In an investigator-initiated study at the University Hospital Zurich, sponsored by LEO Pharma, we aimed to gain deeper insights into the molecular mechanisms underlying Tralokinumab's clinical effects. Specifically, in our laboratory, we investigated its accumulation in the serum and skin of patients after 4 and 16 weeks of treatment. To assess Tralokinumab accumulation in the skin, we first optimized a proteomics workflow for skin swabs, a non-invasive sampling method. By comparing different extraction protocols, we identified a method that enabled the detection of approximately 1000 proteins per sample, considerably more than obtained with skin strips. In the clinical study, serum samples, skin biopsies, and skin swabs were analysed using targeted mass spectrometry with parallel reaction monitoring (PRM), incorporating heavily labelled synthetic peptides to detect unique peptides from Tralokinumab, Periostin, and Loricrin. Our analyses confirmed the previously reported increase of Tralokinumab in serum after 4 weeks of treatment. Additionally, we detected Tralokinumab accumulation in the skin both in biopsy and skin swab samples. These findings suggest that Tralokinumab accumulates in the skin to capture IL-13, contributing to symptom improvement at sites distant from the injection site. Furthermore, we demonstrate that skin swabs provide a valid, non-invasive alternative for assessing the skin proteome, with potential applications for future dermatological studies.

Workshop Abstracts

W01 Sepsis induced tissue specific dysregulation analysed through model of 3D iPSCs derived organoids.

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Sepsis and septic shock are characterized by dynamic immune system changes resulting in deregulated inflammation and homeostasis failure. Circulating neutrophils, monocytes, and other innate immune cells are the first responders recognizing and clearing pathogens while producing a plethora of immune mediators. This prompt activation of the immune system eventually results in negative outcomes, including the induction of fundamental damage on many levels. Sepsis-injured hematopoiesis produces immune cells with altered functionality, whereas mucosal tissues also lead to further tissue remodulation. All these processes can eventually dampen the patient's recovery after sepsis. This project aims to characterize the processes orchestrating the onset of sepsis reflect dynamics and its progression, using several unique models of 3D tissue organoids. The project aims to define factors governing the damage and further remodulation of mucosal tissue and hematopoiesis impeding full recovery from sepsis using models of iPSCs-derived organoids. Cytokine and chemokines signatures were identified in blood samples of septic shock patients collected within first 12 hours of ICU admission. The signatures have been associated with sepsis severity and survivorship and used to trigger hematopoiesis and innate response in iPSC derived mucosal organoids in order to model sepsis progression and recovery. We described distinct cytokine patterns associated with sepsis severity and outcome. We defined the role of cytokines in the sepsis-induced remodeling of mucosal tissues, where we observed dampened tissue integrity and increased permeability. We also used a preclinical model of bone marrow based on human iPSCs, depicting profound changes in tissue homeostasis and cell migration induced by sepsis-born factors. This project identified how combinations of cytokines associated with septic shock impact homeostasis in various tissue systems. Such an approach based on a fully human 3D preclinical model may propose future personalized therapy targeting improved septic shock recovery.

W02 Micro- and nanoplastics with diverse sizes and chemical structures compromise barrier integrity, cause extensive epithelial cell injury, and induce oxidative and endoplasmic reticulum stress

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Plastic pollution is an escalating global crisis, and growing evidence suggests that microplastics can accumulate in various biological systems. This study comprehensively examined the effects of micro- and nanoplastic particles of varying sizes and chemical structures on human gut epithelial cells, peripheral blood mononuclear cells (PBMCs), and nasal organoids. We used commercially available polyethylene particles (1–4 µm), polystyrene (PS) particles with diameters of 0.17 µm, 1–1.4 µm, 4.8–5.8 µm, and 9.5–11.5 µm as well as polyethylene terephthalate (PET) particles developed in-house. A microfluidic gut-on-a-chip system was employed to create a tubular barrier using Caco-2 cells. Epithelial barrier integrity was assessed via transepithelial resistance measurements and paracellular flux assay. Cell viability was evaluated using propidium iodide staining in flow cytometry, and 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) assays, and cell proliferation was analyzed through ^{3}H-thymidine incorporation. In addition, 2′,7′–dichlorofluorescin diacetate (DCFDA) assay was used to determine reactive oxygen species (ROS) levels in Caco-2 and airway cell lines. We performed RNA-seq and targeted proteomics to investigate the effects of microplastics at the molecular level. Smaller-diameter PS particles induced significant cell death even at lower doses. PS (0.17 µm, 1–1.4 µm) and PET impaired epithelial integrity in both gut-on-a-chip and nasal organoids, with PET disrupting the barrier even at low exposure levels (<1000 particles/mL). Upregulated genes were primarily associated with apoptosis, endoplasmic reticulum (ER) stress, and oxidative stress. Notably, ATF4, CHOP, and GRP78 exhibited increased expression at higher PET microplastic concentrations, suggesting that sustained ER stress, induced by protein misfolding, intersects with oxidative stress pathways, ultimately triggering apoptotic cascades. Interestingly, PET, a widely used plastic in daily life, exhibited a recurring pattern that its elevated concentrations induced canonical stress-response elements (NQO1, SOD2, HSPA1B, FOXO3) alongside apoptotic effectors (Bax, CASP3, TRAIL). Higher doses of PS and PET also led to significantly remarkable changes in the targeted proteomics. In conclusion, our results highlight the multifaceted nature of microplastic-induced damage, characterized by impaired barrier function, reduced cellular viability, and widespread transcriptional shifts converging on oxidative stress, ER stress, and programmed cell death pathways.

W03 LPS presence promotes, but is not required for, an ovalbumin induced type 2 mucosal immune response in vitro

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Concurrent mucosal immune activation, via e.g. LPS binding Toll-like receptor 4 (TLR4), has been linked to promoting allergic sensitization. This study investigated the contribution of LPS to ovalbumin (OVA), the major allergen in hen's egg, induced mucosal immune activation in vitro. HT29 human intestinal epithelial cells (IEC) were exposed for 4-24h to LPS or OVA, containing LPS (96ng/mL (OVA-LPShigh), 3,6ng/mL (OVA-LPSlow)) or without LPS (OVA-LPSfree). IEC and/or monocyte-derived dendritic cells (moDCs) were exposed to the OVAs for 48h. Primed moDCs were cocultured for 5 days with allogenic naïve Th cells. Cytokine secretion and moDC phenotype were assessed. Secretion of IL8 and CCL20 increased significantly upon IEC exposure to OVA-LPShigh and OVA-LPSlow, but not with LPS. RNA-sequencing confirmed IEC activation by LPS-containing OVA, in contrast to LPS. OVA-LPSfree induced different gene expression patterns compared to LPS-containing OVAs. MoDCs exposed to OVA-LPShigh and OVA-LPSlow secreted higher IL8 and IL6 levels compared to control. IEC/moDC exposed to OVA-LPShigh showed decreased IL6, IL12p70, and IL10 secretion, while increasing the percentage CD80+ moDCs. OVA-LPSfree exposure decreased IL6 and TNF-alpha secretion compared to control. TGF-beta secretion and RALDH expression were decreased in OVA exposed IEC/moDCs, regardless of LPS content. Subsequent coculture of OVA exposed moDCs with naïve Th cells increased IL13 secretion and decreased IFN-gamma by Th cells, significant for OVA-LPShigh. In contrast OVA-LPSfree reduced both IFN-gamma and IL10 secretion when exposed via IEC. Simultaneous exposure to LPS and ovalbumin in vitro yields a more prominent IEC/moDC response, not solely explained by LPS-induced effects. LPS is not required to steer a type-2 T cell cytokine response in vitro. This study signifies a potential interaction between TLR4 activation and allergen exposure. In vivo relevance is to be explored, as a healthy gut naturally contains LPS.

W04 IL-33-mediated fibroblast-myeloid cell crosstalk controls intestinal granuloma formation

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Formation of highly dynamic and spatially organized granulomas is a common feature of inflammation. However, the intricate interplay between immune cells and fibroblastic stromal cells during the formation of intestinal granulomas has remained largely elusive. Here, we show that the induction of the nuclear alarmin interleukin-33 (IL-33) in lamina propria fibroblasts during the granulomatous immune response to the intestinal helminth Heligmosomoides polygyrus bakeri (Hpb) has a profound effect on granuloma formation and worm clearance. Ablation of IL-33 in intestinal fibroblasts targeted by the Cxcl13-Cre-transgene resulted in impaired cellular composition

and protective properties of granulomas. IL-33-mediated signals initiated the activation of interleukin 1 receptor like 1 (IL1RL1)-positive myeloid cells including the upregulation of discrete singling pathways to support macrophage attraction and fibroblast activation within granulomas. Consequently, IL-33-dependent regulatory circuits led to the induction of the eosinophil chemotactic chemokine CCL11 in fibroblasts, and the subsequent accumulation of eosinophils within granulomas. Overall, these findings highlight the pivotal role of fibroblast-derived IL-33 as a key mediator in controlling local immunological processes within intestinal granulomas.

W05 Food emulsifier polysorbate 80 causes gut barrier disruption and inflammation

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Polysorbate 80 (P80), a widely used emulsifier in processed foods has been linked to alterations in gut barrier function and inflammation. This study investigates the effects of P80 on the gut epithelial barrier and systemic inflammation, using colon cancer cell lines, iPSC-induced human intestinal organoids (HIO), intestine on-a-chip, and murine models. MTT (3-(4, 5-dimethylthiazolyl-2)-2, 5-diphenyltetrazolium bromide) and DCDFA(2',7' –dichlorofluorescin diacetate) assays were used in both CaCo2 cell lines and HIO to detect the effect of p80. NF-kB reporter HCT116 cells were used to detect the effect of p80. Eight-week-old female C57BL/6 mice were treated with 2.5% p80 in their drinking water. After 4 days of treatment, the mice were sacrificed and their gut, aorta, liver, stomach, and sera were analyzed by targeted proteomics, RNA sequencing, and non-targeted proteomics. p80 treatment resulted in cell death down to 0.05% solutions in CaCo2 cell lines and HIO samples. There was up to a fourfold increase in reactive oxygen species (ROS) formation in a dose-dependent manner. p80 treatment resulted in up to a 150-fold increase in NF-kB stimulation which was reversed by N-acetylcysteine administration, demonstrating the role of oxidative stress on NFkB activation. Treatment of mice with p80 in their drinking water resulted in oxidative stress, endoplasmic reticulum stress, failures in DNA repair, cell death by apoptosis, and proinflammatory mediators. Our findings demonstrate that P80 induces significant cytotoxicity, ROS production, and NF-κB activation in both cell-based and murine models, implicating oxidative stress and multiple mechanisms of cellular stress and inflammation in gut barrier dysfunction. N-acetylcysteine's reversal of these effects suggests a potential therapeutic strategy to mitigate P80-induced inflammation and barrier damage. Further analysis is ongoing to explore DNA damage, mitochondrial damage, and proteomics in affected tissues& cells.

W06 Hookworms shape tolerogenic dendritic cell function via metabolic reprogramming

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Atopic diseases arise from inappropriate immune responses to innocuous antigens and are a significant economic burden in industrialised countries. They are difficult to treat and rely on systemic immune suppression and/or symptom management. We have identified a hookworm-derived protein named Anti-inflammatory protein 2 (AIP-2) capable of restoring allergen tolerance and effectively "cure" allergic diseases. AIP-2 shows remarkable immunomodulatory capabilities by specifically enhancing the tolerogenic function of mesenteric conventional dendritic cells type 1 (DC1). However, the molecular mechanisms induced by AIP-2 remain unknown. We have used a multiOMICS systems immunology approach using gene expression, chromatin accessibility, as well as proteomics to identify the protein-receptor interactions, the transcriptomic profiles and epigenetic modification involved in AIP-2 ligation in cDC1s. The cells were sorted according to their tolerogenic function determined by the enzymatic activity of aldehyde dehydrogenase (ALDH) 1a2 responsible for the catalysis of retinoic acid. 10,000 isolated nuclei from each of the four groups (AIP-2 treated high/low ALDH activity, Vehicle treated high/low ALDH activity) were sequenced usingsingle nuclei sequencing and the RNA and ATAC profiles were analysed. Total RNA of the whole cell was also investigated by next generation bulk RNA sequencing. Total cellular protein was extracted and an coprecipitation was conducted to identify potential cell surface binding partners of AIP-2. Two unique cDC1 transmembrane proteins were identified to interact with AIP-2. AIP-2 also induced unique transcriptomic and chromatin profiles in the high ALDH activity. Enriched pathway analysis, chromatin changes, and the surface receptors lead us to propose a mechanism on how AIP-2 is modulating cDC1 tolerogenicity by directly acting on inflammation signalling and mitochondrial metabolism. Elucidating the mechanism of action of AIP-2 is a critical step towards commercial translation, and also provides a foundation for the identification of further novel drug targets for ameliorating inappropriate responses from the adaptive immune system.

W07 IL-33 expands plasma cells, disrupts germinal centers, and increases autoantibody production

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IL-33 is a pro-inflammatory cytokine that plays a critical role in asthma, COPD and autoimmune diseases. The role of IL-33 on B cell maturation and tolerance, however, is poorly understood. Here, we show that IL-33 can induce the differentiation and accumulation of plasmablasts and plasma cells of all isotypes in the spleen leading to increased antibody production. Specifically, we demonstrate that IL-33 induces IL-5 driven production of IgM and IgG2a, as well as CD4+ T cell driven production of IgG1 and IgE. This IL-33 induced antibody production is accompanied by disrupted splenic architecture and elevated autoantibody production, indicating a break in peripheral tolerance. Consistent with this, overexpression of IL-33 exacerbated autoantibody production, kidney damage and decreased survival in a mouse model of lupus. Additionally, intranasal delivery of IL-33 and exposure to house dust mite extract (HDM) both increased autoantibodies in the lung. Notably, blocking IL-33 reduced the autoantibodies generated during HDM exposure, indicating that HDM induced autoantibody production is IL-33 dependent. Taken together, our data demonstrate that IL-33 expands plasma cells, disrupts germinal centers and promotes autoantibody production.

W08 The role of IgD in the development of natural and induced tolerance to allergens

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Introduction: B cells play a role in maintaining immune tolerance through IL-10 production, but there is limited knowledge about additional mechanisms. Although immunoglobulin D (IgD) has been associated with naive populations, it has recently been shown that memory antigen-specific and secreted IgD could be a potential key regulator of homeostasis in allergy and tolerance. Our study aims to explore the complex role of IgD in allergy, natural tolerance (NT), and high-dose allergen exposure models. Methods: Peripheral blood and tonsillar mononuclear cells (PBMCs and TMCs) were cultured with CpG, inducing IL-10-producing regulatory B cells, and expression of IgD and tolerance-related markers were analyzed by flow cytometry. In addition, PBMC-purified B cells were stimulated in conditions such as CpG, sCD40L, IL-21, IL-4, and IL-10. Total Ig(tIg) isotypes were measured in supernatants by multiplex assay. Total IgD and specific IgD(sIgD) and memory (CD27+) IgD+ B cells were evaluated from cow's milk-specific immunotherapy (OIT) cohort, atopic dermatitis patients treated with dupilumab (anti-IL4Ralfa) and bee venom-exposed beekeepers. Results: CD19+IgD+IL-10+ population significantly increased in PBMCs after CpG stimulation. IgD+IgM- B cells co-express CD22 (BCR signalling inhibitor) and Notch2 (marginal zone (MZ) B cell development) however the expression of IL-10 is limited to cells that also express IgM. CpG or IL-21+sCD40L+IL-4 induces higher production of IgD in purified B cells. Circulating CD27+IgD+ B cells express a higher proportion of CD22 and NOTCH2 compared with CD27+IgD- in PBMCs and TMCs. Despite of IL-4 effect in IgD production in vitro, dupilumab (anti-IL-4Ralfa) did not reduce tIgD or CD27+IgD+ B cells in treated patients after 6 months. In the cow's milk cohort, αS1-casein-specific IgD increased dramatically after the OIT group and in NT, compared with before OIT. Finally, frequencies of CD27+IgD+ B cells were higher in beekeepers with long-term allergen exposure and TMCs compared to new beekeepers and non-exposed controls. Conclusions: Memory IgD+ B cells express tolerance and MZ-related markers. CpG and IL-4 seem to induce IgD production by B cells in vitro along with activation and differentiation stimuli but dupilumab treatment does not change the production of IgD. NT, OIT and high-dose allergen exposure increase the levels of sIgD. Higher frequencies of CD27+IgD+

cells were found in long-term allergen exposure and in TMCs. These findings reveal the potential role of IgD in the establishment of immune tolerance however specific mechanisms need to be elucidated.

W09 B cell and Antibody Response to Influenza Vaccination with Thermally Denatured Hemagglutinin

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Background: Hemagglutinin (HA) is the major surface glycoprotein of influenza A virus, involved in receptor binding and viral fusion. Majority of HA research has been conducted using the native folded protein, however during viral entry, acidic conditions within endosomes causes conformational changes of HA, allowing the fusion between the virus and the endosome. Thermal denaturation has previously been shown to unfold HA in a similar manner. In this study we set out to answer two questions: i) What are the differences in B cell and antibody (Ab) response after immunization with native folded vs. thermally denatured HA and ii) Do B cell and Abs recognize different forms of the antigen and what is their functional relevance. Methods: HA was thermally denatured at 37°, 65° or 100° C. C57BL/6 mice were immunized and boosted with each HA protein. Mice were euthanized and their spleens and draining lymph nodes (LN) were collected at the end of the each study for flow cytometric analysis using native or denatured HA conjugated to different fluorophores. Blood serum was collected and tested by ELISA, neutralization assay, and hemagglutination inhibition assay. ELISA plates were coated using native and denatured HA proteins. Results: Flow cytometric analysis demonstrated that Immunization with Native folded HA results in a potent Germinal Center (GC) B cell response compared to denatured HA, however neutralization and hemagglutination assays showed that denatured HA provided a strong neutralization effect against authentic IAV. Ab detection by ELISA showed that regardless of which HA was used for immunization, most HA-species were still recognized. Conclusion: Our data demonstrates that immunization with native and denatured proteins produces a strong B cell and Ab response but denatured HA immunization induces more potent Abs. Furthermore, we show that both native and denatured HA can target a variety of HA-species.

W10 Impact of Surfactants in Oral Care Products on Epithelial Cell Activation and Barrier Dysfunction in Eosinophilic Esophagitis

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Introduction: Eosinophilic esophagitis (EoE) is a chronic immune-mediated condition characterized by esophageal inflammation and tissue remodeling, driven by type 2 immune responses. Both genetic predispositions and environmental factors, such as dietary allergens and irritants are implicated in its pathogenesis. Surfactants like sodium dodecyl sulfate (SDS/SLS)) and cocamidopropyl betaine (CAPB), commonly found in oral care products, may contribute to esophageal epithelial barrier dysfunction. This study aimed to compare the effects of SDS and CAPB on epithelial integrity and immune responses in cells and organoids derived from EoE patients. Methods: Esophageal biopsy samples from five EoE patients were used to develop organoids. SDS (12.5 µg/mL) and CAPB (12.5 µg/mL), relevant to human exposure were applied on day 11. RNA samples were collected after 24 hours for sequencing. Targeted proteomic analysis was conducted on supernatants collected after 48 hours. Air-liquid interface (ALI) cultures were treated with the same compounds, and barrier integrity was assessed via transepithelial electrical resistance (TER) and FITC-dextran assays. Results: Both SDS and CAPB significantly disrupted epithelial barrier function within 48 hours, with SDS having a more pronounced effect. Proteomic analysis revealed key alterations in proteins related to cell metabolism and immune response (e.g., ADGRG1, NECTIN2, CES2, and TGF-alpha). RNA sequencing showed substantial gene expression changes, with 7,234 genes affected by SDS and 7,461 by CAPB. A shared set of 2,560 upregulated and 2,360 downregulated genes suggested common mechanisms, particularly in pathways related to autophagy, cell growth, epithelial differentiation, keratinization, and lipid metabolism. Moreover, cellular response to unfolded proteins and mast cell activation pathways are upregulated. Notably, PRDX5, DUOX1, DUOX2, and SOD2 genes which are important indicators of cellular response to oxidative stress are upregulated. SDS more strongly affected pathways involved in keratinocyte differentiation and digestive system development. Conclusions: This study demonstrates that commonly used surfactants, SDS and CAPB, at doses relevant to everyday exposure, can significantly disrupt esophageal epithelial integrity and alter immune responses. SDS, in particular, exhibited a stronger disruptive effect on both epithelial barrier function and molecular pathways. These findings underscore the potential for oral care products containing these surfactants to exacerbate EoE by impairing epithelial barriers and inducing pro-inflammatory responses.

W11 On the role of Interleukin-1 in regulating allergic B cell responses

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The production of IgE by B cells in response to allergens drives allergic sensitization and inflammation. Recent studies have shown that IgG antibodies can suppress allergic inflammation by acting as negative regulators of IgE function through various mechanisms. Thus, deviating pathogenic IgE responses towards protective IgG responses is a major goal in allergy immunotherapy (AIT). We and others have demonstrated that this can be achieved by allergen display on virus-like particles (VLPs), which boost allergen-specific IgG:IgE ratios. However, the molecular mechanisms by which such approaches deviate germinal center (GC) responses remain incompletely understood. Here, we investigated the role of interleukin-1 (IL-1) in regulating the IgG:IgE balance using mouse models of allergic anaphylaxis. Our findings reveal that follicular T helper (Tfh) and regulatory cells (Tfr) modulate this balance through their IL-1 receptor expression pattern. Notably, B cells themselves emerge as a source of IL-1 following VLP immunization, contributing to the generation of protective IgG responses. Furthermore, we demonstrate that recombinant IL-1 injections enhance allergen-specific IgG:IgE ratios and exhibit both preventive and therapeutic effects in mouse models of AIT. In conclusion, our study identifies IL-1 and its receptors as critical regulators of the IgG:IgE balance, controlling allergic sensitization and inflammation. Potentially, these effects of IL-1 could be harnessed to improve AIT strategies.

W12 PDL1-expressing macrophages infiltrate diffuse large B-cell lymphoma and promote lymphoma growth in a MYC-driven experimental model

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The infiltration of diffuse large- and other mature B-cell lymphomas with T- and myeloid cells is a key tumor microenvironmental feature but is not currently factored into treatment decisions. Here, we have used multiplex immunofluorescence microscopy to quantify the immune infiltrates of >260 diffuse large B-cell- (DLBCL), follicular- (FL) and mantle cell lymphomas (MCL), and chronic lymphocytic leukemias (CLL) relative to clinical outcomes, mutational landscape and phenotype. MCL were found to be the “coldest” and DLBCL the “hottest” entities. The lymphoma microenvironment of DLBCL featured numerically dominant populations of CD8+ and T-follicular helper (Tfh) T-cells that were indicative of superior prognosis. Mutations in EZH2, PTEN and KMT2D were overrepresented in DLBCL with low CD8+ T-cell infiltration. A unique feature of DLBCL was its infiltration by large numbers of PDL1+ macrophages that constituted up to 70% of total cellularity. PDL1+ macrophage infiltration was mutually exclusive with regulatory T-cell infiltration. The inducible ablation of PDL1 on macrophages was sufficient to improve immune control of MYC-expressing lymphoma in a syngeneic immunocompetent model. These results implicate the macrophage/CD8+ T-cell axis as a key pathogenetic determinant and immunotherapeutic

target in a subset of DLBCL patients with poor prognosis.

W13 Impact of cDC2s on ILC2s and eosinophilia in allergic bronchopulmonary aspergillosis

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Allergic bronchopulmonary aspergillosis (ABPA), a severe form of eosinophilic, allergic asthma is caused by the airborne fungal mold Aspergillus fumigatus (Af). The predominant immune response to this pathogen is type 2 immunity-driven, especially T helper 2 (Th2) cells are crucial for the ABPA pathology. However, the contribution of other type 2 immune cells, like type 2 innate lymphoid cells (ILC2s) and type 2 conventional dendritic cells (cDC2s) remains to be investigated. We have established a mouse model that mimics ABPA, which is based on repeated intranasal treatment with a low dose of living Af conidia. Our study revealed that beside Th2 cells, ILC2s play a crucial role for eosinophilia in this ABPA model. Mice lacking cDC2s showed an impaired type 2 immune response with less Th2 cells, eosinophils and ILC2s. Lung cDC2s from ABPA mice expressed the alarmin cytokine IL 33. Selective deletion of IL-33 in cDC2s did not impair the Th2 response, but resulted in lower Gata3 levels in ILC2s, which correlated with diminished lung eosinophilia specifically in male mice. Based on these results, we conclude that cDC2s can enhance Gata3 expression in ILC2s via IL-33, which subsequently promote lung eosinophilia.

W14 Unraveling the Role of Mucosal-Associated Invariant T Cells (MAITs) in Type 2 Inflammation induced by alarmins

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Mucosal-Associated Invariant T cells (MAITs) are unconventional T lymphocytes with a relevant role recently described in respiratory infections. However, MAITs-driven functions remain scarcely investigated in non-infectious inflammatory processes displaying dominant T helper 2 (Th2) components such as allergies. Allergic inflammation processes are initiated by the secretion of the epithelial cell-derived alarmins (IL-33, TSLP, IL-25), often secreted in response to exogenous agents, including allergens. Recent studies have suggested a protective role of MAITs in allergic mice experimental models. However, how human MAITs respond to the presence of alarmins and their actual contribution to the Th2 cell-derived responses has not yet been thoroughly explored. The aim of this study is to investigate the role of circulating human MAITs in Th2-driven inflammatory responses induced by the alarmins. For this purpose, PBMCs from healthy donors were exposed to the alarmins with or without the presence of MAIT-specific activating signals such as 5-OP-RU. In addition, these cells were exposed to antigen-independent signals relevant in both allergic inflammation and MAIT cell biology, such as IL-12. How these alarmins affect cell viability, activation and function of MAIT was examined by flow cytometry. In parallel, we analyzed the effects of alarmins +/- 5-OP-RU +/- IL-12 exposure onto CD4+ T cells by assessing the expression of genes related to the differentiation and function of Th1, Th2 and Th17 cell subsets. Our study demonstrated that alarmins themselves did not alter either the activation or the viability of MAITs. However, alarmins (and specifically IL-33) only when combined with IL-12 significantly induced a Th1-biased phenotype onto the MAITs, contributing to the observed downregulation of Th2 cells-related genes (e.g. IL4, IL5). Further exploration of the molecular mechanisms controlling this pro-Th1 immunophenotype switching on MAITs and its actual contribution at counteracting Th2-driven responses occurring on allergic inflammation are currently under investigation.

W15 Glutathione regulates natural killer cell immunity and mediates tumor control

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Natural killer (NK) cells perform their regulatory and cytotoxic functions in highly oxidative environments, such as during viral infections and tumor growth. However, the antioxidant requirements of NK cells, particularly like glutathione (GSH), remain poorly understood. In this study, we used a mouse model with conditional abrogation of GSH production in NK cells to investigate this relationship. We demonstrated that GSH is indispensable for IL-15-mediated activation of NK cells, a key process in their function. In the absence of the antioxidant GSH, in vitro activated NK cells accumulate reactive oxygen species (ROS) in the mitochondria, leading to reduced mitochondrial fitness and lower energy capacity. This results in impaired proliferation and cytokine production, along with diminished mTOR and STAT5 signaling. During acute viral infections, NK cells in mutant mice fail to control the anti-viral T cell response effectively. Additionally, the lack of GSH in NK cells significantly impairs their ability to control tumor spread. Therefore, GSH appears to be a critical checkpoint for NK cell activation and function.

W16 The human bone marrow may offer an IL-15-dependent survival niche for EOMES(+) Tr1-like cells

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Maintenance of memory T-cells in the bone marrow and systemically depends on the homeostatic cytokines IL-7 and IL-15. An immunological memory may also exist for regulatory T-cells. EOMES(+)type 1 regulatory (Tr1)-like cells express GzmK and have a rapid in vivo turnover, but if they are short-lived effector cells or could be maintained long-term has not been investigated. EOMES(+)Tr1-like cells were enriched among CD69+Ki67-T-cells in the bone marrow of healthy donors, suggesting that they became quiescent and bone marrow-resident. Conversely, CD4(+)GzmB(+) effector T-cells were excluded from the bone marrow-resident fraction. The dichotomy between GzmK(+) and GzmB(+)T-cells was also observed in the CD8(+)T-cell compartment, both in healthy individuals and in multiple sclerosis. Intriguingly, bone marrow-resident CD4(+) memory T-cells expressed increased levels of IL-7R, while EOMES(+)Tr1-like cells were consistently IL-7Rlo. However, EOMES(+)Tr1-like cells expressed the IL-2/15R-beta chain, and the latter was induced upon forced expression of EOMES in primary human CD4(+)T-cells. Finally, IL-15 rescued EOMES(+)Tr1-like cells from death by neglect but was not required for CD4(+) memory T-cell survival. These findings suggest that the bone marrow may provide a survival niche for EOMES(+)Tr1-like cells, whereas GzmB(+)CTL might represent short-lived effector cells. The different IL-7 and IL-15 receptor expression patterns of CD4(+) memory T-cells and EOMES(+)Tr1-like cells suggest furthermore that they compete for different homeostatic niches.

W17 ILC3s are Required for Intestinal Adaptation to Fasting and Feeding

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Upon food ingestion, the small intestine initiates a coordinated response to digest and absorb nutrients while defending against possible infectious threats from foodborne and intestinal microbes. This intricate balance relies on dynamic interactions between gut epithelial cells, the microbiota, and the intestinal immune system. Together, these systems activate local defense and repair mechanisms during each feeding cycle, ensuring tissue homeostasis. However, it remains unclear whether the circadian challenge of feeding avoids

becoming pathogenic due to the absence of harmful factors or the presence of efficient counteracting mechanisms.In this study, we explore the role of type 3 innate lymphoid cells (ILC3s) in facilitating intestinal adaptation to fasting and feeding. Our findings reveal that ILC3s are rapidly activated activated by feeding with a lipid-rich meal that increases intestinal permeability, followed by rapid normalization of intestinal, inflammatory and metabolic parameters. Using a model that enables targeted ILC3 depletion, we show that mice progress to critical metabolic failure if ILC3s are absent before feeding. We observe that ILC3s are essential for suppressing basal type 1 immune responses, which, in turn, supports the generation of fasting-induced enterocytes (FIEs) that optimize the absorption of glucose, lipids, and ions.This study uncovers a pivotal role for ILC3s in maintaining intestinal and metabolic stability amidst the recurring challenges posed by feeding and fasting cycles. Our findings emphasize the critical function of ILC3s in priming intestinal tissues for nutrient uptake and preserving the integrity of the gut barrier, thereby ensuring overall intestinal health and systemic homeostasis.

W18 Influence of serotonin-signalling on maturation and cytokine production of dendritic cells in comparison with BPE and influence on T cell priming

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Background: Own previous work showed that 5HTRs were regulated after a nasal challenge with birch pollen extract (BPE) and BPEs contain biogenic amines, among them serotonin, raising the question of serotonin effects in birch pollen allergy. Methods: DCs were differentiated from CD14+ monocytes of birch-pollen (bp) allergic and non-allergic donors. Immature DCs (iDCs) were stimulated with BPE and serotonin, with and without inhibitors (Risperidone, Asenapine). 5HTR isotypes and serotonin transporter (SERT) expression was assessed in iDCs and LPS-matured DCs. Naïve CD4+ T-cells from allogenic, non-atopic donors were co-cultured with pre-stimulated DCs (non-atopic, bp-allergic). After 9 days the T cell's expression of transcription factors (T-bet, GATA-3, ROR-gT, FoxP3) was studied by flow cytometry. Results: SERT and nearly all 5HTR isotypes were expressed on iDCs and were partly regulated upon stimulation with LPS. Serotonin led to a dose-dependent upregulation of maturation markers in non-atopic iDCs, which was attenuated by Asenapine and Risperidone. BPE mimicked the serotonin effect on CD80 expression. In LPS- and atopic DCs, serotonin had no effect on maturation marker expression. In iDCs, serotonin stimulation resulted in a dose-dependent release of IL-6, while BPE induced secretion of IL-6 and IL-10 (both blocked by Asenapine and Risperidone). In the co-culture we observed different baseline expression of T-Bet, GATA-3 and FoxP3 in CD4+ T-cells primed with DCs from non-allergic or bp-allergic donors, while baseline ROR-gT expression was similar. BPE and serotonin resulted in identical changes in the GATA3 expression of T cells primed with non-atopic and bp-allergic DCs; the expression of the other TFs followed similar, but not identical patterns in response to both stimuli. Conclusion: Our systematic comparison of DC functions in response to serotonin and birch pollen exposure suggests that serotonin signaling might play a role in DC-primed recall responses to birch pollen exposure.

