ÖGMBT

ABSTRACTS

17 th ÖGMBT Annual Meeting

„FROM MOLECULES TO ORGANISMS – INTERACTIONS AND INTERVENTIONS“

September 24-26 2025

universität innsbruck

MEDICAL UNIVERSITY INNSBRUCK

Life Sciences Awards Austria 2025

Österreichische Gesellschaft für Molekulare Biowissenschaften & Biotechnologie
Austrian Association of Molecular Life Sciences and Biotechnology

ÖGMBT Benefits

Infos & Updates

- Newsletter
- Annual Meeting
- Jobs
- Career Events
- Grants
- Event Calendar
- Job Market
- Chemiereport Magazine
- Further Education Board

Your Network

- Membership in FEBS, FEMS, EFB
- Grants
- Fellowships
- Discounts
- ÖGMBT Members
- Connection to Stakeholders

Young Life Scientists Austria

ÖGMBT YLSA

- Career Events
- Company Visits
- Job Profiles
- Networking Events

Annual Meeting

- Discount on Registration
- Interdisciplinary Exchange
- Industry Exhibition
- Best Talks/ Best Posters Prizes

Life Sciences Career Fair

- Career Workshops
- Employer Pitches
- CV Check
- Talent Pool

Life Sciences Awards Austria

Research & PhD

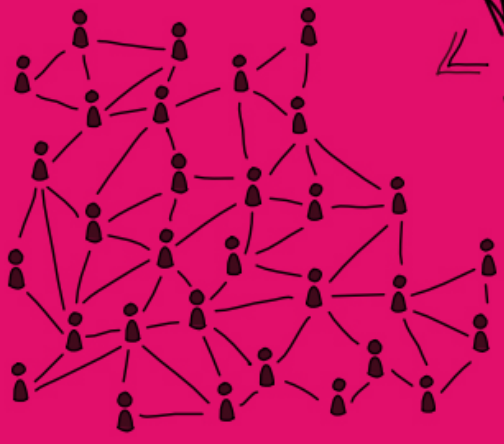
Travel Grants

- National
- International

Engage & Participate

- Shape the Future of Life Sciences as a Volunteer! (ÖGMBT)
- Become an ÖGMBT Member!

More about us!
www.oegmbt.at



Austrian Association of Molecular Life Sciences and Biotechnology

Österreichische Gesellschaft für Molekulare Biowissenschaften und Biotechnologie

17th ÖGMBT Annual Meeting 2025 "From Molecules to Organisms - Interactions and Interventions"

TIP:
Use the bookmark function of your PDF reader to quickly navigate this abstractbook

September 24 - 26, 2025
CCB Innsbruck

Medical University of Innsbruck & Leopold Franzens University of Innsbruck, Austria

Chairs / Scientific Committee

Francesco Baschieri
Medical University of Innsbruck, AT

Sarah Brandl
Medical University of Innsbruck, AT

Giorgia Del Favero
University of Vienna, AT

Theresia Dunzendorfer-Matt
Medical University of Innsbruck, AT

Frank Edenhofer
University of Innsbruck, AT

Matthias Erlacher
Medical University of Innsbruck, AT

Hesso Farhan
Medical University of Innsbruck, AT

Heidelinde Fiegl
Medical University of Innsbruck, AT

Andrea Garvetto
University of Innsbruck, AT

Johanna Gostner
Medical University of Innsbruck, AT

Hubert Hackl
Medical University of Innsbruck, AT

Ludger Hengst
Medical University of Innsbruck, AT

Sebastian Herzog
Medical University of Innsbruck, AT

Lukas A. Huber
Medical University of Innsbruck, AT

Katharina Hüfner
Medical University of Innsbruck, AT

Heidelinde Jäkel
Medical University of Innsbruck, AT

Cornelia A. Karg
University of Innsbruck, AT

Andreas Koeberle
University of Graz, AT

Verena Labi
Medical University of Innsbruck, AT

Michaela Lackner
Medical University of Innsbruck, AT

Sabine Liebscher
Medical University of Innsbruck, AT

Markus Mandl
University of Linz, AT

Pablo Monfort Lanzas
Medical University of Innsbruck, AT

Simone Moser
University of Innsbruck, AT

Sigrid Neuhauser
University of Innsbruck, AT

Johannes Passecker
Medical University of Innsbruck, AT

Joel Riley
Medical University of Innsbruck, AT

Sabrina Sailer
Medical University of Innsbruck, AT

Michael Sauer
OMV AG, AT

Oliver Schmidt
Medical University of Innsbruck, AT

Angelika Seeber
University of Innsbruck, AT

Joachim Seipelt
Nuvonis Technologies GmbH, AT

Eduard Stefan
University of Innsbruck, AT

François Tyckaert
Medical University of Innsbruck, AT

Günter Weiss
Medical University of Innsbruck, AT

Organizing Committee

Johanna Gostner
Medical University of Innsbruck, AT

Ludger Hengst
Medical University of Innsbruck, AT

Lukas A. Huber
Medical University of Innsbruck, AT

Table of Contents

Welcome words

Dear ÖGMBT Members,
Dear Colleagues,

We are delighted to welcome you to the **17th ÖGMBT Annual Meeting**, taking place at the **Centre for Chemistry and Biomedicine (CCB)** in **Innsbruck** from **September 24-26, 2025**. This year's engaging and thought-provoking theme is: **"From Molecules to Organisms – Interactions and Interventions"**

This meeting is designed to bridge the gap between fundamental life sciences, translational research, and applied fields. It provides a dynamic and interactive platform to showcase cutting-edge research, featuring presentations from leading scientists, lively discussions, and extensive networking opportunities.
Among the key themes explored are:

- **From Cells to Organisms: Understanding Biological Interactions**
  Discover how biological mechanisms function across organelles, cells, tissues, and organisms, and how they adapt through development, health, and disease. Topics include stem cells, cell cycle, cancer biology, and cell death.
- **Bridging Knowledge for Scientific Progress**
  Explore how interdisciplinary approaches and advanced techniques—such as machine learning, protein and cell dynamics, and cell adhesion mechanics—drive scientific innovation.
- **Translating Basic Research into Innovation**
  Find out how discoveries in RNA regulation, lipid biology, and natural products are driving progress in drug development, biotechnology, and pharmaceuticals.
- **Immune System, Environmental, and Health Interactions**
  Examine the impact of chemical exposures, microbiomes, and climate on health, with discussions on toxicology, risk assessment, infection, immunity, and antimicrobial resistance.
- **Metabolic and Mental Health Across the Lifespan**
  Investigate how aging, metabolism, and exercise shape biological processes, and gain insights into neurological and metabolic disorders as well as psychiatric conditions.

What can you expect from the meeting?
We are honoured to welcome renowned international scientists who will present their latest discoveries and engage in stimulating discussions with attendees.

Highlights of the ÖGMBT Annual Meeting include the Life Sciences Research Awards Austria and the PhD Life Sciences Awards Austria, which recognize outstanding contributions from young researchers. We look forward to their inspiring presentations.

A family room will be available to support participants with families.

We anticipate exciting exchanges of ideas and interdisciplinary collaborations that will connect scientists across disciplines and career stages, pushing the frontiers of life science.

We are looking forward enjoying an inspiring meeting with you!

Johanna Gostner

Ludger Hengst

Lukas A. Huber

Chairs Scientific/Organizing Committee

General Information

TAXI

Order a taxi via +43 512 5311

VENUE

Center for Chemistry and Biomedicine (CCB),
Medical University of Innsbruck, Biocenter
Innrain 80, 6020 Innsbruck
Kindly find the venue plan on page 8.

Wi-Fi

… is available at the venue. Please ask for the log-in data at the registration desk.

MEETING OFFICE AT THE VENUE

The registration desks will be staffed throughout the Annual Meeting. Please contact us with any related queries in person or by e-mail (office@oegmbt.at).

LUNCH & COFFEE BREAKS

Food and beverages during lunch & coffee breaks will be offered in the foyer in front of the main lecture hall (M.EG180/L.EG 200)

BADGES

We ask you to always wear your badge clearly visible, especially during breaks and at social events to make connecting and networking easier for all.

LANGUAGE

The language of the meeting is English.

SMOKING

… is not permitted at the venue. Kindly use the outdoor smoking facilities.

PHOTO/VIDEO

By taking part in the annual meeting, you agree to us using any photo/video taken at the event without the expressed written permission of those included in the photograph/video. Attendees are not allowed to take any audios of talks or photos of presentation materials (Powe Points, posters, etc.) without the author's permission.

ABSTRACT BOOK/LIST OF PARTICIPANTS

… are available in the registration system after login.

CONFIRMATION OF ATTENDANCE

… will be available after the event in the registration system (login required).

LIFE SCIENCES AWARDS AUSTRIA 2025 / RISING STAR LECTURES

Come to the Life Sciences Awards ceremony on Wednesday, Sept 24, 17:45 – 18:20, and celebrate with us the brightest young Life Sciences minds of Austria who will either receive a Research or a PhD Award. The PhD Awardees will present their talks directly after the award ceremony followed by the Research awardees holding their talks in the Rising Star Lectures.

ORAL PRESENTATIONS

Presentations must be held in English. Please, hand in your presentation in Power Point or PDF format on a USB-stick to the technician in the lecture hall during a break, at least 2 hours before your session. The program is very tight, so please adhere to the time allotted for your presentation.

POSTER SESSIONS

All posters are assigned to one of the 3 poster sessions. All posters will be on display for the whole meeting. Poster presenters: Please be present at your poster during your respective poster session. You can view the poster assignments in the poster tables on pages 28ff.

- **Poster session 1**: Wednesday, Sept 24, 13:00 - 14:15
- **Poster session 2**: Thursday, Sept 25, 13:15 - 14:15
- **Poster session 3:** Friday, Sept 26, 13:30 – 14:30

BEST TALK / BEST POSTER PRIZES

Each early career scientist who presents their work can win:

- 1 prize à € 500.- for Best Talk sponsored by Microsynth Austria & ÖGMBT
- 1 prize à € 200.- for Best Poster sponsored by FEBS Open Bio

The prize presentation will take place during the Closing Ceremony on Sept 26th from 17:30 – 18:00.

INDUSTRY EXHIBITION & EXHIBITORS QUIZ

In the foyer of the venue 30 companies will be displaying their products and services (see venue plan and exhibitor list on page 8). As attendee you have the chance to win great prizes – so take part in the exhibitor quiz. You will find the exhibitor quiz flyer in your goodie bag which you will receive at the registration desk. Rules and prizes for the quiz are described in the quiz flyer. The first exhibitor quiz prize drawing will take place on Friday, Sept 26, during the afternoon coffee break in the foyer whereas the second prize drawing with the main prizes will take place on the same day during the closing ceremony.

ÖGMBT General Assembly

Be an active part of ÖGMBT and shape the future with us! We cordially invite all ÖGMBT members to participate in the ÖGMBT General Assembly on Friday, Sept 26, from 14:00 – 15:00.
You are not an ÖGMBT member yet, but wish to join? You are welcome to attend the General Assembly meeting as well (without voting rights, though).

SOCIAL MEDIA

Follow us on for information about our upcoming events.
LinkedIn Linked in. Facebook

NETWORKING EVENT "WINE & SCIENCE"

Together with the exhibitors, we invite all participants to our networking event Wine & Science on Wednesday, Sept., 24, 19:00 – 22:00 in the foyer of the CCB Innsbruck.

SOCIAL EVENT "Walking Tour & Get Together@Nattererboden"

Exploring the beautiful environment of Innsbruck we will take a guided walk (approx. 85 min) starting at the CCB Innsbruck. Local guides will show the groups around and share some facts about Innsbruck.

All groups will end up at the traditional restaurant "Nattererboden". A welcome drink and flying snacks are on us. Additional culinary delights can be chosen from an event menu. The groups will walk back to the CCB with our guides and some really fancy gadgets afterwards. For those preferring to use public transportation take into account it takes 16 minutes to reach the bus stop. The last regular bus leaves at 10:00 pm. To inquire your connection kindly use this QR code.
Space is limited. So kindly sign in on our event list at the registration desk upon registration and choose from the elaborate menu. We are very much looking forward enjoying a lovely evening with all of you.

FAMILY ROOM

We want to make it easy for parents to take part in our annual meeting. A family room in M.01.392 is available on the first floor. You are welcome to use it at your own risk Children have to be under personal supervision at any time.

“Your ideas, our next move” – WORLD CAFÉ

During the conference you will have the chance to share the issues and topics that matter most to you – whether well-known areas such as career development or networking, or completely new aspects and unmet needs we may not have considered yet – by writing them on our Idea Walls. **Until Thursday (Sept 25) afternoon**, participants can contribute their ideas openly and freely. On Thursday afternoon, the submitted ideas will be collected and clustered by the ÖGMBT team and the moderator – so that on **Friday, Sept 26, 10-11 am**, we can bring a clear and structured set of topics into our World Café session.
The **World Café** will be a guided and moderated process by Petra Buchinger (www.buchinger.org, buchinger Life Science Solutions, AT) where we discuss, explore and deepen these themes together in small groups. The aim is not to create a binding list of priorities, but to capture inspiration and identify what really moves the community. Some participants may even form self-organized groups to take ideas further, while ÖGMBT and YLSA may provide support where possible. If you would like to stay informed about the outcomes and next steps, you will also have the opportunity to sign up during the session.

Picture credit: https://theworldcafe.com/tools-store/hosting-tool-kit/image-bank/

“Connecting Generations” – NETWORKING CARD GAME

Networking goes next-level with Connecting Generations. This game is a unique opportunity for experienced scientists to connect with enthusiastic students, share insights and inspire the next generation organized by ÖGMBT YLSA. On the other side, students get the chance to engage with top scientists, learn from their experiences and exchange ideas. A bonus for students: they have the chance to win an exciting prize—all while making real connections.

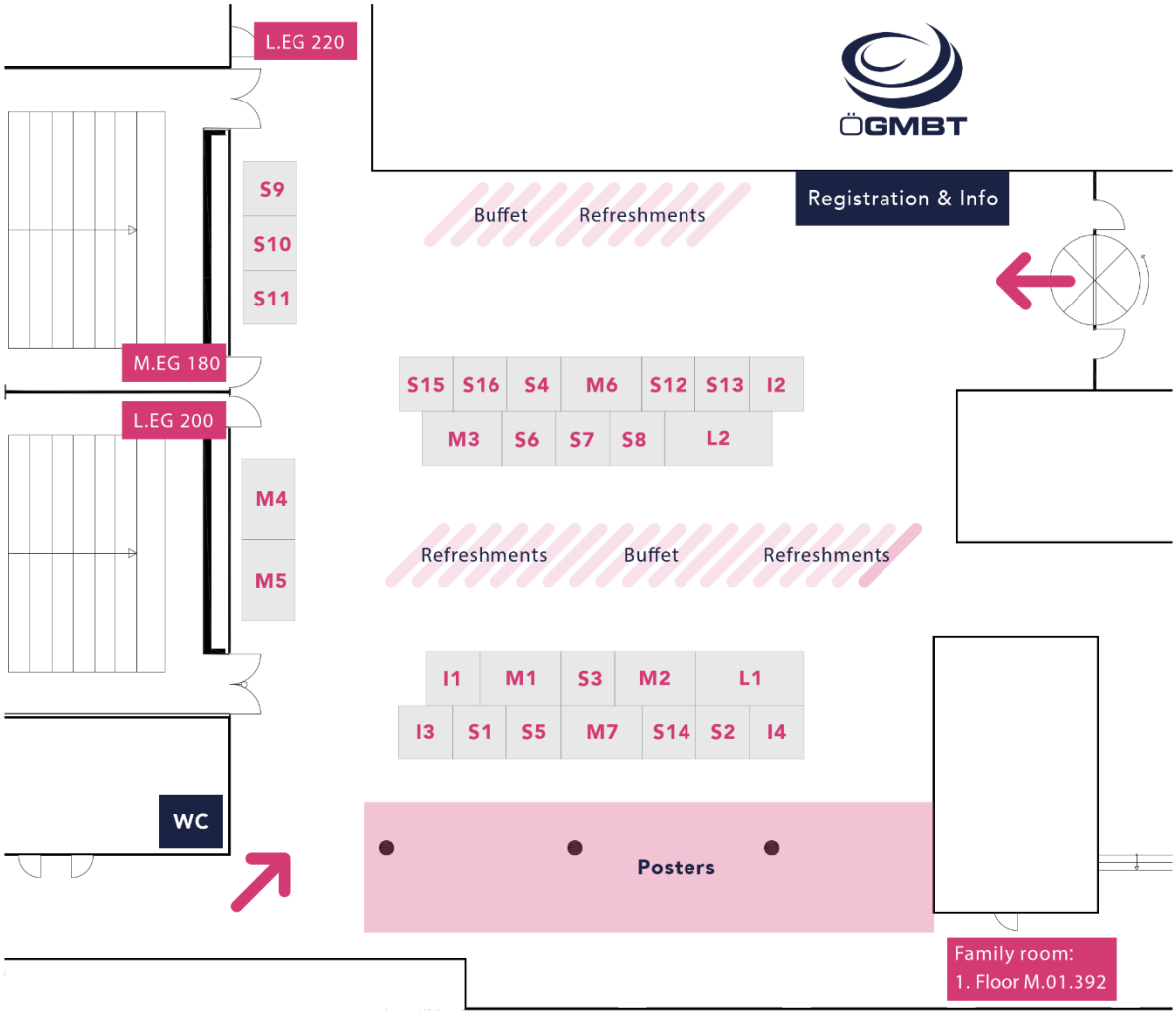
How it works:

- Spot the experienced scientists – Scientists who are in the game will have a coloured dot on their conference badge. That’s your signal to start a conversation!
- Talk First, Collect Later – Each experienced scientist has a unique card with their portrait, career insights and fun answers to kick off a great discussion.
- Here’s the catch: you have to actually talk, do not only ask for the card.
- Build Your Collection – The more conversations you have, the more cards you’ll collect.
- **Throw your collection into the Card Box at the registration desk until Friday, Sept 26, 13:30.**
- Win big time – on the same day, 17:30- 18:00, we’ll raffle off a prize to the student with the most cards.

This is your chance to break the ice, get inspired and make (maybe) career-changing connections in a fun and informal way.

Program Overview

17th ÖGMBT Annual Meeting								
	Wednesday, 24.09.			Thursday, 25.09.			Friday, 26.09.	
09:00-11:00	Registration		9:00-9:40	Plenary 2: Anne Simonsen		9:00-9:40	Plenary 3: Georg Kustatscher	
			9:40-10:25	PhD Session		9:40-10:00	Science flashes 3	
			10:25-10:45	Science flashes 2		10:00-11:00	"Your ideas, our next move" - World Café	
11:00-11:20	Opening		10:45-11:05	Coffee Break		11:00-11:20	Coffee Break	
11:20-12:00	Plenary 1: Veronika Sexl		11:05-12:35	S5: Infection and immunity	S6: Mechanical aspects of cell adhesion and migration	11:20-12:50	S11: Stem cells, cell cycle and cancer	S12: Natural products in life science research
12:00-12:20	Science flashes 1							
12:20-13:00	Lunch		12:35-13:15	Lunch		12:50-13:30	Lunch	
13:00-14:15	Postersession 1		13:15-14:15	Postersession 2		13:30-14:30	Postersession 3	
						14:00-14:30	Company Workshop Thermo Fisher Scientific	
						14:00-15:00	ÖGMBT General Assembly	
14:15-15:45	S1: Neural circuits in health and disease	S2: Environment and microbiology	14:15-15:45	S7: Organelle and membrane biology	S8: Advances in toxicology and risk assessment	15:00-16:30	S13: Cell death in health and disease	S14: Machine learning and perturbation in cellular systems
15:45-16:05	Coffee Break		15:45-16:05	Coffee Break				
16:05-17:35	S3: The multifaceted world of lipids	S4: Aging, mental health, exercise and metabolism	16:05-17:35	S9: RNA in gene regulation	S10: Unveiling protein and cell dynamics	16:30-16:50	Coffee Break & 1. Quiz drawing	
						16:50-17:30	Plenary 4: Peter Murray	
						17:30-18:00	Closing Prizes for best talks/posters 2. Quiz Drawing	
	Break							
17:45-18:20	Life Sciences Awards Austria Ceremony		17:40-17:45	Group Photo				
18:20-19:00	Rising stars Lectures							
19:00-22:00	Wine & Science		17:45	Walking Tour & Get-together @ Nattererboden				



BOOTH	COMPANY
S8	Bartelt
S5	Berthold Technologies
M3	Biozym Biotech Trading
I2	CliniSciences
S12	e-BLOT Life Science (Shanghai)
M2	Eppendorf Austria
S14	Eurofins Genomics Germany
S7	GenScript Biotech (Netherlands)
S15	handshake Consulting
S16	HVD Life Science Vertriebs
S13	Integra Biosciences Deutschland
S11	LabBuddy
S9	LabConsulting
M7	Macherey-Nagel
M5	Merck Life Science
S2	Microsynth Austria
M1	New England BioLabs
S1	Novogene
S3	Promega
I1	Shimadzu
S4	SLAS
S6	SZABO-SCANDIC
S13	Takara Bio Europe
M6	Tecan Sales Austria
I4	Thermo Fisher Scientific
L1	THP Medical Products
S10	VWR International
I3	XPseq Analytics

17th ÖGMBT Annual Meeting

FLOOR PLAN

Invited Speaker Bio Sketches

Christoph Bock, CeMM & Medical University of Vienna, AT

Christoph Bock is a principal investigator at the CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences, professor of medical informatics and head of the Institute of Artificial Intelligence at the Medical University of Vienna. His research combines experimental biology (high-throughput sequencing, epigenetics, CRISPR screening, bioengineering) with computational methods (bioinformatics, machine learning, artificial intelligence) – for cancer, immunology, and precision medicine. Before coming to Vienna in 2012, he was a postdoc at the Broad Institute of MIT and Harvard (2008-2011) and a PhD student at the Max Planck Institute for Informatics (2004-2008). Christoph Bock is also scientific coordinator of the Biomedical Sequencing Facility of CeMM and MedUni Vienna, member of the Human Cell Atlas Organizing Committee, fellow of the European Lab for Learning and Intelligent Systems (ELLIS), and elected board member of the Young Academy in the Austrian Academy of Sciences. He has received important research awards, including an ERC Starting Grant (2016-2021), an ERC Consolidator Grant (2021-2026), the Otto Hahn Medal of the Max Planck Society (2009), the Overton Prize of the International Society for Computational Biology (2017), and the Erwin Schrödinger Prize of the Austrian Academy of Sciences (2022).

Andreas Boland, University of Geneva, CH

Andreas Boland is an Associate Professor at the University of Geneva. He studied Biology at the University of Jena and joined the lab of Dr. Elisa Izaurralde at the MPI in Tuebignen for his PhD work, where he discovered his passion for Structural Biology. In his postdoc work with Dr. David Barford at the MRC-LMB in Cambridge, he used cryoEM to investigate mechanisms that control cell division. His laboratory in Geneva uses structural, biochemical and biophysical methods. During cell division, each daughter cell needs to receive an identical set of sister chromatids. Duplicated chromosomes are held together by the ring-shaped cohesin complex. Separation of chromosomes at anaphase is triggered by separase, a protease that cleaves the cohesin subunit SCC1. The Boland lab studies separase regulation. Andreas has received Young Investigator Awards from the Helmut Horten Foundation and EMBO.

E. Ada Cavalcanti-Adam, University of Bayreuth, DE

E. Ada Cavalcanti-Adam is a Full Professor for Cellular Biomechanics at the University of Bayreuth. Previously, she was Group Leader at the Max Planck Institute for Medical Research in Heidelberg from 2017 until 2023.
Her interdisciplinary research integrates mechanobiology, cell-matrix interactions, and bioengineering approaches to study how physical and chemical cues at the cellular interface regulate adhesion, signalling, and force transmission. She holds a habilitation in Physical Chemistry and Cell Biology from Heidelberg University, and her academic path spans degrees and residencies in Dentistry and Orthodontics (Italy and USA), a PhD in Biosciences (Heidelberg), and international experience at institutions including the University of Pennsylvania and the Max Planck Institute for Intelligent Systems.
She is a fellow of the Max Planck School Matter to Life and associate editor at *Science Advances*. Her contributions have been recognized with numerous awards, including the UNESCO-L'Oréal Prize for Women in Science (2008), a Marie Curie Fellowship (2003), and multiple honors from the University of Pennsylvania and professional societies.

Astrid Collingro, University of Vienna, AT

Astrid Collingro is a senior scientist at the Centre for Microbiology and Environmental Systems Science at the University of Vienna. She studied microbiology at the Technical University of Munich and earned her PhD from the University of Vienna in 2004.
Astrid's research focuses on obligate intracellular bacteria, with a particular emphasis on chlamydial symbionts of protists. She investigates the diversity and evolution within the chlamydial phylum to better understand what distinguishes symbionts of protists from human pathogens. One of her main goals is to expand the number of available isolates to further explore the wide range of chlamydiae-host interactions.
Following a research stay at the Australian Institute of Marine Science, Astrid developed a strong interest in marine hosts such as corals, sponges, and algae, and the role chlamydiae play in their microbiomes. Currently, she is examining the environmental prevalence of chlamydiae and their influence on microbial eukaryotic hosts and, by extension, on microbial communities and the ecological processes they underpin.

Katia Cosentino, UNIMORE-University of Modena and Reggio Emilia, IT

Katia Cosentino studied Chemistry at the University of Calabria, Italy, and obtained a PhD from the same institution. During her doctoral studies, she spent time at ETH Zurich, where she developed a strong interest in biophysics and membrane biology. After completing her PhD, she joined the group of Ana Garcia-Sáez, first at the German Cancer Research Center (DKFZ) in Heidelberg, and later as a Max Planck Fellow and senior scientist at the Institute of Biochemistry in Tübingen, Germany. In 2018, she was awarded a Baden-Württemberg Elite Program grant to establish her independent research group, and in 2019 she was appointed Junior Professor of Molecular Cell Biophysics at the University of Osnabrück. Since 2025, she has been based at the University of Modena and Reggio Emilia, where she leads the Cell Death Biophysics group.
Her research combines biophysics, biochemistry, cell biology and high-resolution fluorescence microscopy to investigate the molecular mechanisms of regulated cell death. Her current work explores the function of Gasdermin proteins and their role in membrane permeabilization during pyroptotic cell death.

Maria Hondele, University of Basel, CH

Maria Hondele is a tenure-track assistant professor of Biochemistry at the Biozentrum, University of Basel, Switzerland since 2020. Her lab investigates cellular self-assembly processes and the formation, regulation, and function of membraneless organelles, especially those associated with RNA processing.
Dr. Hondele studied biochemistry at the University of Regensburg and trained at the University of Massachusetts on a Fulbright scholarship. She completed her PhD in chromatin biology at EMBL Heidelberg and the University of Munich with Prof. Andreas Ladurner, and conducted her postdoctoral research in RNA and condensate biology at ETH Zurich in the laboratory of Prof. Karsten Weis.

Johanna Klughammer, Genecenter LMU, DE

In my research I use high-dimensional (spatio)molecular data in combination with computational approaches to understand how cells work together efficiently in order to form multicellular organisms and what happens if they fail to do so in the case of diseases such as cancer. I am interested in molecular (epigenome, transcriptome, proteome) as well as evolutionary aspects of this fascinating phenomenon. I completed my undergrad studies in Biomedicine at the University of Würzburg in 2012 and my PhD studies in computational epigenomics and malignant disease at CeMM and the Medical University of Vienna in 2017. After a short postdoc phase, I moved to the Broad Institute in Boston for my postdoctoral research in computational (spatio)genomics. In September 2021 I started my own lab for Systems Immunology at the Gene Center of the LMU Munich.