W19 Deletion of the proton-sensing receptor GPR4 reduces tumor progression in mouse models of colon cancer

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G protein-coupled receptor 4 (GPR4) is a pH-sensing receptor that is activated by neutral or acidic extracellular pH. GPR4 is expressed primarily in vascular endothelial cells (ECs). Intestinal tissue from patients with inflammatory bowel disease (IBD) shows increased expression of GPR4 in inflamed tissue. Patients with IBD are at significantly increased risk of developing colorectal cancer (CRC). We used the MC38 and AOM/DSS murine models of CRC to assess the influence of GPR4 deficiency on tumor growth. Tumor development was assessed by size and weight. Tumor tissue was analyzed by immunohistochemistry (IHC), real-time quantitative polymerase chain reaction (qPCR) and flow cytometry. In the MC38 model, Gpr4-deficient mice showed significantly reduced tumor size and weight compared to wild-type (WT) mice. This effect correlated with a significantly increased number of NK1.1+ cells in tumor tissue as determined by IHC. qPCR and flow cytometry confirmed increased numbers of NK and NKT cells, and revealed significantly decreased numbers of macrophages and neutrophils. In the AOM/DSS model of CRC, Gpr4-deficient mice showed significantly reduced tumor size and weight, compared to WT mice. Likewise, Gpr4-deficient mice showed a significantly increased number of NKp46+ cells in tumor tissue and increased numbers of NK cells were confirmed by qPCR and flow cytometry. In conclusion, the absence of GPR4 significantly attenuated the tumor progression in the colon of mice, and this result correlated with increased cytotoxic cell activity and reduced presence of tumor-associated macrophages and neutrophils. The data suggest that acidosis sensing by endothelial GPR4 modulates anti-tumor immune responses. GPR4 represents a potential new target for therapeutic intervention.

W20 MHC-I upregulation safeguards neoplastic T cells in the skin against NK cell-mediated eradication in mycosis fungoides

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Cancer-associated immune dysfunction is a major challenge for effective therapies. The emergence of antibodies targeting tumor cell-surface antigens led to remarkable advancements in the treatment of hematopoietic malignancies, particularly blood cancers. Yet their impact is constrained against tumors of hematopoietic origin manifesting in the skin. In this study, we employ a clonality-supervised deep learning methodology to dissect key pathological features implicated in mycosis fungoides, the most common cutaneous T-cell lymphoma. Our investigations unveil the prominence of the IL32β - major histocompatibility complex (MHC)-I axis as a critical determinant in tumor T-cell immune evasion within the skin microenvironment. Notably, in patients' skin, we find MHC-I to detrimentally impact the functionality of natural killer (NK) cells, diminishing antibody-dependent cellular cytotoxicity and promoting resistance of tumor skin T-cells to cell-surface targeting therapies. Through murine experiments, we demonstrate that disruption of the MHC-I interaction with NK cell inhibitory Ly49 receptors restores NK cell anti-tumor activity and targeted T-cell lymphoma elimination in vivo. These findings underscore the significance of attenuating the MHC-I-dependent immunosuppressive networks within skin tumors. Overall, our study introduces a novel strategy to reinvigorate NK cell-mediated anti-tumor responses to overcome treatment resistance to existing cell-surface targeted therapies for skin lymphoma.

W21 Preclinical Potential of Gamma Delta T Cells with Novel Nanoparticles for Antigen-Directed Immunotherapy in Triple-Negative Breast Cancer

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Introduction: Triple-Negative Breast Cancer (TNBC) is an aggressive subtype with limited treatment options, high recurrence rates, and poor outcomes. Personalized cancer vaccines leveraging virus-like particles (VLPs) represent a promising strategy with the potential to induce durable immune responses. Recent research highlights the innate and adaptive properties of gamma delta T cells, emphasizing their potential in cancer immunotherapy. However, how VLPs interact with gamma delta T cells to enhance activation remains poorly understood, warranting investigation. We engineered next-generation plant-derived VLPs incorporating TLR ligands, characterized by cryo-electron microscopy and biochemical techniques. We assessed the interaction of VLPs with gamma delta T cells in transgenic mice and through image streaming. The vaccine's effects were tested in a preclinical 4T1 metastatic mammary carcinoma model. Our findings demonstrate that gamma delta T cells effectively phagocytosed VLPs in both wild-type and knock-out mice. Our VLPs expanded gamma delta T cells in tumor-draining lymph nodes (tdLNs). In mice lacking TLR7/8, reduced gamma delta T cell interaction and response to VLP immunization were observed. Subtype analysis revealed distinct activation profiles of Vgamma-1 and Vgamma-4 gamma delta T cells. Assessment of tdLNs and tumors indicated an early gamma delta T cell expansion, highlighting innate properties. Depleting gamma delta T cells abolished antitumor efficacy, suggesting adaptive characteristics. Additionally, our personalized vaccine enhanced CD4, CD8, and gamma delta T cell tumor infiltration, increased cytotoxic markers, reduced recurrence and metastasis, and improved survival despite low tumor mutational burden. Ongoing research focuses on gamma delta T cell recruitment mechanisms and scRNA sequencing. Our findings uncover novel innate and adaptive characteristics of gamma delta T cells in response to our next-generation VLPs, which are loaded with diverse innate immune stimuli. These groundbreaking insights have the potential to reshape the field of cancer vaccines by harnessing gamma delta T cells as key players in antitumor immunity.

W22 Agonistic GITR treatment enhances antitumor immune responses and suppresses tumor progression in pancreatic ductal adenocarcinoma

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Pancreatic ductal adenocarcinoma (PDAC) remains a significant challenge in oncology, with limited efficacy of immunotherapy attributed to its profoundly immunosuppressive tumor microenvironment (TME). Effective strategies to modulate the TME are urgently needed to enhance antitumor immune responses. Glucocorticoid-induced TNFR-related protein (GITR) has emerged as a promising immunotherapeutic target, but its activation in PDAC has not been fully investigated. In this study, we investigated GITR activation using the Pan02 murine PDAC model and analyzed human PDAC samples from treatment-naïve patients and those receiving neoadjuvant chemotherapy. Human samples were profiled using FACS, single-cell RNA sequencing (scRNA-seq), spatial transcriptomics, and immunofluorescence. Our findings demonstrate that GITR is significantly overexpressed in PDAC tissues compared to normal adjacent pancreatic tissue, with further upregulation observed following neoadjuvant chemotherapy. These results were mirrored in the Pan02 model, where GITR activation led to a reduction in regulatory T cells (Tregs) and an increase in activated cytotoxic effector cells within the TME. Functionally, this immune modulation resulted in suppressed tumor growth and extended survival in vivo. Spatial transcriptomic analysis revealed that GITR expression in human PDAC was predominantly localized to lymphocytes adjacent to tumor cells, with high GITR expression correlating with improved patient survival, underscoring its clinical relevance. Collectively, our findings identify GITR as a key regulator of the immunosuppressive TME in PDAC. By enhancing effector cell activation and functions, GITR represents a compelling target for novel immunotherapeutic strategies. Combining GITR activation with standard chemotherapy holds potential for synergistic benefits and improved clinical outcomes in PDAC patients.

W23 Accessory lymph nodes support local control of tumor growth

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Lymph nodes (LNs) are strategically positioned throughout the mammalian body and provide local base camps for immune cells. The establishment of complex microenvironments for cellular interactions in LNs is of utmost importance for the defense against invading pathogens and the control of tumor growth. LN organogenesis in mice is a programmed process dominated through the interaction between lymphoid tissue organizer (LTo) cells and hematopoietic lymphoid tissue inducer (LTi) cells. Lymphatic endothelial LTo cells initiate LN organogenesis through Sphingosin-1-Phosphate (S1P) receptor mediated retention of LTi cells in LN anlagen. Modulating S1P receptor signaling through the provision of FTY720/fingolimod in utero enhanced LTi cell retention in LN anlagen and induced the formation of accessory LNs in mice. Here, we performed single cell RNA sequencing and high resolution microscopy analysis of LN anlagen to address the role of the S1P receptor-driven retention of LTi cells in the embryonic tissue. Specifically, we molecularly characterized different LTo cell populations in the embryo and determined the signaling pathways that coordinate their engagement with LTi cells under conditions of accessory LN formation. Furthermore, we found that accessory LNs contributed to the generation of the anti-viral immune response and the control of regional tumor growth in adult mice. In sum, our findings provide novel insights on cellular interactions that orchestrate LN organogenesis and highlight options to strengthen immune reactivity during malignant diseases.

W24 Path to the clinic: design, validation and manufacture of an lgr5-targeting CAR-T against colorectal cancer

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Cancer stem cells (CSC) are a small population of cells within a tumour with the capacity to self-renew, differentiate, and initiate new tumours. CSC are resistant to chemotherapy and radiotherapy and are enriched in residual disease. Targeting CSC is a strategy to reduce the tumours' ability to generate new cells. Leucine-rich G protein-coupled receptor 5 (LGR5) is a marker of CSC and LGR5+ cancer cells are implicated in tumour progression and metastasis. We designed and tested a chimeric antigen receptor (CAR) targeting the extracellular domain of LGR5. LGR5-targeting CAR-T cells showed significant antigen-specific cytotoxicity and IFN release against colorectal cancer (CRC) cell lines in vitro, and in vivo efficacy in a CRC xenograft mouse model. We confirmed the specificity and safety of the LGR5 targeting CAR-T cells by testing against normal human tissues. GMP ready protocol for clinical scale manufacture of LGR5-targeting CAR-T cells has been developed using CD3+ T cells from healthy donors. We have successfully tested this protocol using CRC patient-derived CD3+ T cells and were able to generate clinically relevant cell numbers (80-fold expansion) with high CAR expression. Cells manufactured using this GMP protocol expressed markers of self-renewing naïve-like and central memory phenotype and showed very low percentage of cells that were triple-positive for PD1, TIM3 and LAG3. This protocol has been successfully tested and validated in a GMP manufacturing facility for the production of LGR5 targeting CAR-T cells, and we have FDA approval for a first in man phase1/2 clinical trial against metastatic colorectal cancer, using a boin design dose escalation protocol, with 4 stages to test dose limiting toxicity. Phase 1 commenced in 2024 and is currently testing dose 3.

W25 The ontogeny of immune tolerance: a model of early-life secretory IgA - gut microbiome interactions

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To achieve immune and microbial homeostasis during adulthood, the

developing immune system must learn to identify which microbes to tolerate and which to defend against. Despite extensive experimental, observational, and clinical data, the concept of 'immune education' has lacked mathematical characterization. We address this gap by synthesizing existing literature to develop a mechanistic mathematical model representing the reciprocal imprinting of gut ecology and adaptive immunity in early life, addressing the urgent need to understand the long-term impact of neonatal immune imprinting on adult health. Our work explores the interplay between the gut microbiome and the gut mucosal adaptive immune response, particularly the multifaceted role of Secretory Immunoglobulin A (SIgA). Using our mathematical framework, we address three questions in early life immunology with both theoretical and practical implications. First, our model provides a predictive perspective on gut microbial composition, illustrating how IgA coating patterns during early and late ontogeny are important candidates for robustly forecasting immunological outcomes. Second, our research indicates that breast milk shapes the gut microenvironment with enduring effects that transcend its temporary presence, unraveling the mystery of how early postnatal influences on the immune system extend into adulthood. Lastly, our findings highlight the transgenerational influence of maternal SIgA, showing how both its deficiency and excess reactivity can lead to specific patterns of immune response and susceptibility to infection in offspring. By pioneering an integrative systems biology approach rooted in a wide array of data and detailed understanding of underlying processes, our model provides a leap from traditional correlational studies to a deeper, mechanistic understanding. We believe that these insights significantly contribute to the field and set the stage for the systematic design and evaluation of future interventions aimed at mitigating the burden of immune-mediated diseases, thus representing a transformative step in both theoretical and applied immunology.

W26 Microbiota-derived metabolite improves lung inflammation by modulating metabolism of alveolar macrophages

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Gut microbiota is a collection of numerous species occupying the human gastrointestinal system that can affect distal organs, including the lungs, via microbial metabolites. Microbiome dysbiosis is implicated in the pathogenesis of multiple inflammatory diseases, including acute lung injury (ALI) related to overactivation of immune cells. We investigated the anti-inflammatory effects of microbial metabolites on primary lung cells by measuring secreted pro-inflammatory mediators using cytometric bead array assays. The most effective metabolite, X, was tested as a treatment in a mouse model of lipopolysaccharide (LPS)-induced acute lung injury (ALI). Both metabolite X and LPS were administered intranasally, and after four days, cytokine levels and lung cell infiltration were analysed through flow cytometry. Additionally, lung cells from the in vivo experiments were further examined using single-cell RNA sequencing analysis. Finally, mitochondrial metabolism was evaluated in alveolar macrophages exposed to LPS with or without metabolite X. Our results show that metabolite X decreases the production of IL-6, CXCL1 and CXCL10 cytokines in murine lung cells. Moreover, the therapeutic administration of metabolite X reduces neutrophil infiltration into the lungs and the secretion of pro-inflammatory cytokines in vivo. Transcriptome analysis reveals that metabolite X exerts its protection through the modulation of mitochondrial metabolism of alveolar macrophages. Subsequent in vitro experiments demonstrated that metabolite X acted through Sphingosine-1-phosphate receptor 2 (S1PR2) to induce metabolic rewiring of alveolar macrophages. To conclude, our data show that metabolite X, a bacteria-derived compound, is capable of rewiring the signalling and metabolism of immune cells and thus presents a promising therapeutic option in ALI and other diseases characterized by excessive pro-inflammatory signalling.

W27 The effects of IL-4, IL-13, and IL-22 in epithelial barrier dysfunction and skin Inflammation

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Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by eczema and barrier dysfunction. While type 2 cytokines (IL-4 and IL-13) are known contributors, the IL-22- role remains less understood. This study elucidates the distinct impacts of these cytokines on AD pathogenesis using cutting-edge methodology as ex-vivo human skin models and multi-omics approaches. The ex-vivo human skin model preserves normal barrier function and resident immune cells. Samples were treated with IL-4, IL-13, IL-4+IL-13, and IL-22. We assessed barrier function using electric impedance spectroscopy (EIS) and performed RNA sequencing (RNA-seq) and non-targeted proteomics. Additionally, we conducted spatial transcriptomics on skin biopsies from healthy and AD donors and analyzed RNA-seq data from dupilumab-treated AD patients. Both type 2 cytokines and IL-22 significantly compromised skin barrier function, evidenced by decreased EIS values. Spatial transcriptomics revealed CLDN1 as a crucial barrier gene downregulated in the epidermis of AD lesions. RNA-seq identified cytokine-specific gene expression patterns, IL-4 and IL-13 combination suppressed genes essential for skin barrier integrity and keratinization. IL-4 induced additional signaling pathways beyond IL-13. Similarly, IL-13 induced the downregulation of IL22RA1 (IL-22 receptor) beyond IL-4. While, IL-22 induced the upregulation of the IL4R, the main receptor for IL-4 and and IL-13 signaling. Type-2 cytokines suppressed antimicrobial peptides, while IL-22 induced their expression. Transferring our dataset to patients treated with Dupilumab, we report that IL-22-related gene changes persisted despite dupilumab treatment, suggesting a distinct pathogenic mechanism, while type-2 genes were mostly restored after 3 months of treatment. The proteomic analysis confirmed that the above-mentioned studied cytokines downregulated key barrier proteins, particularly claudin-1. This comprehensive study provides insights into the differential effects of IL-4, IL-13, and IL-22 on ex-vivo human skin, highlighting their complex interplay in disrupting skin barrier function and modulating innate immune responses. These findings may inform more targeted therapeutic approaches for AD management.

W28 Aspergillus and Beta-glucan sensing by basal progenitor cells reprograms airway epithelial differentiation.

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Asthma and chronic rhinosinusitis (CRS) patients have significantly impaired airway barrier function, mucus hypersecretion and ineffective mucociliary clearance. Acute respiratory infections and fungal antigen sensitisation are known to potentiate asthma and CRS, however the underlying programming events that drive long-term epithelial changes remains poorly defined. We hypothesised that disease-associated epithelial changes results from infection induced reprogramming of basal cells, as this persistent progenitor population is responsible for differentiating into the specialised cells of the upper airway epithelium. The presence of fungus such as Aspergillus spp. in the airways is associated with severe airway inflammation, IgE sensitisation and poor airway function in asthma and CRS patients. Hence, we investigated whether basal cell exposure to Aspergillus and the fungal cell wall component, Beta-glucan, altered differentiation outcomes. Exposure of basal cells to Beta-glucan for 5 days induced the upregulation of 178 genes and downregulation of 333 genes. Upregulated genes were associated with innate immune responses, pyroptosis, and anabolic cellular processes, whereas downregulated genes were related to stemness and regulation of allergic airway inflammation. Using air-liquid interface (ALI) epithelial differentiation models, we found that epithelium derived from basal cells exposed to either Aspergillus extract or Beta-glucan prior to differentiation preferentially developed into CD151+/CD66c+ secretory cells, with increased MUC5AC staining quantified by immunofluorescence, compared to controls. A reduction in FOXJ1+ cells was also evident in ALI epithelium. These data indicate that sensing of fungal antigens by basal cells re-directs lineage choice towards a more secretory predominant phenotype, consistent with epithelial changes associated with CRS and asthma. We propose that airway exposure to fungal antigens may contribute to the chronic epithelial changes associated with disease via reprogramming of

basal cell function and differentiation. Ongoing studies aim to investigate the epigenetic changes induced by fungal antigen exposure in basal cells and how this governs differentiation outcomes.

W29 Anti-inflammatory functions of indole-3-propionic acid

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The gut microbiota protects the gastrointestinal system's homeostasis by producing antimicrobial substances, vitamins, and metabolites, strengthening the gut epithelial barrier, inhibiting opportunistic pathogen colonization, and regulating the immune system. In addition, the gut microbiome has prominent roles in skin epithelial homeostasis (gut-skin axis), which can be seen in inflammatory skin diseases such as atopic dermatitis. We showed that Indole 3 propionic acid improves gut epithelial barrier development speed and integrity as demonstrated in gut-on-a-chip 3D cultures. The application of 0.25, 1- and 4-mM doses of IPA significantly increases the gut epithelial barrier integrity compared to control by almost 2 times up to 800 ohm x cm2 during the gut development phase of the gut epithelial barrier. The transcriptomic analysis shows that it upregulates gene expression associated with xenobiotics metabolism, ion transport, water transport, glucose transport, and amino acid transport pathways. It increases the tight junction protein claudin-1 gene expression. It shows an anti-inflammatory activity, as demonstrated with decreased chemokines (CXCL-5,10 and 11, CCL-20,23 and 25, CSF-1 and MCP-1) and IL-1a levels in culture medium detected by proximity extension assay. Untargeted proteomics analysis revealed that 4 mM IPA upregulates glycolysis, tricarboxylic acid cycle, and oxidative phosphorylation and downregulates lipid metabolism pathways-related proteins. Next, we assessed its effect on skin epithelial barrier integrity with an ex vivo skin tissue model. Treatment of systemic circulation-relevant doses of IPA (0.25,1 and 4 uM) alone rescued the surfactant, cocoyl methyl glucamide-induced skin epithelial barrier damage within 24 hours. In addition, it reversed the inflammation caused by cocoyl methyl glucamide demonstrated by decreased IL-18, CSF-1, PRDX-3 and PD-L1 protein levels. In conclusion, our data highlights IPA, a gut microbiome metabolite, as a promising agent for preventing, rescuing, and treating gut and skin epithelial barrier impairment.

W30 Microbiota-derived bile acids attenuate lung inflammation: Evidence from mouse models and human-derived lung organoids

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The gut microbiota plays a crucial role in shaping immune responses both locally in the gut and distally in other organs like the lungs, primarily through the action of microbial metabolites released into circulation. Secondary bile acids derived from the transformation of host-derived bile acids by the gut microbiota, have recently been identified as potent anti-inflammatory mediators in the intestine, influencing CD4+ T cell differentiation and dendritic cell function. However, the specific bile acid species responsible for these effects and the underlying mechanisms remain unclear. We have identified a particular species (named here as Metabolite X due to a pending patent application) able to profoundly ameliorate the inflammatory response in the lungs in a murine model of LPS-induced acute lung injury (ALI) and bacterial pneumonia (Klebsiella pneumoniae). This metabolite acts on alveolar macrophages through the Sphingosine-1-phosphate receptor 2 (S1PR2) inducing their metabolic rewiring, dampening the production of chemokines and reactive oxygen species. Moreover, using human-derived bronchial lung organoids in co-culture with human fibroblasts we have been able to investigate the anti-inflammatory properties of Metabolite X in several models of lung inflammation such as bacterial (LPS and K. pneumoniae) and viral infections [Poly(I:C)] as well as allergic asthma (HDM). While the treatment with metabolite X mitigates the inflammatory response, especially IL-6 and IL-8 chemokines, it also contributes to maintaining the epithelial barrier integrity. All these data point to Metabolite X as a promising therapeutic approach, given its ability to ameliorate lung inflammation both in vitro and in vivo.

W31 Disease Activity-Dependent Siglec-1 Expression on Monocyte Subsets of Patients with Idiopathic Inflammatory Myopathies

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Background: Idiopathic inflammatory myopathies (IIMs) are systemic autoimmune disorders with varying clinical presentations and disease pathomechanisms. Interferon pathway is one of the key potential therapeutic targets in selected IIM patients. Siglec-1, an interferon-inducible receptor, is a potential biomarker for disease activity, particularly in dermatomyositis (DM). Aims: To analyze Siglec-1 expression on classical (cMO), intermediate (iMO), and non-classical monocytes (ncMO) in IIM subtypes and investigate its association with clinical activity measures. Methods: Siglec-1 expression was measured by 8-color flow cytometry in IIM patients classified into DM, antisynthetase syndrome (ASS), immune-mediated necrotizing myopathy (IMNM), and inclusion body myositis (IBM), and in healthy controls (HC). Disease activity was assessed using IMACS Core set measures. Results: 54 IIM patients participated in the study (32 DM, 16 ASS, 3 IMNM and 3 IBM). Active DM patients exhibited significantly higher Siglec-1 mean fluorescence intensity (MFI) compared to other active IIM subgroups and HCs in every monocyte subsets. Siglec-1 expression levels did not differ significantly between IIM subgroups and HCs without stratification by activity. The correlation of Siglec-1 expression on monocyte subsets and different disease activity measures in the whole IIM population were the strongest regarding global (Physician Global Activity), skin (CDASI, Skin-VAS), and gastrointestinal (GIT-VAS) activity markers (positively) and muscle force (negatively). Siglec-1 expression was heterogeneous in active ASS patients suggesting different disease pathogenesis in the same subgroup. Intermediate monocytes displayed the highest Siglec-1 expression across all groups and the strongest associations between disease activity markers and Siglec-1 expression were observed on intermediate monocytes. Conclusion: Siglec-1 expression on intermediate monocytes is elevated in active DM and correlates strongly with organ specific clinical and biochemical markers of disease activity. These findings highlight that Siglec-1 is a candidate biomarker for monitoring IIM disease activity, and could be useful in patient selection for interferon targeted treatments.

W32 Pericardial lymphoid clusters control cardiopathogenic T-cell activation and differentiation during autoimmune myocarditis

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The parietal pericardium contains fat-associated lymphoid clusters (FALCs), which monitor the pericardial cavity for immune signals before substances are reabsorbed into the circulation, acting as immune surveillance hubs of the cardiac cavity. However, surprisingly little is known about the involvement of these non-classical secondary lymphoid organs in cardiac inflammation. Here, we investigated the activation and differentiation of cardiac-specific T cells in pericardial FALCs. Using a mouse model of autoimmune myocarditis, we found a close correlation between cardiac and pericardial inflammation. Following initial activation in heart-draining lymph nodes, cardiac myosin-specific memory CD4+ T cells accumulated in pericardial FALCs. Single-cell transcriptomic analysis of immune and stromal cells from pericardial FALCs indicated the presence of distinct cellular niches that serve as amplifiers of cardiopathogenic T cell responses. CD4+ T cells in FALCs were underpinned by CCL19-expressing fibroblastic reticular cells (FRCs), which instructed T cell activation and differentiation. Bioinformatics analysis identified FRCs as major T cell interaction partner that controls T cell differentiation toward the Th17 pathway via IL-6. Indeed, antibody-mediated blockade of

IL-6 reduced the infiltration of IL-17+ T cells in both the pericardium and heart, thereby preventing progression to inflammatory cardiomyopathy and heart failure. In sum, this study highlights the role of pericardial FALCs in cardiac inflammation and reveals key mechanisms regulating T cell behavior in this specific microenvironment.

W33 Autoantigen-Dexamethasone Conjugate-Loaded Liposomes Halt Arthritis Development in Mice

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There is no curative treatment for chronic auto-inflammatory diseases including rheumatoid arthritis, and current treatments can induce off-target side effects due to systemic immune suppression. Our group has previously shown that dexamethasone-pulsed tolerogenic dendritic cells loaded with the arthritis-specific antigen human proteoglycan can suppress arthritis development in a proteoglycan-induced arthritis mouse model. To circumvent ex vivo dendritic cell culture, and enhance antigen-specific effects, drug delivery vehicles, such as liposomes, provide an interesting approach. Anionic 1,2-distearoyl-sn-glycero-3-phosphoglycerol liposomes were prepared with enhanced loading of the arthritis-specific peptide human proteoglycan-dexamethasone conjugates by cationic lysine tetramer addition. Liposomes were tested in vitro and in vivo to assess immunological effects on dendritic cells and antigen-specific T cells, and in a mouse model for arthritis to assess their ability to prevent or treat disease. Phenotypic markers were measured by flow cytometry, and cytokine production was measured by ELISA and qPCR. The arthritis score was evaluated by a paw scoring system. Antigen-pulsed tolerogenic dendritic cells induced by liposomal dexamethasone in vitro enhanced antigen-specific regulatory T cells to a similar extent as dexamethasone-induced tolerogenic dendritic cells. Mice injected with antigen-dexamethasone liposomes have significantly higher antigen-specific type 1 regulatory T cells than mice injected with antigen only. The liposomes significantly inhibit the progression of arthritis compared to controls in preventative and therapeutic proteoglycan-induced arthritis mouse models. This coincides with systemic tolerance induction and an increase in IL10 expression in the paws of mice. A single administration of autoantigen and dexamethasone-loaded liposomes seems to be a promising antigen-specific treatment strategy for arthritis in mice.

W34 Investigating autoreactive T cells in IgLON5-antibody associated encephalopathy.

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IgLON5-antibody associated encephalopathy is a rare, severe, and progressive neurological disorder marked by sleep disturbances and neurodegeneration, with a high mortality rate. It is characterized by the presence of antibodies targeting the neuronal cell adhesion protein IgLON5 and is strongly associated with specific HLA class II alleles, particularly HLA-DRB1*10:01 and HLA-DQB1*05:01. Despite this evidence, the role of T cells in its pathogenesis remains poorly understood. In this study, we employed a highly sensitive in vitro screening approach to investigate autoreactive T cells in patients with IgLON5 disease. We identified memory CD4+ T cells specific for IgLON5 in 5 out of 7 screened patients, isolating roughly 60 autoreactive single T cell clones. Systematic analysis of these clones described a polyclonal T cell receptor (TCR) repertoire, defined the targeted epitopes and highlighted a predominant HLA-DR restriction. Notably, most autoreactive T cells responded to both the native and naturally occurring deaminated forms of recognized IgLON5 peptides. Intracellular staining demonstrated that these T cell clones produce IFN-γ, TNF-α, and granzyme B, suggesting a pro-inflammatory phenotype. Collectively, our findings support a role of autoreactive memory CD4+ T cells in IgLON5-antibody associated encephalopathy, providing new insights into the underlying immunopathology and offering new avenues for biomedical applications.

W35 Cellular and Molecular Immunoprofiling of Lupus Panniculitis: Elucidating the Roles of Cytotoxic T Cells, B Cells, and Complement Activation

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Lupus panniculitis (LP) is a subtype of cutaneous lupus erythematosus (CLE) that affects subcutaneous adipose tissue. The pathomechanisms underlying LP are largely unknown. In this study, we aimed to obtain deeper insights into LP through the characterization of cellular and molecular immune patterns. Using imaging mass cytometry (IMC), we analyzed the cellular infiltrates in deep skin biopsies from LP patients (n=8) and healthy controls (n=6). Concurrently, we performed nCounter nanostring technology to quantify the mRNA expression of immune-related markers. The IMC analysis revealed that T cells (CD3+) predominated in LP More precisely, they exhibited a predominantly skin-homing (CLA+), cytotoxic phenotype (CD8+, granzyme B+), indicating site-specific immune activation within skin tissue. B cells (CD20+) were also present. They constituted a significant portion of immune cells, alongside with the presence of dendritic cells and macrophages. Differential gene expression analysis revealed an upregulation in pathways associated with adaptive and innate immune responses. This included T cell receptor signaling (upregulation of CD247, LCK), lymphocyte activation (ZAP70, CD3D), cytokine signaling (STAT1, MYD88), and MHC antigen presentation (HLA-DRA, TAP1/2). Additionally, there was an upregulation of genes associated with the Complement system (C1QA/B, C4A/B). Our results suggest that a cytotoxic T- and B-cell-predominated immune response and complement activation is involved in LP. This points towards a pathogenesis that is different from other types of panniculitis.

W36 Chronic hand eczema revealed as a Type 2 Disease: Evidences from Clinical Trial and Molecular Profiling

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Background. Chronic hand eczema (CHE) is a debilitating skin condition characterized by pain, itch, and chronic inflammation, with a complex multifactorial origin. Its diverse presentations, including overlapping traits of atopic dermatitis, contact dermatitis, and psoriasis, make diagnosis and treatment particularly challenging. Despite

being the most common occupational skin disease, the underlying immune mechanisms of CHE remain poorly understood. Methods. Here we conducted a comprehensive molecular profiling of CHE patients of all etiologies and morphologies and performed a phase 2b randomized, multicenter, double-blind, placebo-controlled clinical trial comparing dupilumab to placebo over 16 weeks. Results. We demonstrated that CHE is a type 2 immunity driven disease, regardless of etiological factors or clinical presentation. Transcriptomic profiles of CHE patients closely resemble those seen in both atopic dermatitis and psoriasis, with dysregulated genes affecting skin barrier function, leukocyte migration, cytotoxicity, and mixed type 1, 2, and 3 immunity. The clinical trial included 94 adults with moderate to severe CHE persisting for at least six months and resistant to potent topical corticosteroids. Compared to placebo control, 16-week dupilumab treatment significantly improved clinical severity and quality of life of CHE patients, while largely restoring appropriate transcriptomic and proteomic programs related to skin barrier and immune homeostasis. Conclusion. These findings demonstrate that IL-4Ralpha signaling is a critical regulator of CHE pathological features, independent of atopic dermatitis background or environmental triggers and support reclassifying CHE as a type 2 immune disorder, positioning dupilumab and IL-4/13 targeted therapies as leading treatments for moderate-to-severe patients. Trial registration. clinicaltrials.gov NCT03861455. Fundings. Sanofi US ISS (DUPECZEMAIN N° RC31/18/0269 both to MT and CP); Almirall IIS-RC Study (to MT); Agence Nationale pour la Recherche (R21009BB to NG); European Research Council (ERC-2023-COG # 101124255 to NG), Acteria Foundation (both to MT and NG).

W37 Fast, pre-seasonal Intralymphatic Immunotherapy for grass pollen allergy reduces the symptom and medication score

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Background: Allergy-specific immunotherapy is the only available disease-modifying treatment for allergic diseases. However, conventional subcutaneous or sublingual administration requires a treatment duration of 3-5 years, has little market penetration and low adherence. Intralymphatic immunotherapy (ILIT) is a promising alternative, requiring only three injections with exceptionally low allergen doses. This study evaluates the efficacy and safety of ILIT using lower doses containing 60 ng Phl p 5 per injection. Method: Adults with grass pollen-induced rhinoconjunctivitis in eastern Jutland on the mainland of Denmark were recruited in spring 2021. After recording medication and symptom scores during the grass pollen season of 2021, they were randomly allocated 2:1 to ultrasound-guided ILIT (283 patients on verum :144 patients on placebo) in the winter 21/22 at one university hospital and three specialist ENT clinics. Injection quality was evaluated after treatment but before unblinding on ultrasound video clips. Only the grass pollen season of 2023 was sufficient to evaluate an effect of ILIT. We grouped patients according to the quality of the injections received as described in Flory 2023 and compared the clinical effect of grouped injections. Results: Compliance was >99%. There were 21.7% mild, local side effects and 5.3% mild systemic side effects and no severe treatment related adverse events. Patients treated with good injection quality reported a significant degree of reduction of cSMS in the grass pollen season of 2023, the second season after treatment (p=0.014). Patients treated with only two or one good injection had a lesser effect (ns), suggesting a dose response. Skin prick test diameters with grass extract of patients with good injection quality were significantly reduced two years after treatment (p=0.02). Conclusion: ILIT offers a safe and fast method for pre-seasonal immune therapy for Allergic Rhinitis. The patient target group is currently not reached by traditional AIT.

W38 Investigation of the effect of the nasal allergen challenge on the volatile organic compounds in exhaled breath of patients with allergic phenotypes of rhinitis

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RATIONALE: The diagnosis of local allergic rhinitis (LAR) needs a nasal allergen challenge (NAC), whereas the confirmation of allergic rhinitis (AR) might also require this test. We assessed the capacity of volatile organic compounds (VOCs) in exhaled breath (EB) to serve as non-invasive biomarkers for allergic phenotypes of rhinitis. METHODS: 61 house dust mite/Alternaria alternata-allergic patients (29 LAR and 32 AR), 29 non-allergic rhinitis (NAR) subjects and 14 healthy non-atopic controls (HC) were recruited prospectively. EB was collected before and 24 hours after a NAC. Saturated hydrocarbons were determined by thermal desorption coupled with gas chromatography-mass spectrometry (TD-GC/MS) in EB samples. A model was constructed by means of LASSO + LS (least absolute shrinkage and selection operator + logistic regression) to discriminate between allergic patients (AR and LAR) and non- allergic subjects (NAR and HC). The study population was randomly divided into a training set (78 subjects) and a validation set (26 subjects). Model performance was estimated by 5-fold cross-validation and testing in the validation set, and permutation test was used for model significance assessment. RESULTS: The NAC did not induce significant differences in VOCs in EB in any study group. A significant model (p=0.006) that selected two VOCs (decane and nonadecane) was built and allowed discrimination between allergic and non-allergic patients at baseline. For this model, AUC (area under the receiver operating characteristic curve) value determined by cross-validation was 0.716, and the AUC obtained by testing on validation set was 0.771 (61% sensitivity and 75% specificity). CONCLUSIONS: These findings show VOC in EB could serve as non-invasive biomarkers for allergic phenotypes of rhinitis.

W39 Establishing Genetically Modified Alveolar Macrophages as Versatile Cell Therapy Against Pulmonary Diseases

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Asthma is a heterogenous pulmonary disease associated with chronic airway type 2 immune inflammation. IL-33 and its receptor ST2 have been reproducibly identified as major susceptibility loci for asthma, supporting a critical role of this signaling pathway. Since alveolar macrophages (AMs) are the main immune cell population found in the alveoli under steady state and the first immune cells to encounter any pathogens or allergens entering the lung, we hypothesize they can be used as novel cell therapy and genetically encoded drug delivery platform. Specifically, we aim to target the IL-33/ST2 axis in models of lung type 2 inflammation by genetically manipulating the AMs to express an IL-33 neutralizing protein, IL33trap, and investigate the efficacy of this novel cell therapeutic approach in a mouse model of Alternaria alternata-induced allergic airway inflammation. We established murine ex vivo cultures of primary AMs (mexAMs) that could be maintained and expanded up to 3 months while retaining their AM identity and the potential to repopulate an empty AM niche in vivo. To enable genetic manipulation of mexAMs using lentiviruses, we optimized lentivirus production and mexAM transduction protocols. We then assessed the therapeutic potential of IL33trap-expressing mexAMs in inhibiting type 2 immune responses by transferring these genetically modified mexAMs into Csf2ra–/– recipients lacking endogenous AM population, followed by challenge with recombinant IL-33 intratracheally. We observed IL33trap-expressing AMs potently blocked activation and proliferation of ILC2s in the lungs. In addition, eosinophilia in the BAL was also prevented by IL33trap-expressing AMs. Notably, IL33trap-expressing mexAM also prevented features of type 2 inflammation induced by the model allergen A. alternata. Overall, our study has the potential to establish a novel and versatile cell therapy approach, using AMs for the local production of anti-inflammatory molecules, which can be implemented to various pulmonary diseases, not limited to asthma.

W40 Early life RSV infection as a preventable risk factor for asthma

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Allergic asthma is increasingly common and strongly influenced by

genes and environment. Human respiratory syncytial virus (hRSV) bronchiolitis is a common cause of early life wheezing, but it is less clear if and how it is a risk factor for persistent asthma. Here, we studied the Danish National Patient and Prescription Registries and found that children admitted to hospital for RSV bronchiolitis in the first 6 months of life had a 3-fold higher risk of hospital-diagnosed asthma until the age of 24 compared with uninfected children. The risk for asthma was highest when either or both parents also had an asthma diagnosis. Particularly children born to an asthmatic mother and hospitalized with hRSV had a 5.4-fold increased asthma risk compared to non-infected children born to non-asthmatic parents. To model this, we infected mice in the first week of life with pneumonia virus of mice, the murine counterpart of hRSV. When exposed to allergen in the perinatal period, infected mice developed more severe asthma features, which was strongly enhanced by maternal allergy. Mechanistically, pneumovirus infection in the pups induced the expression of activating Fc receptors on dendritic cells (DCs). Neonatal DCs used antibodies transferred from allergic dams to recognize allergen, explaining enhanced Th2-polarized allergen-reactive T cells in offspring of allergic mothers. Given the recent recommendations of RSV immunoprophylaxis to all newborns, we administered cross-protective neutralizing RSV antibodies to lactating dams, and this abolished the enhancing effects of PVM infection on Th2 priming and asthma risk in the offspring. Combined, these epidemiological and mechanistic data show that early life RSV infection is a preventable risk factor for asthma, influenced by parental asthma history. Since 15% of childhood asthma is attributable to RSV irrespective of severity, universal immunoprophylaxis in the perinatal period could have profound effects on asthma incidence and healthcare needs.

W41 PAPER TCR transgenic CD4+ T cells reveal the requirement for papain's enzymatic activity in the induction of Th2 responses.

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Allergic diseases such as asthma, hay fever, and eczema affect up to 700 million people worldwide, driven by T helper 2 (Th2) cells. These cells differentiate upon exposure to diverse environmental allergens, but the mechanisms underlying early Th2 differentiation remain unclear. Using a PAPain Enzyme Reactive (PAPER) TCR transgenic mouse model—where all CD4+ T cells respond to papain—we traced the activation and differentiation of antigen-specific Th2 cells in the lung and lung-draining lymph nodes following exposure to the clinically relevant allergen papain. Papain, a cysteine protease from the peptidase C1 family (which includes the HDM-derived protease Der p 1), is a widely used type-2 adjuvant. It is often mixed with antigens like ovalbumin (OVA) to induce Th2 responses and serves as a commercial enzyme in food, cosmetics, and biochemical applications. Despite its experimental use as an adjuvant, the papain-specific Th2 response has largely been overlooked. In this study, we dissected key factors contributing to Th2 skewing: antigen presentation and TCR signaling, costimulation, and post-translational cytokine processing. Our findings demonstrate that papain's proteolytic activity is critical for inducing a robust Th2 response in the lung and draining lymph nodes.

W42 Gut-derived microbial metabolite P-cresol sulfate modulates chemokine production in nasal and bronchial epithelial cells in vitro

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Asthma is a lung disease characterized by chronic airway inflammation and structural remodeling, leading to variable airflow obstruction and hyperresponsiveness to various stimuli. Epithelial cells in the nasal and bronchial mucosa serve as a protective barrier, regulating immune responses and producing mucus. However, when their function is impaired, they contribute to the development of asthma. Growing evidence suggests that the gut microbiota is crucial in protecting against allergic asthma due to their immunomodulatory properties. The microbiota ferments dietary fibers into metabolites that enter the circulation and may act elsewhere, such as in lung tissue. A recently identified metabolite, P-cresol sulfate (PCS), produced during L-tyrosine metabolism in the intestine, has been shown to protect mice against allergic airway inflammation following L-tyrosine or PCS treatment. Part of this protective effect is through the inhibition of CCL20 production from airway epithelial cells. PCS has also been negatively associated with asthma incidence in children. However, the impact and mechanisms of action of gut-derived microbial metabolites on human airway epithelium remain poorly understood. Here, we investigated the immunomodulatory effects of PCS on in vitro primary human airway epithelial cell models. We used mucociliary differentiated cultures of human primary nasal and bronchial epithelial cells (PNEC and PBEC) generated by culture at the air-liquid interface. We studied the responses of PBEC and PNEC to PCS in the presence or absence of inflammatory stimulation, using protein and gene expression analyses from pools of two to five donors. We confirmed that PCS reduced CCL20 release by 10% in PBEC and 20% in PNEC without affecting IL8 levels. Next, we aim to explore the molecular pathways PCS activates in the human airway epithelium. This research seeks to elucidate how gut-derived PCS prevents allergic airway responses and investigates its potential as a future strategy for preventing or treating allergic asthma.

W43 Comprehensive multi-omics analysis reveals the immunomodulatory role of platelet content in healthy subjects

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Platelets are small anucleate cell fragments that contribute to homeostasis in vascular injury. Despite the increasing evidence of their role in inflammatory disease, studies analysing the content of resting platelets in homeostatic conditions are still lacking. Here, we evaluated the lipidomic, protein, and transcriptomic content of platelets by analysing matched platelet-rich plasma (PRP) and platelet-poor plasma (PPP) samples from 10 healthy subjects. Untargeted lipidomics revealed a clear clustering when comparing both PPP and PRP samples. These differences were driven by increased levels of plasmalogens and serotonin conjugates and decreased levels of lysophosphocholines (LPCs 14:0, 15:0, 16:0, 18:2, 22:6), carnitines (CAR 8:0, 10:0, 10:1, 14:1), and oxidized fatty acids in PRP. Further analysis of the oxidized lipid content of platelets showed that PPP and PRP were clearly differentiated by their oxylipin content, with PRP having increased levels of several oxylipins including arachidonic acid derivatives such as prostaglandin (PG)J2, PGE2, PGF2a, and PGD2, thromboxane (TX)B2, 20-OH-leukotriene (LT)B4, lipoxin A4, and several hydroxy-eicosatetraenoic acids (HETEs), such as 8-, 9-, 11-, 12-, and 15-HETE. These changes were greatly associated with inflammation-related pathways, including arachidonic acid, eicosanoid, and prostaglandin metabolism. PRP transcriptomics showed that platelets have an enrichment in transcripts related to wound healing, blood coagulation, haemostasis, and platelet aggregation and activation, all well-known functions of platelets, but also to immune processes such as cell-cell adhesion and antigen presentation. Furthermore, platelets had transcripts encoding for immune interaction (HLA, SELP) and eicosanoid synthesis (PTGES, FADS) proteins. Finally, we validated these transcriptomic results, finding increased levels of inflammatory and tissue healing-related proteins (IL-17, IL-33, IL-25, TSLP, PDGBB, HGF, VEGF) in PRP. Overall, these results point towards platelets having a role in the regulation of inflammation and advance the identification of beneficious components that could be used for future treatment of blood and inflammatory-related diseases.

W44 Innate Immune Memory and Metabolic Reprogramming in the Lower Airway Epithelium of Patients with Allergic Asthma

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Asthma is a complex disease influenced by clinical, molecular, and environmental factors. Exacerbations, often triggered by respiratory viral infections such as rhinovirus (RV), are frequent in asthma patients, unlike in healthy individuals, where RV typically causes mild symptoms. The intrinsic immunometabolic reprogramming of airway epithelium in asthma, which may alter responses to RV infection and allergens, remains poorly understood. Interestingly, a reduction in viral exacerbations is often observed with successful allergen immunotherapy (AIT) in allergic asthma, although the underlying mechanisms are unclear. This study investigates the interplay between metabolic reprogramming and the antiviral response of airway epithelium in allergic asthma and examines the impact of AIT on these processes. We utilized in vitro cultures of primary bronchial epithelial cells in an air-liquid interface repetitively infected with RV, along with ex vivo analyses of bronchoalveolar lavage and bronchial biopsies from healthy controls and allergic asthma patients, including those undergoing AIT. Employing RNA-seq, RT-qPCR, proteomics, metabolomics, confocal microscopy, and bioinformatics of publicly available datasets, we analyzed immune responses and metabolic activity. Asthmatic bronchial epithelium displayed distinct baseline and post-infection metabolic profiles, with increased glycolysis and reduced oxidative phosphorylation. Single-cell RNA-seq of healthy bronchial epithelium under type 2 inflammation revealed similar metabolic remodeling in ciliated and secretory cells. Repetitive RV infections induced pronounced metabolic and proteomic changes, especially in asthma, implicating pathways of cell senescence, epigenetics, and glucose metabolism. These findings suggest immune and metabolic reprogramming resembling trained immunity or tolerance. AIT-induced metabolic shifts in the lung microenvironment, notably in carbohydrate, amino acid, and oxidative stress pathways, were associated with enhanced antiviral responses. Our results indicate that airway epithelial metabolic reprogramming shapes asthma pathogenesis and that AIT partially reverses these immunometabolic alterations, potentially mitigating disease exacerbations.

W45 Obesity reprograms bone marrow derived macrophages to promote anti-tumor immunity

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Obesity has been identified as the number two modifiable risk factor for cancer, behind only smoking. This prolonged exposure to excessive nutrients and altered systemic metabolism can promote a distinct immunosuppressive state to limit tumor immunosurveillance. Studies have revealed that innate immune cells can be primed by an initial innate stimulus such as chronic inflammation or increased lipids, to enhance subsequent activation to a different innate stimulus, coined “innate immune memory” or “trained innate immunity”. Obesity has also shown to have a detrimental effect on bone homeostasis by altering bone marrow and hematopoietic stem cell differentiation by shifting stem cells in favor of myeloid progenitors. Further These obesity-induced changes in the bone marrow microenvironment can lead to dramatic bone marrow remodeling, compromising immune cell functions, which in turn impact host response to systemic inflammatory diseases and regulation of whole-body metabolism. However, there is limited evidence to mechanistically identify obesity induced innate immune memory in bone marrow progenitor cells that alter function in peripheral tissue microenvironments. Interestingly we found that bone marrow derived macrophages (BMDMs) taken from obese (HFD) mice maintain an altered metabolic phenotype, exhibiting increased basal OCR and ECAR compared to BMDMs from lean mice. Additionally, HFD BMDMs exhibited increased mitochondrial ROS production, increased lipid uptake and increased pro-inflammatory markers such as MHCII and CD86. Further, transplanted bone marrow from obese mice into irradiated lean mice resulted in significantly reduced tumor incidence and tumor size when subcutaneously injected with MC38 tumor cells. Additionally, mice that received HFD bone marrow exhibited increased macrophages and CD8 T cell infiltration into tumors. Together these data suggest that an “innate memory” of obesity is preserved in the bone marrow which can impact subsequent anti-tumor immunity and tumor growth.

W46 The molecular and metabolic mechanisms of TCR-indpendent activation of human CD8+ effector memory T cells

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It has been shown that CD8+ effector memory T cell (TEM) activation via TCR is largely regulated by mTORC2 over mTORC1. This raises the question of whether TCR-independent CD8+ TEM activation also involves the mTOR pathway and if so, which complex dominates. Additionally, mTORC1 regulates IRE1-alpha during ER stress, and amino acids enable mTORC1 activity in effector Treg cells. However, the role of mTOR and amino acids in cytokine-driven CD8+ TEM cell activation is unclear. This study aims to investigate whether the amino acids-mTORC1-IRE1-alpha pathway is involved in cytokine-induced CD8+ TEM cell activation. In this study, human primary peripheral blood mononuclear cells (PBMCs), CD8+ T cells and total T cells were used. Small guide RNA and Cas9 protein or chemical inhibitors were applied to study the function of proteins including mTORC1, mTORC2 and IRE1-alpha. The knockout efficiency was measured by western blotting. The expression of IFN-gamma and spliced X-box binding protein 1 (XBP1s) were measured by flow cytometry or enzyme-linked immunosorbent assay (ELISA). I found that CD8+ TEM cells were the main cytokine producer in CD8+ T cells when activated TCR-independently; Chemical inhibition of mTORC1 had a more pronounced downregulation effect on cytokine-induced IFN-gamma production than mTORC2; Both chemical inhibition and genetic knockout of IRE1-alpha potently supressed XBP1s expression and reduced the production of cytokine-induced IFN-gamma in CD8+ T cells; Amino acids upregulate the expression of cytokine-driven IFN-gamma, which was diminished by dual inhibition of mTORC1/C2. In conclusion, this study shows that TCR-independent CD8+ TEM cell activation utilizes a metabolic mechanism which is distinct from TCR-dependent one: mTORC1, rather than mTORC2, contributes more to this metabolic response. Additionally, our data suggest that cytokine-induced CD8+ T cell activation is mediated through amino acids-mTOR-IRE1-alpha-XBP1s pathway.

W47 Thymic Stromal Lymphopoietin (TSLP) imprints a metabolic and epigenetic reprogramming in human CD1c+ myeloid dendritic cells promoting Th2 polarization

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Human thymic Stromal Lymphopoietin (TSLP) is a member of the IL-2 family of cytokines that is mainly produced by epithelial cells under both homeostatic and inflammatory conditions. Increased levels of TSLP are involved in the exacerbation and chronification of asthma. TSLP enhances the capacity of human dendritic cells (DCs) to trigger type 2 responses by favouring the polarization of naïve CD4+ T cells towards Th2 cells. Clinical trials have demonstrated that treatment with Tezepelumab, a monoclonal antibody selectively binding to TSLP, is effective in asthma patients. The interplay between metabolic and epigenetic rewiring is fundamental for the induction, maintenance and regulation of DC functionalities. However, the capacity of TSLP to regulate the function of DCs and their polarization capacity in different inflammatory contexts is not fully elucidated. Therefore, the main aim of this project is to study the molecular mechanisms by which TSLP imprints metabolic and epigenetic reprogramming in human DCs and their functional consequences in the initiation and chronification of pathological immune responses. Freshly isolated CD1c+ myeloid DCs (mDCs) from healthy donors do not express TSLP receptors (TSLPR and CD127), but 24h of culture with complete RPMI significantly increases the number of TSLPR+CD127+ cells. Tezepelumab impairs the TSLP-induced expression of OX40L, HLA-DR, CD40 and CD83, as well as Th2 chemokine production (TARC/CCL17 and MDC/CCL22) in mDCs. TSLP-activated mDCs display a metabolic reprogramming towards an increase of glycolysis and mitochondrial oxidative phosphorylation, as well as an epigenetic reprogramming that enhances gene transcription. TSLP blockage by Tezepelumab prevents metabolic rewiring in mDCs and their capacity to polarize naïve CD4+ T cells towards Th2 responses. Overall, our findings enhance the knowledge on how TSLP induce metabolic and epigenetic rewiring in human DCs and their functional implications, as well as how TSLP restore healthy responses.

W48 ACC1 regulates adipose type 2 innate lymphoid cell differentiation to maintain metabolic health

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Group 2 innate lymphoid cells (ILC2) residing in the adipose tis-

sue play an important role in maintaining the metabolic health and energy balance of the organisms. In obesity ILC2 numbers are reduced and their function is impaired, leading to the progression of metabolic inflammation. However, which events impact on ILC2 biology in the adipose tissue in obesity remains unresolved. Here, we show that high fat diet (HFD)-induced obesity results in the metabolic reprogramming of adipose ILC2, decreasing the expression of acetyl-CoA carboxylase 1 (ACC1), which is critical for maintaining the citrate shuttle, and thus a metabolic program allowing cellular differentiation. Investigating a possible connection between ACC1 and obesity-induced changes in ILC2, we uncover that fatty acids regulate the expression of ACC1, while pharmacological inhibition of ACC1 diminishes mitochondrial function and ILC2 metabolism. Furthermore, deletion of ACC1 in ILC2 phenocopies the overall reduction and functional impairment of ILC2 observed in obesity, which ultimately leads to increased triglycerides in circulation, adipose tissue hypertrophy and inflammation, even in the absence of HFD. We further uncover that HFD-feeding or deletion of ACC1 results in the accumulation of undifferentiated ILC2 and local ILC progenitors in the adipose tissue, suggesting that ACC1 may primarily regulate the maturation of ILC2. These findings suggest that obesity primarily impacts type 2 immunity by impairing adipose ILC2 differentiation and activation via ACC1 expression, rather than causing cell death through lipid overload and lipotoxicity, offering an explanation for the inefficacy of ACC inhibition in obesity.

W49 Exposure of nasal epithelial cells with pollen aerosols and coronaviruses in a near-physiological in vitro model

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Background: We had previously shown that pollen exposure resulted in an increased susceptibility of respiratory epithelial cells to infection with rhinovirus due to a blunted type I and type III interferon response. During the first and second waves of the COVID-19 pandemic, positive correlations were observed between airborne pollen concentrations and SARS-CoV-2 infection rates, both worldwide and in Augsburg, Germany. Due to our previous findings, we hypothesized that pollen might render nasal epithelial cells more susceptible to infection with coronaviruses. Methods: Primary nasal epithelial cells (HENCs) were isolated from conchotomic surgery specimens and cultured at the air-liquid interface. Fully differentiated HNECs were pre-exposed to clean air or to pollen aerosols (birch, timothy grass) for 10 min, 12h or 24h and subsequently infected with hCoV 229E or SARS-CoV-2 (0.25 MOI). Plaque assay was performed 24h and 48h post infection (p. i.) with Huh-7 (hCoV 229E) or Vero-6 (SARS-CoV-2) cells to determine infectious particle production; dPCR or qPCR was used to determine viral genomes. Apical and basolateral supernatants were collected for cytokine and chemokine analysis. Results: Exposure of HNECs to pollen aerosols led to excessive mucus production at 12h and 24h post-exposure. Plaque assays revealed infectious virus particle production 48h after infection of HNECs with 229E or SARS-CoV-2, however, there was no increase over time, indicating poor virus replication in the HNECs. Significant increases in infectious virus particle production were seen in birch pollen pre-exposed cells. Grass pollen pre-exposure only led to a trend-wise increase in virus infectivity. The virus PCRs showed similar results. The effects of pollen co-/pre-exposure were very similar in the hCoV 229E and SARS-CoV-2 infection models. Conclusion: Our near-physiological in vitro model results support the hypothesis that high airborne birch pollen concentrations during springtime could facilitate coronavirus transmission via their interaction with nasal epithelial cells.

W50 Reprogramming lipid-laden foamy macrophages and exosomes production in lung inflammatory diseases

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Chronic Obstructive Pulmonary Disease (COPD) is common chronic respiratory disease with high morbidity and mortality rate. The risk factors, such as cigarette smoke and air pollution, cause an imbalance in the expressions of proteolytic enzymes and reactive oxygen species (ROS), which contribute to the damage to the alveolar structure and the production of inflammatory mediators. We previously found that increased foamy macrophages in patients with COPD, and the lipid-laden foamy macrophages (LLFM) contribute the development of COPD. Moreover, pulmonary surfactant protein D (SP-D) has shown protective role for LLFM-induced lung inflammation. In this study, we investigated how LLFMs contribute to the progression of COPD, and address the mechanisms, molecular targets, and therapeutic potential involved in reprogramming LLFMs and regulating exosome production via SP-D. We found foamy macrophages produced high levels of inflammatory cytokines and ROS. In comparison of the difference of exosomal microRNAs released from macrophages and foamy macrophages using RNA seq, we found miRNA let-7 was significantly reduced in the foamy macrophage-derived exosomes compared to normal macrophages. Overexpression of let-7 reduced the number of foamy macrophages induced by oxidized low-density lipoprotein (oxLDL). We further examined how let-7 mediated the lipid metabolism and found that let-7 promoted lipid catabolism through inhibiting the expression of the ring finger protein 8 (RNF8) and retinoid X receptor (RXR) in lipid-laden foamy macrophages. Furthermore, let-7 also reduced the expression of inflammatory cytokines, interleukin 6 and TNF-alpha that were highly expressed in the foamy macrophages. In conclusion, we demonstrated that miRNA let-7 mediated the lipid metabolism via RNF9 and RXR pathway in foamy macrophages and further prevented the formation of foamy macrophages. This study reveals a novel insight of foamy macrophages and miRNA in the pathogenesis of COPD, and provide target therapy opportunity for this incurable disease.

W51 Effect of Physical Exercise on the Immune System: Proteomic Profiling Reveals Endotype Variations Associated with Activity Level and Intensity in Athletes

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Physical exercise affects the immune system depending on its intensity, duration, and training load. It modulates immune response through changes in cytokines, chemotactic factors, adhesion molecules, and reactive oxygen species. Regular moderate-to-vigorous exercise promotes an anti-inflammatory state, enhances immune surveillance, and offers protection against chronic diseases, infections, and potentially cancer. In contrast, vigorous exercise can induce a pro-inflammatory state and impair immune function. Endurance sports focus on slow-twitch muscle fibers, while anaerobic sports target fast-twitch fibers for power and speed. In this study, we used proximity extension assay (PEA)-based targeted proteomics to assess the impact of exercise on organ damage, immune response, and inflammation in winter sport athletes, amateur athletes, and non-athletic controls. Our results show that endurance training reduces levels of IL-6, IL-15, and FGF-21, with higher exercise intensities inversely affecting these proteins. Chronic intense training without recovery may suppress immunity, but regular exercise improves chemotaxis and immune functions. Parvalbumin, important for muscle relaxation, is found more in fast-twitch fibers, while TNNI3 up-regulation could improve cardiac performance. The PI3K-Akt pathway supports cardiac hypertrophy, and its changes, alongside MAPKs activated by IL-18, promote pro-inflammatory cytokine production for tissue regeneration. High-intensity exercise enhances the innate immune response to viral infection, especially during the acute training phase, by increasing chemokines, leukocyte chemotaxis, T cell activation, and angiogenesis. IL-8, involved in neutrophil migration and angiogenesis, is produced locally in muscles during exercise with minimal systemic effects, while intense exercise can also raise IL-10, leading to immunosuppression. Professional athletes tend to have a pro-inflammatory immune profile, with variations linked to activity type and intensity. Endurance athletes show a more anti-inflammatory profile. In conclusion, omics approaches offer valuable insights into athlete health, exercise-immune interactions, and the identification of biomarkers to distinguish between normal recovery and overtraining, ultimately helping to balance immune health and optimize performance.

W52 Lymphocyte-derived IFN-γ primes alveolar macrophages for ZBP1-mediated death during influenza infection

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Alveolar macrophages (AMs) are lung-resident innate immune cells located in the alveolar space that are important for the maintenance of lung homeostasis. AMs act as sentinel immune cells and are crucial for initiating proper immunological responses to respiratory pathogens. The absence or dysfunction of AMs typically results in the accumulation of cellular debris from dying epithelial cells and pulmonary alveolar proteinosis, which impairs gas exchange and ultimately leads to lung failure. In the context of respiratory infections, such as infection with influenza A virus (IAV), a phenomenon known as the 'macrophage disappearance reaction' occurs, leading to a depletion of resident AMs and contributing to disease pathogenesis. Using ex vivo culturing systems of primary AMs from mice and IAV infection mouse models in vivo, we aimed to comprehensively characterize the mechanisms underlying AM disappearance. Our findings demonstrate that AMs are directly infected and undergo inflammatory cell death, exhibiting both apoptotic and pyroptotic features. We have identified the innate immune sensor Z-DNA binding protein 1 (ZBP1) as a critical mediator of AM death, as its deletion using CRISPR-Cas9 protects AMs. Interestingly, in vivo, we show that ZBP1 induction depends on interferon (IFN)-gamma production by T cells and NK cells. In contrast, autocrine type I IFN production by infected AMs is critical for ZBP-1 induction and cell death observed ex vivo. The inhibition of IFN-gamma signaling and, consequently, AM death reduces the severity of IAV infection and mitigates the risk of serious secondary bacterial infections. These findings suggest that targeting AM survival may provide a therapeutic strategy to control lung inflammation and improve outcomes during severe respiratory infections.

W53 Alternative splicing of Nod-like receptor (NLR) isoforms

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Nod-like receptors (NLRs) are a family of pattern recognition receptors (PRRs) responsible for sensing a variety of microbial and cellular stress signals to initiate innate immune signalling. Regulation of NLR activity is vital for maintaining homeostasis and optimal tissue function, where dysregulation of such processes can contribute to tissue damage and disease. Alternative splicing of pre-mRNA is one such regulatory mechanism. Our group and others have previously shown that alternative splicing of NLRP3, a pro-inflammatory PRR, can reduce its activity. However, alternative splicing mediated regulation of other NLRs has not been explored, nor is it known if or how alternative splicing of NLRs is implicated in disease. We have utilised a targeted long-read sequencing approach to identify splice isoforms within the leucine-rich repeat domain of several NLRs involved in innate immune signalling. Furthermore, our preliminary data suggests that there is a subset of NLR isoforms that is differentially expressed between peripheral blood mononuclear cells and human monocyte-derived macrophages. This implies that alternative splicing may be a mechanism by which different cell types can regulate NLR signalling and hence modulate innate immunity.

W54 A network of interferon-stimulated genes regulates human LINE-1 retrotransposition

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Persistent activations of innate immune responses caused by endogenous mobile genetic elements are suggested to contribute to sterile inflammation, which may lead to age-related inflammation and autoimmune phenotypes. Human Long Interspersed Element-1 (LINE-1 or L1) retrotransposon is the only active and autonomous mobile genetic element in the human genome, which can “copy-and-paste” its own sequences to be inserted into different locations in the genome through a process termed retrotransposition. L1 retrotransposition cycle will produce L1 RNA, L1 proteins (ORF1p and ORF2p that bind to L1 RNA to form L1 ribonucleoprotein complex), and L1 cDNA reverse transcribed by ORF2p. L1 RNA and cDNA can trigger innate immunity with type I interferon (IFN) production independent of retrotransposition, potentially upregulating the downstream interferon-stimulated genes (ISGs) expression to inhibit L1 intermediates and/or retrotransposition. However, the identity and mechanism of action of these ISGs remain to be elucidated. Our immunoprecipitation-coupled mass spectrometry of the L1 ORF1p complex in HeLa cells revealed a network of ISG proteins that associate with the L1 complex. Retrotransposition assays uncovered several ISG proteins that inhibit L1 retrotransposition when overexpressed, including: (1) HECT and RLD domain containing E3 ubiquitin protein ligase 5 (HERC5); (2) helicase with zinc finger 2 (HELZ2); and (3) 2'-5'-oligoadenylate synthetase-like (OASL). We focused on HELZ2, a protein that contains two helicase domains and an exoribonuclease RNase II/R (RNB) domain. We found that the helicase activity is required for significant reduction of the steady-state level of L1 RNA, ORF1p, and retrotransposition efficiency. Notably, the L1 5’ UTR was found to be the target of HELZ2-dependent L1 RNA destabilization. We also demonstrated that L1 RNA was sufficient to induce the type I IFN response and HELZ2 overexpression strikingly reduced L1-dependent IFN-α upregulation by ~16-fold. In sum, we reported an ISG network that inhibits L1 retrotransposition.

W55 Benefitial effects of gluten-free diet in the chonic model of MPTP-induced alpha-synucleinopathy (Parkinson´s disease) in C57Bl/6 mice

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Recent data suggest, that due to existence of the brain-gut axis, and even possible spreading of alpha-synuclein from the gut to the brain, chronic intestinal inflammation may contribute to the pathogenesis of neurodegenerative diseases, e.g. the Parkinson`s disease (PD). Dietary gluten/gliadin display pro-inflammatory properties.
The aim of this study is to test possibly beneficial, anti-inflammatory effects of gluten-free diet (GFD) in the chronic MPTP-induced mouse model of PD. C57Bl/6 mice received three weekly i.p. injections (20mg MPTP/kg) for period of 8 weeks. One week later, the mice were used for behavioral testing (open-field test), detection of dopamin and its metabolites in the brain, and collection of lymphoid organs for flow cytometry analysis. Interestingly, mice fed the GFD displayed higher exploration values in the open field test indicating an increased willingness to engage with their environment, whereas mice fed STD demonstrated slightly decreased locomotor activity. Flow-cytometry analysis revealed tendency to increased proportion of CD4+Foxp3 Tregs in almost all lymphoid organs studied in animals on the GFD. In addition, similarly to effects of GFD in some other immune-mediated diseases, our data also documented increased proportion of gamma/delta T cells in mice fed GFD, suggesting a potential regulatory role for gamma/delta T cells in PD. No changes were observed in proportions of CD4+CD45RB-low T cells, IL-10-positive CD4+ and IFNgamma-positive CD8+ T cells, and in various (CD27+, CD27-, NKG2D-high) subsets of NK cells. Our data indicate subtle positive effects of the GFD in the chronic MPTP mouse model of PD. Further experiments are needed to clarify the effect of GFD in PD, as dietary interventions may represent a safe and promising approach to improve clinical symptoms of PD
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W56 Gluten-free diet reduces severity of DSS-induced colitis in BALB/c mice

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Inflammatory Bowel Disease (IBD), is a chronic inflammatory condition in which gut microbiota, intestinal permeability, and nutrition play critical roles. While probiotic bacteria or beneficial metabolites have been subject of intense research, dietary interventions attracted less attention. Dietary gluten/gliadin display pro-inflammatory, LPS-like properties, and thus gluten-free diet (GFD) has even been proposed for IBD patients. We examined the effect of GFD in the mouse model of dextran sulphate sodium (DSS)-induced colitis in two regimens.