Georg Kustatscher, University of Edinburgh, GB

Georg studied Molecular Biology at the University of Salzburg, Austria, and obtained a PhD from the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany, working on epigenetics in the lab of Andreas Ladurner. From 2008 to 2020 he was a Postdoc in Juri Rappsilber's proteomics group at the Welcome Centre for Cell Biology in Edinburgh, UK. In 2020 he established a research group at the University of Edinburgh. The aim of his lab is to understand, from a systems biology perspective, how cells regulate protein levels and how these processes are disrupted in cancer cells. The group addresses this question by combining wet-lab proteomics and computational approaches, including machine-learning.

Jonathan Lindsey, North Carolina State University, US

Jonathan S. Lindsey (b. 1956) grew up in Indiana, did his undergraduate studies at Indiana University in Bloomington (1974–1978), and graduate and postdoctoral studies (1978–1984) at The Rockefeller University with Prof. David C. Mauzerall. He was on the faculty at Carnegie Mellon University for 12 years before joining North Carolina State University in 1996. His interests concern the science and creation of tetrapyrrole macrocycles (porphyrins, chlorins, bacteriochlorins) and their roles in photosynthesis-like phenomena. A continual focus over the years has concerned synthetic methodology in the tetrapyrrole arena, which has in recent years been directed to gain access to natural members including chlorophylls and open-chain derivatives, the phyllobilins. To advance the photo sciences, he also has developed the PhotochemCAD program and spectral databases.

Philip Marx-Stölting, BfR, DE

Philip Marx-Stoelting, Dr. rer. nat., ERT, is serving at the German Federal Institute for Risk Assessment as a scientific director heading the unit 'Testing and assessment strategies' in the pesticides safety department and the BfR working group on endocrine disruptors. He is involved in several large research projects on NAM development including PARC, where he is leading the work-package 'hazard assessment'. He is also involved in several expert panels on EU and international (OECD) level and chairing the 3R working group of the German Society for Toxicology (GT).

Peter Murray, Max-Planck-Institute of Biochemistry, DE

Peter Murray is a senior group leader at the Max-Planck-Institute for Biochemistry in Martinsried, Germany (near Munich) where he moved in 2017 after 19 years at St. Jude Children's Research Hospital in Memphis, Tennessee. He is also an Honorary Professor in the medical faculty at the Technical University of Munich. Murray's laboratory is focused on immune regulatory events mediated by metabolic crosstalk. He is best known for work on macrophages, IL-10 and arginine metabolism in immunity. Current research is his laboratory centers on how the immune system control ferroptosis and more specifically anti-ferroptosis through regulated amino acid metabolism. An extension of this work concerns pro-cancer effects of the immune system that suppress ferroptosis in stressed malignant cells. Further information can be found: http://www.biochem.mpg.de/murray.

Valerie O'Donnell, Cardiff University, GB

Valerie O'Donnell completed her PhD in Biochemistry at the University of Bristol, and post-doctoral fellowships in Switzerland and USA where she studied free radical biology and its intersection with lipid oxidation, inflammation and blood pressure regulation. Her ongoing research focuses on applying mass spectrometry to the identification of new lipids that regulate innate immunity and inflammation, in particular families of oxidized phospholipids generated by enzymes that promote blood clotting and thrombosis. With her colleagues, she has shown that enzymatic lipid oxidation through lipoxygenases and Lands cycle can form unique bioactive phospholipids in diverse blood cells that contribute to vascular inflammatory disease through driving clotting. She is also lead of LIPID MAPS, an ELIXIR Core Data Resource that houses the globally used LIPID MAPS Classification and Nomenclature for lipids as well as numerous informatics tools and educational resources for lipid researchers.

André Rendeiro, CeMM Research Center for Molecular Medicine, AT

I am a Principal Investigator at CeMM - the Research Center for Molecular Medicine of the Austrian Academy of Sciences and a Research Group Leader at the Ludwig Boltzmann Institute for Network Medicine at the University of Vienna, leading a research group on computational and molecular methods to study human aging and pathology.
My group develops computational methods for the analysis of spatial data (spatial transcriptomics, highly multiplexed imaging), and its integration with various modalities of molecular and clinical data of individuals along their lifespan. I am particularly interested in the organization of cells at the micro-anatomical level and understanding how this changes during the lifespan of individuals and at the onset of disease.
https://rendeiro.group/

Verena Ruprecht, University Innsbruck, AT

Verena Ruprecht is Professor at the University Innsbruck (UIBK) Austria and Affiliated Group Leader at the Centre for Genomic Regulation (CRG) Barcelona, Spain. She studied biophysics and completed her doctoral work in super-resolution microscopy and cellular biophysics at the Johannes Kepler University Austria. She continued her postdoctoral work in the field of cell and developmental biology at the Institute of Science and Technology (IST) Austria. Her laboratory studies single cell and multicellular dynamics during tissue development and homeostasis, with a focus on how mechanical forces regulate cell plasticity, multicellular self-organization and tissue clearance. Work of the lab further addresses cellular morphodynamics and cell fitness in the context of cancer metastasis. Her lab uses an interdisciplinary approach that combines quantitative methods from physics and biology and bridges in vivo model systems and synthetic bottom-up in vitro assays.

Katharina Schmack, Francis Crick Institute, GB

Katharina Schmack received her medical and doctoral degrees from Charité, Berlin in 2008 and 2009, respectively. She then completed her postdoctoral training, clinical scientist fellowship and psychiatry specialization at Charité, Berlin.
In 2018, she moved to Cold Spring Harbor Laboratory, New York, for a research fellowship. In 2021, she joined the Crick Institute as a Clinical Group Leader.
Her research focuses on psychosis. Her lab investigates the neural circuits and immune processes giving rise to hallucinations and other psychotic symptoms. Using a cross-species approach, her lab studies both patients and mice with behavioural tests, computational models, and in-vivo measures and manipulations.

Veronika Sexl, University of Innsbruck, AT

Veronika Sexl, MD Rector, University of Innsbruck Prof. Dr. Veronika Sexl is a distinguished Austrian scientist and medical professional, with decades of expertise in pharmacology, cancer research, and translational medicine. Currently serving as the Rector of the University of Innsbruck, Dr. Sexl has a storied academic and research career, including leadership roles at the Medical University of Vienna and the Veterinary University of Vienna. Her research is internationally recognized, particularly her contributions to understanding the JAK-STAT signalling pathway, leukemia progression, and the novel regulatory role of CDK6 in tumor biology. She has supervised over 20 PhD students and published over 200 scientific papers with over 16,000 citations. As a member of the and numerous scientific boards, Dr. Sexl has helped advance hematology and oncology research globally. Her accolades include the prestigious ERC Advanced Grant, the Novartis Prize for Medicine, and membership in the Austrian Academy of Sciences and the German National Academy of Sciences “Leopoldina”.

Anne Simonsen, Oslo University Hospital, NO

Professor Anne Simonsen leads the Autophagy research group at the Inst for Cancer Research, Oslo University Hospital, and is the co-director of the Centre of Excellence CanCell (Centre for Cancer Cell Reprogramming) at the University of Oslo, Norway. She received her PhD in 1996 and during her postdoc, she identified the FYVE domain as a specific PtdIns(3)P binding domain and EEA1 as a PtdIns(3)P and RAB5 effector protein important for endosome fusion. She started her laboratory at the University of Oslo in 2009 where she became a full professor in 2011. The main objective of the Simonsen laboratory is to unravel the molecular mechanisms involved in selective types of autophagy and their role in normal health and disease. Specific focus areas include characterization of the role of hypoxia-induced mitophagy in cancer development and protein aggregate clearance in neurodegenerative disease. Her lab also has a continued interest in ALFY and other BEACH-domain-containing proteins. They use mammalian cell lines, various in vitro approaches, and zebrafish for their discoveries. She has authored more than 120 papers and has an H-index of 66. She is a member of the Norwegian Academy of Sciences and an elected member of EMBO.

Abdou Rachid Thiam, CNRS/ENS, FR

Bridging Physics and Biology to Understand Lipid and Organelle Function Trained as a physicist, I transitioned into the study of lipid and organelle biology through a multidisciplinary lens, integrating physical chemistry, cell biology, and biophysical techniques. My research focuses on developing and applying in vitro and ex vivo approaches to dissect the dynamic regulation of membrane-bound organelles. By exploring the kinetic and energetic principles that govern membrane-associated processes, my team investigates how these mechanisms shape organelle function and contribute to cellular organization and homeostasis across scales.

Workshop

Workshop is open to all participants.

Glacios 2 and SmartEPU automation for accessible, high-throughput structure determination and drug discovery

Speaker: Javier Fernandez Collado, Thermo Fisher Scientific

Date: Fri, Sept 26, 14:00 - 14:30,
Location: Lecture room L.EG.220

Cryo-EM has revolutionized biology by resolving protein structures at high resolutions. The Glacios 2 Cryo-TEM equipped with Smart EPU software enables users of all levels of expertise to obtain high resolution data. In collaboration with the Greber lab (Institute for Cancer Research), the structure of CDK-activating kinase (CAK) bound to different ligands was rapidly resolved to ~4 Å and ~3 Å resolutions using 1-hour and 4-hour sessions. Greater user accessibility and increased throughput enable cryo-EM to drive structure-based drug discovery. Additionally, the state-of-the-art E-CFEG pushes resolution even further, achieving the record at 200 kV with a 1.5 Å reconstruction of Apoferritin.

Detailed Program

Wednesday, September 24th, 2025

11:00 - 11:20	Opening	**OPENING CEREMONY** *Moderation: Johanna Gostner (Medical University of Innsbruck, AT),* *Lukas A. Huber (Medical University of Innsbruck, AT),* *Ludger Hengst (Medical University of Innsbruck, AT)* *Welcome words by Michael Sauer (ÖGMBT President)*	**M.EG.180/ L.EG.200**
11:20 - 12:00	Plenary	**PLENARY 1** *Chair: Ludger Hengst (Medical University of Innsbruck, AT)* **Veronika Sexl (University of Innsbruck, AT)** From JAK-STAT to CDK6 A scientist`s journey through signaling in leukemia	**M.EG.180/ L.EG.200**
12:00 - 12:20		**SCIENCE FLASHES 1** *Chair: Ludger Hengst (Medical University of Innsbruck, AT)*	**M.EG.180/ L.EG.200**
		Jackson Fontaine (Medical University of Innsbruck, AT) Novel passive transfer mouse model of Anti-IgLON5 disease to study circuit mechanisms underlying motor dysfunction	
		Daniel Ramel (University of Graz, AT) Tackling the knotweed problem by its roots, using an RNAi-based herbicide.	
		Dominik K. Großkinsky (AIT Austrian Institute of Technology, AT) Exploring the role of endophytes for improving cryopreservation of potato	
		Jakob Prömer (Medical University of Vienna, AT) Characterizing serine phosphorylation in Muscle Specific Kinase (MuSK)	
		Lena Guerrero Navarro (University of Innsbruck, AT) TFEB orchestrates stress recovery and paves the way for senescence induction in human dermal fibroblasts	
		William Olson (Institute for Biomedical Aging Research, AT) Age-associated B cell fate choice is dependent on Bach2 upregulation	
		Alice Cassiani (BOKU University, AT) In depth investigation of *actinobacterial* coproporphyrin ferrochelatase	
		Natalia Regina Melo Santos (Medical University of Innsbruck, AT) Metabolic features of cancer cells during contact guidance migration	
		Adam Pollio (Medical University of Innsbruck, AT) The elucidation of TM9SF4 function in migration and polarization.	
12:20 - 13:00		**LUNCH**	**Foyer**
13:00 - 14:15		**POSTER SESSION 1**	**Foyer**
14:15 - 15:45	Track 1	**S1: NEURAL CIRCUITS IN HEALTH AND DISEASE** *Chairs: Sabine Liebscher (Institute of Neurobiochemistry, AT),* *Johannes Passecker (Medical University of Innsbruck, AT)*	**M.EG.180/ L.EG.200**
14:15 - 14:45	Keynote	**Katharina Schmack (Francis Crick Institute, GB)** Striatal neuromodulators in hallucination-like perception	
14:45 - 15:00		**Elfriede Dall (Universität Salzburg, AT)** Conformational and Functional Regulation of SET by Legumain Cleavage	
15:00 - 15:15		**Mariana Spetea (University of Innsbruck, AT)** Mu and delta opioid receptor polypharmacology as a promising strategy for effective analgesia with reduced CNS-mediated risks of tolerance and physical dependence	

15:15 - 15:30		**Alexander Wallerus (Medical University of Innsbruck, AT)** Neurokraken - a fully flexible, open-source, python-based behavior platform for circuit neuroscience research	
15:30 - 15:45		**Shenyi Jiang (Ludwig Maximilian University of Munich, DE)** Impact of distinct TDP-43 pathologies on neuronal health *in vivo*	
14:15 - 15:45	Track 2	**S2: ENVIRONMENT AND MICROBIOLOGY** *Chairs: Sigrid Neuhauser (University of Innsbruck, AT), Andrea Garvetto (University of Innsbruck, AT)*	**L.EG.220**
14:15 - 14:45	Keynote	**Astrid Collingro (University of Vienna, AT)** Bacterial symbionts of protists and their unexplored impact on ecosystems	
14:45 - 15:00		**Katharina Russ (University of Innsbruck, AT)** Genomic and Experimental Analysis of Bacteria Interacting with *Serpula lacrymans*	
15:00 - 15:15		**Alexander Eschlböck (University of Innsbruck, AT)** Regulation of 6-pentyl-α-pyrone production in *Trichoderma atroviride*: The role of *pks1* and beyond	
15:15 - 15:30		**Nikolaus Falb (BOKU University, AT)** Knockout studies & molecular enzymology of Coproheme decarboxylase: New insights into anaerobic heme biosynthesis	
15:30 - 15:45		**Jakob Ender (BOKU University, AT)** Importance of heme biosynthesis in *Porphyromonas gingivalis*	
15:45 - 16:05		**COFFEE BREAK**	**Foyer**
16:05 - 17:35	Track 1	**S3: THE MULTIFACETED WORLD OF LIPIDS** *Chairs: Andreas Koeberle (University of Graz, AT), Sabrina Sailer (Medical University of Innsbruck, AT)*	**M.EG.180/ L.EG.200**
16:05 - 16:35	Keynote	**Valerie O'Donnell (Cardiff University, GB)** Delineating the role of lipoxygenases in innate immunity, thrombosis and wound healing	
16:35 - 16:50		**Hubert Schaller (IBMP CNRS, FR)** Distinct functions of cycloartenol-derived sterols in plants	
16:50 - 17:05		**Nicolas Vitale (INCI CNRS UPR3212, FR)** Illuminating neurosecretion: Optogenetic and click chemistry novel tools highlight the multiple roles of phosphatidic acid in neurotransmitter release.	
17:05 - 17:20		**Victoria Stefan (University Hospital of the Paracelsus Medical University Salzburg, AT)** A Ketogenic Diet boosts Neuroblastoma Immunotherapy in mice	
17:20 - 17:35		**Janik Kokot (Medical University of Innsbruck, AT)** Mathematical modeling of lipid diversity by reconstructing lipid class specific fatty acyl compositions	

16:05 - 17:35	Track 2	**S4: AGING, MENTAL HEALTH, EXERCISE AND METABOLISM** *Chairs: Markus Mandl (JKU Medical Faculty, AT), Katharina Hüfner (Medical University of Innsbruck, AT)*	**L.EG.220**
16:05 - 16:35	Keynote	**André Rendeiro (CeMM Research Center for Molecular Medicine, AT)** Histological aging signatures enable tissue-specific disease prediction from blood	
16:35 - 16:50		**Johannes Burtscher (University of Innsbruck, AT)** Combining exercise and hypoxia to promote healthy brain aging – a review	
16:50 - 17:05		**Linda K. Rausch (University of Innsbruck, AT)** Going to altitude with anxious-depressive symptoms - a randomized pilot trial in individuals with and without mental disorders	
17:05 - 17:20		**Sonja Großmann (University Innsbruck, AT)** Role of Dipeptidyl peptidase-4 in Adipose stem/progenitor cells	
17:20 - 17:35		**Elisabeth Heuböck (Johannes Kepler Universität Linz - Zentrum für medizinische Forschung, AT)** Epicardial adipose tissue as an underestimated factor of cardiovascular diseases: Isolation and characterization of functional adipogenic stem-/progenitor cells to study pathophysiological processes *in vitro*	
17:35 - 17:45		**HEALTH BREAK**	
17:45 - 18:20		**LIFE SCIENCES AWARDS AUSTRIA 2025** *Moderator: Michael Sauer (OMV AG, AT)*	**M.EG.180/ L.EG.200**
Bundesministerium Wirtschaft, Energie und Tourismus		***LIFE SCIENCES AWARDS 2025 CEREMONY*** *Opening words by BMWET representative (BMWET, AT)*	
Boehringer Ingelheim		*Life Sciences PhD Award Austria 2025 – Basic Science* **Yannick Weyer (Medical University of Innsbruck, AT)** The Dsc ubiquitin ligase complex identifies transmembrane degrons to degrade orphaned proteins at the Golgi	
POLYMUN SCIENTIFIC Immunbiologische Forschung GmbH		*Life Sciences PhD Award Austria 2025 – Applied Research* **Max Josef Kellner (Helmholtz Zentrum für Infektionsforschung, DE)** Preparing for Future Pandemics: Rapid Virus Identification in Resource-Limited Settings and Modeling Zoonotic Virus Infections in Natural Reservoir Species	
18:20 - 19:00		**RISING STAR LECTURES** *Chair: Joachim Seipelt (Nuvonis Technologies, AT)*	**M.EG.180/ L.EG.200**
Bundesministerium Wirtschaft, Energie und Tourismus		*Life Sciences Research Award Austria 2025 – Basic Science* **Victoria Deneke (Research Institute of Molecular Pathology, AT)** A conserved fertilization complex bridges sperm and egg in vertebrates	
Bundesministerium Wirtschaft, Energie und Tourismus		*Life Sciences Research Award Austria 2025 – Applied Research* **Rémi Hocq (TU Wien, AT)** Teaching a microbe how to breathe carbon monoxide: When transposons rewire metabolism	
Bundesministerium Wirtschaft, Energie und Tourismus		*Life Sciences Research Award Austria 2025 – Excellence & Societal Impact* **Eugenia Pankevich (CeMM Research Center for Molecular Medicine, AT)** Systematic discovery of CRISPR-boosted CAR T cell immunotherapies	
19:00 - 22:00		**WINE & SCIENCE**	**Foyer**

LIFE SCIENCES AWARDS AUSTRIA 25

Rising Stars Lectures
Sept 24
18:20

VICTORIA E. DENEKE

"A conserved fertilization complex bridges sperm and egg in vertebrates"

Winner of Research Award 2025 – **Category Basic Science**

RÉMI HOCQ

"A megatransposon drives the adaptation of Thermoanaerobacter kivui to carbon monoxide"

Winner of Research Award 2025 - **Category Applied Research**

EUGENIA PANKEVICH

"Systematic discovery of CRISPR-boosted CAR T cell immunotherapies"

Winner of Research Award 2025 – **Category Excellence & Societal Impact**

YANNICK WEYER

„Functional characterization of a novel post-ER associated degradation system"

Winner of PhD Award 2025 – **Category Basic Science**

MAX JOSEF KELLNER

"Preparing for Future Pandemics: Rapid Virus Identification in Resource-Limited Settings and Modeling Zoonotic Virus Infections in Natural Reservoir Species"

Winner of PhD Award 2025 – **Category Applied Research**

Awards Ceremony
Centre for Chemistry and Biomedicine (CCB)
Sept 24
17:45

THE ÖGMBT CONGRATULATES THE WINNERS 2025

ÖGMBT

Thursday, September 25th, 2025

09:00 - 09:40	Plenary	**PLENARY 2** *Chair: Hesso Farhan (Medical University of Innsbruck, AT)* **Anne Simonsen (Oslo University Hospital, NO)** Regulation of mitochondrial quality control and cellular bioenergetics during hypoxia	**M.EG.180/ L.EG.200**
09:40 - 10:25		**PHD SESSION** *Chairs: Angelika Seeber (University of Innsbruck, AT), Pablo Monfort-Lanzas (Medical University of Innsbruck, AT)*	**M.EG.180/ L.EG.200**
09:40 - 09:55		**Lea Emmy Timpen (University of Innsbruck, AT)** Impact of the E2F1-BASP1 complex on regulating *MYC* expression	
09:55 - 10:10		**Julia Arapovic (University of Vienna, AT)** Establishment of a transient ALFA-Tagged Uncoupling Protein 3 expression system in H9c2 cells to benchmark mitochondrial protein localization, detection, and isolation workflows	
10:10 - 10:25		**Urban Leitgeb (BOKU University, AT)** The sugar connection: N-glycosylation and dimerization in myeloperoxidase biosynthesis	
10:25 - 10:45		**SCIENCE FLASHES 2** *Chairs: Angelika Seeber (University of Innsbruck, AT), Pablo Monfort-Lanzas (Medical University of Innsbruck, AT)*	**M.EG.180/ L.EG.200**
		Baris Bekdas (Medical University of Innsbruck, AT) Orm2 at the crossroads between sterol and sphingolipid metabolism	
		Ilaria Dorigatti (Medical University of Innsbruck, AT) Beyond ether lipid metabolism: PEDS1 as an orchestrator in immunology	
		Laura Sammarco (Medicine University of Innsbruck, AT) Characterization of the trafficking of VIP36 and VIPL and identification of new cargos	
		Martina A. Höllwarth (Medical University of Innsbruck, AT) Unveiling the subunit topology of BORC assemblies at the lysosomal membrane using crosslinking mass spectrometry	
		Marco Reindl (Medical University of Graz, AT) Charged for action: precision delivery of an antimicrobial peptide via polymer-coated nanoparticles enhances efficacy	
		Lucia Parráková (Medical University of Innsbruck, AT) Formaldehyde exposure alters cell cycle progression and metabolic activity in human monocytic cells	
		Kamila Nykiel (Medical University of Innsbruck, AT) Engineering covalent small molecule–RNA complexes in living cells	
		Annkatrin Bressin (Max-Planck-Institute for Molecular Genetics, DE) New insights into the molecular basis of ARID1B haploinsufficiency associated with the Coffin-Siris syndrome	
		Thomas Gabler (BOKU University, AT) The origin of coproporphyrin III presence in *acne vulgaris* caused by pathogenic *Cutibacterium acnes* type 1 strains in human skin	
		Hannah Marie Cebula (St. Anna's Children's Cancer Research Institute, AT) Investigating dose-dependent ß-catenin activity in wilms tumor	
10:45 - 11:05		**COFFEE BREAK**	**Foyer**

11:05 - 12:35	Track 1	**S5: INFECTION AND IMMUNITY** *Chairs: Guenter Weiss (Medical University of Innsbruck, AT), Michaela Lackner (Medical University of Innsbruck, AT)*	**M.EG.180/ L.EG.200**
11:05 - 11:35	Keynote	**Christoph Bock (CeMM & Medical University of Vienna, AT)** Programmed Cells? Epigenetics and Cell Engineering for Immunity and Cancer	
11:35 - 11:50		**Yelyzaveta Miller-Michlits (Medical University of Innsbruck, AT)** High-Definition Spatial Profiling of the Skin Microenvironment in Post-COVID Small Fiber Neuropathy	
11:50 - 12:05		**Martin Hermann (Medical University of Innsbruck, AT)** Clinical relevance of circulating blood microaggregates and reactivation of Epstein-Barr virus in long-term Post-COVID patients	
12:05 - 12:20		**Lourdes Rocamora Reverte (Institute for Biomedical Aging Research, University of Innsbruck, AT)** Identification of highly suppressive human regulatory T cells in old age	
12:20 - 12:35		**Natascha Kleiter (Medical University of Innsbruck, AT)** Loss of NR2F6 reduces tissue-resident macrophages and protects from *Salmonella* Typhimurium infection.	
11:05 - 12:35	Track 2	**S6: MECHANICAL ASPECTS OF CELL ADHESION AND MIGRATION** *Chairs: Francesco Baschieri (Medical University of Innsbruck, AT), Francois Tyckaert (Medical University of Innsbruck, AT)*	**L.EG.220**
11:05 - 11:35	Keynote	**E. Ada Cavalcanti-Adam (University of Bayreuth, DE)** Forces in receptor-mediated cell adhesion	
11:35 - 11:50		**Pere Patón González (University of Innsbruck, AT)** Topographically driven migration of cancer cells	
11:50 - 12:05		**Melanie Emma Groninger (Medical University of Innsbruck, AT)** Unraveling the YAP1-TGFb1 axis: a key driver of androgen receptor loss in prostate cancer-associated fibroblasts	
12:05 - 12:20		**Victoria Levario Diaz (University of Bayreuth, DE)** Spatial engineering of collagen ligand nanopatterns to study integrin-dependent migration in cancer	
12:20 - 12:35		**Maximilian Jobst (University of Vienna, AT)** Metabolic modulation and mechanotransduction in T24 bladder cancer cells	
12:35 - 13:15		**LUNCH**	**Foyer**
13:15 - 14:15		**POSTER SESSION 2**	**Foyer**

14:15 - 15:45	Track 1	**S7: ORGANELLE AND MEMBRANE BIOLOGY** *Chairs: Oliver Schmidt (Medical University of Innsbruck, AT), Hesso Farhan (Medical University of Innsbruck, AT)*	**M.EG.180/ L.EG.200**
14:15 - 14:45	Keynote	**Abdou Rachid Thiam (CNRS/ENS, FR)** Lipid storage and interorganelle communication	
14:45 - 15:00		**Luca Szabo (Medical University of Innsbruck, AT)** The role of the Retriever in polarized plasma membrane recycling	
15:00 - 15:15		**Astha Purwar (Medical University of Innsbruck, AT)** Characterizing a protective function of the ESCRT machinery at the stressed plasma membrane	
15:15 - 15:30		**Niklas Schomisch (Zellbiologie, AT)** Mechanistic dissection of the ER export of the sphingolipid biosynthesis regulator Orm2	
15:30 - 15:45		**Isabel Singer (Medical University of Innsbruck, AT)** LAMTOR1 phosphorylation orchestrates protein interactions and metabolic signalling at the lysosome	
14:15 - 15:45	Track 2	**S8: ADVANCES IN TOXICOLOGY AND RISK ASSESSMENT** *Sponsored by* ASTOX *Chairs: Johanna Gostner (Medical University of Innsbruck, AT), Giorgia Del Favero (University of Vienna - Faculty of Chemistry, AT)*	**L.EG.220**
14:15 - 14:45	Keynote	**Philip Marx-Stölting (BfR, DE)** NAMs in risk assessment – challenges and perspectives	
14:45 - 15:00		**Pablo Monfort-Lanzas (Medical University of Innsbruck, AT)** Dose-response modeling from omics data in toxicology	
15:00 - 15:15		**Janice Bergen (University of Vienna, AT)** Describing the role of shape-dependent toxicity for foodborne contaminants in a human Intestinal cell model	
15:15 - 15:30		**Sophie Strich (Medical University of Innsbruck, AT)** Unraveling AKT isoform-specific activity and drug responses using cell-based assays	
15:30 - 15:45		**Celina Ablinger (Paracelsus Medical University Salzburg, AT)** Combination of lenvatinib and antibiotics: A new strategy to overcome resistance in differentiated thyroid cancer?	
15:45 - 16:05		**COFFEE BREAK**	**Foyer**