SPF BALB/c mice were fed standard (STD) or gluten-free (GFD) Altromin diets for periods of 4 weeks prior the one-week exposure to 2.5% dextran sulphate (DSS). In the second scheme, GFD diet was introduced only 2 days before and again during the one-week exposure to 2.5% DSS. Colon lengths, intestinal bleeding, weight loss, histological parameters of the colon, flow cytometry analysis of colonic leucocytes as well as of Tregs, memory/effector T cells, and NK cells in lymphoid organs were used to characterize the exposure to GFD. Four-week exposure to GFD prior to DSS-administration led to highly statistically significant preservation of colon lengths (p<0.001), decreased intestinal bleeding, significantly improved histology (crypt length) and decreased inflammatory infiltrate in colon (e.g. Ly6C+ monocytes), and also to changes in proportions of T-cell subsets of mesenteric lymph nodes (MLNs). Interestingly, even short exposure to the GFD during induction of DSS-colitis preserved the colon lengths (p<0.05) and influenced several T cell subsets in MLNs. Thus, the long-term exposure to GFD substantially reduced DSS-induced colitis in SPF BALB/c mice and had even some effect if applied only during the course of the IBD induction. We think that dietary interventions with GFD represent a safe therapeutic strategy for translation to clinical trials (this work was supported by grant no. NU22-06-00269 from the Ministry of Health, CZ).

W57 Asthma-protective in vitro farm-dust stimulation modulates dendritic cell co-inhibition and co-stimulation in childhood asthmatics

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Asthma is one of the most common chronic diseases in childhood. Its prevalence is increasing in Western countries with high hygiene standards, while children growing up in farming areas are protected from childhood asthma. This phenomenon, known as the “asthma-protective farm effect” was replicated repeatedly in epidemiological studies. This study aimed to identify underlying immunological mechanisms with a focus on dendritic cells (DCs) by gene expression analysis. Therefore, DCs isolated from peripheral blood mononuclear cells of allergic asthmatics (AA) and healthy children (HC) were analyzed upon 24h of in vitro farm-dust stimulation using the NanoString-PanCancer Immune Profile Panel (5AA/7HC). Pathway analysis was performed using the annotations provided by NanoString. Moreover, expression of selected maturation, coinhibitory and costimulatory molecules was further examined using qRT-PCR of differentiated monocyte-derived DCs upon 24h of in vitro farm-dust stimulation (5AA/3HC). Following in vitro farm-dust stimulation, analysis of NanoString data revealed significant regulation of 378 (in HC) and 255 (in AA) genes from which 127 (in HC) and 85 (in AA) remained significant after adjustment for multiple testing. Significantly regulated genes in both phenotypes were inter alia related to innate and adaptive immune genes, cell-type specific signaling, regulation of immune and inflammatory response, T cell differentiation, and basic cell function. Transcriptional regulators, TNF superfamily genes, and genes associated with inflammatory response, and T cell polarization were only modulated in HC. qRT-PCR upon in vitro farm-dust stimulation of monocyte-derived DCs demonstrated upregulated expression of CD274 (<0.05 for AA and HC), CD83 (<0.05 for AA and HC) and CCR7 (<0.05 for AA)). These findings suggest a crucial role of DCs, their maturation and their coinhibitory properties for the asthma-protective farm effect and may point to a potential future therapeutic application using farm-dust (components).

W58 Revisiting the Hygiene Hypothesis – Impact of Siblings on Early Life Microbiome Composition and Metabolism

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The hygiene hypothesis was first proposed by Strachan in 1989, following his observation that hay fever was less common among children with older siblings. Subsequent studies supported the association of birth order with allergic sensitisation. We hypothesised that siblings might be an important reservoir of non-spore forming microbes, influencing and inducing early life gut microbiome development and immunoregulatory networks within the host. Metagenomic sequencing of infant faecal samples from the CORAL study at 6 and 12 months of age was performed. Metaphlan and Humann3 analysis pipelines were used to characterize microbial taxa and map their functional potential through metabolic pathway abundance. Metagenomic data was integrated with associated metadata to enable comparative analyses of infants with (n=187) or without (n=160) siblings. Microbiota composition at 6 months of age was not substantially influenced by the presence of siblings. However, at 12 months of age, infants with siblings had significantly higher levels of immunoregulatory microbes such as Bifidobacteria, Doria and Faecalibacteria, with lower levels of pathobionts such Veillonella, Citrobacter and Enterococcus. The relative abundance of 51 microbial pathways were significantly different at 6 months of age (15 pathways higher in infants with siblings), while 215 microbial pathways were significantly different at 12 months of age (13 pathways higher in infants with siblings). Multiple microbial pathways relevant to host immune responses were associated with the presence of siblings, including short chain fatty acid, histamine and bile acid metabolism. The presence of siblings within the home has a profound effect on infant early life gut microbial composition and associated metabolic activity. These microbiome differences may mediate the protective effects associated with birth order on allergy risk. Our data suggests that we need to revisit and update the hygiene hypothesis, which remains a misleading misnomer that incorrectly encourages unhygienic practices including exposure to infections.

W59 A rodent model to explore the impact of farm-like environmental conditions on gut barrier, immune regulation and disease outcomes

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Laboratory rodents in barrier facilities may fail to develop a diverse microbiome and immune training, risking poor translatability to humans. We have established a housing system exposing lab to farm-like conditions including soil and domestic animal excrements, representing a realistic living habitat for the house mouse. In a range of experiments we have found that these “feralized” mice shifted their gut microbiota, obtained a matured immunophenotype, showed improved barrier integrity and became more resistant to intestinal inflammation and colorectal cancer development. The feralized microbiota provided resilience to the induction of intestinal inflammation by dextran sodium sulphate (DSS). Interestingly, when given fiber controlled diets, feralized fiber-rich eaters were particularly protected, while clean fiber-rich eaters mice were the most susceptible to DSS-induced inflammation, the fiber-low groups falling inbetween. In some experiments, we added cohousing with wild-caught mice to donate murine commensals and pathobionts. Wild mouse cohousing further improved intestinal barrier markers, microbiota and increased presence of resident memory CD8+ T-cells in the intestinal wall, and more signs of systemic immunity maturation. We have not observed clinical disease as a result of wild mice cohousing. In response to a parenteral influenza vaccine, feralization and wild cohousing did not affect the antibody response. In contrast, when cohousing with pet store mice, vaccine response was compromized. Pet store mice brought more numerous and severe pathogens, and often clinically affected the cohabitants. In conclusion, exposure of lab mice to farm-like conditions conveyed a shift of the gut microbiota, gut barrier and immune functions. Exposure to wild mice potentiated these changes, but donors carrying too great pathogenic burden may compromize health and immune responses. Altogether, lab mice feralized in a farm-like environment may add translational value to mucosal immunity modeling, and presents as an opportunity to explore how environments varying in microbial pressure may affect disease conditions.

W60 The role of bacteria-derived histamine in allergy associated airway diseases

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The prevalence of allergic diseases affects up to 40% of the population worldwide, with respiratory allergies being among the most common ones. Chronic rhinosinusitis (CRS) is an inflammatory disease of the upper respiratory tract (URT). Type 2-CRS and other

respiratory conditions associated with allergic reactions are complex diseases presenting with common etiologies of inflammation and/or infections. Histamine secreted by host cells during allergic reactions is well recognized, however the presence and mechanisms of action of histamine-secreting bacteria within the host has just started to be investigated. To identify and characterize the URT bacterial histamine producers we collected nasal swabs from healthy volunteers and nasal secretions from patients with type 2 CRS and control subjects. To check the amount of secreted bacterial histamine we determined the level of histamine secreted to the supernatant by inoculating the samples in rich microbiological media. The measurement of secreted histamine was done by the UPLC-DAD method. We identified one strain of Staphyloccocus capitis that in-vitro secreted more histamine than positive controls. Afterwards, using nose secretion cohort, we have inoculated BHI media with mucus samples to allow whole bacteria consortiums to grow. In screened nasal secretion samples, we have observed that the amount of histamine secreted by bacteria was lower in the CRS type 2 patients compare with control subjects. Bacteria that are able to produce and secrete histamine are present in URT. Even though it might seem surprising that bacterial histamine level is lower in CRS type 2 patients compared to control, the outcome is in line with my previous finding, showing significant decrease in the lung inflammation in animals' gavaged with bacteria that secrete histamine, compared to positive control. The histamine secretion from bacteria most probably have influence on allergic responses and can have immunological consequences, however the effects required detailed further studies.

W61 Single-cell spatial transcriptomics reveals the mucosal landscape at the airway wall in health and asthma

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Understanding the mucosal landscape of complex disorders such as asthma is essential to define novel pathways for diagnosis and therapeutical approaches. Omics and imaging approaches have revolutionized our vision of the cellular complexity of mucosal surface and how disease impacts not only the essential function of cells but also their interactions between each other. We recently employed spatial transcriptomics to decipher lung architecture in childhood asthma (Joulia et al. JCI 2024), analysing changes in the pulmonary vasculature. Here, we extended this analysis of the airway wall by employing the single-cell spatial transcriptomic platform, Xenium in combination with full transcriptome platform GeoMX. We characterised more than 97,000 cells from endobronchial biopsies taken from 9 healthy and 20 asthma donors undergoing treatment with biologics or a tyrosine kinase inhibitor (i.e. imatinib). We identified sub-populations of basal cells and endothelial cells cooperating at the airway wall, that expressed large amounts of alarmins such as IL-33 as well as chemokines. Imatinib treatment greatly reduced the ability of these cells to express pro-inflammatory mediators and modified their cellular interactions. Furthermore, we provide an in-depth phenotype analysis of mast cells and discovered how imatinib inhibited their expression of proteases such as CPA3 or mediators such as amphiregulin. Finally, we provided an innovative approach to evaluate drug/target interaction in situ using the modified drugtocell pipeline. This study provides an unprecedented overview of the pulmonary mucosal barrier and the cellular communities that reside in distinct anatomical niches, while exploring new facets of lung response to current therapies. Funded by the Wellcome Trust.

W62 Novel cytokine pattern associated with severe childhood asthma

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Mild-to-moderate and severe asthma can be categorized into distinct endotypes based on various immunological phenotypes and cytokine profiles. Severe asthma is associated with significant morbidity, implying the importance to better understand the underlying immune mechanisms. We aimed to characterize severe childhood asthma by gene expression and cytokine secretion to identify potential new therapeutic targets. Gene expression profiles from isolated peripheral blood mononuclear cells (PBMCs) of school-age children between healthy (HC), asthmatic (A) and severe asthmatics (SA) were compared using bulk mRNA sequencing (total n=190). Differential gene expression analysis (Limma R-package) and Gene Set Enrichment Analysis (GSEA) were performed (p-values were corrected for multiple testing). Cytokine secretion of unstimulated and stimulated PBMCs was measured (n=342). Statistical analysis was performed by linear regression. Gene expression analysis revealed 640 significantly higher and 420 significantly lower expressed genes in SA compared to HC. Moreover, 150 significantly higher and 70 significantly lower expressed genes were identified in SA compared to A. No significant difference in gene expression was found between A and HC. GSEA analysis using GO terms revealed that genes lower expressed in SA than in HC and A were mainly related to chemokine activity. Geneset analysis using KEGG pathways showed that genes lower expressed in SA than in HC and A were mainly related to cytokine-cytokine receptor interaction, IL-17-, TLR- and TNF-signaling pathways (FDR ≤ 0.05). Cytokine secretion assays demonstrated that without stimulation, CCL7 secretion was significantly lower in SA compared to A and HC. After LpA stimulation, CXCL10 secretion was significantly lower in SA compared to A and HC, while IL-17 and IL-23 secretion was significantly higher in SA compared to A and HC (p-values ≤ 0.05). IL-17 and IL-23-associated immune pathways may be relevant for asthma severity, whereas decreased CXCL10 and CCL7 secretion may point to impaired IFN and IL-1beta/TNFalpha-responses, respectively.

W63 Fast itch relief during dupilumab predicts clinical efficacy in bullous pemphigoid

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Background: Dupilumab has emerged as a promising treatment option for bullous pemphigoid (BP). Rapid identification of responders could avoid the need of additional immunosuppressive treatments that are associated with increased morbidity and mortality. Methods: To investigate the course of itch as an early indicator of treatment response, data of 12 BP patients treated with dupilumab at the University Hospital of Zurich were retrospectively evaluated. Disease severity was assessed by bullous pemphigoid disease area index (BPDAI) and pruritus by a numeric rating scale (NRS, 0-10) at baseline, day 1, 3, 14, month 1, 2 and last follow-up. Results: 8/12 patients (67%) had complete, and 4/12 patients (33%) had partial response during dupilumab treatment. Notably, a highly significant reduction of pruritus (p < 0.0001) was observed already on day 1 with further improvement at later time points. Moreover, fast relief of itch could predict treatment response with a significant correlation to clinical response on day 14 (Pearson correlation R 0.64, p-value 0.047) and an almost significant correlation by day 3 (R 0.68, p-value 0.061). Additionally, 92% (11/12 patients) were on dupilumab monotherapy at last follow-up without any concomitant systemic or topical treatment for BP. Currently, serum proteomics (OLINK) at baseline and follow-up is ongoing for further mechanistic data to support the clinical response. Conclusions: The rapid and significant decline in BP-associated pruritus observed with dupilumab correlated significantly with disease remission. Early pruritus response after the initial dupilumab injection could indicate treatment response. Therefore, this could change how bullous pemphigoid is treated in the future and avoid additional immunosuppressive treatment in BP. Larger data is needed to confirm our findings.

W64 Metabolomic and Proteomic Profiling of Severe Olive-Allergic Patients Treated with Dupilumab

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Allergy is one of the most prevalent chronic diseases worldwide, with approximately 10% of allergic individuals developing severe phenotypes characterized by Th2-driven chronic inflammation and a dysregulated Treg response. Severe allergic patients often do not respond to conventional treatments, highlighting the need for personalized therapeutic approaches. Particularly, olive tree (Olea europaea) pollinosis is a major cause of respiratory allergy in the Mediterranean basin, with severe phenotypes commonly associated with a strong sensitization against minor allergens like Ole e 7, predominant in areas of extreme pollen exposure. In the last decade, biological agents targeting the exacerbated Th2-derived signalling, such as Dupilumab. This monoclonal antibody targets IL-4/IL-13-controlled pathways and has shown clinical efficacy in different allergic contexts, such as asthma and atopic dermatitis. However, its systemic immunometabolic effects remain unclear. This study evaluates the effect of a 6-month Dupilumab treatment in severe asthmatic patients (GINA steps 4-5) sensitized to Ole e 7. Serum samples collected from non-treated (n=10) and treated (n=12) severe allergic patients at baseline (T0) and after 6 months of Dupilumab administration (T1) were analyzed through targeted metabolomic (including fatty acids, sphingolipids, carnitines, amino acids and lysophospholipids among others) and proteomic (including chemokines, cytokines and growth factors among others) approaches. The analysis revealed that Dupilumab treatment induced significant changes in the metabolomic and proteomic profile of these patients after 6 months (e.g. decrease in fatty acids and increase in IL-4 and CCL2) and when comparing to the non-treated group (e.g. decrease in LPCs and TNFSF12 and increase in IL-4). Altogether, these results points towards a reduction of pro-inflammatory molecules after Dupilumab treatment. These findings offer valuable insights into the immunometabolic effects of Dupilumab in severe allergic asthma, highlighting the existence of potential serum biomarkers for clinical validation of treatment monitoring.

W65 Eosinophils control intestinal commensalism to sustain homeostasis

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Eosinophils are bone-marrow-derived granulocytes that reside at mucosal interfaces, playing a pivotal role in gastrointestinal tissue morphogenesis and homeostasis. While the bidirectional relationship between eosinophils and bacterial communities is increasingly recognized, its underlying mechanisms remain poorly understood. Here, we provide novel insights into this dynamic interplay. Using transient and complete eosinophil-deficiency models combined with 16S rRNA microbial sequencing, multiplexed imaging, flow cytometry, and in vitro immunological assays, we demonstrate that eosinophils are essential for maintaining balanced gut microbiotal communities, particularly mucus-dwelling bacteria, Helicobacter species and members of the Clostridia class. Notably, eosinophil-deficient mice exhibit alterations in colonic villi architecture and a thinner mucus layer, bringing microbes into closer proximity to the epithelium and facilitating inflammation. We further show a key role for neonatal eosinophils in establishing immune homeostasis and regulating the microbiota composition. Their selective depletion prior to weaning results in microbial dysbiosis, which increased their susceptibility to developing allergic and metabolic diseases in adulthood. Transplanting the microbiome from eosinophil-deficient mice into wild-type recipients further resulted in microbial dysbiosis and systemic bacterial dissemination, further confirming the pivotal role of eosinophils in regulating microbiome-host interactions Additionally, a screen of over 20 bacterial strains revealed that specific microbes differentially activate eosinophils through TLR4-dependent mechanisms, highlighting a bidirectional relationship where eosinophils shape bacterial communities while bacteria selectively influence eosinophil function. Altogether, our findings underscore the critical role of eosinophils in shaping the intestinal microbiota and maintaining gut-immune homeostasis. Disruptions in this interplay have profound and lasting consequences on host physiology and disease susceptibility.

W66 Unveiling GPR35 as a Metabolic Hub in Eosinophilic Esophagitis: Connecting 8-methoxykynurenate, Macrophages, and Epithelial Dysfunction

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Eosinophilic esophagitis (EoE) is a chronic inflammatory disorder driven by disrupted epithelial barrier integrity and complex cytokine signaling. Emerging evidence highlights GPR35 as a key regulator of cytokine activity and epithelial preservation, though its precise role in EoE remains unclear. This study explores Gpr35's function in EoE using patient-derived organoids and an EoE mouse model. Analysis of esophageal biopsies from patients with active EoE revealed significant upregulation of GPR35 expression. Using the Gpr35-tdTomato reporter mouse model, we identified that Gpr35 expression in the esophagus is predominantly localized to macrophages and dendritic cells. Deletion of Gpr35 in macrophages attenuated the EoE phenotype, reducing eosinophil infiltration, Th2 cytokine expression, and IL-18 levels in the esophagus. Stimulation of patient-derived organoids with IL-18 impaired the expression of epithelial barrier-associated genes and proteins. Computational docking experiments identified 8-methoxykynurenate (8-MK), a tryptophan derivative, as a potential endogenous ligand for GPR35, offering insight into its classification as a formerly orphan receptor. In vitro studies revealed that 8-MK stimulation of BlaER1 cells and bone marrow-derived macrophages increased IL-18 expression, while immunoblotting confirmed that cleaved IL-18 release is NLRP3-caspase-1 dependent. These findings reveal that Gpr35 orchestrates cytokine-driven inflammation and epithelial barrier dysfunction via macrophages in EoE, positioning it as a metabolic hub and potential therapeutic target for this disease.

W67 Arginase 1 and 2 as regulators of the B cell response

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Most vaccines confer protection against infection by induction of specific antibodies. The effectiveness of vaccines depends on the sustained production of long-lasting, high-titre antibody responses. However, recent experiences with the COVID-19 pandemic have highlighted a lack of fundamental understanding of how these vaccine-induced antibody responses can be sustained over the long term, an essential goal in the field of vaccinology. Our experiments have shown an increased expression of Arginase 2 in MBC compared to GCB, while Arginase 1 was higher in GCB cells compared to MBC. Both arginases convert L-Arginine to Urea and L-ornithine and thus compete with inducible nitric oxide synthase (iNOS or NOS2) for the L-Arginine substrate and thus can regulate the nitric oxide (NO) pathway, a known regulator of immune function again via NF-κB. This led us to generate a CD19creArg1lox mouse line to study the role of Arginase 1 in B cells and GC versus plasma cell formation. We found levels of antigen-specific IgG antibody in these mice are initially similar to wild type mice after immunization with VLPs. However, after day 21, these mice fail to maintain high levels of antigen-specific IgG, indicating a failure to generate long-lived plasma cells as we have previously seen in complement-receptor deficient mice. In contrast, deletion of arginase 2 in B cells led to an early increase and earlier decline of antibody responses. These data indicate a critical role for arginase metabolism in the antibody response and, surprisingly, a dual role of the two enzymes in the regulation antibody responses.

W68 Tracking antigen specific T cell responses during myocardial aging

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Aging induces profound changes in the immune system paralleled by increased cardiovascular risk and heart failure incidence. We previously reported that T cells in heart draining mediastinal lymph nodes

(medLN) accumulate an age-dependent interferon-gamma (IFN-gamma) signature, accompanied by a distinct T cell receptor (TCR) repertoire clonal expansion pattern. Herein, we sought to dissect factors triggering age-related clonal expansion of IFN-gamma producing T cells and identify their antigen specificity. First, to address whether age-related clonal expansion is triggered by life-long microbial exposure, we characterized cardiac and medLN T cells in aged (18 months old) germ-free mice. Flow cytometry and single-cell sequencing analyses indicated that despite the absence of microbial exposure, aged mice still maintained the T cell effector and IFN-gamma production phenotype in the heart and in medLNs, suggesting that clonal expansion is triggered by intrinsic factors. Next, to assess whether age-associated myocardial oxidative stress and injury could be the cause of clonal expansion in heart-draining LNs, we analyzed aged mice over-expressing mitochondrial catalase (mCAT) in cardiomyocytes. Interestingly, aged mCAT mice maintained the T cell IFN-gamma production phenotype both in aged heart and medLNs, indicating that these responses are not induced by myocardial oxidative damage. To test whether IFN-gamma-producing T cells that undergo clonal expansion with aging are enriched for cardiac antigen specificity, we selected 23 highly expanded TCRs from IFN-gamma-producing CD4, CD8 and, regulatory T cells of aged medLNs for expression, functional characterization, and testing their putative cardiac antigen specificity. Taken together, this study suggests that the spontaneous T cell clonal expansions observed in aged mice are not triggered by life-long exposure to pathogens, nor to cardiomyocyte damage associated with oxidative stress. Ongoing experiments based on TCR tools will address whether these mechanisms are dependent on cardiac antigens and eventually lead to the identification of cardiac epitopes relevant during aging.

W69 Ineffective L-phenylalanine metabolism aids pro-inflammatory Th2 phenotype in severe allergy

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Changes in T cell metabolism guide and determine their fate. Efficient T cell metabolism is crucial for cellular activation, proliferation, function and memory formation. However, the metabolism and metabolic reprogramming exhibited by CD4+ T cells and their subsets in allergic diseases remains poorly understood. In order to address these knowledge gaps, we first performed metabolomics of circulating memory CD4+ T effector (Teff) and T regulatory (Treg) cells from healthy subjects which revealed significant enrichment in pathways related to amino acid and L-phenylalanine (Phe) metabolism. Hence, we studied the effect of Phe on CD4+ T cell energy metabolism and observed that Phe significantly enhanced total and memory CD4+ T cell glycolysis while limiting mitochondrial oxidative phosphorylation. Furthermore, Phe limited memory CD4+ T cell proliferation via an Interleukin-4-induced-1 oxidase (IL4I1)-dependent mechanism which was confirmed using siRNA and CRISPR gene modifications. Next, we studied the energy metabolism of Th2 and Treg cells under the influence of Phe, using recently developed Single Cell ENergetIc metabolism by profilIng Translation inhibition (SCENITH), and observed that Phe specifically and significantly increased Th2 cell glycolytic capacity while decreasing their mitochondrial dependence. Phenotypic assessment of in vitro differentiated Th2 cells revealed that Phe not only limited Th2 cell proliferation, as seen in memory CD4+ T cells, but also mRNA expression of critical type 2 transcription factors and cytokines such as mTOR, BACH2, BATF, IL-4, IL-5, and IL-13. Furthermore, Phe also reduced the expression of CD161, a previously reported pathogenic Th2a cell marker. Finally, metabolomics and ex vivo assessment of CD4+ Teff cells and serum of allergic patients revealed significantly lower intracellular abundance of Phe in circulating memory CD4+ Teff cells of a subset of severe allergic patients, elevated serum Phe concentration, and a significant negative correlation between LAT1, an important Phe transporter, and serum Phe. Altogether, these data highlight that Phe regulates Th2 cell metabolism and development of pathogenic Th2 cells and this mechanism in impaired in severe allergy.

W70 Proteomic and Transcriptomic Insights into Diet-Induced Modulation of Neonatal T Cell Development

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Introduction: Diet plays a critical role in gut microbiome health, with poor macronutrient composition linked to reduced microbial diversity, compromised gut barrier integrity, and a systemic pro-inflammatory immune phenotype. These disruptions likely perturb the balance between effector T cells and regulatory T cells (Tregs). This study investigates early-life microbiome-immune system interactions influencing T cell-mediated tolerance and T cell receptor (TCR) repertoire diversity. Our findings aim to highlight the pivotal role of microbiome-induced regulatory Treg TCR diversity in preventing allergen sensitisation. Methods: To assess diet's influence on immune development in neonatal mice, progenitors were fed a non-starch polysaccharide (NSP) fibre-enriched or saturated fat (SF)-enriched diet for three weeks premating, with diets maintained through weaning. Offspring microbiome samples were collected between postnatal days 14 and 28, followed by proteomic analysis of bacterial lysates. Single-cell RNA and TCR VDJ sequencing were performed on CD4+ T cells from mesenteric lymph nodes and Peyer's patches of day 21 mice. Results: Proteomic analysis revealed more unique proteins in the NSP group than the SF group. Single-cell sequencing identified distinct CD4+ T cell subpopulations, including Naïve, Memory, Effector, and Tregs, with transcriptomic differences between dietary groups. TCR repertoire analysis links luminal antigens with TCR diversity. Conclusions: This study provides evidence that early-life dietary interventions alter the luminal antigen pool, shifting the TCR repertoire and transcriptional profiles of CD4+ T cells. These findings suggest that even subtle dietary changes during critical developmental windows can have lasting effects on immune function and may influence atopic disease susceptibility. Further research could lead to dietary strategies to prophylactically reduce atopic disease risk.

W71 A dys-regulatory T-cell? Defects in CD8+ T-cell suppression by Foxp3-dE2 regulatory T-cells

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Regulatory T-cells (Tregs) are essential for the maintenance of immune homeostasis and self-tolerance. Tregs are programmed by the transcription factor FOXP3 which has two major alternatively spliced isoforms in humans: One full-length version containing all 11 coding exons (FOXP3-FL) and one version lacking the second exon (FOXP3-dE2). Although healthy humans have Tregs programmed by either or both isoforms, humans with sole FOXP3-dE2 expression develop lethal autoimmunity. The overall goal of this study is to identify the phenotypic and functional defects in suppression by FOXP3-dE2 Tregs. Here, we use a novel Foxp3-dE2 mouse model to show that Foxp3-dE2 Tregs have a cell-intrinsic reduction in the expression of key regulatory molecules—including CD25, CTLA-4, and IL-10. Reduced CD25 expression on Foxp3-dE2 Tregs leads to reduced pSTAT5 signaling in response to IL-2 stimulation. Diminished IL-2 regulation by Foxp3-dE2 Tregs associates with enhanced CD8+ T-cell activation and memory formation in response to influenza viral infection. Thus,

reduced expression of key inhibitory molecules on Foxp3-dE2 Tregs results in diminished IL-2 regulation and enhanced CD8+ T-cell activation and memory formation. These findings are critical for understanding the defects in suppression by Foxp3-dE2 Tregs and how these cells may contribute to aberrant immune responses.

W72 Characterization of ADRB1-specific CD4+ T-cells in patients with myocardial infarction

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Heart specific T cells emerge as critical orchestrators of post MI inflammation and repair. However, few cardiac antigens and their specific TCRs have been validated in humans. Recently, we identified a beta 1 adrenergic receptor ADRB1 derived epitope that stimulates antigen specific CD4 T cell responses in HLA DRB1 13 MI patients. Herein, we sought to identify and functionally characterize the specific TCRs recognizing this class II restricted cardiac antigen. PBMCs from DRB1 13positive subjects were stimulated in vitro with antigenic ADRB1167-182 peptide and the expanded antigen specific CD4 T cells (OX40positive4 1BBpositive) were sorted for downstream scRNA TCR-sequencing. TCR repertoire analysis confirmed that in vitro ADRB1 stimulation led to clonal expansion of specific CD4 T cells, with unique TCR repertoires. Expanded IFN gamma producing CD4 T cells were found in 2 out of 5 subjects, expanded Tregs were found in 2 out of 5 subjects, and expanded IL5 expressing cells were found in 1 out of 5 subjects. Limited TCR overlap was observed across individuals. However, GLIPH2 analysis revealed a distinct TCR beta motif exclusively found in IFN gamma producing CD4 positive T cells expanded in the presence of ADRB1167-182. To confirm antigen specificity, 9 TCRs carrying the identified TCR motif were expressed in in-house-generated transgenic BW5147 G.1.4 TCR reporter cell-lines, tgTCR, expressing CD3, humanized CD4 and NFAT ZS green. Co culture of tgTCR cells with human DRB1 13positive PBMCs confirmed that the identified TCR motif binds to ADRB1 167-182 presented on HLA DRB1 13. These findings were further validated by using MHC II restricted tetramer against ADRB1167-182. Taken together, these findings establish ADRB1167-182 as a functional cardiac antigen and identify conserved TCR motifs expressed in ADRB1 specific T cells poised with an IFN gamma signature, thereby advancing our understanding of antigen specific T cell responses in MI.



Poster Abstracts

P01 The effect of PM2.5 and microplastic fibres in model of chronic epithelial injury.

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Background. A significant association between increased levels of air pollution and elevated risk of mortality and morbidity has been demonstrated. The chronic exposition to noxious factors leads to cumulative damage to the alveolar compartment and reduced diffusion capacity and lung function. Aim. The aim of the study was to characterize the response of bronchial epithelial on damage associated with particulate matter and microplastisc in in vitro model of chronic epithelial injury. Material and methods. Primary, normal bronchial epithelial cells (ATCC, StemCell, Promocell, Lonza) were cultivated in air–liquid interface (ALI) for 7 days after that with 5% freshly prepared cigarette smoke extract (CSE) from 1R6F with filter (University of Kentucky) for total of 21 days. Cells were then stimulated with microplastic fibres (200 µg/cm2) and PM2.5 (50 µg per insert) applied to the top of the epithelial cells layer for 48 hours. Simultanusly, cells were were divided in two groups: uninjured or physically injured, scratch. Results. We did not find cytotoxic effect in any of investigated group. We observed a different pattern of transepithelial electrical resistance (TEER) changes in CSE cultivated epithelial cells. TEER was decreased after injury in all CSE cultivated cells (control, PM2.5 and microplastic treated) after 48 hours compared to normal cells. The upregulation of MMP-9 mRNA expression was the most common marker of injury in epithelial cells. The mRNA expression of COL-6A, IL-19, MMP-7 was decreased in PM2.5 treated injured cells with chronic CSE stimulation. The higher expression of EGF was observed in microplastic treated injured cells in the evaluated model. Conclusion. The healing of the epithelial damages caused by components of air pollution is different during short term and chronic lung injury. The structural impairment of airway epithelium caused by chronic lung injury might increase the permeability and toxic effect of PM2.5 and microplastisc.