16:05 - 17:35	Track 1	**S9: RNA IN GENE REGULATION** *Chairs: Sebastian Herzog (Medical University of Innsbruck, AT), Matthias Erlacher (Medical University of Innsbruck, AT)*	**M.EG.180/ L.EG.200**
16:05 - 16:35	Keynote	**Maria Hondele (University of Basel, CH)** DEAD-box ATPases are global regulators of membraneless organelles	
16:35 - 16:50		**Malou Hanisch (Medical University of Innsbruck, AT)** Experimental identification of preQ$_1$-binding RNAs in the pathogenic bacterium *Listeria monocytogenes*	
16:50 - 17:05		**David Klingler (New York University, US)** The interplay between RNA chemical probes and RNA binding proteins: cautionary tale or new opportunity?	
17:05 - 17:20		**Magdalena Fickl (Medical University of Innsbruck, AT)** The impact of Nsun2-mediated 5-methylcytosine on mRNA dynamics during mESC differentiation	
17:20 - 17:35		**Anna Ploner (Institute of Organic Chemistry, AT)** The stability of RNA G-quadruplexes in the gas phase	
16:05 - 17:35	Track 2	**S10: UNVEILING PROTEIN AND CELL DYNAMICS** *Chairs: Theresia Dunzendorfer-Matt (Medical University of Innsbruck, AT), Eduard Stefan (University of Innsbruck, AT)*	**L.EG.220**
16:05 - 16:35	Keynote	**Verena Ruprecht (University Innsbruck, AT)** Organelle mechano-signalling and error correction in the early embryo	
16:35 - 16:50		**Ruth Herbst (Medical University of Vienna, AT)** Unraveling the MuSK Network: A Time-Resolved Proteomic Map of Neuromuscular Signalling	
16:50 - 17:05		**Valentina Sladky (Medical University Innsbruck, AT)** The AID2 system offers a potent tool for rapid, reversible, or sustained degradation of essential proteins in live mice	
17:05 - 17:20		**Alexandra Fritz (University of Innsbruck, AT)** Empowering the identification and validation of drug candidates targeting oncoproteins and E3 ligase functions	
17:20 - 17:35		**Veronika Temml (Paracelsus Medical University Salzburg, AT)** Unravelling dopamine receptor selectivity: Combining in vitro studies with molecular dynamics to gain mechanistic insights	
17:45 - 22:00		**WALKING TOUR & GET-TOGETHER @ NATTERERBODEN**	

Friday, September 26th, 2025

09:00 - 09:40	Plenary	**PLENARY 3** *Chair: Lukas A. Huber (Medical University of Innsbruck, AT)* **Georg Kustatscher (University of Edinburgh, GB)** Protein covariation advances functional annotation of the human proteome	**M.EG.180/ L.EG.200**
09:40 - 10:00		**SCIENCE FLASHES 3** *Chair: Lukas A. Huber (Medical University of Innsbruck, AT)*	**M.EG.180/ L.EG.200**
09:40 - 09:42		**Aleksandra Fesiuk (Medical University of Vienna, AT)** Therapeutic targeting of thyroid hormone pathway in prostate cancer	
09:42 - 09:44		**Sofia Angelini (University of Innsbruck, AT)** Modelling Batten Disease employing iPSC-derived organoids reveals early progenitor loss and accelerated neuronal differentiation	
09:44 - 09:46		**Cristina Schöpf (Medical University of Innsbruck, AT)** The antibacterial activity and therapeutic potential of an amphibian derived peptide	
09:46 - 09:48		**Armin Oberosler (University of Innsbruck, AT)** MAA analytics Analytical considerations in the purification of mycosporine-like amino acids from marine organisms	
09:48 - 09:50		**Felix Eichin (Medical University of Innsbruck, AT)** The PIDDosome - between ploidy control and cell death	
09:50 - 09:52		**Marlene Lochner (Medical University of Innsbruck, AT)** Discovering new players in inflammatory cell death	
09:52 - 09:54		**Leonie Madersbacher (Medical University of Innsbruck, AT)** Myeloid checkpoints as targets for combination immunotherapy in ovarian cancer	
09:54 - 09:56		**Katja Rungger (Medical University of Innsbruck, AT)** The intratumoral microbiome and their effects on AHR-driven immune responses in pancreatic adenocarcinoma	
09:56 - 09:58		**Lucija Kucej (Medical University of Innsbruck, AT)** Identification of a Golgi quality control network in mammalian cells	
09:58 - 10:00		**Eva Rauch (Medical University of Innsbruck, AT)** Optimisation of an XL-MS workflow to investigate the architecture of native lysosomal LAMTOR assemblies	
10:00 - 11:00		**"YOUR IDEAS, OUR NEXT MOVE" - WORLD CAFÉ** *Moderator: Petra Buchinger (buchinger Life Science Solutions, AT)*	**M.EG.180/ L.EG.200**
11:00 - 11:20		**COFFEE BREAK**	**Foyer**

11:20 - 12:50	Track 1	**S11: STEM CELLS, CELL CYCLE AND CANCER** *Chairs: Heidelinde Jäkel (Medical University of Innsbruck, AT), Frank Edenhofer (University Innsbruck, AT)*	**M.EG.180/ L.EG.200**
11:20 - 11:50	Keynote	**Andreas Boland (University of Geneva, CH)** Structural studies of chromosome segregation.	
11:50 - 12:05		**Alessia Schirripa (University of Veterinary Medicine Vienna, AT)** Adaptive CDK Pathways Underpinning Therapy Resistance	
12:05 - 12:20		**Omar Torres-Quesada (Medical University of Innsbruck, AT)** Novel functions of the small $p27^{KIP1}$ uORF-encoded peptide	
12:20 - 12:35		**Utku Horzum (Medical University of Innsbruck, AT)** A novel ERAD-to-mTORC1 signalling axis constitutes a vulnerability of multiple myeloma cells to targeting secretory proteostasis	
12:35 - 12:50		**Amelie Schurer (University of Innsbruck, AT)** Novel stem cells from the human brain - cellular and epigenetic plasticity of eNSPCs	
11:20 - 12:50	Track 2	**S12: NATURAL PRODUCTS IN LIFE SCIENCE RESEARCH** *Chairs: Cornelia Karg (University of Innsbruck, AT), Simone Moser (University of Innsbruck, AT)*	**L.EG.220**
11:20 - 11:50	Keynote	**Jonathan Lindsey (North Carolina State University, US)** Synthesis of phyllobilins and bacteriochlorophylls – valuable phytochemicals	
11:50 - 12:05		**Stefan Hofbauer (BOKU University, AT)** Heme biosynthesis in prokaryotes - enzyme mechanisms, interactions and more	
12:05 - 12:20		**Thomas Josef Zech (Ludwig-Maximilians-Universität, DE)** The alkaloid derivative 2-Desaza-annomontine (C81) impedes angiogenesis through inhibition of CDC2-like kinases (CLKs) and β-catenin activity.	
12:20 - 12:35		**Petra Huber-Cantonati (Paracelsus Medical University Salzburg, AT)** From Molecule to Mechanism: Understanding Benzylated Dihydrochalcones in Breast Cancer Therapy	
12:35 - 12:50		**Pamela Vrabl (University of Innsbruck, AT)** Harnessing *Penicillium* and *Talaromyces* species for scalable production of potent photoantimicrobials and photoanticancer agents	
12:50 - 13:30		**LUNCH**	**Foyer**
13:30 - 14:30		**POSTER SESSION 3**	**Foyer**
14:00 - 14:30		**COMPANY WORKSHOP: THERMO FISHER SCIENTIFIC**	**L.EG.220**
14:00 - 15:00		**ÖGMBT GENERAL ASSEMBLY**	**M.EG.180/ L.EG.200**

15:00 - 16:30	Track 1	**S13: CELL DEATH IN HEALTH AND DISEASE** *Chairs: Joel Riley (Medical University of Innsbruck, AT), Verena Labi (Medical University of Innsbruck, AT)*	**M.EG.180/ L.EG.200**
15:00 - 15:30	Keynote	**Katia Cosentino (UNIMORE-University of Modena and Reggio Emilia, IT)** Membrane pores in cell death at the nanoscale: assembly, structure and regulation	
15:30 - 15:45		**Leonie Weber (University of Innsbruck, AT)** The BASP1 protein interferes with WNT pathway signalling	
15:45 - 16:00		**Ahmad Salti (Johannes Kepler University Linz, AT)** Transcriptomic and functional characterization of patient-derived PRPF31- retinal organoids of retinitis pigmentosa	
16:00 - 16:15		**Paul Petermann (Medical University of Innsbruck, AT)** The PIDDosome-p53 axis dictates cell fate after cell-cell fusion	
16:15 - 16:30		**Nadine Kinz (University of Innsbruck, AT)** The role of sub-lethal mitochondrial permeabilization in B cell mutagenesis and oncogenic transformation	
15:00 - 16:30	Track 2	**S14: MACHINE LEARNING AND PERTURBATION IN CELLULAR SYSTEMS** *Chairs: Heidi Fiegl (Medical University of Innsbruck, AT), Hubert Hackl (Medical University of Innsbruck, AT)*	**L.EG.220**
15:00 - 15:30	Keynote	**Johanna Klughammer (Genecenter LMU, DE)** Multi-modal Spatial and Single-cell Profiling of Metastatic Breast Cancer and Integrated Computational Analysis	
15:30 - 15:45		**Alexander Kirchmair (Medical University of Innsbruck, AT)** Spatial profiling of cell niches to uncover mechanisms of immune evasion in cancer	
15:45 - 16:00		**Lorenzo Merotto (Dept. of Molecular Biology / Digital Science Centre (DiSC), AT)** omnideconv: a unifying framework for single-cell-informed deconvolution of transcriptomic data	
16:00 - 16:15		**Mieke Nicolaï (Medical University of Innsbruck, AT)** Deciphering the role of the healthy tissue microenvironment in early-stage NSCLC	
16:15 - 16:30		**Bernhard Eder (University of Innsbruck, AT)** Rectangle: robust cell-type deconvolution informed by single-cell RNA sequencing data	
16:30 - 16:50		**COFFEE BREAK & 1. QUIZ DRAWING**	**Foyer**
16:50 - 17:30	Plenary	**PLENARY 4** *Chair: Johanna Gostner (Medical University of Innsbruck, AT)* **Peter Murray (Max-Planck-Institute of Biochemistry, DE)** Immunometabolic circuits that control cell viability	**M.EG.180/ L.EG.200**
17:30 - 18:00	Closing	**CLOSING CEREMONY** *Chairs: Johanna Gostner (Medical University of Innsbruck, AT), Lukas A. Huber (Medical University of Innsbruck, AT), Ludger Hengst (Medical University of Innsbruck, AT)*	**M.EG.180/ L.EG.200**

LIFE SCIENCES CAREER FAIR

ÖGMBT

+ WORKSHOPS & PRESENTATIONS WITH COMPANIES AND INSTITUTIONS FROM AUSTRIAN LIFE SCIENCES SECTOR

MAY 12, 2026
HOCHSCHULE CAMPUS WIEN

FREE REGISTRATION
OEGMBT.AT/EVENTS/LIFE-SCIENCE-CAREER-FAIR

SUPPORTED BY:

LISA LIFE SCIENCE AUSTRIA

Bundesministerium Wirtschaft, Energie und Tourismus

ÖGMBT

18th ÖGMBT Annual Meeting

LIFE SCIENCES STRONGER TOGETHER!

September 14-17 2026

Vienna BioCenter / UBB, Vienna, AT

Life Sciences Awards Austria 2026

https://oegmbt.at/events/annual-meeting

Poster Table – Poster Session 1

Wednesday, Sept 24, 13:00 - 14:15

Poster #	Presenter	Title
S1: Neural circuits in health and disease		
PS1-S1-SF01	**Jackson Fontaine**	Novel passive transfer mouse model of Anti-IgLON5 disease to study circuit mechanisms underlying motor dysfunction
S2: Environment and microbiology		
PS1-S2-PP01	**Lukas Birstonas**	Elucidating the contribution of Ugp1 in *Aspergillus fumigatus* 5-fluorocytosine activity.
PS1-S2-PP02	**Sara Hnaien**	Effects of cold drought and land use on plasmodiophorids/grass interactions
PS1-S2-PP03	**Hannah-Sophie Auricht**	Using gas chromatography and mass spectrometry (GC-MS) for the detection of drought and heat stress effects on the metabolome of *Solanum tuberosum* varieties
PS1-S2-PP04	**Anagha Santhosh**	Localized ROS as a Feature of *Maullinia ectocarpii* Infection in *Ectocarpus siliculosus*
PS1-S2-SF01	**Daniel Ramel**	Tackling the knotweed problem by its roots, using an RNAi-based herbicide.
PS1-S2-SF02	**Dominik K. Großkinsky**	Exploring the role of endophytes for improving cryopreservation of potato
S4: Aging, mental health, exercise and metabolism		
PS1-S4-PP01	**Florian Hatzmann**	Role of the Glycolytic Enzyme Aldolase C in Adipocyte Metabolism and Function
PS1-S4-PP02	**Christina-Marie Baumbach**	The equine fascial system: first insights into its cellular composition
PS1-S4-PP03	**Victoria Strobl**	Matrix metalloproteinases in modulating white adipose tissue
PS1-S4-PP04	**Johannes Pallua**	Advancing Diagnostic Spectroscopy: Raman and Infrared Imaging in Bone, Tissue, and Forensic Applications
PS1-S4-PP05	**Marlies Eder**	Exploring metabolic sleep regulation dependent on Drosophila's brain regions
PS1-S4-PP06	**Tobias Huberts**	Dietary methionine modulates tissue-specific metabolomic profiles and aging-related pathways in rats
PS1-S4-PP07	**Jose Miguel Ramos Pittol**	CRISPR activation of FXR potentiates the up-regulation of a subset of metabolic genes by obeticholic acid in liver cells
PS1-S4-SF01	**Jakob Prömer**	Characterizing serine phosphorylation in Muscle Specific Kinase (MuSK)
PS1-S4-SF02	**Lena Guerrero Navarro**	TFEB orchestrates stress recovery and paves the way for senescence induction in human dermal fibroblasts

Poster #	Presenter	Title
S5: Infection and immunity		
PS1-S5-PP01	**Denisa Cont**	Fluorescence-based point-of-care device for rapid detection of respiratory RNA viruses in clinical settings
PS1-S5-PP02	**Katharina Wagner**	Functional status and amino acid profiles - sex-specific findings one year after COVID-19
PS1-S5-PP03	**Lynn Muller**	Trained Immunity Enhances Valvular Calcification: The Role of Age and Sex in Calcific Aortic Valve Disease
PS1-S5-PP04	**Markus Nagl**	Development of N-chlorotaurine: Efficacy and tolerability of inhalation in fungal pneumonia in the mouse model
PS1-S5-SF01	**William Olson**	Age-associated B cell fate choice is dependent on Bach2 upregulation
PS1-S5-SF02	**Alice Cassiani**	In depth investigation of *actinobacterial* coproporphyrin ferrochelatase
S6: Mechanical aspects of cell adhesion and migration		
PS1-S6-PP01	**Gisa Gerold**	Encephalitic alphavirus infection of human iPSC-derived neurospheres alters Rho GTPase pathways and impairs neurite outgrowth
PS1-S6-SF01	**Natalia Regina Melo Santos**	Metabolic features of cancer cells during contact guidence migration
PS1-S6-SF02	**Adam Pollio**	The elucidation of TM9SF4 function in migration and polarization.
Varia		
PS1-V-PP01	**Elizabeth Cloos**	Inducible expression systems for AAV production in mammalian cells
PS1-V-PP02	**Sophie Huber**	REMBAC - A Rapid Efficient Manifold Baculovirus Transduction Platform for stable cell line development
PS1-V-PP03	**Jochen Gitzl**	Unlocking Gene Expression Potential: Investigating viral protein-driven enhancement in mammalian cells exploiting recombinant baculoviruses
PS1-V-PP04	**Jonas Carlsson**	RNA duplexes in the gas phase - can we use native electrospray ionization mass spectrometry to probe duplex formation and stability in solution?
PS1-V-PP05	**Maria Toth**	Recombinant AAV production: Insights from stable cell lines and adenovirus infection

Poster Table – Poster Session 2

Thursday, Sept 25, 13:15 - 14:15

Poster #	Presenter	Title
S3: The multifaceted world of lipids		
PS2-S3-PP01	**Daniela Weber**	Integrative analysis of multi-omics data to elucidate potential antitumor mechanisms of a ketogenic diet in melanoma
PS2-S3-PP02	**Sophia Pichler**	Functional analysis of Lcb1 and Lcb2 phosphorylation sites in *S. cerevisiae*
PS2-S3-PP03	**Konstantin Adrian Siegmann**	Lipids and their role in membrane protein degradation pathways.
PS2-S3-PP04	**Denise Kummer**	Plasmalogen catabolism: a new fluorescent HPLC-based Assay
PS2-S3-PP05	**Nina Weidacher**	Isotopic tracing of enzyme-mediated regulation of cardiolipin biosynthesis and remodelling
PS2-S3-PP06	**Viktorija Juric**	PPARα- links mitochondrial β-oxidation disorders with membrane lipid remodeling
PS2-S3-SF01	**Baris Bekdas**	Orm2 at the crossroads between sterol and sphingolipid metabolism
PS2-S3-SF02	**Ilaria Dorigatti**	Beyond ether lipid metabolism: PEDS1 as an orchestrator in immunology
S7: Organelle and membrane biology		
PS2-S7-PP01	**Doris Stepic**	Delineating hepatocytic apical trafficking defects in MyoVb associated liver disease
PS2-S7-PP02	**Alexander Plesche**	Effects of mechanical stress on the lipid homeostasis of the endoplasmic reticulum
PS2-S7-PP03	**Antonia Degen**	Advanced modelling of LCHADD/VLCADD with 3D-bioprinting and induced-pluripotent stem cell technology
PS2-S7-PP04	**Nikolas Marchet**	Alpha-arrestin mediated control of cellular nutrient uptake and its role in metabolic signalling
PS2-S7-PP05	**Mariana Eca Guimaraes de Araujo**	Evolutionary conservation and structural flexibility in BORC and BLOC-1
PS2-S7-PP06	**Yannick Weyer**	The Dsc ubiquitin ligase complex identifies transmembrane degrons to degrade orphaned proteins at the Golgi
PS2-S7-PP07	**Amal Mathew**	BORC segregates synaptic vesicle and lysosomal proteins through motors UNC-104/KIF1A and UNC-116/KIF5
PS2-S7-SF01	**Laura Sammarco**	Characterization of the trafficking of VIP36 and VIPL and identification of new cargos
PS2-S7-SF02	**Martina A. Höllwarth**	Unveiling the subunit topology of BORC assemblies at the lysosomal membrane using crosslinking mass spectrometry

Poster #	Presenter	Title
S8: Advances in toxicology and risk assessment		
PS2-S8-PP01	**Aldrien Ryan Naces Reynaldo**	Effects of azole antifungals on immunobiochemical pathways
PS2-S8-PP02	**Martin Paparella**	Evolving regulatory frameworks through case studies focused on uncertainty characterization for the assessment of developmental neurotoxicity
PS2-S8-SF01	**Marco Reindl**	Charged for action: precision delivery of an antimicrobial peptide via polymer-coated nanoparticles enhances efficacy
PS2-S8-SF02	**Lucia Parráková**	Formaldehyde exposure alters cell cycle progression and metabolic activity in human monocytic cells
PS2-S8-ASTOX	**ASTOX**	ASTOX Poster
S9: RNA in gene regulation		
PS2-S9-PP01	**Isabell Gonnella**	tRNA superwobbling - the decoding of valine codons in M. capricolum and E. coli
PS2-S9-PP02	**Mara Gortan**	Expanding the genetic code via novel codon–anticodon pairs
PS2-S9-PP03	**Jennifer Wuggenig**	mRNA modifications in translation and RNA stability
PS2-S9-SF01	**Kamila Nykiel**	Engineering covalent small molecule–RNA complexes in living cells
PS2-S9-SF02	**Annkatrin Bressin**	New insights into the molecular basis of ARID1B haploinsufficiency associated with the Coffin-Siris syndrome
S10: Unveiling protein and cell dynamics		
PS2-S10-PP01	**Ela Zdenkovic**	Investigating the reaction mechanism of coproheme decarboxylase from *Bacillus subtilis* reacting with FMN
PS2-S10-PP02	**Annalena Habeler**	Ligand shuffling – comparison of different porphyrins in complex with chlorite dismutase from *Dechloromonas aromatica.*
PS2-S10-PP03	**Isabella Fegerl**	Structural analysis of TPO oligomerization and the functional role of its domains
PS2-S10-SF01	**Thomas Gabler**	The origin of coproporphyrin III presence in *acne vulgaris* caused by pathogenic *Cutibacterium acnes* type 1 strains in human skin
PS2-S10-SF02	**Hannah Marie Cebula**	Investigating dose-dependent ß-catenin activity in wilms tumor

Poster Table – Poster Session 3

Friday, Sept 26, 13:30 - 14:30

Poster #	Presenter	Title
S11: Stem cells, cell cycle and cancer		
PS3-S11-PP01	**Anju Kombara**	Extracellular matrix signalling pathway crosstalk in primary human mesenchymal stromal cells
PS3-S11-PP02	**Niklas Schweiger**	Transcriptional trajectory and single cell gene expression analysis reveal barriers of iPSC reprogramming
PS3-S11-PP03	**Miriam Unterkofler**	The protein interaction network of p27 in prometaphase
PS3-S11-PP04	**Martina Podlesnic**	Single-cell profiling of striatal organoids derived from Leigh syndrome patients highlights gene network dysregulated in neurodevelopment
PS3-S11-PP05	**Verena Sturmlehner**	Development of a 3D-bioprinted Mesothelium-on-Chip system to study Ovarian Cancer
PS3-S11-PP06	**Betul Sari**	A novel isoform of Skp2 generated by alternative translational initiation
PS3-S11-PP07	**Michael Kullmann**	Identification of Novel $p57^{Kip2}$ Phosphorylation Sites: A Key Tyrosine Modification Blocks Cyclin-CDK Binding
PS3-S11-PP08	**Carlos Castillo Giron**	Role of the CDK-Inhibitor $p27^{Kip1}$ on Myeloid/Lymphoid Neoplasm with rearrangement of PDGFRα
PS3-S11-PP09	**Sem Peijnenborgh**	Taming the Double-Edged Sword: How FoxM1 Regulates Its Own Power in Senescence and Cancer
PS3-S11-SF01	**Aleksandra Fesiuk**	Therapeutic targeting of thyroid hormone pathway in prostate cancer
PS3-S11-SF02	**Sofia Angelini**	Modelling Batten Disease employing iPSC-derived organoids reveals early progenitor loss and accelerated neuronal differentiation
S12: Natural products in life science research		
PS3-S12-PP01	**Vanessa Kern, Carmen Bendetta**	Establishing a screening protocol for the detection of antitumoral photosensitizers in *Penicillium* spp., *Talaromyces* spp. and *Hamigera* spp.
PS3-S12-PP02	**Niccolò Mariani**	Triggering photosensitizer production in *Talaromyces islandicus*
PS3-S12-PP03	**Cornelia Karg**	UVISION - from sea to cell: translating marine Mycosporine-like amino acids into biomedical UV filters
PS3-S12-PP04	**Satinee Loh**	Investigating the effect of immobilising α-galactosidase onto magnetic, CMD-coated iron oxide nanoparticles on its activity and storage, for ease of separation in blood samples
PS3-S12-PP05	**Friederike Luise Glauch**	The light of us: Photoantimicrobial activity of extracts from selected *Talaromyces* and *Penicillium* species
PS3-S12-PP06	**Birgit Lengerer**	Chitin and glycan-binding proteins in *Hydra's* adhesive system: unveiling potential for future biomimetic applications
PS3-S12-PP07		Merged with PS3-S12-PP01

Poster #	Presenter	Title
PS3-S12-PP08	**Annelies Oismüller**	Discovery of a novel pieicidin-family metabolite through activation of a cryptic biosynthetic gene cluster in *Nocardia terpnica*
PS3-S12-PP09	**Filip Gallob**	The natural product Nostatin A inhibits V-ATPase activity and gives novel insights into consequences of lysosomal perturbations
PS3-S12-SF01	**Cristina Schöpf**	The antibacterial activity and therapeutic potential of an amphibian derived peptide
PS3-S12-SF02	**Armin Oberosler**	MAA analytics Analytical considerations in the purification of mycosporine-like amino acids from marine organisms
S13: Cell death in health and disease		
PS3-S13-PP01	**Tamara Lang**	Stress Pathway Activation Induced-Macropinocytosis in p53-Deficient Cells Following Fine Dust Exposure
PS3-S13-SF01	**Felix Eichin**	The PIDDosome - between ploidy control and cell death
PS3-S13-SF02	**Marlene Lochner**	Discovering new players in inflammatory cell death
S14: Machine learning and perturbation in cellular systems		
PS3-S14-PP01	**Felix Petschko**	Scaling immune-cell receptor analysis with Scirpy to millions of single cells
PS3-S14-PP02	**Constantin Zackl**	spacedeconv: deconvolution of tissue architecture from spatial transcriptomics
PS3-S14-SF01	**Leonie Madersbacher**	Myeloid checkpoints as targets for combination immunotherapy in ovarian cancer
PS3-S14-SF02	**Katja Rungger**	The intratumoral microbiome and their effects on AHR-driven immune responses in pancreatic adenocarcinoma
Poster Session 3: PhD Session		
PS3-PhD-PP01	**Nils Leibrock**	A tale of two TOLs: *PIN*-pointing the issue for high temperature adaptation
PS3-PhD-PP02	**Thanida Laopanupong**	SZT2 in ER/Lysosome Crosstalk and the maintenance of proteostasis
PS3-PhD-PP03	**Dominik Hau**	Radiation-induced calcific aortic valve disease: a viral mimicry disorder?
PS3-PhD-PP04	**Alexandra Tsal-Tsalko**	Characterization of the Axl/Gas6 signalling pathway following receptor inhibition by peptide ligands and siRNAs.
PS3-PhD-PP05	**Adrian Lendvai**	REGIMOPROT: Identification and Characterization of Extracellular Matrix Components involved in Bone Regeneration
PS3-PhD-PP06	**Nevra Pelin Cesur**	Unravelling Tendon Degeneration: Cellular and Metabolic Insights from SPARC-Deficient Model
PS3-PhD-SF01	**Lucija Kucej**	Identification of a Golgi quality control network in mammalian cells
PS3-PhD-SF02	**Eva Rauch**	Optimisation of an XL-MS workflow to investigate the architecture of native lysosomal LAMTOR assemblies

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

Abstracts – Day 1, Wed, 24.9

.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

Plenary 1

Chair:

Ludger Hengst
Medical University of Innsbruck, AT

Plenary Lecture

P1-PL01 From JAK-STAT to CDK6 A scientist`s journey through signaling in leukemia

Veronika Sexl, Karoline Kollmann, Dagmar Gotthardt
Universität Innsbruck, Austria

Although significant progress has been made over the last decades, we are still searching for ways to successfully fight cancer. This talk will present an overview over signaling processes involved in leukemia and highlight insights on JAK-STAT signaling in hematopoiesis. A novel role of the cell cycle kinase CDK6 in leukemic stem cells and leukemia development will be discussed.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

Science Flashes 1

Chair:

Ludger Hengst
Medical University of Innsbruck, AT

PS1-S1-SF01 Novel passive transfer mouse model of Anti-IgLON5 disease to study circuit mechanisms underlying motor dysfunction

Jackson Fontaine, Sabine Liebscher

Systems Neuroscience, Medical University of Innsbruck, Austria

Anti-IgLON5 disease is a rare form of autoimmune encephalitis characterized by the occurrence of autoantibodies targeting the cell adhesion molecule IgLON5 in the central nervous system. Patients present with an overlapping array of neurological symptoms, primarily characterized by a sleep disorder and progressive gait disturbances. These movement disorders often mimic other neurodegenerative diseases, such as progressive supranuclear palsy, Parkinson's disease, or multi-system atrophy. The actual underlying mechanisms of how autoantibodies disrupt neural circuit function to drive gait abnormalities remain poorly understood. To elucidate how anti-IgLON5 antibodies affect neuronal function, we employed a passive-transfer mouse model and deep learning to quantify movement and coordination abnormalities in combination with a brain-wide immunohistochemical assessment of markers for neuronal activity. Mice receiving 14 days of intracerebroventricular IgLON5 antibody infusion displayed progressively worsening motor disturbances as seen in more frequent foot slips on the ladder rung, shorter latency to fall on the rota-rod, and the development of a "hunched" posture while ambulating. Our kinematic analysis also revealed a shorter toe-to-crest distance, smaller knee joint extension, and longer stride length, all together indicating significant alterations to the step cycle. To identify neural circuit mechanisms underlying altered motor function, we performed a brain-wide assessment of the expression of cFOS, an early immediate gene, known to positively correlate with neuronal activity levels and phosphorylated pyruvate dehydrogenase (pPDH), known to negatively correlate with neuronal activity. Preliminary data highly suggest that IgLON5 antibodies disrupt information processing in the cortico-ponto-cerebellar loop as evidenced in a reduction of cFOS expression in the pontine grey and consecutively an upregulation of pPDH in the downstream cerebellar cortex, with prominent expression within purkinje neurons. Future direct monitoring of individual circuit elements in the cerebellar cortex will help to uncover mechanisms by which the antibodies compromise microcircuits, leading to the rise of ataxic gait disturbances.

PS1-S2-SF01 Tackling the knotweed problem by its roots, using an RNAi-based herbicide.

Sebastian Mayer, **Daniel Ramel**, Jakob Dujmovits, David Dorner, Markus Weichenberger, Javier Figueroa, Karoline Kalcher, Simon Safron, Lisa Hagen, Julia Jernejcic, Max Schosteritsch, Fabian Gether, Florian Haneder, Christoph Dax, Hannah Winkler, Simone Derntl

"NAWI Graz Austria" iGEM-Team 2025, Institute for Molecular Biosciences, University of Graz, Austria

Japanese Knotweed (Reynoutria *japonica,* synonym *Fallopia japonica*) is an invasive plant species that displaces native species in Europe and North America and permanently alters ecosystems. In addition, *R. japonica* causes significant economic damage by destabilizing critical earthen infrastructure like flood prevention dams, dikes and river banks as well as acting as a biological soil contaminant. Conventional methods of control are often inadequate because of *R. japonica*'s extensive root system and its ability to resprout from small rhizome remnants, making it particularly resistant to chemical and mechanical removal. With Knotaut, we aim to create an environmentally friendly and specific alternative based on the RNA-interference (RNAi) mechanism. To achieve this, we design double-stranded RNAs (dsRNAs) that are complementary to sections of vital *R. japonica* genes, specifically genes essential for root physiology. The dsRNA is packaged in liposomes to increase durability and improve uptake and transport by the plant. The liposome packaged dsRNA is applied as a suspension to the leaves of the plant and transported via the phloem to the roots. In the cells, a Dicer like (DCL) protein splits the dsRNA into smal interfering RNAs (siRNAs), which then serve as guide-RNAs for the RNA-induced silencing complex (RISC). The active RISC then degrades the mRNAs of the target gene, resulting in post-transcriptional gene silencing. The current focus of our research is on target gene identification, and optimization of dsRNA design and production as well as liposome composition. With Knotaut, we want to show that dsRNA-agents are a serious alternative to non-specific and environmentally harmful herbicides.

PS1-S2-SF02 Exploring the role of endophytes for improving cryopreservation of potato

Hanna Koch[0], Friederike Trognitz[0], Alexa Sanchez Mejia[1], Anton Peterson[1], Milica Pastar[0], Theresa Ringwald[0], Livio Antonielli[0], Manuela Nagel[1], **Dominik Großkinsky[0]**

[1] Leibniz Institute of Plant Genetics and Crop Plant Research (IPK), Corrensstraße 3, 06466 Seeland-Gatersleben, Germany
[0] Center for Health and Bioresources, AIT Austrian Institute of Technology, Austria

The potato ranks as the fourth most important food crop. Thus, it is essential to maintain the heterozygous genotypes in vitro to preserve its genetic diversity. In vitro culturing includes surface sterilization to remove external bacteria and fungi, followed by propagation under sterile, sugar-rich conditions. However, this approach is labor-intensive as the plants require periodic transfer to fresh growth medium. Therefore, cryopreservation approaches have been established and implemented in genebanks for long-term storage to preserve vegetatively propagated collections. For this, meristematic tissues, i.e. apical or lateral shoot tips, undergo tissue dissection, osmotic adaptation, cryoprotection, cryogenic treatment using liquid nitrogen to halt all biochemical activity and preserving genetic integrity, and controlled rewarming. However, rewarming can trigger the colonization of endophytes around the explant, which can compromise its ability to develop into a plant.

In this project, we analyzed 382 potato accessions for their regrowth potential post-cryopreservation. While 50% showed a good regrowth (≥60% of plants regrown), 39% recovered poorly (≤60% of plants regrown) and 11% failed to recover. To investigate microbial influences, an ITS and 16S rRNA gene amplicon survey was conducted on all these accessions. As anticipated, the microbial diversity was in general low due to sterile cultivation conditions. A total of 637 bacterial amplicon sequencing variants (ASVs) spanning 53 different orders were identified. While some ASVs might originate from exogenous sources, others belong to known plant-associated groups, including Bacillales. In addition, bacteria were isolated from 19 potato accessions resulting in 52 bacterial isolates, belonging to 19 different strains based on 16S rRNA gene sequence comparison. The isolates were characterized for their potential in producing IAA, siderophores and osmolytes, as well as in ACC deamination, and phosphate solubilization. This characterization guided the selection of strains isolated from both well and poorly recovering accessions to test their impact on in vitro plant performance and to analyze their genomes. In conclusion, this study provides first insights in the microbial communities associated with potato cryopreservation and their functional traits, representing a crucial step towards enhancing regrowth success and refining long-term preservation strategies in genebanks.

PS1-S4-SF01 Characterizing serine phosphorylation in Muscle Specific Kinase (MuSK)

Jakob Prömer[0], Sara Wolske[0], Castets Perrine[1], Geeske van Woerden[2], Cinzia Barresi[0], Kevin O'Connor[3], Yuko Tsutsui[4], James Murphy[4], Mark Lemmon[4], Ruth Herbst[0]

[1] Department of Cell Physiology and Metabolism, University of Geneva, Geneva, CH
[2] Departments of Neuroscience and Clinical Genetics, Erasmus Medical Center, Rotterdam, NL
[3] Departments of Neurology and Immunology, Yale School of Medicine
[4] Department of Pharmacology, Yale School of Medicine
[0] Institute for Specific Prophylaxis and Tropical Medicine, Medical University of Vienna, Austria

The neuromuscular junction (NMJ) is a highly specialized chemical synapse that transduces excitatory stimulation from lower motor neurons to muscle cells. NMJ formation is characterized by high density clustering of acetylcholine receptors (AChR) and is governed by the receptor tyrosine kinase muscle specific kinase (MuSK). Dysregulation of MuSKs signaling cascade causes myasthenic syndromes and mice lacking MuSK die perinatally. MuSK activation involves autophosphorylation on tyrosine in the activation loop (AL) of its intracellular tyrosine kinase domain (TKD). The present study characterizes a novel serine residue (S751) that was recently identified and is phosphorylated *in vivo*. We used a baculovirus expression system to produce the TKD of human MuSK and engineered a phosphomimicking mutant MuSK^{S751D}. Comparative enzyme kinetic measurements showed that MuSK^{S751D} had higher affinity for an artificial substrate, as well as for ATP. We next performed x-ray diffraction experiments and determined structures of the wild-type and mutant TKDs. Our 2.2 Å structure of wild-type MuSK supports a closed conformation of the AL, as previously reported in the study of rat MuSK. However, we were unable to model the AL of MuSK^{S751D} in a 2.6 Å dataset. We are currently testing the idea of increased flexibility of the activation loop using hydrogen-deuterium exchange mass spectrometry. We next performed radiometric kinase profiling and identified Ca^{2+}/calmodulin dependent protein kinase II beta (CaMK2β) as kinase that phosphorylates S751. We validated this result with overexpression experiments in heterologous cells. While Crispr/Cas9 mediated ablation of CaMK2β in cultured muscle cells perturbed AChR clustering, MuSK phosphorylation in these cells was unaffected. Furthermore, neither global CaMK2β deletion, nor the secondary deletion of its muscle specific splice variant CaMK2β_M in mice decreased MuSK phosphorylation, leaving the physiological role of this regulation at question. Our detailed characterization indicates a novel kinase regulatory mechanism at the NMJ.

PS1-S4-SF02 TFEB orchestrates stress recovery and paves the way for senescence induction in human dermal fibroblasts

Lena Guerrero-Navarro[1], Pablo Monfort-Lanzas[2], Vinzenz Krichbaumer[1], Mariana E. G. De Araújo[3], Jlenia Monfregola[4], Lukas A. Huber[3], Andrea Ballabio[4], Pidder Jansen-Dürr[1], Maria Cavinato[1]

[1] Institute for Biomedical Aging Research, University of Innsbruck, Austria
[2] 3 Institute of Medical Biochemistry, Biocenter, Innsbruck Medical University, Innsbruck, Austria 4 Institute of Bioinformatics, Biocenter,Innsbruck Medical University, Innsbruck, Austria
[3] 5 Biocenter, Division of Cell Biology, Innsbruck Medical University, Innsbruck, Austria
[4] 6 Telethon Institute of Genetics and Medicine (TIGEM), Naples, Italy

In the realm of stress-induced premature senescence (SIPS), cells confront oxidative stress and widespread cellular damage, with mitochondrial integrity playing a crucial role. Central to mitigating this damage is the promotion of autophagy, particularly through an increase in lysosomal number. This study explores the dynamics of lysosomal quality control in this context, specifically investigating lysosomal signaling pathways during SIPS induced by tert-Butyl hydroperoxide (tBHP). Our findings delineate distinct signaling responses between the initial stress phase and subsequent senescent phase. In the stress phase, we observe an escalation in lysosomal damage, paralleled by an increase in reactive oxygen species (ROS) and mitochondrial dysfunction. This surge in ROS triggers AMP-activated protein kinase (AMPK) activation and Akt inactivation, leading to mammalian target of rapamycin (mTOR) suppression. The inactivation of mTOR during this phase facilitates the activation of Transcription Factor EB (TFEB), a key player in modulating ROS levels, augmenting autophagy, and enabling cellular survival. Interestingly, TFEB knockdown cells under stress showed increased apoptosis, highlighting TFEB's protective role in stress response. As cells transition into the senescence phase, the prior activation of TFEB, having facilitated the clearance of damage through autophagy, becomes less crucial; consequently, with the reduction in damage, TFEB activity is suppressed. The reduction in ROS levels normalizes AMPK and Akt signaling, reactivating mTOR. This reactivation of mTOR, pivotal in establishing the senescent state, mediates the inactivation of TFEB. Our results demonstrate a dynamic interplay between TFEB and mTOR, highlighting their critical roles in modulating cellular fate during the transition from stress response to senescence.

PS1-S5-SF01 Age-associated B cell fate choice is dependent on Bach2 upregulation

William J. Olson, Emmanuel Derudder

Institute for Biomedical Aging Research, Austria

Upon activation by the antigens associated with invading microbes or vaccine components, B cells diversify their responses by taking on a number of cell fates with differing functions. These include, germinal center B cells (GCB) which undergo selection for increased affinity toward antigens, both short- and long-lived antibody secreting cells (ASCs) that promote pathogen clearance and long-term protection from reinfection as well as memory B cells (MBCs) which act as rapid responders upon re-encounter with antigens. Recently, a subset of activated B cells termed age-associated B cells (ABCs) have been described, though not yet well characterized, they are thought to have a detrimental impact on B cell development and total naïve B cell numbers during aging. In addition, ABCs appear to be drivers of a number of autoimmune diseases including systemic lupus erythematosus. While other reports indicate they play a protective role in response to intracellular pathogens such as malaria. The molecular mechanisms underpinning B cell fate choice has long been the subject of study, although, ABC differentiation has only just begun to be unraveled. To date, very few transcription factors have been linked with the ABC fate, including T-bet, Zeb2 and Stat3. Here we provide evidence that one of several transcription factors known to play a role in B cell fate choice, Bach2 favors ABC differentiation. High levels of Bach2 have been associated with memory B cell formation while low levels allow for ASC differentiation and its deletion fully abrogates GC B cells. We find that during in vitro ABC differentiation, Bach2 upregulation is associated with ABC generation, and that lowering Bach2 levels via hemin treatment reduces ABC proportions. Overall, our work is the first to link Bach2 with ABC differentiation and suggests that tight control of Bach2 levels are required to balance ABC formation relative to the other fates and solidifies a central role for this transcription factor in B cell fate choice.

PS1-S5-SF02 In depth investigation of *actinobacterial* coproporphyrin ferrochelatase

Alice Cassiani, Alina Destinger, Paul G. Furtmüller, Thomas Gabler, Stefan Hofbauer

Department of Natural Sciences and Sustainable Resources, BOKU University, Austria

Heme is an iron-containing porphyrin required in numerous biochemical processes essential for all forms of life and it is involved in many metabolic pathways as enzyme cofactor. It also plays a key role in bacterial pathogenesis. Gram-positive bacteria, namely *Firmicutes* and *Actinobacteria* synthetize heme following the coproporphyrin-dependent (CPD) pathway. Many of these monoderm bacteria, so-called superbugs, are dangerous pathogens with multiple resistances to common antibiotics. Coproporphyrin III ferrochelatases (CpfCs) are enzymes involved in the intermediate step within the CPD pathway. CpfCs catalyse the insertion of ferrous iron into coproporphyrin III leading to the formation of coproheme. While the *Firmicutes* CpfCs do not have any bound cofactors, most *actinobacterial* CpfCs feature a [2Fe-2S] cluster, which is also present in most of the protoporphyrin IX ferrochelatases (PpfCs), including the human dimeric PpfC. Research is currently conducted on CpfC from *Corynebacterium diphtheriae* (*Cd*CpfC), in which the presence of the cluster has been spectroscopically proven using UV-Visible and Resonance Raman Spectroscopy. In addition, the X-Ray crystal structure (unpublished) shows that three of the four cysteines coordinating the cluster are present in the C-terminal extension of the peptide sequence (C353, C357, C358), while the fourth ligand is part of the main core of the protein (C127). To evaluate the function of the [2Fe-2S] cluster and further investigate the catalytic insertion of ferrous iron, research is additionally conducted on a C-terminally truncated variant, featuring a peptide sequence truncated before C357, which is spectroscopically proven to be unable to bind the cofactor. Using UV-Visible Spectroscopy and Mass Spectrometry it was observed that the absence of the [2Fe-2S] cluster lowers the affinity of the enzyme for its native substrate, coproporphyrin IIII, but it does not prevent the insertion of ferrous iron and the formation of ferric coproheme. The kinetics studies of the overall process are in progress, as a better understanding of the structure-function relationship in this key enzyme is an essential precondition for the design of inhibitors and, as a final goal, to the development of lead substances for novel antibiotics.

PS1-S6-SF01 Metabolic features of cancer cells during contact guidence migration

Natália Melo Santos, Maria Reichhold, Utku Horzum, Francois Tyckaert, Pere Patón González

Institute of Pathophysiology, Medical University of Innsbruck, Austria

Cancer cells often reprogram their metabolism to meet increased energetic and biosynthetic demands, particularly during migration. The energy required for migration is influenced by microenvironmental factors such as substrate rigidity and topography. Notably, cancer cells can exploit the extracellular matrix's heterogeneous topography to facilitate movement in a process called contact guidance. Although observed already a century ago, contact guidance remains poorly understood at the molecular level.Focal adhesions (FAs) link the actin cytoskeleton to the extracellular matrix, transmitting forces required for migration and are considered essential for contact guidance. However, using metastatic breast cancer MDA-MB-231 cells depleted of Talin1, a key FA component, we found that FAs are dispensable for this type of migration. Since FA maturation requires energy-intensive acto-myosin contractility, we hypothesized that FA-independent migration may be more energy-efficient.To test this, we cultured cells on polydimethylsiloxane (PDMS) substrates engineered with ridge-like nanotopographies functionalized with collagen. Preliminary immunofluorescence analysis showed significant increase in mitochondria number in cells on ridges compared to those on flat surfaces. Interestingly, FA-deficient cells exhibited an increased number of mitochondria on ridges, but decreased ATP production. Additionally, adhesion on ridges seemingly increases the proportion of mitochondria positive for pyrroline-5-carboxylate synthase (P5CS), a mitochondrial enzyme and marker for mitochondrial subpopulations specialized in amino acid production. This may reflect a metabolic shift favoring proline synthesis, which could be related to a reduced need for cells to produce ATP when on ridges. Collectively, these results could indicate a contact guidance-induced metabolic adaptation.

PS1-S6-SF02 The elucidation of TM9SF4 function in migration and polarization.

Adam Pollio, Luca Szabo, Doris Stepic, Georg Vogel

Zellbiologie, Medical University of Innsbruck, Austria

TM9SF4 is a Golgi-resident protein previously associated with cancer progression, but its mechanistic role in regulating cell behavior remains incompletely understood. Prior work in epithelial Caco-2 cells demonstrated that TM9SF4 depletion alters the subcellular localization of DPP4, suggesting a role in trafficking and polarity. Building on these findings, we now focus on the functional contribution of TM9SF4 to cancer cell migration and the pathways by which a Golgi-localized protein may influence migratory behavior.

In this study, we examine the effects of TM9SF4 depletion across several cancer-derived cell lines, employing siRNA-mediated knockdown to interrogate changes in morphology, motility, and cytoskeletal organization. Our aim is to elucidate how Golgi-localized trafficking components regulate dynamic cell behaviors such as migration. Using fixed and live-cell imaging, we assess the spatial organization of TM9SF4 during migration and characterize phenotypic consequences of its loss. In addition to examining migratory parameters, we evaluate expression changes in key adhesion molecules. In MDCK cells, we observe that TM9SF4 knockdown leads to altered expression levels of integrins αv and α5—two integrins closely tied to cell-matrix interactions and directional migration—suggesting that TM9SF4 may modulate surface receptor composition or trafficking.

To better understand the mechanisms underlying these observations, we combine biochemical analysis with confocal microscopy to investigate candidate pathways downstream of TM9SF4. Together, our findings support a broader role for TM9SF4 in coordinating intracellular trafficking and integrin dynamics, with direct implications for migratory plasticity in epithelial and cancer cells.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

Poster Session 1

NOTE: The Science Flash poster abstracts from Poster Session 1 are listed in the Science Flash Session 1

S1: Neural circuits in health and disease

S2: Environment and microbiology

S4: Aging, mental health, exercise and metabolism

S5: Infection and immunity

S6: Mechanical aspects of cell adhesion and migration

Varia

PS1-S2-PP01 Elucidating the contribution of Ugp1 in *Aspergillus fumigatus* 5-fluorocytosine activity.

Lukas Birštonas, Alexander Kühbacher, Fabio Gsaller

Institute of Molecular Biology, Medical University of Innsbruck, Austria

Introduction

Compared to the other antifungal agents used in the clinical setting, the antifungal 5-fluorocytosine (5-FC) is not toxic per sé. To unfold its toxicity, it has to be metabolized within the cell into 5-fluorinated nucleotides such as 5-fluorouridine triphosphate (5-FUTP), an analog of the RNA building block uridine triphosphate (UTP). 5-FUTP can be incorporated into RNA instead of UTP leading to adverse effects in RNA and protein metabolism. In addition to its role in RNA metabolism, UTP is a crucial precursor for nucleotide sugars which provide essential components for cell wall polymers like glucans.

Objectives

In the first step of nucleotide sugar synthesis, the enzyme UDP-glucose pyrophosphorylase (Ugp1) catalyzes the formation of UDP-glucose from UTP and glucose-1-phosphate. Based on the hypothesis that 5-FUTP affects nucleotide sugar metabolism, for instance by directly acting on Ugp1 enzyme activity, in this work we aimed to elucidate a potential novel mode-of-action related to 5-FC.

Materials and methods

A. fumigatus conditional expression mutants of *ugp1* were generated to monitor 5-FC activity during its downregulation and overexpression. In addition to phenotypical assays, minimum inhibitory concentrations (MICs) were analyzed using a broth microdilution assay coupled with high-throughput microscopy. An assay is being developed to determine whether Ugp1 activity is altered in response to 5-FC treatment.

Results

Downregulation of *ugp1* led to severe defects in hyphal morphology and rendered *A. fumigatus* more susceptible to 5-FC. In line, its overexpression increased 5-FC resistance.

Conclusion

Taken together, our initial data suggests a new mode-of-action for 5-FC related to nucleotide sugar biosynthesis.

PS1-S2-PP02 Effects of cold drought and land use on plasmodiophorids/grass interactions

Sara Hnaien, Alex Schwarz, Andrea Garvetto, Sigird Neuhauser

Microbiology, Universität Innsbruck, Austria

As climate change continues to impact ecosystems globally, understanding the interactions between microbes and host plants is increasingly important. This study focuses on the interaction between soil-borne plasmodiophorid parasites (in particular Polymyxa and Tetramyxa spp.) and the alpine grass Poa alpina, which is prevalent in alpine and subalpine regions. Given the increase in cold drought events due to climate change, this research investigates how varying drought conditions influence plasmodiophorid interactions with grasses. We aim to analyze the dynamics of this parasite-host interaction by simulating cold winter drought conditions in a controlled greenhouse environment. Three soil types will be utilized, and Poa alpina will be subjected to different irrigation treatments to assess the impact of water availability on infection rates and plant recovery. The study will evaluate key factors such as plant growth, resilience, and the prevalence of plasmodiophorid infections under these stress conditions. Additionally, the research will explore how recovery from drought impacts the fitness of Poa alpina post-drought. By employing phenotypical assessments, molecular analyses, and microscopy, this study seeks to provide insights into the ecological implications of climate-related stressors on plant-microbes dynamics. The findings will enhance our understanding of how environmental changes may shape the interactions between plasmodiophorids and Poa alpina.

PS1-S2-PP03 Using gas chromatography and mass spectrometry (GC-MS) for the detection of drought and heat stress effects on the metabolome of *Solanum tuberosum* varieties

Hannah-Sophie Auricht, Bushra Ijaz, Markus Teige, Alexandra Ribarits, Cristina Lopez-Hidalgo, Wolfram Weckwerth

Molecular Systems Biology (MOSYS), University of Vienna, Austria

Potato (*Solanum tuberosum* L.) is among the highest-yielding staple crops worldwide, making its resilience to abiotic stress a critical factor in global food security. Yet, the potato yield is strongly dependent on many abiotic factors. Pressuring matters like climate change urge to understand plant stress response to abiotic factors, such as drought. This knowledge will be essential in breeding more adaptable crop varieties to maintain food security. Previous studies showed changes in plant stress-related metabolites [1,2]. **Methods:** Ten potato varieties were tested for their drought and heat stress response in a field trial. The samples for the analysis were collected from both irrigated (control) and non-irrigated (treatment) fields 2024 in two time points in July (at the onset of flowering). Leaf discs were grinded, and their weight normalized. Primary metabolites were targeted in the analysis by collecting the polar phase of the Methanol-Chloroform-Water extract. The metabolites were quantified and identified using Gas chromatography-mass spectrometry analysis. Further processing was done using MS-Dial and statistical analysis with R. **Results:** Preliminary results indicate separation between the control and the treatment group. Between the potato varieties and treatment metabolite changes (e. g. in proline) could be measured. **Discussion:** The differences could depend on varying conditions in the soil, the microclimate and pests in a field trial which were partially assessed and further analyzed by AGES. **Conclusion:** We were able to characterize metabolic changes in *Solanum tuberosum* that are likely related to the applied drought stress conditions.

PS1-S2-PP04 Localized ROS as a Feature of *Maullinia ectocarpii* Infection in *Ectocarpus siliculosus*

Anagha Santhosh, Andrea Garvetto, Sigrid Neuhauser

Department of Microbiology, University Of Innsbruck, Austria

Brown algae are ecologically and economically vital marine phototrophs that belong to the class Phaeophyceae. In the past years, marine aquaculture involving brown algae has gained enormous momentum. However, these algae are vulnerable to a range of prokaryotic and eukaryotic pathogens. One such major parasite is *Maullinia ectoacarpii*, an obligate biotrophic parasite of the class Phytomyxea. Reactive oxygen species (ROS) are known to play a central role in algal defence, functioning both as direct antimicrobial agents and as mediators of downstream defence pathways. While ROS are generated under normal metabolic conditions, their production is often enhanced during pathogenesis. Although interest in brown algal host–parasite interactions is growing, the underlying mechanisms remain poorly understood. Here, we present a microscopic analysis of ROS accumulation in the brown algae *Ectocarpus siliculosus* infected with *M. ectocarpii*. Using microscopy, we detected light-independent ROS production across multiple stages of infection. Notably, the mature plasmodia of *M. ectocarpii* exhibited a distinct accumulation of oxidative species or compartments. This suggests the establishment of a unique oxidative environment within mature feeding plasmodia and parasite-induced modulation of host redox homeostasis. This work implicates oxidative stress and metabolic adaptation in *M. ectocarpii- E. siliculosus* pathosystem, thereby highlighting promising avenues for dissecting the underlying interaction mechanisms.

PS1-S4-PP01 Role of the Glycolytic Enzyme Aldolase C in Adipocyte Metabolism and Function

Vinzenz L. Krichbaumer[2], Katja Silbernagl[2], Alexander K. H. Weiss[1], José Ramos Pittol[2], **Florian Hatzmann[2]**

[1] Institute for Biomedical Aging Research, University of Innsbruck
[2] Institute of Biochemistry, University of Innsbruck, Austria

Aging and obesity with their comorbidities comprise major challenges for health care systems. Adipose tissue functions decline upon aging and obesity accelerates this process, highlighting the need to address age- and obesity associated adipocyte malfunctions to improve metabolic health. Maintaining glucose homeostasis by taking up and processing excess glucose is a central function of adipocytes. Disturbances in this process, which are frequently observed upon aging and obesity, for instance due to disrupted glycolysis interfere with adipocyte functions and lead to metabolic diseases. However, the main regulators of glycolytic flux in adipocytes and their relationship to age- and obesity-associated dysfunction are poorly understood.

Aldolases A (AldoA), B (AldoB), and C (AldoC) are isozymes that catalyze the reversible conversion of fructose-1,6-bisphosphate to glyceraldehyde-3-phosphate and dihydroxyacetone phosphate in glycolysis. AldoA is preferentially expressed in muscle but also predominant in adipose tissue and AldoB is mainly expressed in liver while AldoC is the main form in brain. However, AldoC was shown to be upregulated in both subcutaneous and visceral WAT upon weight-loss after bariatric surgery. To investigate the role of Aldolase isozymes in adipocytes we subjected 3T3-L1 preadipocytes to adipogenic differentiation and found that AldoC shows different expression dynamics than AldoA while AldoB expression was mostly not detectable. Utilizing the CRISPR synergistic activation mediator (SAM) system in 3T3-L1 cells, we generated a preadipocyte cell line with overexpression of endogenous AldoC to analyze its role in adipocyte metabolism and functions. Typically, the glycolytic enzymes hexokinase and phosphofructokinase which mediate the energy-consuming early phosphorylation steps in glycolysis, as well as glucose transporters are considered the rate-limiting steps for glycolytic flux. However, we show that overexpression of AldoC results in increased glycolytic rate in 3T3-L1 cells. Additionally, we show the effects of metabolic rewiring due to AldoC overexpression on adipogenic differentiation. Taken together, we will discuss the implications of enhanced glycolytic flux on adipocyte functions resulting from increased expression of AldoC.