P02 Mechanisms of gut barrier dysfunction: Effects of detergents and food additives on epithelial integrity

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Since the early 2000s, the prevalence of allergic diseases, such as food allergies and eosinophilic esophagitis, has increased to epidemic levels considered. The "Epithelial Barrier Theory" has been suggested to explain the connection between the significant rise in these disorders and the damage to epithelial barriers caused by exposures to environmental toxic substances. Professional dishwashing detergents and food emulsifiers, such as polysorbate 20 (P20) and polysorbate 80 (P80), are widely used globally. We performed several studies to investigate the influence of these compounds on the integrity of the epithelial barriers. Detergent toxicity was observed under the exposure of rinse aid in a dose-dependent manner up to 1:20,000 v/v dilution. P20 and P80 showed cytotoxicity starting at 0.1% (v/v). We revealed that these toxic substances decreased transepithelial electrical resistance, increased paracellular flux and heterogeneous tight junction immunostaining by using models based on human tissues, such as induced pluripotent stem cell-derived human intestinal organoids, colon organoids, organ-on-a-chips, and liquid-liquid interface cultures. Alcohol ethoxylates, which is the main ingredient of rinse aid, was discovered to be mainly contributed to this kind of damage. The RNA-seq and proteomics results demonstrated significant upregulation in key biological processes. In detergent study, the results demonstrated upregulation in cell death, signaling and communication, development, metabolism, proliferation, and immune and inflammatory responses of epithelial cells. After exposure to P20 and P80 at 0.05% v/v, a concentration that didn't induce direct cell toxicity, enhanced expression of genes related to epithelial cell development, cell signaling, proliferation, apoptosis, inflammatory response, and oxidative stress were observed. The disruption is caused by cellular death and molecular toxicity, which lead to the activation of many genes and proteins that induce inflammatory responses in epithelial cells, referred to as 'epithelitis'. These results suggest that widely used dishwashing detergents and food emulsifiers may have potential adverse effects on gut health, warranting further research into the safety of their long-term use

P03 The halophilic archaea, Halorhabdus rudnickae, positively enhance the barrier integrity of the human epithelial cell line Calu-3

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INTRODUCTION. The epithelium of the upper respiratory tract represents the initial barrier against external agents present in the air. In addition to pollutants, allergens, and pathogens, the epithelium may also come into contact with non-pathogenic microorganisms. Halophilic archaea constitute a group of non-pathogenic microorganisms that are able to thrive in highly saline conditions, such as salt mines or in food with a high salt content. Despite their widespread presence, their effects on the human body remain largely unexplored. AIM. The objective of this study was to examine the interaction between the halophilic archaea, Halorhabdus rudnickae, and the human epithelial cell line Calu-3 in the context of its capacity to enhance cell barrier integrity. MATERIALS AND METHODS. The human cell line Calu-3 was used as a model of the human epithelium barrier. The cytotoxic and genotoxic effects of halophiles were evaluated using a CCK-8 kit and an alkaline version of comet assay, respectively. The cell proliferation was analysed using a wound assay with xCELLigence RTCA eSight utilized together with AccuWound 96 Scratch Tool. The expression and quantification of ZO-1 were performed using Leica TCS SP8 confocal microscope. ELISA kits were used to detect cytokines secretion. RESULTS. The stimulation of Calu-3 cells with Hrd. rudnickae did not result in a notable increase in cytotoxicity or genotoxicity. Furthermore, stimulation with halophiles resulted in a significantly higher rate of cell proliferation in comparison to unstimulated cells. Moreover, Calu-3 cells stimulated with Hrd. rudnickae exhibited a markedly elevated expression of ZO-1, coupled with a notable reduction in TGF-beta 1 secretion, in comparison to unstimulated cells. CONCLUSIONS. The presence of halophilic archaea in specific, salty environments may be beneficial for human epithelial cells. The lack of cyto-/geno-toxicity and enhancement in cell barrier integrity may lead to the discovery of novel methods to reduce epithelial disruptions.

P04 Inflammation infiltration weakens innate defense against air pollutants in nasal mucosa

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Background: Indoor air pollution is responsible for an estimated 3.7 to 4.2 million annual deaths worldwide, associated with the onset and exacerbation of upper and lower respiratory diseases such as asthma and chronic rhinosinusitis. Method: We explored the crosstalk effect between various air pollutants in the presence or absence of IL-13-induced inflammation. For epithelial cell culture, a three-dimensional (3D) culture model, nasal epithelial spheroids (NES) was developed. NES were exposed to formaldehyde, acetaldehyde and PM4 for 2 days,with or without IL-13 to mimic eosinophilic inflammatory responses in airway. Results: According to paracellular flux assay, formaldehyde, acetaldehyde and PM4 caused epithelial barrier damage at 104 µg/m3. Notably, when NES were co-treated with IL-13, barrier damage occurred at a lower pollutant concentration of 102 µg/m3. Formaldehyde, acetaldehyde and PM4 reduced mRNA level of CLDN-1, PM4 also downregulated occludin. In the presence of IL-13, formaldehyde, acetaldehyde and PM4 further decreased CLDN-4 expression, and formaldehyde, in combination with IL-13, led to a reduction in ZO-1. RNA sequencing analysis revealed that formaldehy-

de and PM4 strongly increase the expression of AhR, and treatment with the AhR inhibitor improved epithelial barrier integrity by mitigating excessive AhR production. Conclusion: We successfully established an in vitro model using NES to simulate nasal type 2 inflammation and air pollution exposure. Our findings demonstrate that air pollutants, even at daily exposure levels, compromise epithelial barrier function. Compared to healthy tissue, inflammatory tissue exhibits greater susceptibility to air pollutant-induced damage. Moreover, AhR inhibition shows promise as a potential therapeutic strategy for restoring epithelial barrier integrity.

P05 Human PBMC can be used as a surrogate to demonstrate the molecular actions of innovative bone materials promoting bone ormation while minimizing inflammatory responses

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Bone health depends on the balance between resorption and formation. Large defects, lacking sufficient autograft volume, require additional osteogenic materials. This study aimed to develop novel bone substitutes and examine their impact on immune cells. The PBMC cultures were designed to investigate the development of an immune response to direct contact between immunologically active cells and the tested materials. PBMC cultures were finely-tuned utilizing commercially accessible compounds, including beta-tricalcium phosphate, tyramine-modified hyaluronic acid (THA) gel, filtrated/unfiltrated bone particles (monolayer/transwell cultures), agarose, fibrin sealant (Evicel®), and their combinations. Experiments involved the incorporation of tritiated thymidine, assessing cell viability using propidium iodide in flow cytometry, and targeted proteomics by proximity extension assay. We also investigated the effects of specially synthesized peptides containing different bioactive epitopes using the same experimental workflow. A synthetic peptide (T) contained a transforming growth factor-beta (TGF-β) binding motif. As a control, a scrambled peptide (E), which has no specific biological target, was used. For comparison, the effects of Peptide E and Peptide T were evaluated alone and in combination with bone particles or Evicel®. The data demonstrated a marginal elevation in the proliferative activity of cells exposed to specific test materials, including gels like THA, agarose, or Evicel® as well as peptide E. Targeted proteomics analysis identified distinct patterns for both Evicel®-related conditions and specific peptides, highlighting matrisome-, plasmacytoma-, apoptosis- and immune response-related proteins. Next, we selected proteins related to bone remodeling from the targeted proteomics (OLINK T-92, inflammation and immune response panels) data and investigated the profiles exhibited by various conditions concerning these markers. We focused on proteins including CSF–1, IFN–gamma, IL–1 alpha, LAP TGF–beta–1, OPG, TNF, and TRANCE. PBMC response to Evicel® and also its combination with filtered bone particles point out reduced bone resorption and potentially excessive bone formation. A reduced general immune response was also observed for this combination. Furthermore, peptide E promoted higher proliferation, while peptide T induced less cell proliferation and increased cell death, likely due to its TGF-β motif, which plays a complex role in immune regulation. These findings have implications for peptide-based tissue engineering and immune modulation. In addition, gels enriched with specifically synthesized targeted peptides should also be considered another valuable option.

P06 Swainsonine protects human thyrocytes from Fas-induced apoptosis: in vitro study on Nthy-ori 3-1 cell line.

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The role of Fas in immune cells is complex and critical for maintaining immune tolerance. The precise pathways and unique functions associated with Fas/FasL-mediated signaling in the immune system are recognized, but we still know little about its regulation. Fas-mediated apoptosis is a way of thyrocyte elimination and thyroid destruction in Hashimoto's thyroiditis (HT). Proinflammatory cytokines, produced abundantly by immune cells in the thyroid in HT, stimulate the expression of Fas in thyrocytes, making them susceptible to apoptosis induced by FasL on immune cells. The present study was designed to determine the effect of Fas N-glycosylation on apoptosis of the human Nthy-ori 3-1 thyroid cell line. To induce thyrocyte apoptosis and assess the impact of Fas N-glycans on this process, an in vitro model was created. Cells were stimulated with IFNy to express Fas and treated with glycosylation inhibitors: kifunensine and swainsonine, which sequentially act on a-mannosidase I to inhibit glycosylation at the stage of oligomannose structures and on a-mannosidase II to block the formation of complex-type structures. Apoptosis was then induced with human recombinant FasL. MALDI-Tof mass spectrometry monitored changes in N-glycosylation of thyrocytes treated with kifunensine and swainsonine, and apoptosis was analyzed by flow cytometry and fluorescence microscopy. We observed that swainsonin significantly reduces Nthy-ori 3-1 apoptosis, and caspase 3 and 7 activity, and restores mitochondrial potential. DAPI staining showed decreased rupture and fragmentation of cell nuclei in the presence of swainsonine. Our study demonstrated for the first time the antiapoptotic effect of swainsonine on Fas-dependent thyrocyte apoptosis, which may indicate a key role of complex-type structures in the regulation of death domain signaling. This finding may have further application in controlling thyrocyte apoptosis, which leads to thyroid destruction in HT. The research was supported by grant No. U1U/P03/NO/03.28 from the IDUJ.

P07 Circulating inflammatory responses to air pollution exposure

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Epithelial tissues lining the respiratory tract provide a critical barrier which protects underlying cells from environmental toxic substances, including air pollutants. Chronic exposure to these substances can compromise the epithelial barrier, increase permeability, and perpetuate inflammation. Airborne contaminants in Fresno, California, have been implicated in diverse health outcomes, particularly through their impact on inflammatory pathways. We used a NULISAseq™ Inflammation Panel 250 assay to compare protein expression among three groups: Controls (n=30), Fresno-exposed/allergic (n=28), and Fresno-exposed/nonallergic (n=35). These comparisons aimed to identify protein targets potentially disrupted by environmental exposures and to distinguish allergen-driven responses from those unrelated to allergic status. Several proteins exhibited significant changes in both exposed groups relative to controls. MMP3 was substantially elevated in exposed individuals, suggesting heightened matrix remodeling or tissue damage. Similarly, other metalloproteinases such as MMP8 and MMP9 exhibited significant upregulation, indicating compromised barrier integrity and increased immune activation. Pro-inflammatory mediators (IL1B, TNFRSF8, CXCL8) also showed robust differences in exposed participants, in line with enhanced cytokine signaling. Interestingly, FAS-ligand was significantly altered exclusively in the exposed but non-allergic group, highlighting immune pathways that respond to environmental substances independently of allergic sensitization. Proteins associated with vascular biology and angiogenesis (FLT4, TEK) were differentially expressed, suggesting potential endothelial dysfunction due to chronic pollutant exposure. Several immune checkpoint molecules (CTLA4, PDCD1LG2) displayed upregulation between controls and exposed groups, highlighting the potential for pollutant-induced immune dysregulation. These findings indicated that individuals living in air pollutant-rich Fresno environments exhibited substantial shifts in inflammatory, immunoregulatory, and tissue remodeling proteins. Although allergic status explains some variabili-

ty, many of the observed changes appeared primarily driven by pollution exposure.

P08 Targeted proteomics reveals distinct circulating inflammation and inflammatory subgroups in healthy individuals

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Understanding the variations in inflammatory states among seemingly healthy individuals can provide important insights into predisposition to chronic diseases. In this study, we employed targeted proteomics to investigate inflammatory markers in a cohort of healthy controls, uncovering distinct subgroups based on inflammatory profiles. Targeted proteomic analysis was performed on serum samples collected from healthy individuals (n = 30). The samples were analyzed using the Olink® inflammation and immune response panels. Our results revealed that the healthy cohort could be divided into two distinct subgroups based on the levels of inflammatory markers: high-inflammatory and low-inflammatory. Individuals in the high-inflammatory subgroup demonstrated elevated levels of key inflammatory cytokines, including IL-6, TNF-α, and multiple chemokines, compared to the low-inflammatory subgroup. Additionally, the high-inflammatory group exhibited increased expression of apoptosis-related proteins, such as caspase-8 and DNA fragmentation factor subunit alpha (DFFA), as well as antiviral response-related proteins, including HEXIM1, DDX58, and IRF9, and oxidative stress markers like PRDX5, suggesting an enhanced state of cellular apoptosis and oxidative stress. Further, markers associated with epithelial barrier damage, IL-33 and AREG, were also found to be significantly increased in the high-inflammatory subgroup. These findings suggest that even within healthy individuals, there can be significant differences in baseline inflammation and apoptosis related proteins, potentially indicative of early and subclinical physiopathological disturbances. Although these individuals may not present any clinical symptoms currently, the sustained elevation of inflammatory and apoptotic markers may predispose them to an increased susceptibility to chronic conditions in the future, including allergic, cardiovascular, metabolic, and autoimmune diseases. This study underlines the importance of assessing subclinical inflammation, as early detection of these subgroups could provide an early indicator for the need and follow up of preventive interventions.

P09 Evaluation of T cell dysfunction in post acute infection syndromes

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Post-acute infection syndromes (PAISs) like long COVID, post treatment Lyme disease syndrome (PTLDS) and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) are a wide range of complex conditions characterized by cognitive, emotional and neurological symptoms that vary in frequency and severity over time. These conditions frequently lead to persistent symptoms such as fatigue, pain, difficulty concentrating and headaches that continue long after the initial infection has resolved. An estimated 100 million individuals are currently affected worldwide, with an annual incidence projected at 1–2% of the population due to ongoing exposure to infections and vaccines. PAISs are often associated with a dysfunction of the immune system, notably progressive T cell exhaustion marked by diminished effector activity, reduced antigen killing, upregulation of exhaustion markers, metabolic reprogramming, mitochondrial dysfunction, and increased oxidative stress. Without proper intervention, T cell dysfunction may progress to terminal exhaustion. Experiments demonstrate that repeated stimulation of peripheral blood mononuclear cells (PBMCs) with SARS-CoV-2 and CMV peptide pools increases the proportion of T cells expressing the activation marker CD69 and exhaustion markers PD-1, LAG-3, TIGIT, TIM-3, and CD39 with each stimulation cycle. The different patterns exhibited by CD4+ and CD8+ T cells are evaluated. Currently, no early diagnostic tools exist for detecting post-viral PAISs. T-cell diagnostics hold massive potential for identifying underlying post-viral infections by measuring adaptive immune responses and monitoring the progression of T-cell functions following chronic antigen stimulation. Due to the high unmet need, Virax Biolabs has decided initiated a number of non-interventional clinical studies to evaluate the role of T cell dysfunction associated with persistent symptoms associated with long COVid, ME/CFS and post treatment Lyme disease.

P10 Alterations in innate and adaptive immune cells among patients with surgical site infections in the spine

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Surgical site infections (SSIs) are a critical complication following spine surgery, leading to prolonged hospital stays, increased morbidity, re-operation rates, and in some cases, heightened mortality risk. This project aimed to detect changes in the immune cell profile of patients undergoing spial surgery that developed an infection with (I, n= 17) compared to controls (NI, n=20) matched for age, BMI, and surgical invasiveness. Peripheral blood mononuclear cells (PBMCs) from the two patient groups were immunophenotyped using high-dimensional mass cytometry, analyzing immune cell types such as T cells, B cells, and dendritic cells, as well as activation and exhaustion markers. Forty-six immune cell clusters were identified by a cluster analysis, thirty of which were significantly different between I and NI groups. Six clusters were upregulated in the infected group and were clusters comprising Monocytes and Neutrophils. Twenty-four clusters were downregulated in I compared to NI patients , and were comprised of cells such as CD4+ T cells and NK cells. Th17 and B cells were significantly increased in I patients compared to NI patients (p=0.0152 and p=0.0305 respectively). CD4+ T cells showed no differences between groups, but activation marker CD69 and HLA-DR were increased in I compared to NI patients (p=0.0023; p=0.0032). DP and gd T cells, as well as innate immune cells such as NK cells and monocytes were decreased in I patients compared to NI patients (p=0.0305; p=0.0070; p=0.0043; p=0.0357). In this study, we demonstrate that patients with a spine-related infection display an altered immune cell profile with increased B cell numbers, and decreased numbers in innate immune cells. Further investigation into activation and exhaustion markers may reveal deeper mechanisms of immune response in these patients.

P11 Nuclear receptor LRH-1 regulates early T cell development in mice

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Liver receptor homolog 1 (LRH-1, Nr5a2) is a member of the nuclear receptor superfamily and is mainly expressed in endoderm-derived tissues. Recent data from our lab, however, revealed that although LRH-1 is only expressed at low levels in mature T cells, it is essential for the development of mature and functional regulatory and effector T cells. Deficiency of LRH-1 in the late double positive (DP) thymocyte development stage (CD4-Cre-mediated) leads to failure of mature CD4 and CD8 T cell functions, but has only minor effects on DP, single positive (SP) CD4 and CD8 immature T cells. In contrast, Lck-Cre-mediated deletion during early double negative (DN) thymocyte stages had also drastic effects on immature T cells, indicating that LRH-1 is indispensable for thymic development. Surprisingly, early LRH-1 deletion in thymocytes resulted in reduced proliferation only at the DN2, DN3 and DN4 stage, where Nr5a2 expression is extremely low compared to the DP and CD4 SP stage. Cells with LRH-1 deletion in early DN thymocyte stages are barely able to differentiate into more mature T cells, and only T cells, which escaped from Cre-mediated deletion survived and populated the periphery. Yet, these mature T cell escapers are hardly able to express T cell activation markers but seem not to be anergic regarding the secretion of pro-inflammatory cytokines in response to T cell receptor activation. Our findings highlight the critical of LRH-1-regulated processes in early T cell development. Furthermore, its low but critical expression in T cells opens a new potential therapeutic window to treat T cell-mediated immunopathologies, such as inflammatory bowel disease, by pharmacological inhibition of LRH-1.

P12 Tmem127 regulates the T cell proteome and homeostatic Interleukin-7 signaling

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Homeostatic proliferation is the main source of new cells to maintain T cell population in humans. While miR-17-92 is critical for T cell development and homeostasis, for the majority of targets the functional relevance of miR-17-92-mediated regulation is unknown. To systematically investigate the consequences of specific target gene repression on T cell function, we performed arrayed CRISPR KO screening of miR-17-92 target genes we had previously validated. We identified Tmem127 as a negative regulator of multiple T cell surface proteins (ICOS, CD25 and CD226) and homeostatic CD4 T cell proliferation. Tmem127 germline KO mice have splenomegaly and benign expansion of all CD62L+T cell populations leading to decreased CD4/CD8 ratio. Using proximity labeling (Bio-ID) and proteomics we identified multiple T cell proteins regulated by Tmem127 in naïve CD8 T cells. We confirmed recently identified interactors (e.g. MHC I) and identified the IL-2 receptor common gamma chain (CD132), Tgfbr2, ICAM1 and 19 other proteins as novel Tmem127-regulated proteins. Tmem127 KO T cells express more CD132 than wildtype T cells which could result in increased IL-7 driven homeostatic proliferation and the observed phenotype. Indeed, naïve Tmem127KO CD8 T cells proliferate faster and display increased Stat5 phosphorylation when cultured with IL-7 in vitro. When transferred into immunocompetent CD45.1 mice, naïve Tmem127KO CD8 T cells proliferate more than wild type. Tmem127KO mice do not display overt signs of immunological disease but have a more rapid disease onset in a MOG-induced experimental autoimmune encephalomyelitis (EAE) model, which is paralleled by an increased frequency of IFNγ secreting CD44+ CD8 T cells. In summary, we have identified the adaptor protein Tmem127 as a key regulator of important surface proteins on naïve T cells and a restrainer of IL-7 induced homeostatic T cell proliferation.

P13 Elucidating the Roles of ETS-1 and GATA-3 in iNKT Cell Differentiation and Effector Lineage Specification

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Invariant Natural Killer T (iNKT) cells are a unique subset of T lymphocytes that bridge innate and adaptive immunity. Their differentiation and effector lineage specification are tightly regulated by various transcription factors. We recently explored the roles of ETS-1 and GATA-3 in modulating iNKT cell development. ETS-1 is critical for the optimal expression of the iNKT TCR and the transcription factor PLZF, promoting early post-selection differentiation. Loss of Ets1 disrupts the peripheral homeostasis of iNKT cells and diminishes their activation and proliferation capabilities. On the other hand, GATA-3 is essential for determining effector subsets of iNKT cells, particularly influencing the development of iNKT2 and iNKT17 lineages. GATA-3 deficiency results in the loss of iNKT2 and iNKT17 subsets and an altered proportion of iNKT1 cells. Thymic iNKT cells lacking GATA-3 exhibit reduced expression of PLZF, RORgammaT and T-bet, along with decreased production of Th2, Th17, and cytotoxic effector molecules. Single-cell RNA sequencing (scRNA-seq) analyses further reveal that both Ets1 and GATA-3 regulate crucial genes, such as Icos and Zbtb16, which are essential for iNKT differentiation and function. The combined insights from these studies indicate that while Ets1 facilitates the initial differentiation and TCR expression, GATA-3 governs the subsequent effector lineage commitment. Restoration of PLZF and ICOS partially rescues iNKT cell differentiation in the absence of these factors, underscoring their pivotal roles. Our findings highlight a cooperative regulatory network involving Ets1 and GATA-3 in orchestrating iNKT cell development, providing new insights into transcriptional control mechanisms that may inform therapeutic strategies for immune modulation.

P14 Seasonal variation in sunlight is associated with differences in levels of T regulatory and T-helper 17 cells in girls and women

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Multiple sclerosis prevalence is up to ten times greater at higher latitudes compared to low latitudes and is associated with reduced sunlight during childhood. Alterations in inflammatory Th17 and regulatory T-cells (Treg) are associated with autoimmunity. We hypothesised that there were differences in the levels of these T cells between summer (long daylight hours) and winter (short daylight hours) at a high latitude in Australia. In Hobart (latitude 42.8 degrees south), thirteen girls (aged 12-13) and sixteen women (total n=29) had blood collected in the evening in daylight after summer - February/March, (post 15 hours daylight) and at the same time in the dark after winter - August/September (post 9 hours daylight). Height and weight were measured. Participants completed online surveys prior around menstruation, sleep, exercise and time outside. Proportions of Th17 (CD4+, CXCR3-, CCR4+, CCR6+, CD161+), total Treg (CD4+, CD25+, CD127low), naïve Treg (CD45RA+, CD4+, CD25+, CD127low) and memory Treg (CD45RA low, CD4+, CD25+, CD127low) were enumerated by flow cytometry (Cytek Aurora). Hours spent outside were greater in summer than winter (12.5 v 10.5, p=0.0003). The percentage of Treg of CD4+ was higher in summer than winter (7.3% vs 7%, p=0.004) including memory Treg (3.1% vs 2.9%, p=0.02) for all females, and naïve Treg were 13% higher in summer in women (3.2% vs 3.8%, p=0.0009), whereas %Th17 remained unchanged. In women, a negative correlation between the number of hours spent outside in summer and %Th17 was observed (r=-0.53, p=0.035). The %Th17 cells was higher in women than girls (4.9% vs 3.1%, p=0.001) whereas girls had a higher total %Treg (7.6% vs 6.7%, p=0.005), consisting of a higher naïve Treg (5.5% vs 3.7%, p=0.0001) whilst the women had a higher %memory Treg (3.4% vs 2.6%, p=0.0001). These light dependent seasonal differences may influence immune development in children and contribute to the latitude differential of autoimmunity, and possibly allergy.

P15 CD8+ Skin-Resident Memory T Cells Require TCR Signaling for their Persistence in a Mouse Model of Allergic Contact Dermatitis

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Epidermal-resident memory CD8+ T (TRM) cells play a significant role in fighting off pathogens. However, CD8+ TRM cells are also central in the pathogenesis of a variety of inflammatory skin diseases. It is unclear whether the generation and persistence of CD8+ TRM cells are dependent on the presence of cognate antigen and T cell receptor (TCR) signaling. The purpose of this study was to determine whether TCR signaling is required for the generation and persistence of epidermal CD8+ TRM cells in a mouse model for allergic contact dermatitis. We examined the responses to four different contact allergens in combination with adoptive transfer and prime-pull experiments. We determined the presence of contact allergen in the skin by Western blot analysis. We found that epidermal CD8+ TRM cells can develop in the absence of the cognate antigen and TCR signaling as determined by Nur77 induction, whereas persistence of epidermal CD8+ TRM cells requires presence of the cognate antigen and correlates with Nur77 expression. In the presence of contact allergen, a selective expansion of specific TCR clonotypes was seen. In conclusion, this study demonstrates that cognate antigen and TCR signaling are required for the persistence of allergen-specific CD8+ TRM cells in the skin.

P16 Cancer immunoediting in melanoma patients from early stage to advanced disease

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Cancer immunoediting comprises complex interactions between tumor and immune cells leading to one of three potential outcomes: elimination, equilibrium, or escape. One mechanism through which tumors escape the immune-mediated destruction is dedifferentiation which, in turn, can be elicited by T cell-derived inflammatory cytokines and results in loss of T cell-mediated tumor control. Here, we address the scarcity of data regarding cancer immunoediting through immune-mediated melanoma dedifferentiation in humans. We first present a case with progressive melanoma dedifferentiation characterized by loss of melanocyte differentiation antigens and SOX10, with reciprocal upregulaion of NGFR and EGFR over a period of twenty years in the absence of any systemic treatment, and in association with antigen-specific T cell responses. We then performed a systematic investigation of four prospective independent cohorts of patients diagnosed with melanoma in all stages of disease confirming the dedifferentiated signatures in therapy-naïve tumors by single-cell RNA-sequencing and AI-assisted digital image analysis, we assessed the presence and magnitude of T cell responses targeting melanocyte differentiation antigens as well as their relationship with tumor dedifferentiation. We conclude that melanoma dedifferentiation driven by activated antigen-specific T cells commences as early as stage I and persists throughout the entire disease progression.

P17 TRBC1: A Key Indicator of T Helper Cell Clonality in Skin Tissues

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Cutaneous T-cell lymphoma (CTCL) is a rare non-Hodgkin lymphoma characterized by the clonal expansion of neoplastic T cells in the skin. Its diagnosis is often challenging due to clinical overlap with benign, non-communicable skin diseases (NCDs). This study investigates the utility of T-cell receptor beta constant region 1 (TRBC1) as a marker for T-cell clonality in formalin-fixed, paraffin-embedded (FFPE) skin biopsies. We analysed single-cell RNA sequencing data from CTCL skin lesions to examine the expression of TRBC1 in T-helper cells. To quantify the extent of TRBC1 polarization, we developed a score dubbed the TRBC1 Clonality Score (TRBC1-CS). Using patient-specific TRBV mRNA probes and TRBC1 antibodies, we demonstrated polarized TRBC1 expression in TRBV-defined clonal T-helper cells in FFPE skin samples. A simplified immunofluorescence panel consisting of T-cell markers and TRBC1 was utilized to differentiate between CTCL and benign NCDs. The findings were further validated in an independent cohort by comparing the TRBC1-CS to PCR-based BIOMED-2 T-cell clonality assays. We identified polarized TRBC1 expression in TRBV-positive clonal T-helper cells within FFPE skin samples. The TRBC1-CS demonstrated high specificity for CTCL, enabling effective differentiation from benign NCDs. Furthermore, when validated in an independent cohort, TRBC1-CS exhibited superior specificity and positive predictive value compared to PCR-based methods. TRBC1 is a practical and highly specific marker for assessing T-cell clonality in FFPE skin biopsies, offering diagnostic advantages over PCR-based approaches.

P18 Multi-omics cytokine screening reveals immunosuppressive microenvironment in cutaneous T-cell lymphoma

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Immune dysregulation has been reported in several skin disorders, including neoplastic and inflammatory diseases. Accumulating evidence suggested the immune system of cutaneous T-cell lymphoma (CTCL) and atopic dermatitis (AD) is skewed toward immunosuppressive Type 2 responses, and therefore promotes the disease progression. A comprehensive study of key immune regulatory molecules will facilitate the understanding of disease microenvironment and may reveal novel therapeutic targets in Th2-biased skin disorders. In this study, we aim to screen cytokine molecules with comprehensive multi-omics approaches, and to identify dominant immunoregulatory factors in patients with Th2-biased skin disorders. Our result showed distinct cytokine profiles between CTCLs, ADs and HDs. In the skin lesions and sera collected from patients with type 2 inflammatory skin disorders we confrimed significant higher levels of Th2-related cytokines such as IL-9 and IL-13. We further detected several potent chemoattractant for Th2 cells, immunosuppressive IL-10 signaling pathway related molecules, and viral protein interaction related cytokines and receptors. These findings were comparable at both transcriptional and translational molecular level. Our datapoint out towards targetable key factors in immunomodulation for patients with Th2-biased skin disorders assist the understanding of disease microenvironment and contribute to the identification of potential new therapeutic targets.

P19 Multi-Harmonic Imaging-Based Automated Recognition of Cutaneous T-Cell Lymphoma

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Cutaneous T-cell lymphomas (CTCL) are a heterogeneous group of non-Hodgkin lymphomas, with mycosis fungoides (MF) being the most common type, accounting for approximately 60% of all lymphomas arising primarily in the skin. The diagnosis of MF is challenging, especially in its early stages when the number of atypical T-cells is small, and clinical and histopathologic changes are often unspecific. This leads to significant delays of three to five years in diagnosis and treatment. Thus, novel diagnostic methods are needed to adjust the diagnostic and therapeutic strategies of CTCL. Nonlinear optical microscopy (NLOM) holds significant promise in this respect due to its ability to detect specific tissue structures through harmonic generation and prospectively extend histological analysis to three dimensions. To image haematoxylin & eosin (H&E) stained skin tissue with NLOM and detect atypical epidermotropism and dermal cells in MF skin samples using an AI model. We employed NLOM to analyse H&E-stained biopsy samples from MF skin lesions. Expert clinicians labelled the images, which were then used to train a neural network to recognise skin lymphocytes. When applied to the testing dataset, the AI model automatically detected atypical epidermotropism and dermal cells with notable accuracy. NLOM successfully imaged H&E-stained MF skin tissue sections, providing sub-micrometric resolution of epidermal and dermal structures. Using an AI model trained on expert-labelled images, the technique achieved automated detection of lymphocyte epidermotropism and dermal infiltration with high accuracy. The combination of harmonic generation and AI-driven image analysis demonstrated the potential to identify characteristic MF features, particularly epidermotropism, in histological samples. This study demonstrates that NLOM, combined with AI, can accurately detect lymphocyte epidermotropism and dermal infiltration in MF skin tissue. This innovative approach offers clinical dermatologists a powerful tool to improve the diagnosis of MF-CTCL, paving the way for more timely and precise therapeutic strategies.

P20 Anti-inflammatory Effect of a Natural Polyphenol, Resveratrol in TNBS-Induced Rat Model of Colitis: the Role of TNFRs

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Inflammatory bowel diseases (IBD) represent a chronic and incurable group of disorders affecting the digestive tract, with persistent inflammation serving as a key factor in their pathogenesis. This inflammation is strongly linked to oxidative and nitrosative stress. The interaction between tumor necrosis factor-alpha (TNF-alpha) and its receptors (TNFRs) is pivotal in regulating inflammation, immune responses, and cell death. TNF-alpha binds to TNFRs on various cell types and activates inflammatory signalling mechanisms. Recently, compounds with antioxidant and anti-inflammatory properties have been extensi-

vely investigated as potential therapeutic options for IBD. Among these, resveratrol (RES), a natural polyphenol, has gained attention for its potential protective effects against IBD. Our aim was to investigate the role of TNFRs in RES–induced protection in experimental IBD. For this purpose, RES was administered orally at a daily dose of 10 mg/kg for 28 days. To induce experimental colitis, 2,4,6-trinitrobenzene sulfonic acid (TNBS) was injected intracolonically on the 25th day. Animals were sacrificed on day 29 for analysis. The anti-inflammatory effects of RES were assessed using enzyme-linked immunosorbent assay (ELISA) and western blot techniques. Histological examination revealed marked differences in gut wall structure, particularly in the tunica mucosa, across the study groups. Planimetric and histological analyses demonstrated that a 10 mg/kg dose of RES significantly reduced colonic ulceration compared to the TNBS group. The observed protective effects of RES at this dose were associated with regulating inflammatory markers. RES also lowered inflammation by suppressing the production of pro-inflammatory cytokines, including TNF-alpha. Immunohistochemical analysis further showed that RES reduced the expression of TNF-alpha receptors, TNFR1 and TNFR2, in the colon compared to the TNBS group. In summary, these findings highlight that the protective role of RES partly relies on attenuating inflammation via reducing TNF-alpha and TNFRs in the TNBS rat model.