PS1-S4-PP02 The equine fascial system: first insights into its cellular composition

Christina Baumbach, Claudia Bergow, Alexandra Petric, Christiane Schueler, Janina Burk

Dpt. Physiology and Pathophysiology, University of Veterinary Medicine Vienna, Austria

The fascial system fulfills important physiological functions in movement, stability and force transmission. Research on its structure and function is gaining attention due to growing evidence that medical conditions such as chronic back pain and stiffness may be connected to myofascial dysfunction, not only in humans but also in companion animals such as equine athletes.

The facial system is a three-dimensional continuum spanning the whole body, organized in several layers of collagen-rich connective tissue. Fibroblasts are the most abundant cell type, yet another distinct cell type was recently found in human *fascia lata*: fasciacytes. Those rounded cells with perinuclear cytoplasm and prominent nuclei were shown to produce hyaluronan which hydrates the tissue, thereby enabling movement and reducing friction. As so far, knowledge on fascia biology in general is limited and even more scarce with respect to the equine species. Therefore, the aim of our study was to further our knowledge about the equine fascial system, with a focus on its cellular components.

Fascia antebrachia of horses euthanized due to unrelated reasons were sampled (n=4). The tissue was disinfected, cut into smaller pieces and subjected to immuno- and histochemistry and cell culture. After about three weeks in culture with regular change of media and trypsinization, cells were sampled for qPCR, Western Blot or immunofluorescence analyses, respectively.

Two distinct cell types were observed. Equine fasciacytes were seen in all samples and, hence, described here for the first time. They resembled human fasciacytes in structure and function: they are rounded with a prominent nucleus surrounded by cytoplasm, but slow in growth and proliferation. *In situ,* they are surrounded by ECM rich in hyaluronan suggesting their involvement in hyaluronan synthesis and regulation. However, so far, it was not possible to propagate them sufficiently for solid molecular biological analyses. The second cell type were elongated spindle-shaped fibroblast-like cells, outnumbering the fasciacytes by far. Among others, they were positive for vimentin, S100A4 and enzymes involved in collagen production and remodeling.

The current study provides first insights into the cellular components of equine fascia, so far suggesting analogy to the human system and thereby pointing towards the horse as a useful model for fascia research.

PS1-S4-PP03 Matrix metalloproteinases in modulating white adipose tissue

Victoria Strobl[1], Sonja Großmann[1], Petra Waldegger[1], Johann-Peter Viertler[1], Sabine Gufler[1], Tina Deutinger[2], Carina Harasser[2], Gerhard Pierer[2], Werner Zwerschke[1]

[1] Cell Metabolism and Differentiation Research (CMDR), Research Institute for Biomedical Ageing Research (IBA), Leopold-Franzens-University Innsbruck, Austria
[2] Department of Plastic, Reconstructive and Aesthetic Surgery, Medical University of Innsbruck

Obesity represents a significant global health challenge, accelerating aging processes in the human body. Weight loss (WL), achieved via dietary restriction (DR) comprises a robust anti-ageing intervention. Our research group aims to better understand adipose stem/progenitor cell (ASC) dynamics during WL interventions such as DR. Using Affymetrix microarray screening, we identified WL target genes in ASC, including the gene encoding for matrix metalloprotease 3 (MMP-3). Previous studies could already demonstrate that matrix metalloproteases (MMPs) play crucial roles in adipose tissue remodelling and ASC regulation. However, the particular MMPs involved in adipose tissue remodelling yet need to be identified. In the present study, we assessed the effects of MMP-3 on ASC proliferation, differentiation, and senescence through loss-of-function experiments, utilizing shRNA-mediated knockdown strategies. Our results suggest that MMP-3 is important for ASC proliferation, stemness and senescence.

PS1-S4-PP04 *Advancing Diagnostic Spectroscopy: Raman and Infrared Imaging in Bone, Tissue, and Forensic Applications*

Johannes Pallua[1,2], Christian Huck[2]

[1] Universitätsklinik für Orthopädie und Traumatologie, Medizinische Universität Innsbruck, Austria
[2] Institute of Analytical Chemistry and Radiochemistry, University of Innsbruck, Austria

Raman and infrared spectroscopy rapidly transform biomedical diagnostics, enabling non-destructive, label-free chemical analysis of tissues and biomaterials. This talk presents our recent advances in applying handheld and microscopic Raman and mid-infrared spectroscopic techniques across various translational research fields—including infection diagnostics, bone integrity assessment, and forensic post-mortem analysis.

Using Raman spectroscopy, we successfully discriminated between *Staphylococcus aureus* and *Staphylococcus epidermidis* in bone grafts and accurately estimated post-mortem intervals in skeletal remains. Complementary IR microscopy enabled detailed chemical mapping of pathological structures, including parasitic lesions and lymphoid malignancies, and tissue-based assessments in echinococcosis and oral carcinoma diagnostics.

Our studies emphasize the power of spectroscopic imaging to reveal pathogen-specific and disease-related biochemical fingerprints in complex biological matrices. When integrated with micro-CT, histopathology, and machine learning, these approaches provide a robust platform for high-throughput, spatially resolved diagnostics.

This talk highlights the collaborative efforts of analytical chemistry and medical imaging to develop clinically relevant, spectroscopy-based diagnostic strategies with high translational potential—from the operating room to the forensic lab.

PS1-S4-PP05 Exploring metabolic sleep regulation dependent on Drosophila's brain regions

Frank Madeo, Jelena Tadic, Andrea Jerkovic, **Marlies Eder**

Biochemie und molekulare Biomedizin, Institut für molekulare Biowissenschaften, Austria

Sleep plays a vital role across animal species, including humans, for maintaining cognitive function, neural communication, and physiological health. There is growing evidence highlighting its involvement in metabolic regulation, immune defence, and clearance of brain toxins. A chronic lack of quality sleep impairs concentration and creation of new memories and is additionally strongly linked to multiple health problems. Considering the increase of life expectancy, sleep disorders are gaining importance due to their association with aging. Although the importance of sleep is widely recognized, the biological mechanisms behind it are still not fully understood. Here, we use the fruit fly as a model organism to investigate some of these unresolved questions, focusing on the role of polyamines; naturally occurring compounds with reported anti-aging effects; in sleep regulation. Behavioural activity was monitored through video tracking with DART (Drosophila Arousal Tracking), a webcam-based software analysing movement. We observed the importance of polyamine metabolism in sleep regulation and provide evidence suggesting the involvement of a specific brain region in polyamine-dependent sleep regulation.

PS1-S4-PP06 Dietary methionine modulates tissue-specific metabolomic profiles and aging-related pathways in rats

Tobias Huberts[1], Hansjörg Habisch[1], Ingrid Matzer[2], Mara Luisa Kießling[2], Senka Holzer[2], Tobias Madl[1]

[1] Medicinal Chemistry, Medical University Graz, Austria
[2] Medical University Graz; Clinical Department of Cardiology

Alterations in energy metabolism, encompassing changes in dietary, energy intake, and expenditure, are intimately linked to aging and lifespan. *L*-methionine, an essential amino acid, plays a pivotal role in various metabolic processes. It is directly implicated in the one-carbon cycle, which produces *S*-adenosylmethionine from methionine and adenosine triphosphate, and is imperative for cellular function. As demonstrated by animal studies, a reduction in methionine intake has been associated with an increased maximum lifespan and exhibited renoprotective effects. Conversely, excessive methionine intake has been demonstrated to result in the accumulation of its metabolic intermediates or byproducts, which has been identified as an independent risk factor for cerebrovascular disorders, including stroke and dementia.

The aim of this study was to examine age-related metabolomic alterations in a rat model, by administering three diets from low to high methionine content (0.12% Met (low), 0.86% Met (control), 2.58% Met (high Met)). The specific diets were initiated at seven weeks of age for a duration of six weeks, where significant changes in body weight development and growth rate were observed.

Following a period of six weeks, the rats were euthanised and a wide range of tissues were harvested, including liver, spleen, heart, brain, serum, blood, skin. These tissues were examined to ascertain specific changes in the metabolomic profile via nuclear magnetic resonance (NMR) spectroscopy. The metabolomic profiling revealed distinct diet-dependent alterations across tissues, indicating significant changes in key metabolic pathways, particularly the tricarboxylic acid (TCA) cycle, the one-carbon metabolism pathway, and the cytidine diphosphate-choline pathway. These findings suggest that dietary methionine levels influence fundamental metabolic networks that may be linked to aging and organ-specific physiological responses.

PS1-S4-PP07 CRISPR activation of FXR potentiates the up-regulation of a subset of metabolic genes by obeticholic acid in liver cells

Nina Heidenhofer, Lino Salcher, Hannah Sophia Juen, Florian Hatzmann, **Jose Miguel Ramos Pittol**

Institute of Biochemistry, University of Innsbruck, Austria

The farnesoid X receptor (FXR) orchestrates hepatic bile-acid, lipid, carbohydrate and amino-acid metabolism, yet its expression declines with metabolic disease and ageing. FXR is expressed as four isoforms (α1-α4) from a single locus that drive transcription from inverted repeat-1 (IR-1) elements as a heterodimer with the retinoid-X-receptor (RXR). FXR isoforms α2/α4 also activate transcription from non- canonical ER-2 everted repeat-2 (ER-2) elements, mediating most metabolic effects of general FXR activation. We recently showed that FXRα2 binding to ER-2 DNA is RXR-independent and that heterodimerisation with RXR in fact suppresses this pathway, suggesting that selectively boosting FXRα2, or the overall FXR:RXR ratio, could enhance therapeutically valuable FXR response to ligands.

Here we evaluated CRISPR–synergistic activation mediator (SAM) as a gene-delivery strategy to up-regulate endogenous FXR in human hepatoma (HepG2) cells. Individual guide-RNA sets were designed for each native FXR promoter and delivered with dCas9-VP64, and MS2-p65-HSF1. Isoform abundance was quantified by isoform-specific qPCR, and downstream transcriptional responses were profiled in the presence or absence of the clinical FXR agonist obeticholic acid (OCA).

CRISPR-SAM increased total FXR mRNA 4- to 8-fold. At this level, FXR did not up-regulate canonical targets (e.g., *SHP*, *BSEP*) in the absence of ligand as seen with other delivery methods. OCA treatment produced additive or synergistic activation that was gene-specific with partial linkage to response element selectivity. These findings demonstrate that CRISPR-based augmentation of FXR creates a transcriptional landscape synergistic to agonists divergent from that achieved by ligand stimulation alone. Gene-activation approaches may therefore enhance the efficacy of current FXR agonists and represent a promising avenue to restore hepatic metabolic fitness in metabolic disease and ageing.

PS1-S5-PP01 Fluorescence-based point-of-care device for rapid detection of respiratory RNA viruses in clinical settings

Denisa Cont, Anita Brindlmayer-Stamminger, Matthias Pilecky

Department for Biomedical Research, University for Continuing Education Krems, Austria

The COVID-19 pandemic exposed critical gaps in our global capacity to respond rapidly and effectively to emerging infectious diseases, particularly due to the limited availability of reliable, rapid diagnostic tools deployable at the point of need, such as in primary care settings, hospitals, and border control points. To address this, the EU-funded PAIR project (*Pandemic Information to Support Rapid Response*) aims to develop and validate two complementary tools: PANPOC, a portable, fluorescence-based point-of-care device for the rapid detection of respiratory RNA viruses with pandemic potential (including Influenza A/B and SARS-CoV-2) and PANRISK, an AI-driven platform for early outbreak prediction. The PANPOC system will combine isothermal amplification with real-time fluorescence detection in a compact, user-friendly format capable of delivering accurate results in under 30 minutes. Our team will be contributing to the clinical validation of PANPOC using human naso-/oropharyngeal swab samples, with performance benchmarked against standard qPCR assays to assess diagnostic accuracy, sensitivity, specificity, and usability. The outcomes will support regulatory approval and provide real-world data to train the PANRISK predictive platform. By bridging ultra-rapid diagnostics with real-time epidemiological modelling, PANPOC and PANRISK together represent a novel One Health approach to pandemic response, facilitating timely interventions across human and veterinary health sectors.

PS1-S5-PP02 Functional status and amino acid profiles - sex-specific findings one year after COVID-19

Katharina Wagner, Daniel Grüner, Pablo Montfort-Lanzas, Lucia Parrakova, Günter Weiss, Katharina Kurz, Johanna M. Gostner

Medizinische Universität Innsbruck, Austria

One year after acute SARS-CoV-2 infection, many patients continue to experience limitations in daily activities. The ECOG performance status provides an objective measure of physical functioning. Recent findings indicate that alterations in amino acid metabolism, particularly in the tryptophan and phenylalanine pathways, may contribute to long-term post-infectious sequelae due to their roles in immune regulation and neurotransmitter synthesis.

This study aimed to examine metabolic and inflammatory factors associated with functional impairment one year after COVID-19, with a particular focus on alterations in amino acid metabolism and hematological parameters.

Eighty-nine patients one year after confirmed COVID-19 infection were included. The functional status was determined using the ECOG performance score. Blood samples were assessed for alterations in aromatic amino acid metabolism in addition to routine laboratory markers. Sex-related differences were observed. Female patients showed significantly lower counts of reticulocytes, monocytes, and eosinophils compared to males, whereas male patients exhibited higher serum levels of tryptophan. Phenylalanine concentrations were inversely associated with impaired performance status, being lower in male patients with an ECOG score >0. Distinct sex-specific patterns in hematological and amino acid profiles were identified one year after COVID-19. Reduced phenylalanine levels correlated with impaired functional status, suggesting a disruption in aromatic amino acid homeostasis in patients with persistent limitations. Elevated tryptophan in males and reduced hematopoietic cell counts in females highlight possible sex-dependent pathways. Whether hormonal or immunological mechanisms underlie these differences remains unclear. Recognition of such metabolic disparities may support more personalized therapeutic strategies in post-COVID-19 recovery.

PS1-S5-PP03 Trained Immunity Enhances Valvular Calcification: The Role of Age and Sex in Calcific Aortic Valve Disease

Lynn Muller[1], Christina Dünser[2], Michael Graber[1], Manuel Fiegl[1], Jakob Hirsch[1], Veronika Niedrist[1], Vanessa Heim[1], Dominik Hau[1], Michael Grimm[1], Johannes Holfeld[1], Can Gollmann-Tepeköylü[1]

[1] Cardiac Surgery Dept., Medical University Innsbruck, Austria
[2] Department of Internal Medicine II, Medical University Innsbruck, Austria

Calcific aortic stenosis (AS) is a leading cause of valvular heart disease, with risk factors including age, sex, hypercholesterolemia, diabetes, and hypertension. Calcific aortic valve disease (CAVD) is characterized by progressive thickening and calcification of the aortic valve leaflets, leading to impaired blood flow. Traditionally considered a passive degenerative process, CAVD is now recognized as an active and complex inflammatory disease. Currently, no pharmacological treatment exists, and surgical valve replacement remains the only therapeutic option.

A growing body of evidence suggests that chronic inflammation is a key driver of CAVD. Increased mechanical stress leads to endothelial injury and activation of valve interstitial cells (VICs), promoting fibrosis and calcification. This activation triggers a pro-inflammatory cascade involving macrophages, IL-6, IL-1β, and TNF-α, as well as the NF-κB pathway, ultimately inducing osteogenic factors such as BMP-2, Notch1, and Runx2.Recent research highlights the involvement of trained immunity in atherosclerosis, a closely related vascular pathology. Trained immunity refers to the epigenetic and metabolic reprogramming of innate immune cells, particularly monocytes and macrophages, following exposure to inflammatory stimuli such as oxLDL. This results in an exaggerated immune response upon subsequent challenges, contributing to chronic inflammation and tissue remodelling. Given the similarities between atherosclerosis and CAVD, trained immunity may play a critical role in the pathogenesis of aortic valve calcification. Hypercholesterolemia and persistent inflammatory stimulation could induce trained immunity in VICs and macrophages, exacerbating the fibrotic and calcific processes.

Trained monocytes exhibited a hyperinflammatory phenotype characterized by elevated IL-6 production *in vitro* and promoted a pronounced calcific response in valvular interstitial cells (VICs) under co-culture conditions. Echocardiographic analysis of aged mice demonstrated age-associated valve degeneration, with male mice exhibiting more severe pathological changes than their female counterparts. These sex-specific differences were corroborated by *ex vivo* experiments.

Innate immune training induces a heightened pro-inflammatory state in monocytes, contributing to enhanced calcification in valvular cells *in vitro*. Monocytes derived from aged male mice display an enhanced pro-calcific capacity, consistent with the sex-specific progression of valvular degeneration observed *in vivo*. These findings provide a compelling basis for further investigation of immune training in calcific aortic valve disease (CAVD) and its potential as a therapeutic target.

PS1-S5-PP04 Development of N-chlorotaurine: Efficacy and tolerability of inhalation in fungal pneumonia in the mouse model

Cornelia Speth[1], Günter Rambach[1], Andrea Windisch[1], Nadine Falbesoner[1], Christoph Schatz[2], Georg Schäfer[2], **Markus Nagl[1]**

[1] Institute of Hygiene and Medical Microbiology, Medical University of Innsbruck, Austria
[2] Institute of Pathology, Medical University of Innsbruck

Background:

N-chlorotaurine (NCT), an endogenous mild active chlorine compound, can be used topically as anti-infective in different body regions. It was the aim of the present study to demonstrate the efficacy and tolerability of inhaled NCT in the mouse model of fungal pneumonia.

Methods:

Specific pathogen free, 7 weeks-old C57BL/6JRj mice were immune-suppressed with cyclophosphamide or cortisone acetate and infected intranasally with 1.5x10E7 spores of *Lichtheimia corymbifera* or 6.5x10E6 spores of *Aspergillus fumigatus* after 7 days.

Subsequently, the animals were treated 3 times daily for 10 min each with an aerosol (< 5 µm) of NCT or 0.9% NaCl (placebo) for 2 weeks.

Results:

Then mice developed pneumonia throughout. In the first study with *L. corymbifera*, 7 out of 9 mice survived in the 1% NCT group in contrast to only 1 of 9 in the control group ($p = 0.0049$). Accordingly, the number of colony-forming units (CFU) per ml homogenized lung tissue in the test group came to median 1.60 log10 (quartiles 1.30; 1.99) compared to 4.26 log10 (Quartile 2.17; 4.53) in the control group. In the second study with *A. fumigatus*, 8 to 9 out of 9 mice survived in test groups treated with 0.5%, 1%, or 2% NCT, but only 0 to 1 out of 9 mice treated with 0.9% NaCl ($p < 0.01$ for each NCT group versus placebo). In mice treated with 0.1% NCT, 5 out of 9 survived ($p = 0.0035$ versus control, $p = 0.03$ versus higher NCT concentrations). The CFU count from the homogenized lung was 1.3 log10 (max. 2.45) in the 1% NCT group and 5.28 log10 (quartiles 4.46; 5.70) in the control group under cyclophosphamide. Results were similar for 0.5% and 2% NCT as well as under cortisone acetate. Secondary parameters, i.e. number of virulent bacteria in the homogenized lung, body weight, body temperature and inflammation parameters improved significantly by NCT therapy, too. Tolerability of inhalations was good without signs of discomfort or toxicity except for a slight rhonchus only in the 2% NCT group.

Conclusions:

Inhaled NCT highly significantly reduced lethality and counts of fungal and concomitant virulent bacteria in the lung in fungal pneumonia in the mouse model. The concentration of 1% NCT appears to be optimal taking into account both tolerability and efficacy, which is in agreement to hitherto studies and case experiences in humans.

PS1-S6-PP01 Encephalitic alphavirus infection of human iPSC-derived neurospheres alters Rho GTPase pathways and impairs neurite outgrowth

Karsten Cirksena[1], Britta Kuehne[1], Lisa Maria Haiber[1], Bettina Seger[1], **Gisa Gerold[2]**

[1] Institute for Biochemistry & Research Center for Emerging Infections and Zoonoses (RIZ), University of Veterinary Medicine Hanover, Hanover, Germany.
[2] Institute of Virology, Medical University of Innsbruck, Austria

Venezuelan equine encephalitis virus (VEEV) is a re-emerging, mosquito-borne virus, which impairs human brain development and function. Models to assess the impact of VEEV on the developing human brain were previously unavailable. Using iPSC-derived neurospheres, we show VEEV infects both neurons and glial cells and that these cells also produce new virus particles. Multi-omics analysis of VEEV-infected neurospheres demonstrates translational shutoff including downregulation of Rho GTPases and cytoskeletal modulators indicative of reduced migratory activity. Shotgun secretomics moreover revealed downregulation of the neurite outgrowth-associated proteins MDK, IGFBP2, IGFBP4. Unbiased microscopy-based quantification of neurite lengths during VEEV infection demonstrates that the virus impairs neurite outgrowth in the human organoids. Thus, neurospheres are a suitable model for assessing molecular mechanisms of teratogenic virus infection of the developing brain, ultimately uncovering possible targets for intervention.

PS1-V-PP01 Inducible expression systems for AAV production in mammalian cells

Maria Toth, Manuel Reithofer, **Elizabeth Cloos**, Astrid Dürauer, Reingard Grabherr

BOKU University Vienna, Austria

For the production of recombinant adeno-associated virus (AAV) in mammalian cells, a triple transfection method using three different plasmids is commonly used. Two plasmids provide the AAV genes rep, cap and the adenoviral (AdV) helper genes. The third plasmid contains the sequence encoding the therapeutic gene to be packaged into the viral particles. Packaging cell lines, that stably express all AAV and AdV components have the advantage that only one plasmid encoding the target gene must be transfected, which markedly increases production efficiency. However, the expression of cytotoxic proteins such as the AAV gene rep in stable cell lines requires a tight regulation of gene expression. Therefore, an inducible expression system is being explored that comprises viral polymerase from a bacterial virus, namely the T7 RNA polymerase. The inducible system is based on the specific interaction of a viral RNA polymerase and the corresponding viral promoter. Thus, expression is activated only when a plasmid encoding the viral polymerase is present in the cell. Therefore, we propose an antibiotic-free alternative to the widely used TetON system. In our study, we investigated the feasibility of inducible systems in HEK293. Therefore, we designed and introduced different plasmids carrying fluorescent proteins under the control of the viral promoter T7. As a benchmark, the TetON system was included and evaluated in our study. Basal and induced expression levels after co-expression of the corresponding RNA polymerase were assessed by flow cytometry. The inducible systems TetON as well as the T7-system derived from E. coli was used to control transcription of recombinant protein. Subsequently, Rep78 was stably integrated using the TetON system. Growth rates and behavior in an uninduced state were comparable to HEK293 without integrated Rep78. For AAV production, all other required components of AAV and the helper genes were provided by plasmid transfection. Our experiments demonstrate the activation of protein expression using viral polymerases and contribute to the development of stable cell lines for the expression of toxic proteins in mammalian cells.

PS1-V-PP02 REMBAC - A Rapid Efficient Manifold Baculovirus Transduction Platform for stable cell line development

Sophie Huber, Sandra Díaz Sánchez, Miriam Klausberger, Reingard Grabherr, Manuel Reithofer

BOKU University, Austria

Efficient recombinant protein production depends on stable cell lines, especially for complex products like virus-like particles (VLPs) and adeno-associated viruses (AAVs) used in vaccines and gene therapy. Conventional transfection methods for these structures often result in inefficiencies and inconsistent product quality, making stable cell lines essential. However, generating these cell lines is time-consuming and challenging, especially for products requiring large transgenes. Current solutions, often based on Chinese hamster ovary (CHO) cells, are effective but don't always meet the quality needs for VLPs and AAVs, which require human glycosylation patterns. Thus, there is a need for a versatile, cell type-independent platform for stable cell line development.

Our system addresses this need using baculoviral transduction of mammalian cells (BacMam), which is cost-effective, scalable, and efficient. BacMam has several key advantages: (i) it doesn't require high-biosafety laboratories, (ii) it efficiently transduces various cell types, and (iii) it integrates large DNA fragments into genomes. We developed the REMBAC platform (Rapid Efficient Manifold Baculovirus Transduction), enabling site-specific genome integration of large transgenes with customizable expression levels. This is especially useful for dealing with cell-toxic proteins, and the system's expression cassette includes insulators to protect against host-cell silencing.

REMBAC facilitates stable cell line development for a wide range of biopharmaceutical applications, including biologics like monoclonal antibodies or bionanoparticles such as VLP vaccines or AAV gene therapy vectors. It ensures efficient gene delivery across different cell types and integrates the transgenes without leaving viral footprints. By combining BacMam's versatility with homologous recombination for site-specific integration, and using a homing endonuclease for precise transgene excision, REMBAC allows the co-expression of multiple transgenes at controlled levels. A library of transfer vectors supports long-term, fine-tuned protein expression.

The platform did not only corroborate its utility for the establishing multicomponent-VLP production cell lines, but also for the generation of antigen-specific reporter cell lines.

PS1-V-PP03 Unlocking Gene Expression Potential: Investigating viral protein-driven enhancement in mammalian cells exploiting recombinant baculoviruses

Jochen Gitzl[1], Sophie Huber[1], Miriam Klausberger[1], Reingard Grabherr[1], Victoria Alfonso[2], Manuel Reithofer[1]

[1] BTLW, Boku University, Austria

[2] Instituto de Agrobiotecnología y Biología Molecular (IABIMO), Instituto Nacional de Tecnología Agropecuaria (INTA)-Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina.

Recombinant baculoviruses (rBV), particularly their transduction of mammalian cells, have long served as a pivotal biotechnological tool for gene delivery, facilitating efficient recombinant protein production. Recently, this system attracted interest due to its numerous advantages over conventional methods, such as the elimination of the need for high biosafety level laboratories, efficient transduction across various cell types, and the capability to transfer large transgenes into host cells. Its versatility offers a broad application spectrum, especially for novel therapeutic approaches such as virus-like particles or gene therapy vectors. Despite the broad range of accessible host cells, some require substantial resource input *i.e.* high multiplicities of infection, to achieve adequate gene delivery. This challenge arises from two primary obstacles: inefficient cellular entry mechanisms/virus internalization, and host defense mechanisms against viruses. The former was addressed by enhancing viral tropism through pseudotyping rBV with the glycoprotein G of VSV. The latter poses a bigger challenge due to the diverse mammalian antiviral response mechanisms. Recent studies highlighted the role of the cGAS-STING pathway, leading to investigations of potential disruptive candidates such as BV derived P26.

Our study aims to develop an rBV capable of overcoming both challenges. We will incorporate proteins from various viral origins passively into the rBV and evaluate their efficacy in either abolishing cellular viral defense mechanisms or enhancing virus uptake in different host cells lines. Initially, cellular uptake will be assessed using various mammalian cell lines to detect potential efficiency improvements. Next, the impact on transgene expression will be determined by analyzing protein levels of our model protein, ACE2*GFP. The most promising membrane protein candidates identified during the study will be utilized to generate stable insect cell lines, enabling the creation of pseudotyped rBV to explore potential synergistic effects.

In the last step, we intend to elucidate the mechanisms underlying enhanced transgene expression through modulation of host cell defense mechanisms by various viral proteins in knockout cell lines to pinpoint the precise downstream targets. This knowledge will assist in the establishment of novel producer cell lines for next-generation therapeutics.

PS1-V-PP04 RNA duplexes in the gas phase - can we use native electrospray ionization mass spectrometry to probe duplex formation and stability in solution?

Jonas Carlsson, Anna Razkova, Ronald Micura, Kathrin Breuker

Organic Chemistry, University of Innsbruck, Austria

Ribonucleic acids (RNA) play important roles in many cellular processes, including protein translation, in which transfer RNAs interact with messenger RNAs (mRNA) and ribosomal RNAs, the recognition of splice sites during mRNA splicing,[1] and the regulation of gene expression through RNA interference.[2] The ongoing discovery of new RNAs and RNA functions, as well as the recent development of RNA therapeutics, has sparked interest in new methodologies for characterizing RNA. In this context, research groups around the world are developing native mass spectrometry (MS) to study RNA structure and interactions. However, little is known to date about the stability of RNA secondary structures in the gaseous environment of the mass spectrometer.

The goal of this project is to contribute to the development of native MS of RNA by studying RNA duplex stability during and after transfer into the gas phase by electrospray ionization (ESI). As model systems for initial studies, we used four different 10 and 12 nt palindromic RNAs with closely related sequences and known duplex stabilities in solution.[3] Native ESI MS of a mixture of the four RNAs gave signals corresponding only to palindromic, but not mismatched, duplexes. This finding demonstrates that even relatively small RNA duplexes can survive transfer into the gas phase, and that the ESI process does not produce species from nonspecific RNA association. Moreover, ESI of solutions at different pH produced monomer and duplex ions whose relative abundances well reflected the extent of alkaline denaturation[4] of the duplexes in solution.

Finally, to investigate RNA duplex stability in the complete absence of solvent, the gaseous duplex ions were subjected
to vibrational activation using energetic collisions with inert gas. These experiments revealed a clear correlation between gas phase and solution stabilities, indicating intact Watson-Crick base pairing, but also showed that ion net charge critically affects RNA duplex stability in the gas phase.

References

1. doi:10.18388/abp.1998_4346

2. doi:10.1038/nature07758

3. doi: 10.1002/chem.202501860

4. doi:10.1261/rna.7177505

PS1-V-PP05 Recombinant AAV production: Insights from stable cell lines and adenovirus infection

Maria Toth, Manuel Reithofer, Astrid Dürauer, Reingard Grabherr

BOKU University, Austria

In their natural life cycle, AAVs enter the cells and integrate into the AAVSI locus of the cellular genome. If a helper virus (e.g. Adenovirus (AdV)) is present, the AAV genome is amplified and DNA containing AAV progeny particles are being produced. Recombinant adeno-associated viruses (rAAVs) that instead of AAV genes contain a gene of interest (GOI) are a valuable tool in gene therapy as they have a good safety profile and can be produced at large scales. However, the currently used transfection processes are costly and cause batch-to-batch variability. Furthermore, in contrast to the wild type AAV, the full to empty ratio of rAAV particles is in the range of 10-30% as compared to 90-100%. Yet, the reasons for the low packaging efficiency in rAAV production are unknown. In order to investigate and better understand what factors are crucial and whether stable integration of the GOI would be advantageous, we generated an engineered HEK293 cell line. A model GOI used for rAAV production - CMV-eGFP-WPRE - was integrated into the AAVSI locus of HEK293 cells with a copy number of one using the RMCE genome integration method. rAAVs were produced with the stable cell line and co-transfection of two plasmids (providing rep, cap and Adenovirus helper genes) and compared to the standard triple transfection process with the parental HEK293 cell line. To further investigate the reasons for the low full to empty ratio, both cell lines were infected with replication competent AdV during rAAV production. The GOI construct exhibits a very high eGFP expression, which might hinder AAV productivity of the stable cell lines. Therefore, the impact of a siRNA which represses eGFP was investigated.

Our experiments showed that the stable cell lines produce lower amounts of filled rAAVs as compared to the standard triple transfection. However, this effect can be alleviated by an antiviral response due to AdV infection and siRNA co-transfection.

Wild type AAVs are being produced in viral replication complex (VRC) in the nucleus which are formed by the helper virus. Recombinant AAV production was more efficient with the infection of adenovirus as compared to the helper plasmid which contained the DNA binding protein, E4 & VA RNA from adenovirus. This indicates that vital genes are missing in the helper plasmid.

This investigation of rAAV production from a stabe cell line with a genome integrated GOI offers a lot of possibilities to explore process optimization from a molecular biology aspect. This highlights that AAV production is still not fully understood and that the helper functions play a vital role in AAV productivity.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

S1: Neural circuits in health and disease

Chairs:

Sabine Liebscher
Institute of Neurobiochemistry, AT

Johannes Passecker
Medical University Innsbruck, AT

S1-IT01 Striatal neuromodulators in hallucination-like perception

Katharina Schmack

Francis Crick Institute, United Kingdom

Hallucinations are a hallmark of psychotic disorders such as schizophrenia, but their neural circuit mechanisms remain poorly understood. A major challenge is the difficulty of modelling hallucinations in species amenable to circuit-level neuroscience. To overcome this, we developed a cross-species computational-behavioural paradigm to quantify hallucination-like perception in both humans and mice. In humans, task-derived metrics correlated with self-reported hallucinations, validating its relevance to subjective experience. In mice, hallucination-like perception was related to altered dopamine and acetylcholine release in the striatum, pointing to a causal role for striatal neuromodulation. Computational modelling suggested that these neuromodulators encode perceptual expectations, supporting a model in which the striatum integrates sensory input with prior beliefs. Together, our results reveal a conserved mechanism for hallucination-like perception and establish a tractable circuit framework for studying hallucinations across species.

S1-ST01 Conformational and Functional Regulation of SET by Legumain Cleavage

Carina Horak, Alexander C. Wieland, Rupert Klaushofer, Peter Briza, Hans Brandstetter, **Elfriede Dall**

Universität Salzburg, Austria

The cysteine protease legumain typically localizes to the endolysosomal system, where it is an important player in the immune system. However, in the context of Alzheimer's disease (AD), legumain has been shown to be translocated to the cytosol, where it cleaves SET, synonymously termed TAF-1 or I2PP2A, an inhibitor of protein phosphatase 2A. SET is primarily found in the nucleus, where it regulates gene transcription, cell cycle progression, and histone acetylation, but can also translocate to the cytoplasm where it regulates cell migration and is implicated in neuronal apoptosis in AD. In this study, we demonstrate that legumain cleaves SET at two major sites: Asn16 at the N-terminal end and Asn175 at the earmuff domain. Contrary to previous findings, our biochemical and crystallographic experiments reveal that the corresponding N- and C-terminal cleavage products remain bound in a stable complex, rather than dissociating. Additionally, we show that the C-terminal acidic stretch of SET is essential for its binding to histone 1, and that cleavage impairs this interaction. Finally, we demonstrate that SET positively modulates PP2A activity. This effect is however abolished upon cleavage by legumain.

S1-ST02 Mu and delta opioid receptor polypharmacology as a promising strategy for effective analgesia with reduced CNS-mediated risks of tolerance and physical dependence

Mariana Spetea, Veronika Ernst, Maria Guastadisegni, Dominik Pircher, Barbara Brunner, Helmut Schmidhammer

Institute of Pharmacy, Universität Innsbruck, Austria

An adequate pain management, particularly chronic pain, is still an area of unmet medical need. Opioids are effective painkillers, with prolonged use of opioids being associated with analgesic tolerance, physical dependence, and addictive potential. Their pharmacological effects are mediated via the mu (MOR), delta (DOR) and kappa (KOR) opioid receptors. All opioid receptors subtypes are members of the seven-transmembrane-spanning G protein-coupled receptor (GPCR) family. The MOR is the primary molecular target for the therapeutic analgesia, but also for the adverse effects with intensive current research on strategies to mitigate the deleterious opioid-related side effects. The concept of polypharmacology (i.e. multitarget drugs) is a promising strategy to discover safer analgesics with additive analgesic effects through binding synergistic targets on the pain pathways at peripheral, spinal and supraspinal levels. In this study, we present the design and biological actions of a series of oxymorphone analogues that emerged as bifunctional MOR/DOR agonists. Binding studies showed the new oxymorphone derivatives to display very high (picomolar to subnanomolar) affinities to neuronal MOR, DOR and KOR in the rodent brain. They were very potent in activating the recombinant human opioid receptors. In mice, the oxymorphone analogues had antinociceptive efficacy after s.c. administration in acute and inflammatory pain models, mediated by both MOR and DOR. Chronic s.c. drug treatment did not cause antinociceptive tolerance and withdrawal syndrome. The dual activation of MOR and DOR by the novel oxymorphone analogues produces effective antinociception without the CNS-mediated liabilities of tolerance and physical dependence. These findings pave the way to new pain therapeutics with limited side effects following both acute and chronic use.

S1-ST03 Neurokraken - a fully flexible, open-source, python-based behavior platform for circuit neuroscience research

Alexander Wallerus, Sofia Castro e Almeida, Aron Koszeghy, Arsenii Petryk, Maja Überegger, Johannes Passecker

Institute of Systems Neuroscience, Medical University of Innsbruck, Austria

The ability to investigate the neural circuits foundational for information processing, learning, and decision formation is often limited by the difficulty of providing accurate and scalable complex experiences and interactions with detailed behavior measurements. Behavior setups are typically optimized for few, often simple tasks with constrained expandability, and priced prohibitively for scale. To address these challenges we developed Neurokraken, an open and flexible easy-use solution to enable easy pursuit of any experiment designs following any series of events and interactions that one can write in python. Neurokraken can integrate any electronics you can connect to a Teensy or Arduino and provides tracking of task variables, camera capturing for on- or offline analysis, easy task-relevant UIs/live plotting, and a library of 3D-printable components for modular experiment setups while keeping material costs in the 3 digits to make complex neuroscience experiments more accessible. Task-based or live Interventions can easily be achieved with demonstrated capabilities like real-time AI vision body tracking or optogenetics control. A wide range of established and novel tasks will be featured, including freely moving or head-fixed rodents interacting with complex environments through various interfaces. One novel task example showcases mice exploring and navigating a fully controllable avatar-based 2D game world using a joystick. We show that mice control the avatar and forage virtually for rewards, exhibiting emergent behaviors and adapting to dynamic challenges in the virtual space. This virtual environment enables a range of new experimental scenarios, previously constrained by physical limitations, to investigate behavior and its underlying neuronal circuits.

S1-ST04 Impact of distinct TDP-43 pathologies on neuronal health *in vivo*

Shenyi Jiang[1], Riddhi Petkar[1], XiaoQian Ye[1], Sabine Liebscher[2]

[1] Ludwig Maximilian University of Munich, Germany
[2] Institute of Systems Neuroscience, Medical University of Innsbruck, Innsbruck, Austria

Amyotrophic lateral sclerosis (ALS) is a devastating disease affecting ~4 in 100,000 people globally, with a lifetime risk of 1:400. It is characterised by progressive degeneration of upper and lower motor neurons, leading to muscle weakness, atrophy, spasticity, and eventual death from respiratory failure within 2-4 years. A key hallmark of ALS is the pathological change of TAR DNA-binding protein 43 (TDP-43). While physiologically localised in the nucleus where it functions as an essential RNA/DNA-binding protein, TDP-43 in ALS undergoes cytoplasmic mislocalisation and insoluble aggregate formation. Remarkably, while mutations in the TARDBP gene (encoding TDP-43) are rare (~4% familial, ~1.5% sporadic), TDP-43 pathology is observed in ~97% of all ALS cases and is also present in other neurodegenerative diseases like frontotemporal dementia or Alzheimer's disease. The actual role of distinct pathological TDP-43 forms for neuronal and network dysfunction, however, remains elusive to date.

To examine how TDP-43 subcellular localisation affects neuronal function, we developed an *in vivo* model system using adeno-associated virus-mediated neuronal expression of distinct human TDP-43 forms in mouse motor cortex. Our design included three constructs: (1) nuclear-localised wildtype TDP-43, (2) cytoplasmic-localised TDP-43 with mutations in the nuclear localisation sequence, (3) RNA-binding deficient cytoplasmic TDP-43 with enhanced aggregation propensity. The impact on neuronal health and function was assessed using immunostaining and *in vivo* two-photon calcium imaging in behaving mice. We found nuclear overexpression of TDP-43 caused rapid and severe neuronal death, in the absence of cytoplasmic mislocalisation and visible aggregation. In contrast, the two cytoplasmic TDP-43 forms did not induce overt rapid neurodegeneration. Concurrently, microglia morphology indicated strong reactivity to neurons overexpressing nuclear TDP-43 but not to those with cytoplasmic forms. Chronic *in vivo* calcium imaging uncovered distinct functional phenotypes associated with the different forms of TDP-43. Neurons expressing cytoplasmic-localised TDP-43 exhibited increased calcium transient frequency, potentially reflecting hyperexcitability. Conversely, neurons expressing cytoplasmic RNA-binding deficient TDP-43 and thus TDP-43 aggregates, showed decreased calcium signal frequencies. While nuclear overexpression seems readily toxic to neurons, cytoplasmic mislocalisation can have a divergent impact on neuronal function without causing direct neurodegeneration, depending on the solubility of the peptide. Our data thus argue for a more complex impact of varying forms of TDP-43 on neuronal health, which is critical for designing novel therapeutic approaches.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

S2: Environment and microbiology

Chairs:

Sigrid Neuhauser
University of Innsbruck, AT

Andrea Garvetto
Universität Innsbruck, AT

S2-IT01 Bacterial symbionts of protists and their unexplored impact on ecosystems

Astrid Collingro

Centre for Microbiology and Environmental Systems Science, University of Vienna, Austria

Protists, or single celled eukaryotes, constitute a large portion of the biomass on Earth. They play key roles in ecosystems like soil, sediments and the water column where they act as predators of microbes, serve as pray for higher trophic levels, and influence nitrogen and carbon fluxes. Many protists host bacterial symbionts, but most of these symbioses and their relevance in the environment are poorly understood, due to the challenges of cultivating both protists and their symbionts in the lab.

In this talk I will use amoebae and their chlamydial symbionts as a model to explore the versatility and ecological relevance of such symbioses. Summarizing findings from our lab I will show that such interactions are adaptable, ranging from parasitic to mutualistic, depending on the species, the surrounding conditions, and the presence of additional interaction partners like *Legionella pneumophila* or giant viruses. Furthermore, chlamydial symbionts affect the feeding behavior of amoebae in soil microcosms, thereby shaping the soil microbiome and influencing ecological cycles.

Together these results suggest that protist symbionts play a so far neglected role in ecosystems by impacting protist survival, microbiome composition, and biogeochemical processes and should be incorporated in existing models.

S2-ST01 Genomic and Experimental Analysis of Bacteria Interacting with *Serpula lacrymans*

Katharina Russ[1], Miguel Rodríguez-Rojas[2], Martin Kirchmair[1], Susanne Zeilinger[1], Sigrid Neuhauser[1]

[1] Department of Microbiology, University of Innsbruck, Austria
[2] Digital Science Center, University of Innsbruck

One of the most potent brown rot fungi on timber is *Serpula lacrymans*, which colonises houses in temperate and boreal regions around the world. The initial colonization with *S. lacrymans* is usually preceded by water damage, as its optimum growth rate is at a moisture level of 30-40%. If there is limited ventilation in addition to high moisture levels, which is often the case in cellars, *S. lacrymans* grows at a faster rate. As soon as the fungus has established itself on built timber, it begins to degrade cellulose and hemicellulose. When *S. lacrymans* is degrading timber in buildings, it has to be taken into account that the fungus does not occur alone, but is accompanied by other fungi and bacteria. Accordingly, it has been shown that bacteria influence the behaviour of *S. lacrymans* in culture. Both bacteria and fungi have a huge set of carbohydrate active enzymes (CAZymes) which play crucial roles in both building and breaking down complex carbohydrates and glycoconjugates. Bacteria, similar to fungi, have biopolymer-degrading properties and therefore may help *S. lacrymans* to attack wood. By identifying the CAZymes encoding genes, we can gain a better understanding of the biodegradation machinery of the tested bacteria. Aim of this study is to identify CAZymes form *S. lacrymans* associated bacteria, which have previously been isolated from fungal fruiting bodies, and test how bacteria with different CAZyme profiles interact with *S. lacrymans* in microcosm experiments.

S2-ST02 Regulation of 6-pentyl-α-pyrone production in *Trichoderma atroviride*: The role of *pks1* and beyond

Alexander Eschlböck[1], Daniel Flatschacher[1], Siebe Pierson[1], Ulrike Schreiner[1], Valentina Stock[2], Arne Schiller[2], David Ruso[3], Maria Doppler[3], Veronika Ruzsanyi[2], Mario Gründlinger[1], Rainer Schuhmacher[3], Susanne Zeilinger[1]

[1] Department of Microbiology, Universität Innsbruck, Austria
[2] Institute for Breath Research, Universität of Innsbruck, Innsbruck, Austria
[3] Department of Agrobiotechnology IFA-Tulln, Institute of Bioanalytics and Agro-Metabolomics, University of Natural Resources and Life Sciences Vienna (BOKU), Austria

The filamentous fungus *Trichoderma atroviride* is a widely used biocontrol agent recognized for its mycoparasitic, antibacterial and antifungal activities. These properties are largely driven by the production of diverse specialized metabolites (SMs). Among them, 6-pentyl-α-pyrone (6-PP) is one of the most prominent, known for its characteristic coconut aroma and its broad biological activities, including antifungal, antibacterial and plant growth-promoting effects. Despite its relevance, the molecular biosynthesis of 6-PP has remained elusive. We recently identified the polyketide synthase *pks1* as essential for 6-PP biosynthesis via CRISPR/Cas9 mediated gene deletion. Functional analysis of the obtained Δ*pks1* mutant confirmed the loss of 6-PP production and revealed impaired mycoparasitic ability, reduced antifungal activity and altered interactions with plants, demonstrating a direct link between *pks1* and key biocontrol effects of *T. atroviride*. To further elucidate the biosynthetic pathway of 6-PP, we performed HPTLC- and LC-MS-based metabolite profiling combined with metabolic network analysis. This approach enabled the identification of putative biosynthetic intermediates or precursors, supporting the polyketide origin of 6-PP. Moreover, cultivation under varying environmental conditions, together with gene expression analyses, provided insight into regulatory factors influencing 6-PP production. Finally, we explore the self-protection strategies employed by *T. atroviride* to identify potentially autotoxic effects of 6-PP. These findings improve our understanding of SM biosynthesis in fungi and highlight *pks1* as a key factor for both fungal-fungal and plant-fungal interactions in the context of biological control.

S2-ST03 Knockout studies & molecular enyzmology of Coproheme decarboxylase: New insights into anaerobic heme biosynthesis

Nikolaus Falb, Stefan Hofbauer

Department of Natural Sciences and Sustainable Resources, Biochemistry, BOKU University Vienna, Austria

In the last decade it has been shown heme biosynthesis does not follow a universal pathway, but different organisms follow different routes of producing this essential molecule. Gram-positive or monoderm bacteria utilize the coproporphyrin dependent (CPD) pathway. Given the ubiquitousness of pathogenic organisms in this clade, the enzymological investigation of its individual steps is a prerequisite for the development of future antibiotics. Here the focus lies on Coproheme decarboxylase (ChdC), the terminal enzyme of the CPD pathway, catalysing the transformation of ferrous coproporphyrin III/coproheme to heme *b* by oxidative decarboxylation. This implies the necessity of an exogenous electron acceptor: In most studies hydrogen peroxide (H_2O_2) has been discussed and used as a model co-substrate. However H_2O_2, due to its cytotoxic effects and need for control is a sub-optimal substrate *in vivo*. This is especially relevant during anaerobic growth, where H_2O_2 and other reactive oxygen species (ROS) are under even tighter control.

First, we show through knockout studies on monoderm model organism *Bacillus subtilis* that Δ*chdC* strains exhibit heme auxotrophic behaviour during aerobic and anaerobic growth, highlighting the enzyme has likely no anaerobic alternative. By time resolved spectroscopy, liquid chromatography, mass spectrometry and polarographic oxygen level determination with free FMN and flavodoxins YkuN and YkuP of *B. subtilis*, the enzyme reaction under anaerobic conditions is studied and characterized.

S2-ST04 Importance of heme biosynthesis in Porphyromonas gingivalis

Jakob Ender, Christina Schäffer, Stefan Hofbauer

Department of Natural Sciences and Sustainable Resources, Institute of Biochemistry, Boku University, Austria

Porphyromonas gingivalis (Pg) is a Gram-negative, pathogenic bacterium that colonizes the oral microbiome and is recognized as a keystone pathogen in the development of periodontitis, a chronic inflammatory oral disease. Periodontitis is a leading cause of adult tooth loss and has been linked to systemic conditions such as Alzheimer's disease, cardiovascular diseases, and cancer.

P. gingivalis is characterized by the formation of distinct black-pigmented colonies, a feature attributed to the accumulation of iron-containing porphyrin heme b. Heme is an essential cofactor involved in various metabolic pathways. Gram-negative bacteria and eukaryotes typically synthesize heme via the protoporphyrin-dependent (PPD) heme biosynthesis pathway. However, *P. gingivalis* lacks many of the essential genes required for this pathway and has evolved alternative mechanisms to acquire this important cofactor. Interestingly, the terminal enzymes of the pathway are present in *P. gingivalis*. For instance, a protoporphyrin ferrochelatase (PpfC), which catalyzes the insertion of ferrous iron (Fe^{2+}) into protoporphyrin IX (PPIX) to form heme.

In *P. gingivalis*, PpfC contains a unique structural feature: a partially occupied [2Fe-2S] cluster. While this cluster is conserved in numerous prokaryotic and eukaryotic ferrochelatases, its precise function remains unclear. Investigating the heme biosynthesis pathway both in vitro and within the organism may provide novel insights into the role of the [2Fe-2S] cluster and the mechanisms of iron and heme utilization in *P. gingivalis*. To further explore the role of PpfC, we have generated a ferrochelatase knock-out strain (ΔppfC) and are characterizing its effect on growth and heme auxotrophy (inability to synthesize heme) under iron- and heme-limiting conditions.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

S3: The Multifaceted World of Lipids

Chairs:

Andreas Koeberle
University of Graz, AT

Sabrina Sailer
Medical University of Innsbruck, AT

S3-IT01 Delineating the role of lipoxygenases in innate immunity, thrombosis and wound healing

Valerie O'Donnell

Cardiff University, United Kingdom

Lipoxygenases (LOX) expressed by circulating blood cells are conserved across mammalian species and mice lacking these enzymes are protected against multiple vascular inflammatory conditions. On the other hand, the role of these enzymes in physiological healing is less clear, especially considering that LOXs generate many different bioactive lipids from several families. In this study, our current knowledge on the actions of LOXs, in particular the leukocyte isoform 12/15-LOX (mice) or 15-LOX (human), and platelet isoform 12-LOX, in innate immunity, thrombosis and wound healing will be summarised. Discovery and characterisation of families of oxidized phospholipids generated through the Lands cycle will be described, summarising recent studies on their roles in driving thrombosis in rheumatoid arthritis and abdominal aortic aneurysm. A study on the role of 12/15-LOX in physiological wound healing will show how multiple lipids from the enzyme act together to activate an anti-inflammatory programme driven by PPARγ.

S3-ST01 Distinct functions of cycloartenol-derived sterols in plants

Hubert Schaller

Institut de biologie moléculaire des plantes, IBMP CNRS, France

Plants present dis-nct sterol biosynthe-c features compared to most of the metazoans and other organisms. Their sterol profiles display several types of 24-alkyl-sterols in propor-ons that vary quite a lot rela-vely to organs or evenmore to cell types. In addi-on, plants use a mandatory route to convert 2,3-oxidosqualene to cycloartenol thereby defining a cyclopropylsterol biosynthe-c segment, from which pathway end-products are biosynthesized. This is shown to exert a specialized func-on in the gametophy-c phase of the plant life cycle. It is proposed that the raison d'être of the chemical diversity of sterols exceeds the role of these lipids as modulators of membrane proper-es. Plants harboring chemical or gene-c inhibi-ons of the sterol pathway have dis-nct morphogene-c and developmental deficiencies according to steroidogenic genes or enzymes that are affected, such as the Arabidopsis mutants defec-ve in sterol-C24-methyltransferases. The loss of 24-ethylsterols in such mutants, maintaining the biosynthesis of 24-methylsterols and brassinosteroids, suggests specific roles of 24-ethylsterols. Here, we will discuss physiological implica-ons of cyclopropylsterols and 24-ethylsterols towards a refined understanding of plant sterol biology.

S3-ST02 Illuminating neurosecretion: Optogenetic and click chemistry novel tools highlight the multiple roles of phosphatidic acid in neurotransmitter release.

Alexander Wolf, Emeline Tanguy, **Nicolas Vitale**

INCI CNRS UPR3212, France

The orchestrated release of neurotransmitters or hormones by secretory cells involves many vesicular trafficking steps for efficient and rapid release. In addition to key proteins, the contribution of lipids in these various steps along the secretory pathway has been recently postulated. Among them, phosphatidic acid (PA), the simplest glycerophospholipid, has been proposed to play pivotal roles in key trafficking steps, especially in membrane fusion and fission events, where lipid remodeling is deemed crucial.

For instance, using genetic knockdown, pharmacological inhibition of PA-producing enzymes, and PA sensors, we have highlighted the diverse contribution of this phospholipid across multiple stages of neurosecretion. Furthermore, lipidomic analysis of fractionated membranes has revealed the widespread presence of PA in numerous subcellular compartments and its active modulation during cellular stimulation. This sheds light on the complexity of PA signaling, with the existence of different PA pools defined not only in space, but also in time. However, establishing a functional link between these pools and the multiple functions attributed to PA has remained impossible using currently available tools. Hence, to overcome both spatial and temporal limitations, we developed a novel optogenetic strategy targeting lipid metabolism to specific organelles and new PA clickable PA analogues.

Hence, using light sensible PA metabolism enzymes to induce recruitment at specific subcellular membranes, we achieved by the minute modulation of PA levels within specific compartments. This precise control of PA levels coupled with confocal imaging to monitor exocytic sites enabled us, for the first time, to establish insights into the distinct pools of PA involved in specific steps of the secretory pathway. Furthermore, to preserve the biological properties of PA synthetic analogues, we developed a novel strategy for the synthesis of azide-based analogues allowing specific fatty acyl chain positioning. After functional validation of mono and poly-unsaturated forms of PA analogues in bovine chromaffin cells, we characterized their functional interactome during neurosecretion leading to the identification of known PA-interactors involved in exocytosis and many additional potential novel interactors. Altogether, these results validate the versality of these tools to study the biological activities of PA and could be extended to other glycerophopsholipids.

S3-ST03 A Ketogenic Diet boosts Neuroblastoma Immunotherapy in mice

Victoria E. Stefan[1], Daniela D. Weber[1], Laura M. Roppelt[1], Julia Tevini[1], Stefanie Gaisbauer[1], Sara Huber[1], Evon Poon[2], Louis Chesler[2], Barbara Kofler[1]

[1] Department of Pediatrics, University Hospital of the Paracelsus Medical University Salzburg, Austria
[2] Division of Clinical Studies, The Institute of Cancer Research, London, UK

Neuroblastoma is one of the most common pediatric malignancies with poor prognosis for high-risk patients. Although immunotherapy has improved survival rates, its efficacy is hindered by severe side effects. A ketogenic diet (KD) has shown potential as an adjunct to neuroblastoma therapy in preclinical models and synergy with immunotherapy in various cancers. This study evaluates the potential of a KD in enhancing the effect of chemo- and immunotherapy on tumor growth and survival in an immunocompetent mouse model of neuroblastoma.