P21 Acute Inflammation-Induced Barrier Dysfunction in a Rat Model of IBD: a Focus on the Gut-Brain Axis

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Inflammatory bowel diseases (IBD) are gastrointestinal tract ailments characterised by inflammation and ulceration of the gut. IBD can be associated with several neurological comorbidities, such as depression, and cognitive dysfunction, thus the role of the gut-brain axis in IBD has been raised. We aimed to investigate the expression of inflammatory markers and tight junction proteins in the colon and the brain tissues in 2,4,6-trinitrobenzene sulfonic acid (TNBS)-induced rat colitis. We used 225-250 g male Wistar Hannover rats during our experiments. To induce colitis, the animals were treated intracolonically (i.c.) once with TNBS (100 mg/kg) dissolved in 50% ethanol after 16 hours of fasting. The animals were euthanised 72 hours after TNBS instillation. The last 8 cm section of the colon from the anus and the whole brain were dissected and were frozen in liquid nitrogen. Biochemical measurements were performed via western blot. Our results showed that the occludin tight junction protein significantly decreased due to acute inflammation compared to the control group in the colon and the brain tissues. Furthermore, an increased expression of the myeloperoxidase (MPO) enzyme was observed in both the intestinal and brain tissues compared to the control groups. Among the nitric oxide synthase (NOS) enzymes, we observed a significant decrease in endothelial nitric oxide synthase (eNOS) expression in the brain tissue and a significant reduction in the colon and brain tissues in neuronal nitric oxide synthase (nNOS) due to TNBS treatment compared to the control group. In conclusion, it can be stated that damage to the barrier functions can be assumed as a result of acute intestinal inflammation, which can be observed both in the colon and brain tissue. Furthermore, our results suggest that peripheral inflammation in the colon can lead to inflammation of the brain parenchyma partly due to the dysfunction of the blood-brain barrier.

P22 IL4-Ralpha and IFN-gamma opposing signals modulate neutrophils effector functions

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Neutrophils are the most abundant immune cells in the human blood and are essential in the fight against microorganisms. Recent work shows that they are transcriptionally active, can respond and adapt to external stimuli and are a heterogenous population. Atopic dermatitis (AD) is a chronic inflammatory multifactorial skin disease that involves genetic predisposition, epidermal barrier dysfunction, skin microbiome dysbiosis, and type-2-T-helper-cells (Th2)-predominant inflammation. Surprisingly, despite being colonized by pathogenic bacteria, neutrophils are absent of the skin lesions in AD patients. Experiments performed in mice have suggested that IL-4 suppressed the neutrophil functions, induced an aging phenotype, and increased susceptibility to bacterial infections.Here, we investigated the functional adaptation of human neutrophils to opposing signals by in-vitro stimulation with IL-4, IL-13, IFN-γ, and their combinations. IL-4 and IL-13 induced STAT-6 phosphorylation, with IL-4 showing faster kinetics, while IFN-γ induced STAT-1 phosphorylation, consistent with prior findings. Co-stimulation with IFN-γ and IL-4 or IL-13 resulted in simultaneous STAT-6 and STAT-1 phosphorylation. Interestingly, IFN-γ attenuated STAT-6 phosphorylation in IL-4-treated neutrophils but enhanced phosphorylation kinetics with IL-13. Functionally, netosis was reduced by IL-4Rα signaling, while IFN-γ promoted this process. Reactive oxygen species (ROS) production was modulated by cytokine priming in a stimulus-dependent manner. These findings highlight the plasticity of neutrophils and the immune-regulatory interplay between opposing cytokine signals in vitro.

P23 HLA-II peptide-binding diversity shapes humoral immune responses and infection risk

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Infectious diseases represent a leading cause of mortality worldwide, and have shaped the evolution of the human immune system. Human leukocyte antigen (HLA) class II molecules are key to the humoral immune response by presenting peptides to helper T cells. The peptide-binding range varies greatly among HLA-II variants, but the role of this variation in humoral immunity and infection susceptibility has remained unexplored. Here, we integrated data on HLA-II immunopeptidomics and antibody responses in ~1,500 individuals, demonstrating that a broad peptide-binding repertoire of HLA-II is linked to antibody production against pathogen-associated proteins and more favourable health outcomes. Specifically, individuals with these HLA-II molecules have a reduced risk of severe infections and up to 40% lower incidence of diseases caused by common pathogens. Hence, the peptide diversity presented by HLA-II variants shapes immune defense and can serve as a risk factor for infections.

P24 Development of a robust methodology for blood-based biomarker discovery in patients with eosinophilic esophagitis

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Eosinophilic esophagitis (EoE) is a chronic inflammatory disorder of the esophagus, marked by an infiltration of eosinophils. The incidence of EoE has risen rapidly over time since its first case description in the early 1990s. EoE patients commonly experience symptoms such as dysphagia, food impaction, and heartburn. The disease is driven by complex mechanisms, including epithelial barrier dysfunction and Th2-mediated inflammation. Allergens often trigger the immune response by breaching the esophageal barrier. Currently, diagnosing and monitoring EoE patients require endoscopy and biopsies, which are time-consuming, uncomfortable, and invasive. Therefore, there is a pressing need for non-invasive, easily detectable biomarkers. The exploration of extracellular vesicles (EVs) as potential blood-based biomarkers is expanding rapidly. EVs are a heterozygous group of stable, nano-sized, membrane-coated particles secreted by every cell type into body fluids to mediate cellular communication. Additionally, the cargo of EVs reflects the molecular signature of their originating cell, thereby providing insights into the cell's state. The unique characteristics of EVs make them an intriguing subject for biomarker research in cancer, neurodegenerative diseases, inflammatory disorders, etc. We have developed and validated a robust methodology to isolate EVs from blood plasma using size exclusion chromatography. Fractions were collected, and the presence of EVs was confirmed using several approaches. Fluorescent lipid nanoparticles, mimicking the EVs' size (166 nm), were used for sample normalization. Western blot and SDS-PAGE allowed us to confirm the presence of characteristic EV-markers (stomatin, CD9, and CD81) while simultaneously assessing

the level of potential plasma protein contaminants by excluding albumin in our EV-fractions. Finally, mass spectrometry-based proteomics was applied to characterize the isolated EVs with an average of 1046 proteins per sample. Ultimately, this optimized method will be applied to identify potential biomarkers in blood plasma, enabling less invasive diagnosis and monitoring of EoE patients.

P25 Basophils in skin-mediated sensitization to allergic lung Inflammation

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Skin is an important barrier exposed to environmental cues. The pruritic skin disease atopic dermatitis (AD) is associated with a damaged skin barrier and affects about 20% of children and 10% of adults in high-income countries. AD is associated with a type 2 immune response involving various innate immune cells that promote inflammation. These induce differentiation of Th2 cells which secrete IL-4 to elicit the generation of IgE antibodies, e.g. against allergens. Generated IgE is distributed systemically and sensitizes mast cells and basophils also in distal organs. This likely contributes to allergic co-morbidities found in AD patients. Here, we consider the local skin inflammation as an early determinant of the later distal immune response, and analyse the contribution of basophils to the quality of allergen-specific IgE formation. We use a mouse model where the Vitamin D analogue MC903 is topically applied to the ear and induces the alarmin TSLP to drive AD-like symptoms. In addition, we also topically apply ovalbumin (OVA) as a model-allergen to trace the allergen-specific response. For local pathology readout, we determine barrier integrity by transepidermal waterloss measurement and inflammation by measuring the ear thickness. To understand the impact of basophils on allergic sensitization, we determine allergen-specific IgG1 and IgE formation by analysis of the germinal center reaction; measure allergen-specific serum titer and determine their capability to induce anaphylaxis; and analyse allergen-specific IgE-loading of effector cells in spleen and lung. We find indications that basophils promote loss of barrier integrity, which likely supports allergen uptake and drives allergen-specific antibody formation and anaphylaxis. Basophil-driven sensitization is also observed in the lung. When lungs of skin-sensitized wild-type mice are challenged with OVA, they develop higher eosinophilia compared to basophil-deficient mice. Therefore, basophils are crucial drivers of IgE formation and lung sensitization to skin-encountered allergen, potentially relevant in asthma development.

P26 Deciphering Immune endotypes within Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome

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Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a severe, delayed-type drug hypersensitivity reaction with varying clinical presentations, from mild forms to life-threatening conditions. The association between these phenotypic differences and underlying immune mechanisms remains unclear. This study aimed to investigate systemic immune profiles in DRESS patients, hypothesizing that disease severity correlates with distinct inflammatory profiles. We conducted a multicentric study involving 26 DRESS patients from Switzerland and South Africa and 6 healthy controls (HC). Serum samples collected at diagnosis were analyzed using targeted high-throughput proteomics (OLINK) to measure inflammation-/immune response-associated proteins. DRESS patients exhibited systemic immune activation, with elevated levels of type 2-/eosinophil-axis cytokines (IL4, IL5, IL13) compared to HC. Additionally, pro-inflammatory mediators (IL6, IL10, CXCL9, IFN-γ) and immune regulatory proteins (PSIP1, ADA, SH2D1A) were upregulated. Regardless of severity, overlapping upregulation of inflammation-related proteins, including CXCL9, CXCL10, IFN-γ, LAG3, and PD-L1, was observed. Unsupervised clustering revealed three distinct immune profiles. Group 1 showed milder immune activation, characterized by elevated IL7 and older age, shorter drug latency, and prolonged hospitalization. Group 2 exhibited a pronounced type 3 immune response, with elevated Th17-related cytokines and Toll-like receptor signaling proteins, correlating with a higher prevalence of HIV-positive patients. Group 3 demonstrated a strong type 2 cytokine response, with high eosinophil counts and eosinophil-recruiting mediators like MCP-4 (CCL13). These findings suggest that DRESS involves systemic immune activation with distinct inflammatory clusters. The heterogeneity in immune profiles, particularly the type 2-/eosinophil-axis dominance in certain groups, highlights the complexity of DRESS pathophysiology. If validated, these immune signatures may inform patient stratification and guide tailored therapeutic approaches, improving outcomes in this challenging condition.

P27 No Grass Pollen Allergy in sub-Saharan Africa? Analysis of Sensitization Patterns to Pollen in Swiss & sub-Saharan African Atopic Dermatitis Patients

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Background: Sensitizations to pollen can directly impact atopic dermatitis (AD) by potentially leading to exacerbation upon exposure. This study aims to gain more insights into the sensitization patterns to pollen allergens of AD patients in Europe compared to sub-Saharan Africa (SSA). Methods: We included 20 AD patients and 10 healthy controls (HC) from each center in Switzerland (CH), Tanzania (TZ) and Madagascar (MD) in this case-control study. We analyzed the sera with the ALEX2 Allergy Explorer, measuring total IgE and 300 specific IgE antibodies. Results: The prevalence of ARC and asthma in AD patients was similar in all countries (RCA: 60% in TZ, 70% in CH, 75% in MD; asthma: 25% in TZ, 30% in CH, 20% in MD). Total IgE levels were significantly lower in the CH HC than in both SSA HC groups (TZ vs. CH: p=0.03, MD vs. CH: p=0.04). We found major differences in sensitization patterns, especially to grass pollen allergens. Swiss AD patients were sensitized to various grass pollen such as bahia grass (Pas n), bermuda grass (Cyn d, Cyn d 1), common reed (Phr c), perennial ryegrass (Lol p 1), rye (Sec c_pollen), and timothy grass (Phl p 1, Phl p 2). However, no AD patient or HC subject from SSA was sensitized to the tested grass pollen. Significantly more Swiss AD patients were sensitized to the tree pollen of silver birch, hazel, alder, beech, olive, and ash compared to African AD patients. Only one AD patient from MD was sensitized to ash and olive. No sensitization to the aforementioned tree pollen was detected in the rest of the African AD or HC. Conclusions: The absence of grass pollen sensitizations in SSA is most likely due to a lack of commercially available sIgEs tailored to the African environment. More research is needed to identify local types and counts of pollen to develop tailored diagnostics and therapies.

P28 Insights into active and spontaneously resolved atopic dermatitis: Meta-analysis of tissue-resident cells from public dataset

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Atopic dermatitis (AD) is a prevalent, complex chronic inflammatory skin condition that typically begins in early childhood but can affect all age groups. AD is characterized by heterogeneous symptoms and trajectories; while over 50% of children experience spontaneous remission, it often persists or recurs with varying phenotypic expression and severity. Despite advances in understanding AD, the mechanisms behind its remission, recurrence, and persistence remain unclear. Several studies describe the transcriptomic atlas of active AD, but data from spontaneous remission donors in particular is sparse. Longitudinal studies providing a detailed characterization of the diverse trajectories of AD are necessary for a better understanding of the mechanisms driving spontaneous remission. A comparative analysis of publicly available transcriptomic data from AD groups (active AD, spontaneous remission, dupilumab-treated) and healthy controls revealed high inter-donor variability in cell subset frequencies. This limits definitive conclusions from our analysis. Nevertheless, there are considerable differences in frequency of CD4+, CD8+ and regulatory T cells, Keratinocytes-1 and NK cells between remission and healthy donors. Melanocytes showed the highest number of differentially expressed genes with enrichment of TGF-β and IL4 signaling pathway genes. T cells exhibited a pro-inflammatory Th1 profile (upregulated

TGFB1, CD81, IL-1, and IL-18 pathways), while NK cells displayed an anti-inflammatory bias (upregulated SOX4, METRNL, IL-4, and TGF-beta pathways). Collectively, gene expression profile among both therapy-induced and spontaneous remission patients were consistent in the meta-analysis. Interestingly, we observed the frequency of recently reported TH2A cells, which are persistent in dupilumab treated donors, is lower in spontaneous remission donors. In summary, our analysis highlights a complex landscape of immune regulation in atopic individuals and warrants the need for further comprehensive study of diverse AD trajectories. This will potentially enhance our understanding of AD progression and help identify therapeutic targets for sustained therapy-free remission.

P29 Monosodium glutamate affects cellular stress, protein folding defect, mitochondrial dysfunction and cell death in intestinal epithelial cells

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The barrier function of the epithelia is crucial for maintaining homeostasis. Environmental exposures may alter the epithelial barrier integrity and influence the development of diseases. Recent studies have shown that food flavor enhancers can damage the epithelial barriers. Here, we report the impact of monosodium glutamate (MSG), disodium guanylate (DSG), disodium inosinate (DSI) and their combined effects on intestinal epithelial cells. Monolayer Caco-2 cells and organ-on-a-chip model were established, and cellular cytotoxicity, transepithelial electrical resistance (TEER), paracellular flux (PF), RNA-sequencing, and reactive oxygen species (ROS) detection were performed at consumer-relevant doses. MSG, DSG, DSI, and their combined effects demonstrated cytotoxicity to Caco-2 cells at concentrations of 1%, 0.5%, 2%, and 0.5%, respectively. A one-day exposure to 1% MSG, 1% DSG or the 1% combined compounds reduced TEER, while DSI didn't show any cytotoxicity. After three days, 1% MSG and the combined treatment significantly increased PF, indicating compromised barrier integrity. RNA-sequencing analysis revealed significant differences in gene expression between the 1% MSG and combined exposure groups compared to controls. Key pathways affected by 1% MSG included oxidative stress, unfolded protein response, mitochondrial dysfunction. In addition, regulation of autophagy, with a notable upregulation of Deptor (a component of the mTORC1 complex) and TORC1 signaling was demonstrated. Combined doses of food flavor enhancers amplified the effects predominantly caused by MSG. 1% MSG and combined compounds increased ROS levels after 24 hours of exposure, while N-acetyl-L-cysteine mitigated 1% MSG-induced ROS. This study highlights the cytotoxic effects of food flavor enhancers on gut epithelial cells. At 1% daily used concentration, MSG and its combination with DSG and DSI damaged intestinal epithelial barriers and induced different biological processes. Given that a compromised epithelial barrier can trigger immune dysregulation and inflammation, it is important to emphasize the potential health risks and mechanisms associated with these food additives.

P30 Detrimental effects of tooth paste ingredients sodium dodecyl sulfate and cocamidopropyl betaine on oral and fecal microbiome balance

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The oral and fecal microbiome, which is composed of a diverse community of microorganisms, plays a crucial role in maintaining oral and gut health. This study investigates the effects of two common surfactants, sodium dodecyl sulfate (SDS) and cocamidopropyl betaine (CAPB), on oral and fecal microbiome growth dynamics. Additionally, we examined the impact of food-flavor enhancers, including monosodium glutamate (MSG), disodium guanylate (DSG), and disodium inosinate (DSI) on gut microbiota growth. Oral and fecal slurry samples were collected from four healthy donors. Bacterial suspensions were standardized using the McFarland method, and the minimal inhibitory concentrations (ranging from 10% and halving across 21 dilutions) were determined for compounds against oral and fecal bacteria under both aerobic and anaerobic conditions. Our findings revealed that SDS inhibited oral bacterial growth at concentrations of 0.00977% under aerobic condition and 0.00488% under anaerobic condition, while fecal bacterial growth was inhibited at 0.00195%. CAPB demonstrated inhibitory effects at 0.00977% aerobically and an impressively showed a low dose of toxicity 0.000305% in anaerobic conditions, and fecal bacterial growth was also inhibited at 0.00195%. Interestingly, some oral bacterial strains, identified via Sanger sequencing as Acinetobacter—a significant pathogen in hospital environments—survived exposure to SDS concentrations higher than the inhibitory thresholds observed in other samples. This suggests a potential selection for more robust or pathogenic strains in the presence of elevated surfactant levels. The three kinds of food flavor enhancers didn't inhibit the growth of gut bacteria, and we will explore whether the composition of gut microbes has changed according to 16s rRNA sequencing. These findings demonstrate the significant impact of surfactants on the oral microbiome, potentially disrupting its balance. Further research is also needed to determine whether food-flavor enhancers alter gut microbiota characteristics, potentially leading to disease, highlighting the importance of this issue for public health.

P31 The effect of PM2.5 and microplastic on cell injury in lipopolysaccharide stimulated bronchial epithelial cells

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Background. The toxic effect of air pollutants on airway epithelium is associated with oxidative stress, pro-inflammatory response, impaired innate immunity reactions and tissue damage. Aim. The main goal of the project was to characterize the main pathways of bronchial epithelial damage caused by particulate matter and microplastic from air pollution in in vitro model of acute lung injury. Material and methods. Primary, normal bronchial epithelial cells (ATCC, StemCell, Promocell, Lonza) were cultivated in air–liquid interface (ALI) for 21 days. Cells were then stimulated with microplastic fibres (200 µg/cm2) and PM2.5 (50 µg per insert) applied on the top of the epithelial cells layer for 48 hours. Simultaneously, cells were stimulated with 5 µg/ml of lipopolysaccharide (LPS) (from Escherichia coli) and physically injured, scratch. Results. Neither PM2.5 nor microplastic caused cytotoxic effect in uninjured or injured epithelial cultures. Injury decreased transepithelial electrical resistance (TEER) in LPS treated epithelial cells compared to controls especially in injured cultures treated with microplastic. The most significant changes in mRNA expression after PM2.5 or microplastic treatment in cell injury were observed for IL-8, IL-19, MMP-7 and MMP-9 in LPS stimulated epithelial cells compared to IL-1β, MMP-9, EGF and COL-6A in unstimulated cells. Conclusion. The acute epithelial injury in the presence of air pollutants is characterised by a different pattern of response than in controls. The acute epithelial injury in presence of air pollutants might be associated with worse health effects.

P32 Micro- and nano-polystyrene impair epithelial barrier integrity

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Introduction: Microplastic pollution has become a major issue to the ecosystem. They were found to deposit in many human organs by inhalation, and injection or dermal contact. Polystyrene (PS) is one of the most reported microplastics which is found in the human body. In this study, we aimed to assess the effects of PS on the integrity of the gut and airway epithelial barrier. Methods: MTT and DCFDA fluorescence-based assays were employed to assess cell viability and ROS levels in Caco-2 and airway cell lines. Microfluidic gut-on-a-chip from Caco-2 and human nasal organoids were treated with different doses of commercial PS particles with the diameters of 0.17-0.19 µm, 1.0-1.4 µm, 4.8-5.8 µm, and 9.5-11.5 µm. Trans-epithelial electrical resistance (TER) value was detected to assess gut epithelial barrier integrity. The FITC dextran permeability test was used to assess the leak of the epithelial barrier in nasal organoids. Results: PS with the diameter of 0.17-0.19 µm and 1.0-1.4 µm significantly decreased the TER value of the gut-on-a-chip and the survival rates of Caco-2 cells at the dose of 0.31, 1.25 and 5 mg/mL. PS with the diameter of 0.17-0.19 µm and 1.0-1.4 µm also increased the permeability of the nasal organoid at the dose of 0.08, 0.31, 1.25 and 5 mg/mL. PS with the diameter of 0.17-0.19 µm and 1.0-1.4 µm also induced the death of Caco-2 and upper airway cell lines, and the high level of ROS in these cells. While PS with diameters of 4.8–5.8 µm and 9.5–11.5 µm had no obvious effects on the barrier functions of the gut-on-a-chip or nasal organoids, the survival rates of Caco-2 cells and airway cell lines

were similarly unaffected. Conclusions: PS with the diameters 1.0-1.4 µm and 0.17-0.19 µm damaged the gut and airway epithelial barrier, which is associated with oxidative stress and cell death.

P33 IL4 and IL13 induce an atopic dermatitis-like phenotype in N/TERT-2G human epidermal equivalents in vitro

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The prevalence of allergic diseases is rising, affecting nearly 30% of the Western population. The onset of allergic diseases often follows a distinct developmental pattern, known as the atopic march, where early-life atopic dermatitis (AD) predisposes for food allergy, allergic asthma and/or allergic rhinitis later in life. AD is characterized by a dysfunctional skin barrier, which may promote allergen sensitization due to higher skin permeability. Here, an in vitro human epidermal equivalent (HEE) model of N/TERT-2G human keratinocytes was employed to induce an AD-like phenotype. During the 10 day air-liquid interface culture period, IL4 and IL13 (both 10ng/mL) were added at day 0, 3 or 7 to induce the AD-like phenotype. Cell cytotoxicity, barrier development, alarmin gene expression, ZO-1 and filaggrin (FLG) levels were determined in the AD-like HEEs at the end of the 10 day culture protocol. Transepithelial electrical resistance (TEER) was less developed when IL4 and IL13 were added to the HEE cultures at days 0 or 3. Decreased gene expression of the alarmins IL33 and TSLP compared to healthy control when IL4 and IL13 were added from day 0 or 3, but not from day 7 was measured. FLG gene expression was decreased when IL4 and IL13 were added from day 0, quantification of FLG protein level upon immunofluorescent staining confirmed a decreased presence of FLG, which was also observed in HEEs exposed to IL4 and IL13 from day 3. ZO-1 levels were not significantly altered by IL4 and IL13 compared to the healthy control. Addition of IL4 and IL13 successfully induced a phenotype in HEEs with typical AD-like characteristics, with earlier addition of IL4 and IL13 leading to more pronounced disruptions in HEE development. These AD-like HEEs can serve as a model to gain insights in the role of atopic dermatitis in allergic sensitization.

P34 Sodium dodecyl sulfate impairs the skin epithelial barrier by inducing oxidative stress in human skin

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Impairment of the epithelial barrier function is associated with various allergic and inflammatory skin disorders. Household cleaning products and their primary components, surfactants have been reported to damage the skin barrier, however, the cellular mechanisms underlying this impairment remain unclear. Our previous studies have shown that electrical impedance spectroscopy (EIS, Nevisense®) is an effective, non-invasive tool for assessing skin barrier integrity in human skin. We recently developed a method to evaluate skin barrier integrity using ex-vivo human skin models (NativeSkin®) with a normal skin structure. We investigated the mechanisms of epithelial barrier dysfunction in human skin induced by sodium dodecyl sulfate (SDS), a common surfactant used in household cleaning products. Ex-vivo human skins were treated with SDS and PBS, and then barrier function was assessed by EIS. RNA sequencing (RNA-seq) and targeted multiplex proteomics analyses (Olink®) were performed on ex-vivo human skin. The treatment and preventive effects of N-acetylcysteine (NAC) and nicotinamide (NAM) were investigated in air-liquid interface cultured normal human epidermal keratinocytes and ex-vivo human skin. Reactive oxygen species (ROS) levels were measured in monolayer cultured primary human keratinocytes. The application of SDS to the surface of native skins for 1 or 5 minutes resulted in a dose-dependent reduction in EIS values. SDS enhanced skin inflammation and immune responses at both mRNA and protein levels analysed after 24 h. Additionally, SDS increased the skin barrier permeability and induced ROS production in keratinocytes. Treatment with NAC and NAM reduced ROS production and alleviated SDS-induced skin barrier dysfunction. In conclusion, we demonstrated that just 1 minute exposure of SDS disrupts the skin barrier integrity. Furthermore, oxidative stress may play a central role in SDS-induced skin barrier damage. NAC and NAM may exert preventive effects on SDS-induced skin barrier damage by inhibiting oxidative stress.

P35 Common non-nutritive sweeteners disrupt the gut barrier and cause inflammation via multiple mechanisms of cellular stress in vitro

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The global consumption of non-nutritive sweeteners (NNS) as sugar alternatives has increased considerably significantly in recent years to lower caloric intake. However, emerging evidence suggests that even small amounts of NNS may have a negative impact on gut health. As demonstrated in previous analyses, the negative effect of NNS on the intestinal epithelial barrier has been observed at doses relevant to consumers, in a timely or acute manner. In this study, a chronic exposure model was employed, with low doses administered every two days in the culture medium over a period of eight days. The microfluidic organ-on-a-chip platform was utilized to generate 3D intestinal tubules using the human epithelial cell line Caco-2, thereby enabling the investigation of the effects of sodium saccharin (NaSA), sucralose, stevia extract (STVE), and steviol (STVO) at doses below the consumption exposure. Transepithelial electrical resistance (TEER) were assessed to evaluate cellular responses. The effects of NNS on the gut epithelial barrier were analysed using RNA-seq. Our findings indicate that NaSA and STVE, at low accumulative doses, do not result in a significant reduction in TEER. Conversely, sucralose and STVO have been observed to induce a significant dose and time-dependent decrease in TEER. Furthermore, transcriptomic data after low doses of all studied NNS in chronic exposure revealed upregulated pathways, which included those associated with the cellular response to stress, oxidative stress, the endoplasmic reticulum stress response, response to unfolded protein, mitochondrial, response to damage stimulus, telomer maintenance, innate immune response, and cell death. The results indicate that commonly used non-nutritive sweeteners at relatively low and daily used doses have the capacity to disrupt gut barrier function and induce inflammation through multiple cellular stress mechanisms in vitro. This finding suggests potential concerns regarding the widespread and chronic consumption of NNS and their implication for gut and systemic health.

P36 Wildfire smoke causes cytotoxicity and activates the AhR pathway on airway epithelial cells.

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The escalating frequency and intensity of global wildfires pose significant public health challenges. Emerging evidence suggests wildfire-derived particulate matter exerts greater respiratory impacts than ambient particulate matter from other sources, yet its specific mechanisms of epithelial barrier damage remain poorly characterized. This study aims to evaluate wildfire smoke-induced airway epithelial damage and explore underlying mechanisms. Wildfire smoke particulates were generated from olive wood burning under high-flame and low-flame combustion conditions. Primary human nasal epithelial cells and airway epithelial cell lines (BEAS-2B and A549) were exposed to smoke extracts. Cellular viability was quantified using MTT assay, intracellular reactive oxygen species (ROS) levels were detected through DCF fluorescence measurement. Aryl hydrocarbon (AhR) receptor activation was assessed with an AhR reporter HepG2 cell line. We used concentrations of 102, 103, 104, 105 and, 106 µg/m3 for both combustion conditions. Both high-flame and low-flame smoke exposure induced dose-dependent cytotoxicity across all epithelial models. AhR reporter cell assay demonstrated robust activation of AhR pathway upon both combustion exposure. However, smoke exposure did not significantly increase intracellular ROS levels. We demonstrate that wildfire smoke directly damages airway epithelial cells. The potent AhR activation observed suggests this pathway may mediate wildfire smoke-induced epithelial barrier dysfunction.

P37 The role of differential expression of HR1 and HR2 on B cell subsets and their functions

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Histamine is an amine involved in physiological and pathological processes including allergic diseases. Four histamine receptors regulate actions of histamine. HR1 and HR2 are predominantly expressed in T helper 1 (Th1) and Th2 cells, respectively. HR1 promotes Th1-type responses, but Th1 and Th2-type responses are suppressed by HR2. Histamine affects the antibody production of B cells. Our group demonstrated that mRNA expression of HR1 and HR2 on B cells is mutually exclusive, which may characterize two distinct B cell subsets with pro-inflammatory and suppressive properties. PBMCs or pure B cells isolated from both TMCs and blood PBMCs were stimulated with stimuli. Cells were subjected to flow cytometry after 0 and 48h. HR1+ and HR2+ B cells were sorted for bulk RNA sequencing. HR1 and HR2 knockout mouse models were generated. We confirmed the exclusive expression pattern of HR1 and HR2 on primary B cells from human PBMCs with flow cytometry. During PBMCs stimulation with CpG showed a tendency to promote HR1 expression on B cells, and stimulation with anti–B cell receptor (BCR), tended to inhibit HR1 expression; HR2 expression on human B cells can be induced by stimulation with IL-10 and inhibited by BCR with IL-4 after 48 hours; Stimulation with IL-10 for 48 hours increased the percentage of HR double-positive B cells. In response to stimulation in pure B cells from TMCs and PBMCs, CpG with or without histamine, or IL-3, IL-4 promoted HR1-expressed B cells from TMCs; HR2+ B cells from TMCs and PBMCs were increased after CpG with IL-4 activation and inhibited by IL-10. HR1KO and HR2KO mice showed significant changes in the B cell amount in diverse tissues compared to WT mice. These data provide essential contributions to the conditions that lead to exclusive expression of HR1 or HR2 on B cells.

P38 An emerging dual role for ProtA in EBV infected B cells

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Epstein Barr virus (EBV), a gamma-herpes virus infecting >90% of the population worldwide, establishes life-long latency in B lymphocytes and is associated with several lymphoid and epithelial malignancies. In vitro, EBV growth-transforms human B lymphocytes into highly proliferating lymphoblastoid cell lines (LCLs) and is known to hijack host metabolic pathways to meet the high energy demands required for its growth program. Our recent work uncovered transient expression of the enzyme Indoleamine 2,3-dioxygenase 1 (IDO1) in EBV infected B cells. In unpublished studies, we identified expression of another EBV-induced host metabolic protein, referred to here as “protA” (for IP protection reasons), that is expressed starting around 4 days post infection (dpi) and is maintained in LCLs. Knocking out/down protA prior to EBV infection reduced tumor burden in vivo and transformation efficiency in vitro, pointing to an essential role in establishing latency in transformed B cells. How protA supports establishing latency, and thus promotes malignancy, remains unclear. To begin elucidating underlying mechanisms, we applied 13C tracing in LCLs and detected a rapid flux towards the enzyme`s substrate. Intriguingly, while flux from the substrate into its product was readily detected in the first week after infection – reflecting enzymatic activity – this flux was unexpectedly slow in LCLs – leading to intra- and extracellular substrate accumulation. Knock-out of protA in LCLs did not affect their viability or proliferation, but resulted in altered EBV-encoded transcript profile. These findings jointly point to a potential dual role of protA in EBV infection: a metabolic function during the initial transformation phase and a potentially non-metabolic role during latency. Understanding the mechanisms underpinning protA’s role in EBV-infected B cells may point at therapeutic targets able to prevent EBV-driven proliferation, latency and associated lymphoproliferative disorders and cancers.

P39 Investigation of allergen specific B cells

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Food allergies are defined as a type 2 IgE-mediated immune response against certain food proteins. The balance between effector and regulatory B cells determines if an individual has an allergic or tolerant response to ingested food. This means there should be significant differences in B cell subsets and, therefore B cell regulation between healthy and allergic individuals. As such, an investigation into the B cell regulation and the development of food tolerance vs food allergy is a promising trail to understand the causal pathways for food allergy. This project aims to characterize B cells of allergic individuals on a transcriptomic level and investigate the differences of their B cell gene expression in comparison tolerant counterparts. We used bio-banked PBMCs from mono- and dizygotic twins that are either food allergy concordant or discordant. We separated the switched and unswitched B cells from the individual donors with FACS and pooled them for total RNA extraction. The extracted RNA was depleted from ribosomal RNA using the probe based approach of the RiboCop rRNA Depletion Kit. After reverse transcription, library generation and pooling the transcriptomic cDNA was sent for sequencing. Expression patterns between healthy and allergic, between allergy discordant, concordant and healthy twins showed that there was no dysregulation in general B cells. What differences there are might only be present in allergen specific cells. Therefore we labelled peanut allergen to sort out allergen specific memory B cells from donors undergoing peanut OIT. In a collaboration with Harvard, PBMCs from participants of the IMPACT study were sorted and sequenced. The analysis focused on differential gene expression from timepoints at the beginning, end and after OIT. This will give insight on the progress of tolerance development on the B cell level and how lasting these changes are.