An immunocompetent NB model was established using syngeneic allografts derived from the transgenic TH-MYCN mouse. When tumors reached ~75 mm^3, mice were randomized to receive either a KD with an 8:1 ketogenic ratio of fat to carbohydrates + protein or a control diet, alone or in combination with temozolomide chemotherapy (2.5 mg/kg, intraperitoneally, three times per week) and/or anti-GD2 immunotherapy (4 mg/kg, intraperitoneally, twice per week). Tumor sizes were measured twice weekly using calipers, and mice were euthanized when tumors reached 1300 mm^3.

A standalone ketogenic therapy did not reduce tumor growth in MYCN-overexpressing neuroblastoma. However, when combined with temozolomide, KD modestly slowed tumor growth and significantly improved survival compared to untreated controls. KD showed synergy with anti-GD2 immunotherapy, leading to complete tumor regression in 80% of mice and 100% survival beyond the 4-week treatment window, compared to 40% survival in mice receiving immunotherapy and a control diet. Notably, the triple treatment with KD, temozolomide, and anti-GD2 showed no added benefit over the KD-immunotherapy combination.

These findings reveals that a KD strongly synergizes with anti-GD2 immunotherapy, effectively abrogating tumor growth and improving survival in an immunocompetent neuroblastoma model. This indicates a KD as a promising adjunct treatment strategy for neuroblastoma. Metabolomics, single cell transcriptomics and multiplexed immunofluorescence imaging will unravel potential underlying mechanisms of the KD-induced antitumor effects.

S3-ST04 Mathematical modeling of lipid diversity by reconstructing lipid class specific fatty acyl compositions

Janik Kokot, Markus Keller

Institute of Human Genetics, Medical University of Innsbruck, Austria

Lipids are complex molecules whose functions are highly dependent on their class and specific fatty acyl side chain composition. Their modular nature gives rise to a huge combinatorial diversity and an interdependent network of metabolic pathways that often reacts sensitively to nutritional inputs and perturbations caused by disease states. Alterations in this reaction network can lead to shifts in abundance and composition of lipid classes, ultimately disrupting membrane dynamics, signaling pathways, and energy homeostasis.

Fatty acyl side chain information is often missing in literature as lipids are only reported at the species level, which makes a comprehensive interpretation of respective datasets more difficult. To recover the unresolved fatty acyl side chain composition of complex lipid profiles without the need for prior MS2-based annotation, we developed a lipid side chain substitution model that computes theoretical, combinatorial lipid profiles from fatty acid profiles. By fitting the model to experimental lipid profiles at the species level, the fatty acyl profiles are recovered.

We validated our workflow using three cardiolipin data sets, covering various conditions and organisms. The reconstructed fatty acyl profiles align closely with experimental data in cultured mammalian cells and tissue samples. The fatty acyl composition of bacteria, which show much narrower lipid profiles, are challenging to reconstruct since multiple distinct fatty acyl profiles can explain the same species level lipid profile.

Our fatty acyl modeling approach not only augments published, “historical” datasets, but also creates the opportunity to recover and impute unresolved fatty acyl information in large scale lipidomics experiments and makes them compatible with different in-depth analysis workflows. Moreover, the combinatorial model may serve as a valuable neutral benchmark for validating the plausibility of lipid annotations. For this reason, we not only provide the model as an open-source Python package but also host it as an easy-to-use web server called “Fatty Acylizer”.

By enhancing quality and depth of side chain substitution information in lipidomic data, Fatty Acylizer is a valuable tool to not only describe, but also explain fatty acyl compositions, laying important groundwork for future predictive models, which in turn is key for uncovering the mechanistic origins of lipid diversity and specificity.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

S4: Aging, mental health, exercise and metabolism

Chairs:

Markus Mandl
JKU Medical Faculty, AT

Katharina Hüfner
Medical University Innsbruck, AT

S4-IT01 Histological aging signatures enable tissue-specific disease prediction from blood

Ernesto Abila[1], Iva Buljan[1], Yimin Zheng[2], Zhilong Weng[3], Maja Nackenhorst[4], Wolfgang Hulla[5], Yuri Tolkach[3], Adelheid Woehrer[6], **Andre Rendeiro[1]**

[1] CeMM Research Center for Molecular Medicine, Austria
[2] CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences, Austria
[3] Institute of Pathology, University Hospital Cologne, Cologne, Germany
[4] Department of Pathology, Medical University of Vienna, Vienna, Austria
[5] Institute of Pathology, Landesklinikum Wiener Neustadt, Wiener Neustadt, Austria
[6] Division of Neuropathology and Neurochemistry, Department of Neurology, Medical University of Vienna, Vienna, Austria; Department of Pathology, Neuropathology and Molecular Pathology, Medical University of Innsbruck, Innsbruck, Austria

Aging, the leading risk factor for numerous diseases, manifests through diverse structural and architectural changes in human tissues, providing an opportunity to quantify and interpret tissue-specific aging. To address this, we present a comprehensive assessment of tissue changes occurring during human aging, utilizing a vast array of whole slide histopathological images from the Genotype-Tissue Expression Project (GTEx), primarily reflecting non-diseased tissue samples. Using deep learning, we analyzed 25,712 images from 40 distinct tissue types across 983 individuals, quantifying nuanced morphological changes that tissues undergo with age.

We developed 'tissue clocks'—predictors of biological age based on tissue images—which achieved a mean prediction error of 4.9 years. These clocks were associated with established aging markers, including telomere attrition, subclinical pathologies, and comorbidities. In a systematic assessment of biological age rates across organs, we identified pervasive non-uniform rates of aging across the human lifespan, with some organs exhibiting earlier changes (20-40 years old) and others showing bimodal patterns of age-related changes. We also uncovered several associations between demographic, lifestyle, and medical history factors and tissue-specific acceleration or deceleration of biological age, highlighting potential modifiable risk factors that influenced the aging process at the tissue level. Finally, by combining paired histological images and gene expression data, we developed a strategy to predict tissue-specific age gaps from blood samples. This approach was validated in independent cohorts covering eight diseases, ranging from acute conditions like stroke to chronic diseases such as cystic fibrosis and Alzheimer's disease. It successfully recovered significant associations with disease-relevant organs and revealed patterns of systemic and tissue-specific aging that may reflect broader physiological changes in health and disease.

This work offers a new perspective on the aging process by positioning tissue structure as an integrator of cellular and molecular changes that reflect the physiological state of organs in health and disease. It underscores the value of histopathological imaging as a tool for understanding human aging and provides a foundation for the monitoring of tissue-specific aging processes in age-associated diseases.

S4-ST01 Combining exercise and hypoxia to promote healthy brain aging – a review

Johannes Burtscher, Katharina Hüfner

University of Innsbruck, Austria

The brain depends on a continuous supply of oxygen and nutrients in the blood. With advancing age both the supply with and the consumption of oxygen become less efficient. This likely contributes to the development of age-related brain diseases, such as neurodegenerative diseases like Alzheimer's disease and Parkinson's disease, but also diseases related to mental health, including depression and anxiety [1]. Regular physical exercise is a potent protective factor against age-related neuropsychiatric diseases, although mechanistically exercise induced benefits on brain-aging are poorly understood.

We present evidence of impaired physiological responses to reduced oxygen availability ("hypoxia"), oxygen transport (cardiovascular system and blood) and oxygen utilization (mainly mitochondria) in the aging brain [2]. Subsequently, reports on improvements of brain oxygenation by aerobic exercise will be summarized. Also, we will evaluate emerging theories about how humoral exercise responses and in particular how hypoxia responses following increased oxygen demand during exercise promote brain health. Implications about the therapeutic effects of ambient hypoxia alone and in combination with exercise on the brain will be discussed.

Moreover, we aim to put our ongoing research (e.g., [3]) on the effects of ambient hypoxia on the brain and brain diseases in the context of the existing literature. We conclude that controlled and well-selected doses of ambient hypoxia, exercise and the combination of both induce molecular and systemic hypoxia responses. Those may explain not only brain benefits due to controlled hypoxia exposures but may also represent crucial mechanisms in brain health-promoting effects of exercise.

References

[1] J. Burtscher, M. Niedermeier, K. Hüfner, E. van den Burg, M. Kopp, R. Stoop, M. Burtscher, H. Gatterer, G.P. Millet, The interplay of hypoxic and mental stress: Implications for anxiety and depressive disorders, Neurosci Biobehav Rev 138 (2022) 104718.

[2] J. Burtscher, R.T. Mallet, M. Burtscher, G.P. Millet, Hypoxia and brain aging: Neurodegeneration or neuroprotection?, Ageing Res Rev 68 (2021) 101343.

[3] C. Gstir, T. Schurr, R. Ehlers, J. Burtscher, J. Sperner-Unterweger, K. Hüfner, Is it Possible for Individuals with Pre-Existing Mental Disorders to Perform Mountain Sports at High Altitude—First Evidence from a Pilot Cross-Sectional Questionnaire Study, High Alt Med Biol accepted (2024).

S4-ST02 Going to altitude with anxious-depressive symptoms - a randomized pilot trial in individuals with and without mental disorders

Linda K. Rausch[1], Victoria Essl[2], Philipp Stürner[1], Tonja Grillenberger[2], Sebastian Färber[1], Johanna Gostner[3], Carina S. Bichler[2], Barbara Mangweth-Matzek[2], Anne Hecksteden[4], Jannes Hantschel[2], Philipp Nelles[2], Martin Faulhaber[1], Hannes Gatterer[5], Željko Pedišić[6], Barbara Sperner-Unterweger[2], Katharina Hüfner[2]

[1] Department of Sport Science, University of Innsbruck, Austria
[2] Department of Psychiatry, Psychotherapy, Psychosomatics and Medical Psychology, University Hospital for Psychiatry II, Medical University of Innsbruck
[3] Division of Medical Biochemistry, Medical University of Innsbruck
[4] epartment of Sport Science, University of Innsbruck; Institute of Physiology, Medical University Innsbruck
[5] Institute of Mountain Emergency Medicine, Eurac Research, Bolzano, Italy.
[6] Institute for Health and Sport, Victoria University, Melbourne, Australia

Acute exposure to hypoxia may impact affective responses and state anxiety among patients with anxious-depressive symptoms. These effects may be linked to alterations in neurotransmitter systems, particularly the serotonin pathway. Previous research suggests that hypoxic conditions can trigger biological processes that shift tryptophan (TRP) metabolism toward the kynurenine (KYN) pathway, potentially impacting mood regulation. Given the associations between altered KYN/TRP metabolism, reduced serotonin availability, and increased depressive or anxious symptoms, hypoxia may serve as a physiological stressor capable of modulating affective states through this biochemical route. This study aims to explore the potential relationship between neurotransmitter precursor amino acids and acute exposure to hypoxia, as well as how this interaction may influence affective responses.

Participants (n= 30) are screened for medical fitness and symptoms of anxiety or depression and complete both 6-hour sessions in a normobaric hypoxic chamber – one in simulated altitude condition (equivalent to 3800m) and one under a placebo (normoxic) condition. Blood samples and symptom assessments using the State-Trait Anxiety Inventory (STAI) and Beck Depression/Anxiety Inventory (BDI, BAI) are collected before and after each session. Affective responses are assessed hourly using the Positive and Negative Affect Schedule (PANAS), the Felt Arousal Scale (FAS), and the Feeling Scale (FS).

We hypothesize that six hours of acute hypoxia (vs. normoxia) will increase KYN/TRP ratios and proinflammatory levels (neopterin) during and after exposure in all participants and that these changes will be associated with heightened anxious-depressive symptoms post-exposure in affected individuals.

Nonetheless, this study represents an important first step toward understanding the neurobiological mechanisms underlying affective responses to acute hypoxia. Insights from this research may contribute to developing evidence-based safety recommendations for high-altitude exposure, particularly for individuals with underlying psychiatric vulnerabilities.

S4-ST03 Role of Dipeptidyl peptidase-4 in Adipose stem/progenitor cells

Sonja Großmann[1], Florian Hatzmann[1], Petra Waldegger[1], Tina Deutinger[2], Gerhard Pierer[2], Werner Zwerschke[1]

[1] University Innsbruck, Austria
[2] Department of Plastic and Reconstructive Surgery, Innsbruck Medical University, Innsbruck, Austria

Adipose stem/progenitor cells (ASCs) are part of the stromal vascular fraction of white adipose tissue (WAT), necessary for maintaining tissue homoeostasis, regeneration and expansion. Only a few markers are described for the characterisation of ASC. We found that the expression of dipeptidyl peptidase-4 (DPP4) on the cell surface subdivides the DLK1−/CD34+/CD45−/CD31− ASC pool of human WAT into two large populations. DPP4- cells possess lower proliferative and self-renewal capacity, while their adipogenic capacity is higher compared to DDP4+ ASCs. The DPP4 knock-down in ASC reduces proliferative and self-renewal capacity and increases adipogenic differentiation. Overexpression of DPP4 inhibits adipogenesis. Our data suggest that DPP4 is a functional marker for an abundant ASC population in human WAT with high proliferation and self-renewal potential and low adipogenic differentiation capacity.

S4-ST04 Epicardial adipose tissue as an underestimated factor of cardiovascular diseases: Isolation and characterization of functional adipogenic stem-/progenitor cells to study pathophysiological processes *in vitro*

Elisabeth Heuböck[1], Peter Benedikt[2], Florian Huber[2], Olga Mamunchak[2], Charnkamal Singh Bhogal[1], Michaela Kotnik[1], Esma Hamzic-Jahic[1], Sara Lugmayr[1], Verena Charwat[1], Andreas Zierer[2], David Bernhard[1], Markus Mandl[1]

[1] Abteilung für Pathophysiologie, Johannes Kepler Universität Linz - Zentrum für medizinische Forschung, Austria

[2] Department of Cardiac, Vascular and Thoracic Surgery, Kepler University Hospital Linz, Linz, Austria

Background and aims

Epicardial Adipose Tissue (EAT) is a highly metabolically active, visceral fat depot directly adjacent to the myocardium. Under physiological conditions, EAT exerts a variety of cardioprotective functions, predominantly through its "brown-like" adipocyte status. During aging, this tissue undergoes a 'brown-to-white' transition associated with a pro-inflammatory phenotype. Due to the physical proximity to the heart, EAT hereby directly affects cardiac functions, contributing to the pathogenesis of cardiovascular disease, plaque formation, atrial fibrillation and fibrosis. However, as EAT is almost absent in rodents, new models are required to study pathophysiological alterations in this fat depot. The objective of this project is therefore to characterize human EAT samples and to isolate Adipocyte stem/progenitor cells (ASCs) to gain appropriate cells for EAT-specific *in vitro* differentiation studies.

Methods

EAT samples were obtained from patients who underwent a cardiac surgery with a full sternotomy and who gave their informed written consent according to the Declaration of Helsinki. Each tissue sample was cut into three parts to obtain material for histology, RNA/protein- and ASC isolation, respectively. Immunohistochemistry was performed on cryosections to analyze adipocyte morphology among others. Simultaneous RNA/protein isolation was done using Trizol. A reproducible protocol for isolating ASCs from the stromal-vascular fraction was established using the Miltenyi OctoDissociator. Stemness was evaluated through trilineage differentiation assays.

Results

Whole-tissue staining using a specific Perilipin1 (PLIN1) antibody showed a characteristic adipocyte-specific pattern and provided the basis for in depth quantification of intracellular lipid droplets. Isolated ASCs from EAT showed strong and consistent viability and proliferation rate, and were able to reliably differentiate into adipogenic, chondrogenic, and osteogenic lineages. This trilineage differentiation was confirmed by RT-qPCR and immunofluorescence.

Outlook

Further validation of the stemness of the identified cell population will be achieved through single-cell sequencing to elucidate their transcriptomic profiles, alongside surface marker analysis using FACS. Additionally, their differentiation potential towards cardiomyocytes will be explored, providing insights into their therapeutic relevance and applicability.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

Life Sciences Awards Austria 2025

Moderator:

Michael Sauer
OMV AG, AT

Awards sponsored by

Life Sciences PhD Award Austria 2025 – Basic Science *Sponsored by* Boehringer Ingelheim

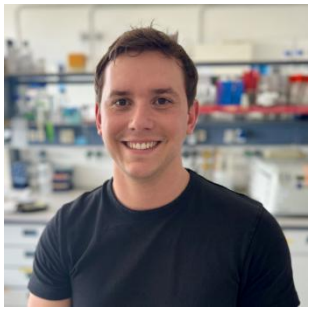
LS-ST01 The Dsc ubiquitin ligase complex identifies transmembrane degrons to degrade orphaned proteins at the Golgi

Yannick Weyer, David Teis

Institute of Molecular Biochemistry, Medical University of Innsbruck, Austria

The Golgi apparatus is essential for protein sorting, yet its quality control mechanisms are poorlyunderstood. Here we show that the Dsc ubiquitin ligase complex uses its rhomboid pseudo-proteasesubunit, Dsc2, to assess the hydrophobic length of α-helical transmembrane domains (TMDs) at the Golgi. Thereby the Dsc complex likely interacts with orphaned ER and Golgi proteins that have shorter TMDs and ubiquitinates them for targeted degradation. Some Dsc substrates will be extracted by Cdc48 for endosome and Golgi associated proteasomal degradation (EGAD), while others will undergo ESCRT dependent vacuolar degradation. Some substrates are degraded by both, EGAD- or ESCRT pathways. The accumulation of Dsc substrates entails a specific increase in glycerophospholipids with shorter and asymmetric fatty acyl chains. Hence, the Dsc complex mediates the selective degradation of orphaned proteins at the sorting center of cells, which prevents their spreading across other organelles and thereby preserves cellular membrane protein and lipid composition.

Life Sciences PhD Award Austria 2025 – Applied Research *Sponsored by*



LS-ST02 Preparing for Future Pandemics:Rapid Virus Identification in Resource-Limited Settings and Modeling Zoonotic Virus Infections in Natural Reservoir Species

Max Josef Kellner

Helmholtz Zentrum für Infektionsforschung, Germany

The spillover of zoonotic RNA viruses into new host populations poses a significant threat to global health and economies, as evidenced by recent outbreaks such as the West African Ebola epidemic, the COVID-19 pandemic, and the panzootic spread of H5N1 influenza. These events underscore the urgent need for enhanced surveillance and assays that can rapidly identify spillover infections, particularly in regions with frequent human–wildlife contact. Furthermore, advancing our understanding of host–pathogen interactions across species is critical for elucidating the molecular determinants of zoonotic viral diseases that are naturally avoided in reservoir species such as bats. My doctoral research addressed both needs through two complementary lines of investigation. First, I co-developed an open-source isothermal nucleic acid detection platform based on Loop-Mediated Isothermal Amplification (LAMP), enabling highly sensitive, colorimetric viral detection without the need for laboratory infrastructure. The system incorporates reagent lyophilization and streamlined sample preparation for field deployment, and was extensively validated with clinical specimens. Second, I established organoid models of mucosal barrier tissues from the Egyptian fruit bat, a natural reservoir for zoonotic RNA viruses including Marburg virus (MARV). These organoids preserved the cellular diversity and functional characteristics of native tissue, enabling direct comparisons of antiviral responses between bat and human epithelial cells. Bat organoids exhibited stronger innate immune responses to MARV, MERS-CoV, and SARS-CoV-2 than human counterparts, mediated by both constitutive and inducible interferon pathways. These findings revealed novel antiviral mechanisms that may underlie bats' resilience to viral disease and suggest new avenues for therapeutic development. Together, these advances integrate innovative diagnostic technologies with fundamental insights into host–virus biology, providing scalable approaches for rapid pathogen detection and novel perspectives on zoonotic disease resilience.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

Rising Star Lectures

Chair:

Joachim Seipelt
Nuvonis Technologies,
AT

Sponsored by

Bundesministerium
Wirtschaft, Energie
und Tourismus

Life Sciences Research Award Austria 2025 – Basic Science

Bundesministerium Wirtschaft, Energie und Tourismus

RS-ST01 A conserved fertilization complex bridges sperm and egg in vertebrates

Victoria E. Deneke[1], Andreas Blaha[1], Yonggang Lu[2], Johannes P. Suwita[1], Jonne M. Draper[1], Clara S. Phan[1], Karin Panser[1], Alexander Schleiffer[1], Laurine Jacob[1], Theresa Humer[1], Karel Stejskal[3], Gabriela Krssakova[1], Elisabeth Roitinger[3], Dominik Handler[3], Maki Kamoshita[1], Jeffrey E. Lee[4], Masahito Ikawa[5], Andrea Pauli[1]

[1] Research Institute of Molecular Pathology, Austria
[2] Premium Research Institute for Human Metaverse Medicine (WPI-PRIMe), Osaka University, Osaka 565-0871, Japan
[3] Institute of Molecular Biotechnology of the Austrian Academy of Sciences (IMBA), Vienna BioCenter (VBC), 1030 Vienna, Austria
[4] Department of Laboratory Medicine and Pathobiology, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canad
[5] Department of Experimental Genome Research, Research Institute for Microbial Diseases, Osaka University, Osaka 565-0871, Japan

Fertilization, the basis for sexual reproduction, culminates in the binding and fusion of sperm and egg. Although several proteins are known to be crucial for this process in vertebrates, the molecular mechanisms remain poorly understood. Using an AlphaFold-Multimer screen, we identified the protein Tmem81 as part of a conserved trimeric sperm complex with the essential fertilization factors Izumo1 and Spaca6. We demonstrate that Tmem81 is essential for male fertility in zebrafish and mice. In line with trimer formation, we show that Izumo1, Spaca6, and Tmem81 interact in zebrafish sperm and that the human orthologs interact *in vitro*. Notably, complex formation creates the binding site for the egg fertilization factor Bouncer in zebrafish. Together, our work presents a comprehensive model for fertilization across vertebrates, where a conserved sperm complex binds to divergent egg proteins—Bouncer in fish and JUNO in mammals—to mediate sperm-egg interaction.

Life Sciences Research Award Austria 2025 – Applied Research

Bundesministerium Wirtschaft, Energie und Tourismus

RS-ST02 Teaching a microbe how to breathe carbon monoxide: When transposons rewire metabolism

Rémi Hocq[1], Josef Horvath[2], Maja Stumptner[2], Mykolas Malevičius[3], Gerhard G. Thallinger[3], Stefan Pflügl[2]

[1] Institute of Chemical, Environmental and Bioscience Engineering, TU Wien, Austria
[2] Institute of Chemical, Environmental and Bioscience Engineering, Technische Universität Wien, Gumpendorfer Straße 1a, 1060, Vienna, Austria
[3] Institute of Biomedical Informatics, Graz University of Technology, Graz, Austria

Introduction

Acetogens are promising industrial biocatalysts for upgrading syngas—a gas mixture containing CO, H_2 and CO_2—into fuels and chemicals. However, CO severely inhibits growth of many acetogens, often requiring extensive adaptation to enable efficient CO conversion ("carboxydotrophy"). Despite the adverse impact of CO on growth rate, acetogenic conversion of CO through the Wood-Ljungdahl pathway (WLP) provides significantly more ATP compared to H_2 and CO_2. As a result, efficient CO uptake theoretically enables the conversion of syngas into ATP-intensive fuels and chemicals (e.g., butanol), which in turn makes engineering carboxydotrophy highly desirable to develop sustainable production processes based on syngas.

The thermophilic acetogen *Thermoanaerobacter kivui* has been previously shown to be adaptable to a carboxydotrophic lifestyle, although its growth rate on CO as sole carbon and energy source remained slow (T_d ~ 40 h, versus ~ 2h for H_2/CO_2). In addition, the precise mechanisms underlying CO adaptation have so far remained elusive, which impedes efforts to rationally engineer carboxydotrophy.

Objective

In this work, we aimed to create a robust chassis for thermophilic bioprocessing of syngas as well as to elucidate the cognate mechanisms conferring CO tolerance and utilization.

Method

We combined adaptive laboratory evolution, bioprocess engineering and multi-omics data analysis to generate a strain rapidly growing on CO as sole carbon and energy source, as well as to quantitatively and qualitatively evaluate its physiological, genetic and metabolic features. We additionally performed genome editing to validate the function of genes putatively linked with carboxydotrophy.

Findings

We adapted the thermophilic acetogen *T. kivui* to use CO as sole carbon and energy source. Isolate CO-1 exhibited rapid growth on CO and syngas (co-utilizing CO, H_2 and CO_2) in batch and continuous cultures (T_d ~ 2.8 h). The carboxydotrophic phenotype was attributed to the mobilization of a CO-dependent megatransposon originating from the locus responsible for autotrophy in *T. kivui*. Transcriptomics illuminated the crucial role the redox balance plays during carboxydotrophic growth. These insights were exploited to rationally engineer *T. kivui* to grow on CO.

Conclusion

Collectively, our work elucidates a primary mechanism responsible for the acquisition of carboxydotrophy in acetogens and additionally showcases how transposons can orchestrate evolution.

Life Sciences Research Award Austria 2025 – Excellence & Societal Impact

Bundesministerium Wirtschaft, Energie und Tourismus

RS-ST03 Systematic discovery of CRISPR-boosted CAR T cell immunotherapies

Paul Datlinger[1], **Eugenia V Pankevich[1]**, Cosmas D Arnold[1], Nicole Pranckevicius[1], Jenny Lin[1], Daria Romanovskaia[2], Moritz Schäfer[2], Francesco Piras[2], Anne-Christine Orts[1], Amelie Nemc[1], Paulina N Biesaga[1], Michelle Chan[1], Teresa Neuwirth[1], Artem V Artemov[3], Wentao Li[1], Sabrina Ladstätter[1], Thomas Krausgruber[2], Christoph Bock[2]

[1] CeMM Research Center for Molecular Medicine, Austria
[2] CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences, Medical University of Vienna, Institute of Artificial Intelligence, Center for Medical Data Science
[3] Medical University of Vienna, Institute of Artificial Intelligence, Center for Medical Data Science

CAR T cell therapy has shown remarkable success in treating blood cancers, but CAR T cell dysfunction remains a common cause of treatment failure. Here we present CELLFIE, a CRISPR screening platform for enhancing CAR T cells across multiple clinical objectives. We performed genome-wide screens in human primary CAR T cells with readouts capturing key aspects of T cell biology, including proliferation, target cell recognition, activation, apoptosis and fratricide, and exhaustion. Screening hits were prioritized using a new *in vivo* CROP-seq method in a xenograft model of human leukemia, establishing several gene knockouts that boost CAR T cell efficacy. Most notably, we discovered RHOG knockout as a potent and unexpected CAR T cell enhancer, both individually and together with FAS knockout, which was validated across multiple *in vivo* models, CAR designs, and patient-derived samples. Demonstrating the versatility of the CELLFIE platform, we also conducted combinatorial CRISPR screens to identify synergistic gene pairs, and saturation base editing screens to characterize RHOG variants. In summary, we discovered, validated, and biologically characterized CRISPR-boosted CAR T cells that outperform standard CAR T cells in widely used benchmarks, establishing a foundational resource for optimizing cell-based immunotherapies

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

Abstracts – Day 2, Thu, 25.9

.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

Plenary 2

Chair:

Hesso Farhan
Medical University of Innsbruck, AT

Plenary Lecture

P2-PL01 Regulation of mitochondrial quality control and cellular bioenergetics during hypoxia

Anne Simonsen

Molecular Cell Biology, Oslo University Hospital, Norway

A healthy mitochondrial population is maintained through a series of quality control pathways and a fine-tuned balance between mitochondrial biogenesis and degradation. Disruption of this delicate balance leads to mitochondrial dysfunction and contributes to aging and several diseases such as neurodegeneration, cardiac disease, and cancer. Mitophagy involves lysosomal degradation of mitochondrial components and can be induced by a variety of stress and damage stimuli, including hypoxia. However, our mechanistic understanding of mitophagy is only just emerging, and no therapies currently target mitochondrial quality control.