P40 Antibody responses to myocardial antigens released in the context of a myocardial infarction

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Recent studies suggest a link between B cells, myocardial antibodies, and ischemic heart failure, influencing post-myocardial infarction (MI) repair. However, the antigenic specificity of these antibodies remains poorly understood. This study aimed to characterize B cell receptor (BCR) repertoires and study specific B cell dynamics in both mice and MI patients focusing on their antigenic targets and specificity. In a "track-and-clone" approach we performed single-cell RNA/BCR sequencing on B cells purified from infarcted mice and peripheral blood mononuclear cells (PBMCs) of MI patients. In mice, unique BCRs emerged in germinal center (GC) B cells and plasma cells after experimental MI, absent in sham-operated controls. Over time, increased GC B cells, clonal expansion, and somatic hypermutation indicated antigen-driven responses and affinity maturation. Similarly, in MI patients, clonally expanded plasmablasts were rapidly mobilized to peripheral blood. Selected expanded BCRs were cloned into immunoglobulin expression vectors, and MI-triggered monoclonal antibodies (MI-IgGs) were expressed in human embryonic kidney cells. When incubated with murine cardiac histological slices as well as human induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs) a portion of expressed BCRs from mice and patients showed binding to myocardial antigens, confirming that MI triggers heart-specific autoimmune responses. At a functional level, we found that iPSC-CMs treated with the monoclonal antibodies produced from MI-BCRseq

experiments showed enhanced beating frequency and sarcomeric irregularity when compared to control iPSC-CMs. When administered into infarcted C57BL/6 mice, these heart-reactive antibodies accumulated in the myocardial scars and were associated with increased GC responses in the heart-draining lymph nodes. These results demonstrate that MI triggers the production of heart-specific antibodies, in both mice and humans. Our "track-and-clone" approach provides novel tools to explore the antigen specificity and functional relevance of myocardial antibodies, and provide critical insights of B cell responses in ischemic heart disease.

P41 Exploring the Role of Type II Cytokines in Alarmin Receptor Regulation in B Cells

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Background: The regulation of B cell function by type II cytokines represents a potential contributor to immune-mediated disorders, including eosinophilic esophagitis (EoE). While EoE is characterized by eosinophilic infiltration in the esophagus, recent findings implicate B cells in its pathophysiology, as evidenced by elevated B cell counts and food-specific IgG4 antibodies in patients. However, the precise mechanisms by which type II cytokines influence B cell function, particularly through the regulation of alarmin receptors, remain poorly understood. This study aims to investigate how type II cytokines and associated activation stimuli modulate alarmin receptor expression on B cells, elucidating their potential contribution to EoE pathogenesis. Methods: B cells were purified from peripheral blood mononuclear cells (PBMCs) and tonsil tissue of healthy donors. In addition immortalized B cells derived from PBMCs of healthy donors and esophageal tissue of EoE patients we analyzed. Cells were treated with IL-4 and other type II cytokines in combination with activation factors such as CD40L, CpG, and BCR crosslinkers. Alterations in B cell phenotype and function were assessed using qPCR, ELISA, Olink proximity extension assay, and flow cytometry. Results: Type II cytokines elicited variable effects on B cell receptor expression. CD40L and IL-4 co-stimulation significantly increased the expression of type II cytokine receptors, such as IL-4R and IL-13RA1, as well as IL-17RB, which may mediate IL-25 signaling. These findings suggest that type II cytokines influence alarmin receptor regulation, potentially altering B cell function in inflammatory conditions. Conclusion: This study highlights the modulatory effects of type II cytokines on alarmin receptor expression in B cells, providing insights into their potential role in EoE pathogenesis. Future investigations are necessary to clarify the mechanisms underlying these interactions and their relevance as therapeutic targets.

P42 Characterization of the Memory B Cell Response to Bee Venom Phospholipase A2 in Novice Beekeepers

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Introduction: Allergen-specific immunotherapy (AIT) induces tolerance through a gradually high dose exposure of the allergen. Beekeepers represent a model of natural immune tolerance, which can provide insight into the mechanisms of AIT. Recently, higher frequencies of type 2-polarized memory B cells (MBC2s) which hold allergen-specific IgE response were discovered in allergic individuals. To investigate the healthy B cell response during allergen tolerance development to honey bee venom (HBV), we longitudinally studied the development of various B cell subsets, including MBC2s, in novice beekeepers. Methods: A six-year prospective study was performed. PBMCs from novice-exposed beekeepers (n=6) were collected before the first exposure to HBV and during different time points after the first sting (days, months, and then seasonal). PBMCs were stained and analyzed by flow cytometry to identify phospholipase A2 (PLA2; major allergen of HBV) and tetanus toxoid (TT; as biological control) specific B cell isotypes and MBC2s (defined as CD23+IL4R+). Results: There were no significant changes in the distribution of the total B cell isotypes after the first sting or re-exposure time points. We observed allergen-specific class-switched B cells expand in response to HBV at 7 to 14 days after exposure. Allergen exposure correlated with the gradual increase of the frequencies of PLA-2 specific B cells. Particularly, IgG1, IgG2, IgA1, and IgG4-expressing B cells were predominantly present among allergen-specific B cells. IgG4 arises from 6 months to one year of constant exposure. The PLA2-specific B cell subset in healthy beekeepers express the previously described MBC2 markers (CD23 or IL-4R) but not always co-expressed together. CD23 expression was more associated with PLA-2-specific B cells than IL-4R expression. IgG1 and IgG4 were the primary isotypes found in allergen-specific MBC2s. Finally, PLA-2-specific B cells express more CD23 compared with TT-specific B cells. Conclusions: IgG1, IgG2, and IgG4 are the predominant isotypes that develop in HBV natural tolerant individuals. Allergen-specific B cells in non-allergic individuals are characterized by CD23+IL4R- expression. These new findings provide valuable insights into the mechanisms of allergen tolerance in healthy individuals and can be extrapolated to patients undergoing AIT, highlighting the role of various B cell subsets in this process.

P43 Unraveling the Complexities of SARS-CoV-2 Antibody Responses: Towards Optimized Vaccination Approaches

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Identifying key factors influencing the severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2)-specific antibody levels after vaccination and/or prior infection was one of the goals during and after the pandemic. This results in important implications for public health strategies and personalized medicine approaches. Therefore, the presented study focused on immune response following SARS-CoV-2 vaccination and/or coronavirus disease 2019 (COVID-19) by considering various influencing factors, including vaccine type and its combinations, time, sex assigned at birth, body mass index (BMI), age, chronic diseases, long-term treatment, and hormones. From January 2022 to March 2023, 2000 adults (≥ 18 years, Salzburg, Austria) participated in this population-based seroprevalence study. SARS-CoV-2-specific IgG antibodies were detected using an anti-SARS-CoV-2 IgG quantitative assay and correlated with data collected by questionnaire (anthropometric factors, vaccination information, medical history). For 77 of the participants, a time-course study up to 24 weeks post vaccination or quarantine end was performed. Convalescent-only subjects had the lowest median antibody titer (65.6 BAU/mL) compared to vaccinated and hybrid immunized subjects (p-value < 0.0001). The type of vaccine as well as vaccine combinations significantly influenced the levels of SARS-CoV-2 spike-protein-specific IgG, ranging from a median antibody level of 770.5 BAU/mL in subjects who were vaccinated only to 3020.0 BAU/mL in hybrid immunized subjects (p-value < 0.0001). Over time, a significant decline in the levels of neutralizing antibodies was found. Depending on the subpopulation analyzed, further significant influencing factors included chronic diseases, medication, and hormones (cortisol, dehydroepiandrosterone (DHEA), testosterone, progesterone). Hybrid immunization led to stronger immune responses, highlighting its value in providing durable and broad-based protection against COVID-19. Importantly, the identification of other key factors - including chronic conditions, medications, and hormones - that influence antibody responses, can aid more personalized vaccination strategies, including the development of next-generation individualized vaccines.

P44 Microbial-Derived Tryptophan Metabolites Selectively Influence Cytokine Secretion, Proliferation and Differentiation of Polarized Human Lymphocytes

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Microbial metabolism of dietary tryptophan generates a wide range of indoles which are important signaling molecules in microbial communities and may contribute to intestinal and systemic immune homeostasis. However, the direct effects of microbial tryptophan-derived metabolites on T cell function have not been thoroughly examined. The aim of this study is to identify the tryptophan-derived metabolites that most effectively modulate T cell differentiation, in particular Th2 polarization. Following naïve CD4+ T cell sorting from human PBMC, lymphocytes were stimulated with HumanTransAct to promote effector T cells differentiation and cytokine secretion. In addition, purified naïve CD4+ T cell was cultured under Th2 polarizing conditions, with or without tryptophan-derived metabolites. Lymphocyte cytokine secretion was measured by ELISA, while Th2 cell surface markers, proliferation and mitochondrial function were examined by flow cytometry. Following anti-CD3/CD28 stimulation, Indole-3-acrylic acid (IA), Indole-3-pyruvate (IPYA) and indole-3-ethanol (IET) significantly reduced secretion of IL-5 and IL-13. IPYA, IET, and Indoxyl 3-sulfate (I3S) have a stronger effect on IFN-gamma secretion than the other indoles. In contrast, IL-10 secretion was increased for many of the indoles, especially IET, Indole-3-propionic acid (IPA) and tryptamine. For IL-17 and IL22 secretion, we found that tryptamine, IA, and Indole-3- glyoxylic acid (IGoxA) reduced IL17 secretion in a dose dependent manner, and many metabolites enhanced IL22 secretion, especially tryptamine, IPYA and IGoxA. Under Th2 polarization conditions, IA and IPA inhibited IL-5 and IL-13 secretion, as well as decreasing the population of CD4+CCR4+GATA3+IL-4+ Th2 cells. IPA also reduced the lymphocytes proliferation rate and influenced functional mitochondria but not the mitochondrial mass. Indoles generated by

microbial metabolism of tryptophan have distinct effects on lymphocyte cytokine secretion, proliferation and polarization. In particular, inhibition of Th2 polarization might be an important mechanism required to prevent mucosal allergen sensitization.

P45 Proteomic Analysis of Extracellular Vesicle Cargo in COVID-19 Patients During Acute and Post-Acute Phase Infection

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The COVID-19 pandemic, caused by SARS-CoV-2, has posed significant challenges to global health, with clinical manifestations ranging from asymptomatic to severe disease. A critical aspect of its pathophysiology involves the immune dynamics during the acute and post-acute phases, where inflammation and immune reprogramming play key roles in disease progression and recovery. To better understand these phases, the proteomic and phosphoproteomic profiles of extracellular vesicles (EVs) derived from plasma samples of COVID-19 patients were analyzed, aiming to uncover the role of EVs and their cargo in SARS-CoV-2 pathogenesis and immune responses, and identify potential biomarkers and therapeutic targets. A comprehensive experimental workflow was developed, including optimization of EV isolation methods, characterization via transmission electron microscopy, flow cytometry, and proteomic analyses using LC-MS/MS. Ultracentrifugation was found to be the most effective technique for isolating exosomes. Key findings revealed distinct protein expression profiles between the acute (P1) and post-acute (P2) phases. Acute-phase samples showed upregulation of innate immune markers, such as ALOX15B and CD14, while post-acute-phase samples exhibited increased expression of adaptive immune proteins, including immunoglobulins and complement components like C5, indicative of recovery and metabolic reprogramming. A pilot study identified 331 unique proteins in total exosome extracts and highlighted phosphorylation-based post-translational modifications (PTMs) in immune pathways, especially the complement cascade. These findings underscore the dynamic immune landscape of COVID-19, with EVs serving as both contributors to and indicators of disease progression. The identification of phosphorylated complement proteins offers novel insights into immune response regulation and potential therapeutic interventions for controlling hyperinflammation.

P46 Bocavirus and/or rhinovirus infection and tonsillar immune responses

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Background: Human bocavirus (BoV) has been implicated in both respiratory and gastrointestinal infections. Yet previous data indicates that it may have immune suppressive effects in virus coinfection, but overall data on the mechanisms of its immune responses remain limited. Objective: We sought to identify differences in immune responses associated with BoV and/or rhinovirus (RV) infection. Methods: Tonsil tissue samples, nasopharyngeal aspirates (NPA), and serum samples were obtained from 65 tonsillectomy patients. BoV and RV were detected by in house PCR and 14 other respiratory viruses were detected by multiplex PCR. RNA-sequencing was performed on tonsillar tissues. Virus coinfections were divided into 4 groups. 1: sole BoV+RV- 2: sole BoV-RV+ 3: sole BoV+RV+ 4: BoV-RV- including other viruses. Bioinformatics analysis including differential expression, pathway enrichment, correlation, and co-expression network analysis were conducted (FDR < 0.05) in R software. Results: The mean age of the patients was 10 years (range 2-65 years) and with equal number of male and female patients. RNA-sequencing of tonsils yielded levels of 17,110 transcripts for analysis. Our comparisons exhibited 384 differentially expressed genes. Sole BoV+RV- compared BoV-RV- group showed upregulation of TNFR2 non-canonical NF-kB pathway, B cell receptor, antigen processing-cross presentation, interferon alpha/beta signaling and interferon gamma signaling. Respectively, sole BoV+RV- showed down regulation of TNF-, NOD-like-, MAPK- NF-kappa B-, chemokine- RIG-1-like and Rc epsilon R1signaling. Sole BoV-RV+ showed upregulation of toll-like receptors 3 and 4 signaling as well as downregulation of Th1, Th2 and Th17 cell differentiation. Sole BoV+RV+ exhibited upregulation of toll-like receptors 3 and 4 signaling as well as downregulation of antigen processing and presentation and asthma pathway genes. Conclusions: The findings demonstrate that respiratory BoV or RV infections are associated with innate, adaptive and antiviral immune responses. BoV appears interesting immune modulator of rhinovirus infections. Keywords: Tonsil, virus, transcriptome analysis, immune response

P47 Characteristic of 15-LOX and 5-LOX oxo-metabolites with Lund-Mackay score in aspirin-exacerbated respiratory disease.

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Background: Aspirin-exacerbated respiratory disease (AERD) is characterized by triad of: asthma, aspirin hypersensitivity and chronic rhinosinusitis with nasal polyps (CRSwNP) combined with imbalance in proinflammatory and anti-inflammatory eicosanoids. We focused on end-oxo-metabolites in 15-lipoxygenase-1 (15-LOX-1) and 5-lipoxygenase (5-LOX) pathway according to radiological changes in sinuses. Rationale: To identify metabolic characteristic with changes in sinuses, we measured level of 15-oxo- and 5-oxo-eicosatetraenoic acids (15-oxo-ETE, 5-oxo-ETE) in plasma and urine in AERD and in aspirin-tolerant-asthma (ATA). Additionally, urinary LTE4 and blood eosinophils were measured. Methods: In AERD (n=78) and in ATA (n=53) group, oxo-metabolites were measured by high-performance liquid chromatography-tandem spectrometry mass (HPLC-MS/MS). Computed-tomography (CT) scans of the sinuses were assessed according to Lund-Mackay score (L-M score). 2 groups in AERD and 2 groups in ATA were constructed. In range of L-M score 0-11 as AERD-/ATA-low L-M. In range of L-M score 12-24 as AERD-/ATA-high L-M. Results: Level of 15-oxo-ETE in plasma was markedly higher in AERD-high L-M compared to ATA-high L-M (p=.02) and ATA-low L-M (p=.04). Differences between urinary 15-oxo-ETE in AERD-high L-M compared to AERD-low L-M were at the limit of statistical significance. There was no differences in level of 5-oxo-ETE in plasma between groups. Level of urinary LTE4 was significantly higher in AERD-high L-M compared to AERD-low L-M (p=.005); ATA-high L-M (p=.001) and ATA-low L-M (p<.001). Blood eosinophils were higher while L-M score was ≥12, in both groups (p<0.001). Only in AERD-high L-M we noticed, positive correlation between (i) urinary 15-oxo-ETE and L-M score (r=0.39, p=.01); (ii) urinary LTE4 and blood eosinophils (r=0.38, p=.01). Conclusions: Higher level of plasma 15-oxo-ETE were common only with advanced pathological changes in sinuses, especially with a high value of L-M score in AERD. Combination of urinary 15-oxo-ETE with LTE4 and blood eosinophils could be a better predictor for CRSwNP than L-M score.

P48 Metabolic phenotypes in type 2 diabetes shape immunometabolic signatures of circulating CD4+ T cells

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People with type 2 diabetes (T2D) are characterized by systemic low-grade inflammation and altered cellular immune responses. Changes in cellular metabolism have been proposed to drive defective T cell responses, but the relationship with systemic inflammation and clinical parameters remains largely unknown. We therefore phenotyped CD4+ T cells from metabolically well-characterized individuals with T2D of short known disease duration of up to five years and glucose tolerant humans (control, CON) from the German Diabetes Study (GDS). Peo-

ple with T2D show a broad upregulation of pro-inflammatory proteins in serum, but not in supernatants of CD4+ T cells 24h after activation. This is paralleled by an altered relationship between inflammatory proteins, both at the systemic and cellular level, with clinical parameters reflecting e.g. hyperglycemia or dyslipidemia. Additionally, positive associations of inflammatory proteins released from CD4+ T cells with intracellular metabolism, e.g. of interleukin-4 and -10 with spare respiratory capacity, exist in CON, but not in T2D. Whereas basal and maximal respiration of untreated CD4+ T cells positively correlated with BMI and fasting C-peptide levels in T2D, this effect was absent in CON. The close interplay of metabolism and inflammation in T2D is also evident from the differential regulation of metabolism- and inflammation-related genes in CD4+ T cells, including genes involved in interferon signaling, the inhibitory receptor CTLA4, and pyrin and HIN domain family member 1 (PYHIN1). Altogether, our results indicate that metabolic phenotypes beyond hyperglycemia, including alterations in C-peptide and circulating lipid levels, shape CD4+ T cell metabolism and inflammatory function in T2D.

P49 Towards new biomarkers in psoriatic arthritis

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Back ground: Psoriatic Arthritis (PsA) is a chronic inflammatory disease with heterogeneous immune cell involvement. Understanding immune profile differences between healthy controls & PsA patients, in addition to immune profile changes after treatment, is crucial for a better understanding of athogenesis. High-dimensional single-cell analysis using CyTof identifies distinct cellular subsets associated with disease progression and treatment respons. Methods: peripheral blood samples were collected from 10 PsA patients and six healthy controls. In addition, blood from 6 PsA undergoing anti-IL-17 biological therapy was collected before and after one and 3 months. samples were processed using CyTof and the panel consisted of the Maxpar Direct ImmuneProfiling assay markers, immune metabolism markers, 2 interleukins, and lipoxin receptors ALX. Results: Baseline Immune profiles in PsA patients showed a significant increase in different subsets like CD8 and CD4 Tcell subsets and among B cells (<0.05). Post-treatment analysis reveled a reduction in these subsets at both 1 months and 3 months timepoints whithout showinng statistical significance.these findins were consistant with different metabolic reporograming trends. Conclusion: Our findings highlight alternations in psoriatic arthritis and suggests that biological therapy reshapes the immune profile.

P50 A novel role in Treg for the transcription factor JAZF1, which orchestrates a transcriptional programme to help maintain Treg lineage fidelity and metabolic homeostasis.

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Disruption of Treg mediated tolerance results in loss of immune homeostasis and drives immune mediated pathology. FOXP3 orchestrates the transcriptional program in Treg and dysregulation of this network is associated with multiple autoimmune diseases. Our lab has mapped the FOXP3 regulatory network to identify transcription factors subordinate to FOXP3 that establish specific transcriptional programmes to reinforce the integrity of Treg. From these studies we identified a FOXP3 induced transcription factor called JAZF1. Very little is known about JAZF1 in the human immune system, but since it helps maintain lipid and glucose metabolism in mouse liver, we speculated that JAZF1 may regulate metabolism in Treg. The metabolic program of immune cells profoundly influences their growth, activation, differentiation, lineage stability, signalling and migration and so when this is disrupted the cell is severely impaired. Thus, maintaining metabolic homeostasis is crucial for cell integrity. Importantly, the human JAZF1 locus contains genetic risk for multiple autoimmune diseases, including IBD, T1D, SLE and RA, suggesting that JAZF1 may protect against autoimmune disease. Our high resolution immunophenotyping has mapped JAZF1 expression to ThR1/17 and ThR22 human Treg memory populations, suggesting a role in maintaining homeostasis at skin and mucosal barrier sites. We now have evidence of metabolic dysfunction and loss of Treg integrity in JAZF1 KO human Treg. Our RNA-seq analysis revealed 543 upregulated and 655 downregulated genes in JAZF1 KO Treg, which included transcription factors, cytokines, chemokines and significantly, downregulation of enzymes regulating every step of glycolysis. Furthermore, pathway mapping indicates perturbations to multiple biological processes (GO) relating to glycolytic metabolism and pathways relating to autoimmune diseases (KEGG) including IBD and T1D in JAZF1 deleted human Treg. Thus, JAZF1 most likely coordinates a transcriptional program to maintain metabolic homeostasis in Treg and may protect against several autoimmune diseases.

P51 Investigating GAD65-CAR Tregs as a Novel Therapy for Type 1 Diabetes

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Regulatory T cells (Tregs) are key players in the maintenance of peripheral tolerance in healthy individuals. Numerous reports suggest that inherent defects in Tregs play a critical role in T1D development. Thus, Tregs have been heavily investigated as a therapeutic target in T1D, with the aim to re-establish islet tolerance. Antigen-specific Tregs are superior to polyclonal Tregs in their migration to and persistence in target tissue, and prevention of systemic suppression. However, they are rare in peripheral blood, requiring significant expansion for therapeutic quantities, which can be costly and time-consuming. Therefore, this project aims to utilise chimeric antigen receptors (CARs) to confer T1D autoantigen-specificity to Tregs. We have generated CAR Tregs specific for the Glutamic Acid Decarboxylase (GAD65), a key autoantigen expressed in islets using lentiviral transduction ofT1D patient derived Tregs. These CAR Tregs were then assayed for functional marker expression, antigen-specific proliferation and suppressive capacity. Following expansion, 80%-96% of CAR Tregs remain FOXP3 positive, and express high level of the functional markers CTLA4 and CD25, showing >80 % and 80-90% positivity respectively. Moreover, their suppressive capacity, when stimulated via their TCR, was not altered by their expression of the CAR when compared to a donor matched un-transduced (CAR negative) control. CAR dependent GAD65-antigen specificity was demonstrated by proliferation in response to GAD65 over a 5- day period both in the presence and absence of IL-2, relative to their CAR-negative control. We have developed a GAD65-CAR Treg which can be further tested in preclinical studies in Tregs as a method for overcoming GAD65 specific autoimmunity in T1D.

P52 Microneedle-based delivery of ovalbumin-loaded mesoporous silica nanoparticles for allergen-specific immunotherapy

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INTRODUCTION. Allergen immunotherapy (AIT) induces long-term immune tolerance. However, current AIT strategies present limitations associated with the administration route. Subcutaneous administration induces a strong immune response but can trigger systemic allergic reaction during administration. Interestingly, allergen delivery to the epidermis appears promising, since the location hosts immune cells and is associated with reduced systemic distribution. However, the stratum corneum is a barrier for the delivery of intradermal therapeutics. Of note, the use of microneedles has been proposed to improve intradermal delivery across the stratum corneum. METHODS Dissolving microneedle array patches (DMAP) containing large-pore mesoporous silica nanoparticles (MSNs) loaded with ovalbumin (OVA) were prepared and characterized. Their biological performance as AIT strategy were evaluated by in vitro (Parafilm model), ex vivo (excised neonatal porcine skin) and in vivo (mice) methods. RESULTS. 12-nm pore MSNs were prepared and loaded with OVA. A preparation method was developed to produce DMAP-containing MSNs in microneedle tips. Dissolution of microneedles and intradermal deposition of nanoparticles were confirmed ex vivo and in vivo using fluorescent nanoparticles. Finally, cellular uptake and biological effect of nanoparticles was evaluated in vitro in dendritic cell model (DC2.4). The results showed strong activation of dendritic cells by OVA-loaded MSN, with over 70% CD40+ cells after this treatment compared to negligible CD40 expression in cells treated with free OVA. OVA encapsulation inside MSN completely prevented the degranulation of RBL-2H3 cells previously sensitized with anti-OVA IgE, showcasing safety improvement. Finally, the immune response to microneedles containing OVA-loaded MSNs in mice was evaluated, observing equivalent specific IgG1 and IgG2b generation as subcutaneously administered nanoparticles. CONCLUSIONS. This work demonstrates the potential of dissolving microneedle array patches containing mesoporous silica nanoparticles for allergen specific immunotherapy. Further work is undergoing to evaluate the therapeutic efficacy of these systems in a murine model of systemic anaphylaxis.

P53 Development of a Novel Platform for Engineered Extracellular Vesicles in Targeted Immunomodulation

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RNA-based therapeutics hold transformative potential for treating a wide range of diseases, including cancer, infections, and immune disorders. However, their clinical success depends on overcoming cellular barriers, and evolutionary mechanisms that prevent RNA entry into cells. The effective delivery of RNA across the lipid bilayer into target cells remains one of the primary challenges hindering the broad application of RNA therapeutics. While various artificial drug delivery systems have been developed, their widespread clinical use is limited by issues such as toxicity, immunogenicity, and suboptimal tissue targeting. Extracellular vesicles (EVs), naturally occurring nanoparticles secreted by every type of cells, represent a promising alternative since they mediate the transfer of functional biomolecules between cells, naturally circulate throughout the body, and traverse biological barriers to deliver cargoes to specific tissues. Among these, red blood cell (RBC)-derived EVs stand out due to their minimal immunogenicity and lack of genomic DNA, reducing potential off-target effects. In this study, we aim to develop a platform leveraging human induced pluripotent stem cells (iPSCs) to produce engineered RBCs capable of delivering therapeutic RNAs. Our approach involves differentiating iPSCs into RBCs using a 28-day protocol guided by growth factors and small molecules. This process is rigorously characterized through Giemsa staining, confocal microscopy, and flow cytometry. The engineered RBCs are designed to express tissue-specific targeting receptors on their surface and encapsulate therapeutic RNA cargoes with high efficiency. To maximize erythropoietic outcome, we are also focusing on introducing targeted mutation to iPSCs through CRISPR-Cas9 gene editing system.This platform aims to establish a novel, biocompatible delivery system for RNA therapeutics, combining the safety profile of RBC-derived EVs with advanced tissue-targeting capabilities.

P54 Monovalent binding of synthetic high affinity Siglec-9 ligands: A potential candidate for allergy immunotherapy?

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Food allergy has a considerable impact on the quality of life of affected individuals. However, treatments with long-lasting effects remain challenging. A possible strategy is the induction of allergen-specific regulatory immune responses by targeting inhibitory sialic acid-binding immunoglobulin like lectins (Siglec), such as Siglec-9 expressed on dendritic cells, with glycan-modified allergens such as beta-lactoglobulin. The use of non-natural, synthetic, high affinity Siglec-9 ligands may reduce the necessity of multivalent ligand presentation, which is required for natural, low affinity, ligands (e.g., 2,3-sialyllactose). To explore this hypothesis, we sought to examine the binding characteristics of high affinity Siglec-9 ligands to the Siglec-9 receptor. Chemoenzymatic synthesis using the peptide ligase technology allowed site-directed and well-defined installation of distinct quantities of synthetical high affinity Siglec-9 ligands and lactose moieties (n = 1, 2, 3, 6 and 9) on the N-terminus of our model protein, the green fluorescent protein (GFP). Mass spectrometry analysis revealed an overall coupling efficiency of approximately 90%. The modified proteins were separated from the starting material by size exclusion chromatography. Installed high affinity Siglec-9 ligands bound in a dose- and quantity-dependent manner to the Siglec-9 receptor on genetically modified HEKBlueSiglec-9 cells, as well as to human primary monocytes naturally expressing Siglec-9. One high affinity Siglec-9 ligand was sufficient to detect binding defined by increased mean fluorescent intensity of an anti-GFP antibody upon application. Hence, high affinity Siglec-9 appear to be a potential candidate to reduce the required number of Siglec-9 ligands for Siglec-9 targeting and in perspective, for the use in allergy immunotherapy. Allergen specific modulation may be achieved by site-directed coupling of those ligands to an allergen, circumventing broad dampening of DCs.

P55 Defining a new role for Charcot-Leyden crystals in Type 2 immunity and airway obstruction

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Protein crystallization is an important feature of type 2 inflammation, as evidenced by the convergent evolution of Galectin-10 crystals in humans, and Ym1/2 crystals in mice. Despite the prevalence of crystals as a principal feature of pathogenic mucus in human diseases such as asthma, chronic rhinosinusitis and allergic bronchopulmonary aspergillosis, their biological importance has not been explored, due to a substantial lack of tools. We have undertaken several novel approaches to investigate these crystals in an in vivo setting. We have developed several mouse lines to understand the role of Galectin-10 (normally absent in mice) in contributing to various features of allergic diseases and inflammation. Transgenic mice that endogenously express Galectin-10 specifically in the lungs demonstrate increased inflammation during IL-33 stimulation, as well as a striking phenotype of mucus production, airway remodeling and airway obstruction; phenotypes which resemble clinical symptoms of severe asthmatics. By immunofluorescence microscopy, we observed Galectin-10 microcrystals in mucus of these transgenic mice. This demonstrates that Galectin-10 is crystallizing through a mucus scaffold and is contributing to inflammation. Furthermore, we crossed these mice to ENaC overexpressing mice that show spontaneous mucus plugging and observed increased inflammation at steady state. Additionally, we have grown lung organoids showing the interaction between Galectin-10 and mucus. In these novel models, we also demonstrate extensive interactions of neutrophils with Galectin-10 crystals leading to the formation of neutrophil extracellular traps (NETs) which contribute to airway plugging and persistent inflammation. This new understanding, together with translational (proof-of concept) studies using human patient samples, provide a unique platform to investigate Galectin-10 crystals as a therapeutic target for an impenetrable aspect of airway disease.

P56 Dynamic changes in plasma biomarkers following oral immunotherapy in multifood allergic patients

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Multi-allergen immunotherapy has gained growing attention as a strategy to induce tolerance in individuals with multiple concurrent food allergies. In contrast to single-allergen approaches, multi-allergen protocols involve added complexity due to cumulative allergic risks and intricate immunologic interactions. Adjunct therapies such as omalizumab, an anti-IgE monoclonal antibody, can enhance both safety and efficacy by mitigating early hypersensitivity events and elevating the threshold for reactivity. Nevertheless, the immunologic mechanisms underlying successful multi-food desensitization remain incompletely understood which need to be further identified. Twenty-five participants with confirmed multiple food allergies, including shrimp and cashew, were enrolled in a combined omalizumab (weeks 0–16) and dose-escalation oral immunotherapy (OIT) regimen (weeks 8–30). Baseline plasma samples were collected before treatment, and matched samples were obtained at week 52. A 250-analyte multiplex immunoassay (Alamar Biosciences, NULISAseqTM inflammation panel) was used to quantify cytokines, chemokines, growth factors, and immunomodulatory receptors. Changes from baseline to week 52 were determined. Of the 250 analytes measured in serums, 29 showed significant changes over the 52-week period. Chemokines such as CXCL6, CXCL13, and CXCL16 were found to decrease, suggesting attenuated pro-inflammatory signaling. In contrast, FGF21 and TNFSF11 were elevated, indicating activation of counter-regulatory or homeostatic pathways. Immune-regulatory markers MERTK, CTSS, and CD80 also showed downregulation during treatment. These findings highlight broad immunomodulatory effects after 52-week of combined omalizumab and multi-allergen OIT. The reduction in inflammatory mediators, coupled with selective activation of regulatory pathways, highlights the immunological complexity of tolerance induction in individuals with multifood allergies. Further research should correlate these molecular changes with long-term clinical outcomes and guide development of more refined, effective immunotherapeutic

strategies.

P57 Extracellular Vesicles for Drug Delivery

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The field of drug delivery has advanced significantly with the development of nanoparticulate systems aimed at enhancing the properties of therapeutics. While liposomes, polymeric nanoparticles, and dendrimers offer targeted drug release, they come with limitations. Viral vectors, including adeno-associated viruses, adenoviruses, and lentiviruses, demonstrate high efficiency in gene delivery but come with safety and production concerns. Lipid nanoparticles, like liposomes and solid lipid nanoparticles, offer biocompatibility and enhanced drug-carrying capacity, yet they lack control over cargo release kinetics and limited loading capacity. Extracellular vesicles (EVs), naturally secreted by most cells, provide a promising alternative. EVs, including exosomes, microvesicles, and apoptotic bodies, circulate through the body, delivering functional proteins and nucleic acids to target cells via membrane fusion, endocytosis, or receptor-ligand interactions. EVs released by red blood cells (RBCs) are particularly attractive. Indeed, RBCs harbor several advantages since they are poorly immunogenic and do not contain DNA, making RBC-derived EVs a natural and safe drug delivery system. This study aims to develop a therapeutic drug delivery platform using EVs. Initially, HEK293 cells will be utilized to optimize therapeutic cargo loading and targeting. We are engineering plasmids to stably express the exporter, cargo (Cre recombinase), and target genes. HEK293 cells will be transfected with these plasmids, and successfully transfected cells will be sorted using flow cytometry. RNA sequencing will be performed to evaluate the specific enrichment of Cre recombinase RNA within EVs compared to cellular RNA content. To test functionality, we will measure Cre recombinase RNA export from donor cells and its transfer to receiver cells, which will activate GFP expression upon Cre recombination. Ultimately, this system aims to use EVs secreted by red blood cells derived from induced pluripotent stem cells.

P58 Protein Expression Dynamics in Female Elite Athletes: Insights into Training, Recovery, Performance, and Menstrual Cycle Impact

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Female athletes are significantly underrepresented in sports science, with only 3% of studies focusing on their training, recovery, and overall well-being. As a result, many unique physiological factors affecting female athletes, such as the menstrual cycle and its impact on performance and immune health, remain largely overlooked. This gender disparity in sports science has led to gaps in understanding the specific needs of female athletes, particularly in relation to how training and recovery processes may differ from their male counterparts. This study aims to address these gaps by investigating the impact of acute training phases on protein expression in female ice hockey elite athletes, with a focus on optimizing recovery and supporting immune health. A mass spectrometry-based proteomics strategy using Data-Independent Acquisition (DIA) was employed to analyze serum samples collected at multiple time points following high-intensity training sessions and a subsequent two-day recovery period. The study's findings revealed significant differential protein expression patterns, shedding light on the molecular mechanisms involved in training adaptation and recovery. During acute training phases, metabolic demands on the body are increased, leading to protein damage and disruptions in protein synthesis and degradation pathways. In contrast, recovery periods provide an opportunity for cellular repair, resolution of inflammation, and tissue remodeling, which are essential to restoring homeostasis and preparing the body for future performance. This research highlights the importance of tailoring recovery protocols to support immune health, particularly in female athletes. The menstrual cycle's impact on training, recovery, and overall health is an area that requires further attention, as it can affect protein expression and immune function. By addressing these critical knowledge gaps, this study advances inclusive sports science, contributing to the health, well-being, and performance of female athletes while promoting a more equitable approach to athletic research and support.

P59 Development of a non-invasive method to collect immune mediators from skin

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Exposure to air pollution, such as ozone (O3), particulate matter (PM), carbon monoxide (CO), sulfur dioxide (SO2), and nitrogen dioxide (NO2) is strongly associated with development of atopic disease of the respiratory tract, the skin, and the eyes. We aim to characterize immune mediators in healthy and inflamed skin, to identify immune-related biomarkers of interest to study further in the context of air pollution. As a proof of principle, we focus on three pathological skin conditions that differ in underlying immune pathogenesis and associated cytokines: 1) atopic dermatitis (AD), a Th2-driven condition; 2) psoriasis, a Th17-driven condition and 3) cutaneous SLE (CLE), an interferon-driven disease and healthy controls. Currently used methods to measure biomarkers in the skin include tape stripping, and collecting suction blister fluid, both invasive methods. We designed and tested a customized skin wash device to non-invasively collect biomarkers from skin. Cytokine and chemokine levels in skin wash fluid were analyzed on protein level. We show we can successfully retrieve spiked protein from skin of healthy subjects using our skin wash device. Furthermore, we can detect endogenously produced cytokines and chemokines after Imiquimod-treatment of healthy subjects. IL-1 alpha and IL-1 beta were expressed highly at baseline and were not induced by Imiquimod treatment. IL-18, IL-23, IFN alpha, IFN lambda 3 and Galectin 9 protein was increased after Imiquimod treatment. Analysis of patient samples is pending, however METC approval has been obtained. We propose this method of biomarker detection will have wider applications in (bio)medical research, including patients with sepsis, chronic complex regional pain syndrome, obesity, systemic immune diseases, and transplant recipients.

P60 Genetic factors of the complement system and suicidality

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Suicide and the mental disorders involved in the development of the suicidal process represent a major public health problem. The relationship between immune and inflammatory processes and mental disorders has been intensively researched. Most studies have focussed on inflammatory markers such as cytokines, and studies looking at the complement system are still scarce. Complement in the central nervous system of those who have died by suicide and its possible role in the development of the suicidal process is a largely unexplored area. We investigated whether there is a statistically significant difference in the expression of genes encoding elements of the complement system between a group of men who died by suicide and controls. Our study included 23 suicide completers (death by hanging), and 28 control subject (sudden cardiac arrest). All subjects were men aged between 18 and 65 years. mRNA was isolated from the brain region BA46 and converted into cDNA. The qPCR method was used to measure the amount of cDNA in the tissue of each sample. The genes of interest were CFB, CFH, C3, C1QA, C1QB, C1QC, C4A and C4B. Statistical analysis was performed using the unpaired Student t-test and the Mann-Whitney test. The p-value indicating statistical significance was set at ≤ 0.05. The expression of the C3 ($p = 0.0155$) and C1QC ($p = 0.0296$) genes was higher in the brain tissue of suicide completers. The expression of the C4A gene ($p = 0.0025$) was higher in the control group. CFH ($p = 0.1828$), C1QA ($p = 0.0503$) and C1QB ($p = 0.1445$) revealed borderline significance. Our research indicates differential gene expression of complement system genes between the two groups. From the findings of other research in this field, we can conclude that the complement system plays a role in the development of the suicidal process.

P61 Transcriptional profiling of immune cells reveals a role for IFN-gamma/CXCL9/CXCL10 pathway in sepsis patients with exaggerated inflammation

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Background: Sepsis is a life-threatening condition marked by immune dysregulation. Rather than treating sepsis as a homogeneous entity, contemporary approaches aim to identify distinct patient endotypes to facilitate personalized medicine. This study aims to investigate immune dysregulation in sepsis patients by analyzing transcriptomic profiles in patients characterized by exaggerated inflammation. Methods: Peripheral blood mononuclear cells (PBMCs) were collected from 124 sepsis patients and 299 healthy volunteers enrolled in the FUSE project, a part of the Human Functional Genomics Romania initiative. RNA sequencing and inflammatory profiles were analysed by proximity extension assay technology. Patients were classified into "High Inflammatory" and "Low Inflammatory" endotypes based on their proteomic status. Differential gene expression was assessed with DESeq2, controlling for age and gender; genes with an adjusted p-value (padj) < 0.05 were considered significant. Pathway enrichment analysis utilized Over-Representation Analysis (ORA). Results: Sepsis patients exhibited transcriptional upregulation of innate immune pathways, including 'antimicrobial peptides' (S100A8, S100A9, TLR2), 'regulation of Toll-like Receptors' (TLR4, CD14), and 'interferon-alpha/beta signaling' (ISG15, IFI27). Adaptive immunity pathways, such as 'T cell activation and differentiation' (BCL11B, GATA3, CD247), were downregulated. No significant transcriptomic differences were found between patients with pneumosepsis and urosepsis, suggesting that disease severity, rather than etiology, influenced the immune response. Comparing the inflammatory endotypes, transcriptomic analysis revealed significant upregulation of interferon-gamma-driven chemokines CXCL9 and CXCL10 in the "High Inflammatory" group. These chemokines are crucial for recruiting activated T cells and modulating inflammatory responses, indicating a potential interferonopathy in this subgroup. Conclusion: Immune dysregulation in sepsis is primarily driven by disease severity. The upregulation of interferon-gamma-CXCL9-CXCL10 pathway in the "High Inflammatory" endotype underscores the importance of identifying patient endotypes to advance personalized medicine in sepsis management. These findings enhance our understanding of innate and adaptive immune responses in sepsis and may guide the development of targeted therapeutic strategies.

P62 Obesity-linked Sphingomyelin d18:1/14:0 (S14) agonises TLR4 in human macrophages

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Obesity has emerged as a global health epidemic, significantly driving the prevalence of non-communicable diseases. Among obesity-related pathologies, insulin resistance and liver steatosis are strongly linked to the expansion of visceral white adipose tissue (vWAT). Adipocytes within vWAT secrete pro-inflammatory cytokines and bioactive lipids, contributing to systemic inflammation via the hepatic portal vein. While chronic inflammation is well-known to exacerbate disease outcomes, the role of complex lipids in promoting or resolving metabolic dysfunction remains underexplored. Our laboratory identified sphingomyelin d18:1/14:0 (S14) in a large Ldlr-KO mouse cohort with atherosclerosis as a potent predictor of obesity-related diseases in mice and humans. S14 binds to, induces dimerization of, and activates Toll-Like Receptor 4 (TLR4). Notably, S14 concentrations in obese patients reach levels sufficient to activate TLR4, suggesting that lipopolysaccharide (LPS)-like bioactive lipids, rather than solely bacterial-derived LPS, may drive TLR4-linked metabolic dysfunction. Intriguingly, preliminary data indicate that S14 activates distinct cell populations compared to LPS. This project aims to characterize S14-driven responses, providing critical insights into the initiation of metaflammation.

P63 Life-threatening CMV encephalitis and RSV infection caused by a TLR3 mutation in twin girls

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Cytomegalovirus (CMV) is a ubiquitous virus which is generally considered benign in immunocompetent individuals. In contrast, patients with inherited or acquired T-cell immunodeficiencies face a heightened risk of severe CMV disease, manifesting as pneumonitis, hepatitis, retinitis, esophagitis, gastroenteritis or encephalitis with end-organ damage. Rarely, seemingly healthy children or adults may experience life-threatening CMV infections. Growing evidence links severe infectious diseases to underlying monogenic type I interferon (IFN) deficiencies. Here, we present the case of two previously healthy 9-month old identical twins, one initially diagnosed with CMV encephalitis and both later developing life-threatening multisystem inflammation triggered by viral infections. Despite prophylactic intravenous immunoglobulin (IVIG) and interferon beta-1a treatment in one twin, both children succumbed to severe systemic inflammation with myocarditis, progressing to multi-organ failure following a respiratory syncytial virus (RSV) infection. Whole exome sequencing revealed a known heterozygous TLR3 p.P554S mutation in both patients, suggesting that TLR3-dependent type I IFN deficiency increases susceptibility to a broader range of viruses beyond herpes simplex virus and can lead to severe central nervous system infections, paradoxically accompanied by hyperinflammatory episodes. Our case underscores the need to screen seemingly healthy children presenting with life-threatening infections, including CMV encephalitis, for monogenic inborn errors of immunity. Further research is crucial to optimize type I IFN therapy in children with life-threatening viral infections linked to these deficiencies.

P64 Beyond bacteria: A novel look at the gut mycobiome's role in Multiple Sclerosis

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Multiple sclerosis (MS) is an autoimmune demyelinating disease of the central nervous system with unclear etiology, influenced by genetic and environmental factors. Recent studies have highlighted a potential role of the gut microbiome in MS, with a specific focus on the bacterial components. However, the impact of the gut mycobiota- the fungal community, on immune function and disease remains underexplored. Interestingly, our results show distinct fungal community profiles in patients with MS compared to healthy controls and the manipulation of the mycobiota in experimental autoimmune encephalomyelitis (EAE), a mouse model mimicking many aspects of MS, indicated an important role on gut microbiome, immune function and disease activity. Based on these findings, we hypothesize that gut fungi play an important role on microbiome-immune interactions and thereby could impact the pathogenesis of MS.

P65 Lawesson's reagent ameliorates inflammation via the modulation of inflammatory cytokines and NET formation in TNBS-induced rat colitis

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Inflammatory bowel diseases (IBD) are chronic disorders, which affect the gastrointestinal tract with inflammation and ulceration. Neutrophils are the first line of defence within the innate immune system and they can release neutrophil extracellular traps (NETs) in response to inflammatory stimuli. It is increasingly clear that NETosis seems to play a role in IBD, however, the exact pathogenesis is still not known. Several studies demonstrated that the gasotransmitter hydrogen sulfide (H2S) has a wide range of regulatory functions in many physiological and pathological processes. In pathological conditions H2S can reduce inflammation, therefore we aimed to investigate the effects of H2S donor treatment on NETs formation and the levels of some neutrophil-associated cytokines and chemokines in an experimental model of IBD. To model colitis 2,4,6-trinitrobenzenesulfonic acid (TNBS) was administered intracolonically to Wistar–Hannover male rats then animals were treated with Lawesson's reagent as an H2S donor per os twice daily for 3 days. From colonic tissues we measured pro-inflammatory cytokines such as tumour necrosis factor-alpha (TNF-alpha), interleukin-6 (IL-6) and important chemokines in neutrophil recruitment such as C-X-C motif chemokine ligand 1 (CXCL1) and C-C motif ligand 2 (CCL2) by ELISA. Furthermore, we determined the expression of members of NETs formation: peptidyl arginine deiminase 4 (PADI4), citrullinated histone H3 (citH3) and myeloperoxidase (MPO) by Western blot. Our results showed that H2S donor treatment

significantly decreased the extent of colonic lesions and the levels of TNF-alpha, IL-6 and CCL2, additionally, markedly ameliorated the level of CXCL1. The expression of NETosis markers PADI4, citH3 and MPO were significantly reduced in the colonic tissue of the H2S-treated group compared to TNBS. In summary, our results suggest that H2S donor treatment seems to exert its anti-inflammatory effects through the inhibition of NETs formation and it provides a promising therapeutic strategy against IBD.



Poster Presenters Overview

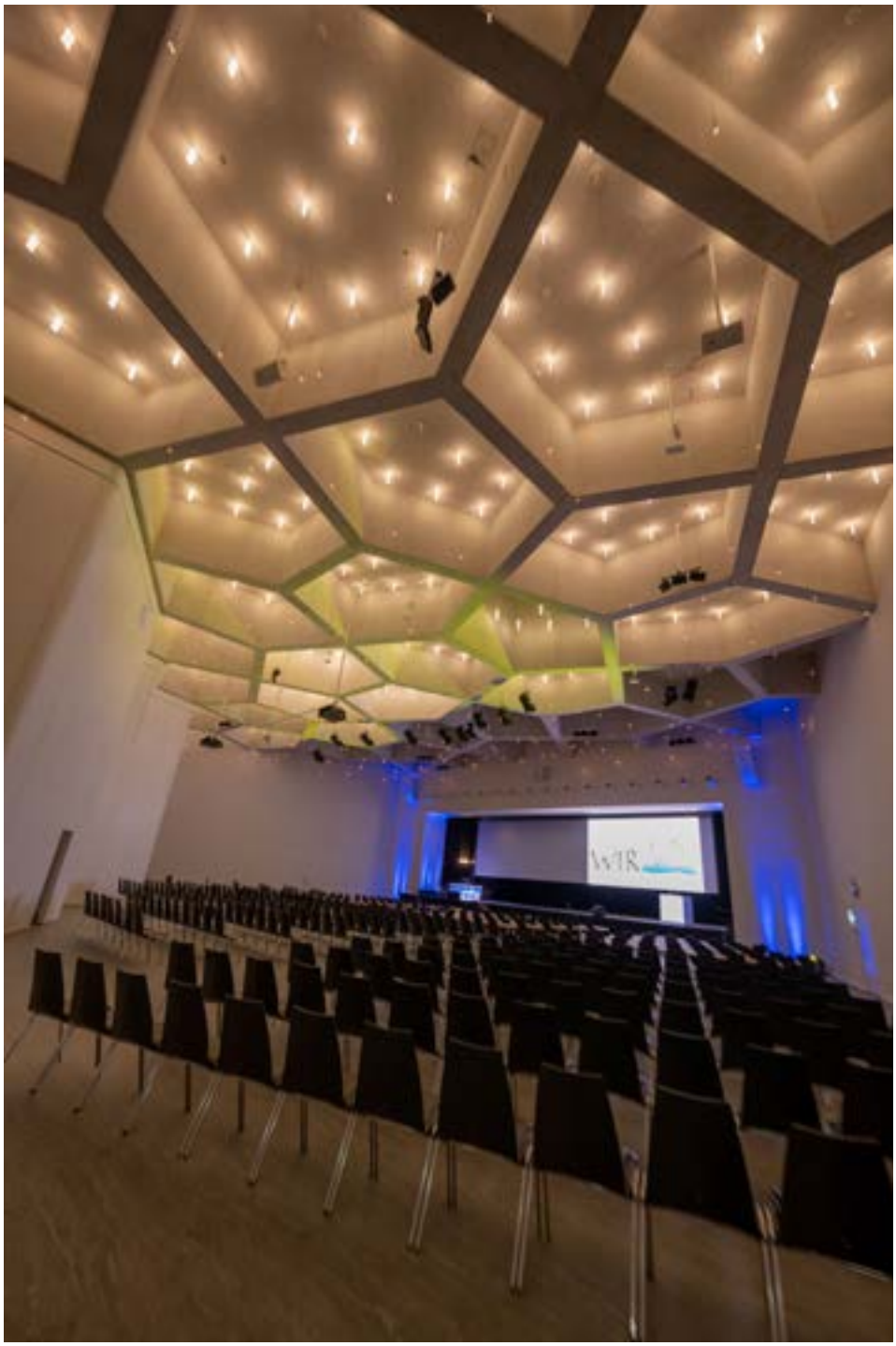
Family Name	First Name	Poster No.	Day	Room	Session-Title
Almasi	Nikoletta	PS21	Day 1	Foyer A1	P3 - Immune response in tumors and chronic inflammation
Ameri	Milad	PS26	Day 2	Foyer A1	P4 - Allergy and Autoimmunity
Ameri	Milad	WS35	Day 2	Forum	W6 - Autoimmunity
Ardicli	Sena	PS05	Day 1	Foyer A1	P1 - Epithelial barrier I
Ardicli	Sena	WS02	Day 1	Davos 1	W1 - Muscosal tolerance and intestinal homeostasis
Ardicli	Ozge	WS10	Day 1	Davos 2	W2 - B cell subsets and immune regulation
Ashour Diyaa	ElDin	WS68	Day 4	Forum	W12 - T and B cell memory and immune regulation
Asuncion Garcia	Maria	PS35	Day 2	Foyer A1	P5 - Epithelial barrier II
Babayev	Huseyn	PS07	Day 1	Foyer A1	P1 - Epithelial barrier I
Babayev	Huseyn	PS08	Day 1	Foyer A1	P1 - Epithelial barrier I
Babayev	Huseyn	PS56	Day 3	Foyer A1	P9 - Novel diagnosis methods, treatments and drugs
Bader	Jackie	WS45	day3	Davos2	W8 - Metabolism and immunity
Barcik	Weronika	WS60	Day 4	Davos1	W10 - Hygiene hypothesis in immune regulation
Barletta	Elena	WS51	Day 3	Forum	W9 - Innate immune response
Barry	Simon	PS51	Day 3	Foyer A1	P8 - Metabolism
Barry	Simon	WS24	Day 2	Davos1	W4 - Immune response to tumors
Beerweiler	Claudia	WS57	Day 4	Davos1	W10 - Hygiene hypothesis in immune regulation
Benne	Naomi	WS33	Day 2	Forum	W6 - Autoimmunity
Boysen	Preben	WS59	Day 4	Davos1	W10 - Hygiene hypothesis in immune regulation
Brown	Cheryl	PS50	Day 3	Foyer A1	P8 - Metabolism
Bu	Xiangting	PS04	Day 1	Foyer A1	P1 - Epithelial barrier I
Burgelman	Jasmijn	PS55	Day 3	Foyer A1	P9 - Novel diagnosis methods, treatments and drugs
Cadosch	Nadine	WS32	Day 2	Forum	W6 - Autoimmunity
Chafle	Sarang	PS28	Day 2	Foyer A1	P4 - Allergy and Autoimmunity
Chang	Yun-Tsan	PS17	Day 1	Foyer A1	P3 - Immune response in tumors and chronic inflammation
Chang	Yun-Tsan	PS18	Day 1	Foyer A1	P3 - Immune response in tumors and chronic inflammation
Chang	Yun-Tsan	PS19	Day 1	Foyer A1	P3 - Immune response in tumors and chronic inflammation
Chang	Lihong	PS32	Day 2	Foyer A1	P5 - Epithelial barrier II
Chang	Yun-Tsan	WS20	Day 2	Davos1	W4 - Immune response to tumors
Cheng	Lin	WS46	Day 3	Davos2	W8 - Metabolism and immunity
Chuang	Ya-Ting	PS13	Day 1	Foyer A1	P2 - Regulatory and effector T cell subsets and cytokines: from bench to bedside
Clark	Margaret	PS14	Day 1	Foyer A1	P2 - Regulatory and effector T cell subsets and cytokines: from bench to bedside
Conde Garcia	Eva	WS07	Day 1	Davos 2	W2 - B cell subsets and immune regulation
Contreras	Nuria	WS64	Day 4	Davos2	W11 - Type II inflammation
Corak	Basak	WS39	Day 3	Davos1	W7 - Novel diagnosis methods, treatments and drugs
Crepaz	Daniel	WS65	Day 4	Davos2	W11 - Type II inflammation
Cui	Ningxuan	WS12	Day 1	Davos 2	W2 - B cell subsets and immune regulation
D'Avino	Paolo	WS27	Day 2	Davos2	W5 - Epithelial barrier and microbiome
Da Choi	E	PS25	Day 2	Foyer A1	P4 - Allergy and Autoimmunity
de Geus	Eveline	PS59	Day 3	Foyer A1	P9 - Novel diagnosis methods, treatments and drugs
De Leeuw	Elisabeth	WS40	Day 3	Davos1	W7 - Novel diagnosis methods, treatments and drugs
De Martin	Angelina	WS04	Day 1	Davos 1	W1 - Muscosal tolerance and intestinal homeostasis
Delafontaine	Selket	PS63	Day 3	Foyer A1	P10 - Innate immune response
Delgado Dolset Maria	Isabel	WS43	Day 3	Davos2	W8 - Metabolism and immunity
Devotta	Hannah	WS58	Day 4	Davos1	W10 - Hygiene hypothesis in immune regulation
Diedro	Mel	PS22	Day 2	Foyer A1	P4 - Allergy and Autoimmunity
Drabonova	Barbora	WS56	Day 4	Davos1	W10 - Hygiene hypothesis in immune regulation
Du	Hang	PS41	Day 2	Foyer A1	P6 - B cell subsets, cytokines and antibody production
Duijzer	Dagmar	PS24	Day 2	Foyer A1	P4 - Allergy and Autoimmunity
Eggestein	Annika	WS49	Day 3	Forum	W9 - Innate immune response
Eguiluz Gracia	Ibon	PS52	Day 3	Foyer A1	P9 - Novel diagnosis methods, treatments and drugs
Eguiluz Gracia	Ibon	WS38	Day 3	Davos1	W7 - Novel diagnosis methods, treatments and drugs
Ehlers	Anna	PS54	Day 3	Foyer A1	P9 - Novel diagnosis methods, treatments and drugs
Engeroff	Paul	WS11	Day 1	Davos 2	W2 - B cell subsets and immune regulation
Enriquez	Josue	WS09	Day 1	Davos 2	W2 - B cell subsets and immune regulation
Fehr	Danielle	PS27	Day 2	Foyer A1	P4 - Allergy and Autoimmunity
Fehrenbach	Pia	PS10	Day 1	Foyer A1	P2 - Regulatory and effector T cell subsets and cytokines: from bench to bedside
Fisch	Laura	WS52	Day 3	Forum	W9 - Innate immune response
Fratea	Andrian	PS61	Day 3	Foyer A1	P10 - Innate immune response
Fric	Jan	WS01	Day 1	Davos 1	W1 - Muscosal tolerance and intestinal homeostasis
Funch	Anders	PS15	Day 1	Foyer A1	P2 - Regulatory and effector T cell subsets and cytokines: from bench to bedside
Funda	David	WS55	Day 4	Davos1	W10 - Hygiene hypothesis in immune regulation
Gavel	Jannes	WS41	Day 3	Davos1	W7 - Novel diagnosis methods, treatments and drugs
Geginat	Jens	WS16	Day 1	Forum	W3 - T cells and innate lymphoid cells
Graf	Lisa-Marie	WS13	Day 1	Forum	W3 - T cells and innate lymphoid cells
Griger	Zoltán	WS31	Day 2	Forum	W6 - Autoimmunity
Grusdat-Pozdeev	Melanie	WS15	Day 1	Forum	W3 - T cells and innate lymphoid cells

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Family Name	First Name	Poster No.	Day	Room	Session-Title
Guendel	Fabian	WS17	Day 1	Forum	W3 - T cells and innate lymphoid cells
Hanif	Tanzeela	PS46	Day 3	Foyer A1	P7 - Immune response to viruses
Harapas	Cassandra	WS53	Day 3	Forum	W9 - Innate immune response
Hasiuk	Marko	PS12	Day 1	Foyer A1	P2 - Regulatory and effector T cell subsets and cytokines: from bench to bedside
Hoffmann	Hans Jürgen	WS37	Day 3	Davos1	W7 - Novel diagnosis methods, treatments and drugs
Ilich	Adrian	WS70	Day 4	Forum	W12 - T and B cell memory and immune regulation
Jardon Parages	Inés	WS44	Day 3	Davos2	W8 - Metabolism and immunity
Joulia	Régis	WS61	Day 4	Davos2	W11 - Type II inflammation
Karl	Tanja	PS43	Day 3	Foyer A1	P7 - Immune response to viruses
Kleinewietfeld	Markus	PS64	Day 3	Foyer A1	P10 - Innate immune response
Kliem	Caroline	WS62	Day 4	Davos2	W11 - Type II inflammation
Kolios	Antonios	WS63	Day 4	Davos2	W11 - Type II inflammation
Kouter	Katarina	PS60	Day 3	Foyer A1	P10 - Innate immune response
Kral	Anita	WS28	Day 2	Davos2	W5 - Epithelial barrier and microbiome
Krawczyk	Krzysztof	PS03	Day 1	Foyer A1	P1 - Epithelial barrier I
Kulkarni	Abhijeet	WS69	Day 4	Forum	W12 - T and B cell memory and immune regulation
Li	Manru	PS34	Day 2	Foyer A1	P5 - Epithelial barrier II
Li	Boran	WS67	Day 4	Forum	W12 - T and B cell memory and immune regulation
Liu	Xiaoqing	PS36	Day 2	Foyer A1	P5 - Epithelial barrier II
Lopez	Juan Felipe	WS08	Day 1	Davos 2	W2 - B cell subsets and immune regulation
López-Rodríguez	Juan Carlos	WS14	Day 1	Forum	W3 - T cells and innate lymphoid cells
Luqman-Fatah	Ahmad	WS54	Day 3	Forum	W9 - Innate immune response
Makowiec	Celia	PS38	Day 2	Foyer A1	P6 - B cell subsets, cytokines and antibody production
Manczinger	Máté	PS23	Day 2	Foyer A1	P4 - Allergy and Autoimmunity
Marchi	Nicolo	PS53	Day 3	Foyer A1	P9 - Novel diagnosis methods, treatments and drugs
Martin-Cruz	Leticia	WS47	Day 3	Davos2	W8 - Metabolism and immunity
McCracken	Nigel	PS09	Day 1	Foyer A1	P2 - Regulatory and effector T cell subsets and cytokines: from bench to bedside
Medea	Veszelka	PS20	Day 1	Foyer A1	P3 - Immune response in tumors and chronic inflammation
Melhem	Hassan	WS66	Day 4	Davos2	W11 - Type II inflammation
Misiukiewicz-Stepien	Paulina	PS31	Day 2	Foyer A1	P5 - Epithelial barrier II
Moise	Cezar-Fabian	PS58	Day 3	Foyer A1	P9 - Novel diagnosis methods, treatments and drugs
Navarro	Severine	WS06	Day 1	Davos 1	W1 - Muscosal tolerance and intestinal homeostasis
Ogulur	Ismail	PS02	Day 1	Foyer A1	P1 - Epithelial barrier I
Papadopoulou	Chrysa	WS23	Day 2	Davos1	W4 - Immune response to tumors
Paplińska-Goryca	Magdalena	PS01	Day 1	Foyer A1	P1 - Epithelial barrier I
Pat	Yagiz	WS29	Day 2	Davos2	W5 - Epithelial barrier and microbiome
Pop	Oltin-Tiberiu	PS16	Day 1	Foyer A1	P3 - Immune response in tumors and chronic inflammation
Ratter-Rieck	Jacqueline	PS48	Day 3	Foyer A1	P8 - Metabolism
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Rodríguez Viso	Pilar	WS30	Day 2	Davos2	W5 - Epithelial barrier and microbiome
Safiat Simboro	Hadja	PS57	Day 3	Foyer A1	P9 - Novel diagnosis methods, treatments and drugs
Sahani	Nitish	PS45	Day 3	Foyer A1	P7 - Immune response to viruses
Schenk	Mirjam	WS22	Day 2	Davos1	W4 - Immune response to tumors
Schneider	Stephan	PS39	Day 2	Foyer A1	P6 - B cell subsets, cytokines and antibody production
Seuwen	Klaus	WS19	Day 2	Davos1	W4 - Immune response to tumors
Sherri	Alaa	PS49	Day 3	Foyer A1	P8 - Metabolism
Siegel	Johanna	PS40	Day 2	Foyer A1	P6 - B cell subsets, cytokines and antibody production
Simpson	Daniel	PS62	Day 3	Foyer A1	P10 - Innate immune response
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Sukenikova	Lenka	WS34	Day 2	Forum	W6 - Autoimmunity
Szatkowski	Piotr	PS47	Day 3	Foyer A1	P8 - Metabolism
Tauber	Marie	WS36	Day 2	Forum	W6 - Autoimmunity
ten Hoopen	Leon	PS42	Day 2	Foyer A1	P6 - B cell subsets, cytokines and antibody production
Tepekule Müller	Burcu	WS25	Day 2	Davos2	W5 - Epithelial barrier and microbiome
Toeroek Szilvia	Agnes	PS65	Day 3	Foyer A1	P10 - Innate immune response
Trzos	Sara	PS06	Day 1	Foyer A1	P1 - Epithelial barrier I
Urban	Swetlana	WS18	Day1	Forum	W3 - T cells and innate lymphoid cells
Viola	Margarida	WS42	Day 3	Davos1	W7 - Novel diagnosis methods, treatments and drugs
Waardenburg	Marlinde	PS33	Day 2	Foyer A1	P5 - Epithelial barrier II
Wang	Jiu-Yao	WS50	Day 3	Forum	W9 - Innate immune response
Weinstein	Kristin	WS71	Day 4	Forum	W12 - T and B cell memory and immune regulation
Wiedmann	Alice	PS11	Day 1	Foyer A1	P2 - Regulatory and effector T cell subsets and cytokines: from bench to bedside

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Family Name	First Name	Poster No.	Day	Room	Session-Title
Wilhelm	Christoph	WS48	Day 3	Davos2	W8 - Metabolism and immunity
Wolska	Magdalena	WS26	Day 2	Davos2	W5 - Epithelial barrier and microbiome
Yang	Minglin	PS37	Day 2	Foyer A1	P6 - B cell subsets, cytokines and antibody production
Yao	Lu	PS44	Day 3	Foyer A1	P7 - Immune response to viruses
Zeyneloglu	Can	WS05	Day 1	Davos 1	W1 - Muscosal tolerance and intestinal homeostasis
Zhao	Bingjie	PS29	Day 2	Foyer A1	P5 - Epithelial barrier II
Zhao	Bingjie	PS30	Day 2	Foyer A1	P5 - Epithelial barrier II
Zuurveld	Marit	WS03	Day 1	Davos 1	W1 - Muscosal tolerance and intestinal homeostasis



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We look forward to seeing you next year:

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