We have recently screened for novel regulators of hypoxia-induced mitophagy in cells expressing mitochondrial reporters. I will here present data showing that several novel autophagy-related proteins are involved in the turnover of selective mitochondrial proteins in response to hypoxia-mimicking conditions and that the modulation of their expression levels is linked to changes in cellular bioenergetics and disease development both in vitro and in a zebrafish model.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

PhD Session

Chairs:

Angelika Seeber
University of Innsbruck, AT

Pablo Monfort-Lanzas
Medical University of Innsbruck, AT

PhD-ST01 Impact of the E2F1-BASP1 complex on regulating *MYC* expression

Lea E. Timpen, Leonie I. Weber, Tobias Kipura, Kane Puglisi, Marta de León, Marcel Kwiatkowski, Markus Hartl

Biochemistry, University of Innsbruck, Austria

The gene regulator MYC controls multiple cellular processes including cell proliferation and differentiation, but MYC is also aberrantly activated in multiple human tumours. For this reason, MYC is considered as major cancer driver representing a promising therapeutic target, although direct MYC inhibition has remained difficult. Therefore, indirect strategies targeting the MYC network appears to be a more suitable approach. One of the downregulated transcriptional MYC targets is the *BASP1* gene, encoding a neuronal signalling protein and a transcriptional corepressor. However, it was also observed that ectopic expression of BASP1 suppresses *MYC* mRNA expression, rendering MYC and BASP1 mutually exclusive. Furthermore, BASP1 overexpression interferes with MYC-induced cell transformation.

To investigate the regulation of *MYC* transcription in the context of BASP1, we performed a reverse chromatin immunoprecipitation (R-ChIP) screen using the colorectal cancer cell line SW480, and SW480 with a CRISPR-activated *BASP1* gene. Using biotin-labelled oligodeoxynucleotides targeting the *MYC* promoter region, crosslinked proteins were pulled down using streptavidin-coated magnetic beads. Subsequently, proteins were detected by mass spectrometry (MS). Thereafter, candidate proteins interacting with BASP1 were identified by co-immunoprecipitation (Co-IP) and other pull-down assays, and their influence on *MYC* transcription was tested by luciferase reporter gene assays.

The R-ChIP screen identified 541 unique proteins binding to the *MYC* promoter, and 107 thereof were specific for BASP1-expressing SW480. Among these, we have identified proteins that are known to interact with the cell cycle regulator E2F1. By performing Co-IP experiments, we found that BASP1 and E2F1 form a complex. Whereas E2F1 upregulates *MYC* transcription in SW480, the presence of BASP1 significantly reduces E2F1-mediated *MYC* activation.

A physical interaction between the cell cycle promoter E2F1 and the potential tumour suppressor BASP1 was discovered. By further investigating the function of the BASP1-E2F1 complex, we expect to gain more insight into the molecular mechanism of oncogenic *MYC* regulation, and to develop novel therapeutic strategies to target oncogenic functions of the gene regulators E2F1 or MYC.

PhD-ST02 Establishment of a transient ALFA-Tagged Uncoupling Protein 3 expression system in H9c2 cells to benchmark mitochondrial protein localization, detection, and isolation workflows

Felix Sternberg[1], **Julia Arapovic[1]**, Kilian M. Heisig[1], Jürgen König[1], Elena E. Pohl[2]

[1] Nutrition, University of Vienna, Austria
[2] Institute of Physiology, Pathophysiology and Biophysics, University of Veterinary Medicine, Vienna, Austria

Mitochondrial energy metabolism plays a central role in various diseases, including neurodegenerative disorders, obesity, type 2 diabetes, and cardiovascular conditions. Mitochondrial proteins coordinate key metabolic pathways such as fatty acid oxidation and glucose metabolism. Uncoupling protein 3 (UCP3), located in the inner mitochondrial membrane of non-proliferating cells including brown adipocytes, cardiomyocytes, and skeletal muscle cells, is upregulated during β-oxidation, characterized by elevated ATP production and maintained mitochondrial membrane potential (Φm). It has been proposed that proton transport via UCP3 is coupled to fatty acid anion export, contributing to Φm regulation. Despite its significance, the (patho-)physiological function of UCP3 and family members such as UCP2, involved in C4 metabolite transport, remains elusive, partly due to limitations in antibody specificity. To address this, we employed transient chemical transfection of H9c2 cardiomyoblasts with ALFA-tagged UCP3 (UCP3-ALFA), suitable as a positive control system for our endogenously tagged UCP2-ALFA cell line. The ALFA tag, a stable 15-amino-acid α-helix, enables highly specific detection via anti-ALFA antibodies. While not establishing a stable cell line, we aimed to validate microscopy staining protocols and optimize affinity purification of native UCP3-ALFA under physiological conditions. The tagged protein was confirmed via column chromatography, and its mitochondrial localization was visualized by immunofluorescence microscopy. This transiently expressed UCP3-ALFA system thus serves as a technical benchmark for establishing imaging and isolation workflows. Future work will apply these workflows to UCP2-ALFA and expand into the biophysical characterization of purified protein thereby investigating properties such as transport kinetics, dimerization, and interactions using fluorescence-based approaches.

PhD-ST03 The sugar connection: N-glycosylation and dimerization in myeloperoxidase biosynthesis

Urban Leitgeb, Paul Furtmüller, Isabella Fegerl, Vera Pfanzagl

Biochemistry, BOKU University, Austria

Myeloperoxidase (MPO) is a heme-containing enzyme essential for neutrophil-mediated killing of phagocytosed pathogens. During the neutrophilic oxidative burst, MPO uses H_2O_2 and halide ions to produce hypohalous acids within the phagosome[1]. The mature enzyme functions as a homodimer with two monomers linked by a single interdomain disulfide bond and each containing five N-glycosylation sites[2]. MPO biosynthesis involves multiple steps: In the endoplasmic reticulum (ER), MPO undergoes co-translational N-glycosylation, signal peptide cleavage, and heme incorporation. The intermediate proMPO exits the ER and undergoes propeptide removal, excision of a hexapeptide, dimerization and finally storage in azurophilic granules[3]. Despite its critical role in innate immunity, MPO biosynthesis is not yet fully understood, particularly the organization of post-ER processing events. Furthermore, the specific role of the five N-glycosylation sites in MPO biosynthesis and their significance for the enzyme's activity remain unclear.

In this study we examine the dimerization step in MPO biosynthesis and explores the impact of N-glycosylation on this process.

We report X-ray structural and small-angle X-ray scattering (SAXS) data for native dimeric MPO (dMPO), monomeric MPO (mMPO), and deglycosylated monomeric MPO (mMPOdg) in combination with biochemical and biophysical analyses. While the crystal structure of mMPO remains dimeric with minor structural differences compared to dMPO, mMPOdg crystallizes as a monomer in a distinct space group and with a different crystal morphology. Furthermore, SAXS data reveal a significant reduction in homodimer affinity for mMPOdg compared to mMPO. Despite these differences, mMPO and mMPOdg retain an enzymatic activity similar to dMPO, though differential scanning calorimetry (DSC) and circular dichroism (ECD) data show reduced thermostability. In summary, these findings emphasize the critical role of MPO N-glycans for dimer formation, leading to an enhanced protein stability. This highlights their importance in MPO biosynthesis, ensuring proper assembly of the mature enzyme and its efficient packaging into azurophilic granules.

[1] Segal, A. W. (2005). How neutrophils kill microbes. *Annu. Rev. Immunol.* **23**, 197–223.

[2] Zeng, J. & Fenna, R. E. (1992). X-ray crystal structure of canine myeloperoxidase at 3 Å resolution. *J. Mol. Biol.* **226**, 185–207.

[3] Nauseef, W. M. (2018). Biosynthesis of human myeloperoxidase. *Arch. Biochem. Biophys*. **642**, 1–9.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

Science Flashes 2

Angelika Seeber
University of Innsbruck, AT

Pablo Monfort-Lanzas
Medical University of Innsbruck, AT

PS2-S3-SF01 Orm2 at the crossroads between sterol and sphingolipid metabolism

Baris Bekdas, Oliver Schmidt, Niklas Schomisch

Cell Biology, Medical University Innsbruck, Austria

Sphingolipids (SL) play a major role in regulation of membrane structure and function. Besides, some (e.g. ceramides) act as important signaling molecules. Yet, SL biosynthesis intermediates are also toxic at elevated concentrations. Therefore, their synthesis in the endoplasmic reticulum (ER) is tightly controlled. The conserved ORMDL family proteins (in budding yeast: Orm1/2) are responsible for SL regulation by confining the rate-limiting enzyme serine-palmitoyl-CoA transferase (SPT) in an inhibited complex (called SPOTS complex). When SL levels are low or cells experience tensile plasma membrane (PM) stress, Orm1/2 dissociate from the SPOTS complex and the SPT enzyme becomes activated. Despite high amino acid sequence identity, Orm1/2 show some different features. E.g. Orm2 inhibits SPT more potently and is additionally regulated by subcellular localization and proteolysis. Whether Orm1/2 have additional functions that are independent of their role as SPT inhibitors is unknown.

We found that Orm2 mutants are hyper-sensitive to anti-fungal drugs that target the biosynthesis of ergosterol (the fungal cholesterol analogue), and also have altered levels and localization of sterols. Using mass spectrometry (MS)-based interactome studies, we found interactions of Orm1 and particularly Orm2 with several ER-localized enzymes involved in the synthesis of ergosterol. Sterols maintain plasma membrane structure and functions in concert with SL, and the literature suggests nodes of communication between the metabolic pathways of these two lipid species. Yet, the underlying molecular mechanisms are unknown. In this project, we investigate a potential new role of ORMDL family proteins in organizing sterol synthesis at the ER and coordinating it with SL metabolism.

PS2-S3-SF02 Beyond ether lipid metabolism: PEDS1 as an orchestrator in immunology

Ilaria Dorigatti[1], Sarah Spöck[2], Denise Kummer[1], Katharina Lackner[3], Georg Golderer[1], Ernst R. Werner[1], Verena Labi[2], Katrin Watschinger[1]

[1] Medical University Innsbruck, Austria
[2] Institute for Developmental Immunology, Biocenter, , Medical University of Innsbruck, Innsbruck, Austria
[3] Institute of Human Genetics, Medical University of Innsbruck, Innsbruck, Austria

Plasmalogens, a subclass of ether lipids, are crucial for membrane organization and stability. Of note, they constitute a significant portion of immune cell membranes. Their synthesis is initiated in peroxisomes and finalized at the endoplasmic reticulum by the enzyme plasmanylethanolamine desaturase (PEDS1). PEDS1 inserts the characteristic vinyl ether double bond at the *sn*-1 position in plasmalogens. Our laboratory recently identified the gene for PEDS1 and a PEDS1-deficient mouse model is available.

In the mouse, disturbances in the first enzymes of ether lipid metabolism result in symptoms resembling those frequently reported in human patients suffering from ether lipid deficiencies arising in Rhizomelic Chondrodysplasia Punctata. These include severe neurological and behavioural symptoms, along with significant impact on bone, eye, and sperm development. Importantly, recent research highlighted significant alterations in the immune system and inflammation depending on plasmalogen levels.

Our examination of the impact of PEDS1 loss on the haematopoietic system revealed notable abnormalities in diverse blood parameters, determined through comprehensive blood count tests and complemented by ELISA analysis of blood serum. Interestingly, we identified a significantly increased number of B cells in the bone marrow and a trend towards impaired humoral immunity. This suggests a crucial role for plasmalogens in the antibody-mediated immune response. To further elucidate these findings we performed flow cytometry analysis on primary and secondary lymphoid organs harvested from PEDS1-deficient mice and controls. Moreover, an intriguing finding from an *in vitro*-induced germinal center B cell culture system unveiled a possible role for plasmalogens in the proficient secretion of immunoglobulins from these cells. These promising observations will be further investigated in an *in vivo* setting.

The overarching goal of our study is to unravel the molecular regulatory function of the metabolic enzyme PEDS1 within the hematopoietic and lymphoid system.

PS2-S7-SF01 Characterization of the trafficking of VIP36 and VIPL and identification of new cargos

Laura Sammarco, Veronika Reiterer-Farhan, Gabriele Stöckl, Hesso Farhan

Pathophysiology, Medicine University of Innsbruck, Austria

The transport of correctly folded secretory glycoproteins out of the endoplasmic reticulum (ER) to the Golgi apparatus is enabled by the coat protein complex type II (COPII) vesicles. Soluble secretory proteins are sorted into these COPII vesicles via so called cargo receptors. This work aims at a better understanding of the intracellular function of two putative cargo receptors VIP36/LMAN2 and VIPL/LMAN2L. These are transmembrane L-type lectins, which interact with the glycoproteins via their luminal domain. Although identified more than 3 decades ago, we know very little about VIP36 and VIPL with respect to the proteins they interact and how they exit the ER.

The first line of research focuses on trafficking of VIP36 and VIPL within the secretory pathway. Both the proteins have a potential cytoplasmic ER exit motif (FY) on their C-termini, while they present different C-terminal ER retrieval motifs: KR in VIP36 and RKR in VIPL. I used the Retention Using Selective Hooks (RUSH) system in combination with export/retrieval deficient mutants to deepen our understanding of how the trafficking is regulated. The potential role of FY motif as an ER export motif is supported by the slowdown of the export kinetics of the construct upon its substitution by alanines. I also investigated VIP36 and VIPL dependency on SEC24, the major cargo binding module within the COPII coat. Knockdown experiments targeting its four paralogs suggest a major involvement of SEC24 in the trafficking of both VIP36 and VIPL, which is impaired mostly by the depletion of SEC24A and SEC24B paralogs.

The second area of work focuses on the search for cargos for both VIP36 and VIPL. Initially we performed an Immunoprecipitation (IP) based approach using RUSH-constructs to distinguish interaction partners in the ER from those in the later secretory pathway. As an IP based approach could suffer from limitations due to the weakness of lectin-glycoprotein interaction we combine this approach screening the secretome of VIP36 and VIPL deficient HepG2 cells to gain a more comprehensive picture.

PS2-S7-SF02 Unveiling the subunit topology of BORC assemblies at the lysosomal membrane using crosslinking mass spectrometry

Martina A. Höllwarth[1], Eva Rauch[1], Victoria Vigorito[2], Luca L. Fava[2], Lukas A. Huber[1], Taras Stasyk[1]

[1] Cell Biology, Medical University of Innsbruck, Austria
[2] Armenise-Harvard Laboratory of Cell Division, Department of Cellular, Computational and Integrative Biology - CIBIO, University of Trento, Trento, Italy

The hetero-octameric BLOC-1-related complex (BORC) regulates lysosomal positioning by recruiting ADP-ribosylation factor-like protein 8 (Arl8) to the lysosomal surface. Arl8 subsequently facilitates anterograde lysosomal transport along microtubules through direct or indirect interactions with kinesin motor proteins. This process is negatively regulated under amino acid- or EGF-depleted conditions by the late endosomal/lysosomal adaptor and MAPK and mTOR activator (LAMTOR/Ragulator). In previous work, we have demonstrated that the BORC subunit Lyspersin serves as the linker between BORC and LAMTOR using chemical crosslinking. Beyond its role in positioning, BORC is also involved in lysosome-autophagosome fusion and lysosomal reformation. However, the molecular architecture and regulatory mechanisms governing these functions remain largely unknown.

Our objective is to elucidate the subunit topology of BORC protein assemblies, define the specific protein-protein interactions involved and investigate their structural dynamics under different physiological conditions. Therefore, we employ crosslinking mass spectrometry (XL-MS) on native BORC complexes isolated by affinity purification from cells expressing endogenously tagged BORC subunits.

Using CRISPR/Cas9 ribonucleoprotein-mediated knockin, we generated hTERT-RPE1 cells with N-terminally ALFA-tagged Diaskedin. This enables the pull-down of native BORC assemblies using ALFA-nanobody-immobilized beads. The purified complexes are subjected to crosslinking and following a bottom-up proteomics approach, crosslinked peptides are analyzed by liquid chromatography-tandem mass spectrometry (LC-MS/MS). To enhance the detection and identification of crosslinked peptides, we optimized the workflow by incorporating an immobilized metal affinity chromatography (IMAC)-enrichable crosslinker. Additionally, we improved the elution specificity by employing competitive elution with the ALFA-peptide, minimizing non-specific background.

We are currently optimizing the experimental workflow by refining the binding efficiency to ALFA-nanobody-immobilized beads, adjusting elution conditions, and evaluating alternative crosslinking strategies. Furthermore, we plan to go beyond steady-state conditions and enrich specific and functionally relevant crosslinks by applying different physiological perturbations, such as starvation/stimulation and also induction of cellular quiescence.

PS2-S8-SF01 Charged for action: precision delivery of an antimicrobial peptide via polymer-coated nanoparticles enhances efficacy

Marco Reindl, Verena Zach, Sebastian P. Schwaminger

Nano Lab, Division of Medicinal Chemistry, Medical University of Graz, Austria

The rapid rise of antibiotic-resistant bacteria poses a critical global health challenge, with infections caused by multidrug-resistant strains becoming increasingly difficult to treat with conventional antibiotics. This has resulted in higher rates of morbidity and mortality, as well as increased healthcare costs worldwide. New strategies are therefore urgently needed to enhance the effectiveness of antimicrobial agents while minimising the development of resistance.

One promising approach is the use of targeted drug delivery systems to improve the stability, bioavailability and efficacy of antimicrobial compounds. In this study, we developed a novel delivery platform based on iron oxide nanoparticles (IONPs) that are coated in situ with a copolymer of acrylic acid and methacrylic acid [poly(AA-co-MAA)]. This coating strategy introduces carboxylate groups that enable the binding of cationic peptides with a high capacity through electrostatic interactions. The resulting particles had a hydrodynamic diameter of 137 nm and zeta potential ranging from –35 to –41 mV), indicating excellent stability in aqueous solutions.

We then investigated the loading of the cationic antimicrobial peptide lasioglossin-III (LL-III) onto the coated nanoparticles. LL-III was rapidly and efficiently absorbed into the nanoparticles in PBS according to a Sips isotherm, with a maximum adsorption capacity of 0.82 g/g at a LL-III concentration of 4 g/L. Following three PBS washing steps, 49% of the peptide could be retained, suggesting stable interactions driven by electrostatics and hydrophobic effects. This performance exceeds the adsorption of bare IONPs and other nanoparticle systems reported in the literature.

Cytotoxicity assays using 3T3 fibroblasts and HEK cells confirmed that both unloaded and LL-III-loaded nanoparticles were non-toxic, highlighting their biocompatibility. Antimicrobial activity was evaluated against Escherichia coli, and it was found that LL-III-loaded nanoparticles significantly reduced the minimum inhibitory concentration (MIC) from 9.82 µM (free LL-III) to 4.59 µM, demonstrating enhanced bactericidal efficacy upon nanoparticle delivery.

These results suggest that ION@P(AA-co-MAA) nanoparticles could be a promising delivery system for antimicrobial peptides, offering improved stability, biocompatibility and therapeutic effectiveness. This system has strong potential for use in the future in treating infections caused by antibiotic-resistant bacteria.

PS2-S8-SF02 Formaldehyde exposure alters cell cycle progression and metabolic activity in human monocytic cells

Lucia Parrakova[1], Pablo Monfort-Lanzas[2], Egon Demtez[3], Piotr Tymoszuk[4], Heideline Jäkel[1], Johanna Gostner[1]

[1] Medical Biochemistry, Medical University of Innsbruck, Austria
[2] Medical University of Innsbruck, Institute of Medical Biochemistry, Innsbruck, Austria,2) Medical University of Innsbruck, Institute of Bioinformatics, Innsbruck, Austria
[3] Department of Internal Medicine II, Immuntherapy Lab, Medical University of Innsbruck, Innsbruck, Austria
[4] Data Analytics As a Service Tirol, Wörgl, Austria

Formaldehyde is a highly reactive aldehyde to which humans are ubiquitously exposed via consumer products, ambient environmental emissions, and occupational settings. Formaldehyde is also produced endogenously by cellular metabolism, thus intrinsic detoxification pathways exist that can mitigate it at physiological concentrations. The primary basis of formaldehyde's cytotoxicity is the covalent cross-linking of nucleophilic biomolecules, including proteins and nucleic acids, leading to the disruption of essential cellular functions.

We investigated the effects of formaldehyde on the human monocytic cell line THP-1 at different concentrations, including such being present endogenously, and across different exposure times. Using flow cytometry to assess cell cycle distribution, we observed an increase of cells in G2/M phase after 24h of incubation with endogenous concentrations of formaldehyde indicating activation of the cell cycle checkpoint. In contrast, higher concentrations are associated with reduced viability. Additionally, dose- and time-dependent effects were also observed for metabolism of aromatic amino acids in formaldehyde exposed THP-1 cells.

Our findings demonstrate that formaldehyde-induced effects on cell cycle progression, apoptosis, and amino acid metabolism depend on both the duration and concentration of exposure, thereby complicating the identification of a clear threshold for irreversible biological toxicity.

PS2-S9-SF01 Engineering covalent small molecule–RNA complexes in living cells

Kamila Nykiel[0], Raphael Bereiter[1], Laurin Flemmich[1], Sarah Heel[1], Stephan Geley[0], Malou Hanisch[0], Clemens Eichler[1], Kathrin Breuker[1], Alexandra Lusser[0], Ronald Micura[1]

[1] University of Innsbruck
[0] Molecular Biology, Medical University Innsbruck, Austria

Covalent labeling of RNA in living cells poses many challenges. Using a structure-guided approach, we have engineered covalent RNA aptamer-ligand complexes by chemical modification of the ligands. We show that highly specific covalent linkage is possible under the physiological conditions of living cells for two distinct aptamer-ligand systems, namely the $preQ_1$ riboswitch and the fluorescent light-up aptamer Pepper. We present several examples for imaging as well as pull-down applications of the covalent Pepper system (*co*Pepper) in living cells. In particular, we demonstrate the unique advantage of the covalent system for FRAP (fluorescence recovery after photobleaching) analyses allowing the monitoring of intracellular RNA dynamics. The ease with which the Pepper FLAP can be converted into a *co*FLAP bodes well for the rapid dissemination of this approach to *in vivo* RNA imaging.

PS2-S9-SF02 New insights into the molecular basis of ARID1B haploinsufficiency associated with the Coffin-Siris syndrome

Annkatrin Bressin, Nicole Eischer, Jelena Ulicevic, Geno Villafano, Nico Soyka, Lukas Behrens, Elisabeth Altendorfer, Susanne Freier, David Meierhofer, Andreas Mayer

Max-Planck-Institute for Molecular Genetics, Germany

Chromatin remodelers are key protein complexes that modify chromatin structure by sliding or disassembling nucleosomes, providing genome accessibility for the transcription machinery. The SWI/SNF chromatin remodelling complex, including its conserved regulatory subunit ARID1B, constitutes the canonical SWI/SNF complex. Heterozygous single-point mutations in *ARID1B* can lead to haploinsufficiency and are associated with neurodevelopmental disorders. In this study, we use a quantitative multi-omics approach coupled with cell engineering and microscopy methods to reveal the functional consequences of ARID1B haploinsufficiency on chromatin and transcription regulation underlying cell function. We show that the most common *de novo* ARID1B mutation causing Coffin-Siris syndrome (CSS) leads to a severe reduction of ARID1B protein levels in human cells. Reduced ARID1B levels result in decreased chromatin accessibility at promoters and putative enhancers of genes associated with developmental disorders and intellectual disability. Consistently, spike-in controlled RNA-seq reveals transcriptional changes, particularly in neurodevelopmental genes associated with disease. In ARID1B-sensitive genes, nascent RNA polymerase II transcription elongation is particularly affected. Our study elucidates the molecular mechanisms of ARID1B haploinsufficiency in human cells and provides an explanation why neurodevelopmental genes are particularly dependent on ARID1B dosage.

PS2-S10-SF01 The origin of coproporphyrin III presence in *acne vulgaris* caused by pathogenic *Cutibacterium acnes* type 1 strains in human skin

Thomas Gabler, Paul Georg Furtmüller, Stefan Hofbauer

BOKU University, Austria

Acne vulgaris is a prevalent dermatological condition characterized by the obstruction of hair follicles, leading to the accumulation of dead skin cells and subsequent inflammation most commonly observed among individuals between the ages of 16 to 20. The severity of acne may be further influenced by specific risk factors, including (i) genetic predisposition, (ii) dietary influences, and (iii) hormonal activity. The second potential cause is an infection with the Gram-positive bacterium *Cutibacterium acnes* (formerly *Propionibacterium acnes*). Despite the absence of a comprehensive understanding of the underlying factors causing the symptoms, coproporphyrin III, an exclusive porphyrin present only in the coproporphyrin-dependent heme biosynthesis pathway of monoderm bacteria, has been associated with the condition since it was demonstrated to accumulate in the affected skin. In addition to the acneic strains of C. acnes (type 1 strains), there are sub-strains (type 2 and 3) that have been identified in healthy skin. As coproporphyrin III is an intermediate porphyrin of the heme biosynthesis pathway of monoderm bacteria, it is evident that the pathway and the enzymes involved must be considered first. Coproporphyrin III is the substrate of coproporphyrin ferrochelatase (CpfC), which yields iron coproporphyrin III and then converted to heme b by coproheme decarboxylases (ChdC) in the final step.

Here, one detail attracts attention. It has been established that CpfC and ChdC are naturally regulated in their own open reading frame, resulting in a monomeric CpfC and pentameric ChdC in almost all known monoderm bacteria. However, a fusion of these genes in one open reading frame has been observed in the pathogenic type 1 strains of *C. acnes*. The fusion of CpfC and ChdC in such a strain was first reported by Dailey and colleagues. The potential impact of this mutation could be manifold, including alterations to (i) oligomerization state, (ii) enzyme kinetics, (iii) the shuttling of porphyrins between CpfC and ChdC, and (iv) the separate regulation of the enzymes at the genetic level. This major difference could be one of the reasons for coproporphyrin III accumulation in *C. acnes* type 1 strains. Here we outline the initial findings of this project, which include the (i) expression and purification, (ii) oligomerization state, (iii) substrate and product binding studies, and (iv) preliminary structural insights into the CpfC_ChdC fusion enzyme.

PS2-S10-SF02 Investigating dose-dependent ß-catenin activity in wilms tumor

Hannah Marie Cebula[1], Maud Plaschka[2], Lukas Watzke[3], Simon Gutwein[4], Ulrike Mann[3], Luis Fernando Montaño-Gutierrez[3], Christoph Hafemeister[2], Cécile Picard[5], Frédérique Dijoud[5], Polina Kameneva[2], Jenny Wegert[6], Manfred Gessler[6], Leo Kager[7], Benoît Dumont[8], Matthias Farlik[3], George D. Cresswell[2], Sabine Taschner-Mandl[2], Florian Halbritter[2]

[1] Developmental Cancer Genomics, St. Anna's Children's Cancer Research Institute, Austria
[2] St. Anna Children's Cancer Research Institute (CCRI)
[3] Medical University of Vienna
[4] Technical University of Vienna
[5] Hospices Civiles de Lyon (HCL)
[6] Julius-Maximilians-Universität Würzburg
[7] St. Anna Children's Hospital
[8] Centre de Recherche en Cancérologie de Lyon (CRCL), Institut d'Hématologie et d'Oncologie Pédiatrique Lyon (IHOPe)

Wilms tumor (WT), the most common pediatric kidney cancer, often involves dysregulated Wnt/ß-catenin signaling, an important pathway in kidney development and tumorigenesis. While activating mutations in *CTNNB1* (ß-catenin) are well-characterized in WT, the impact of different levels of ß-catenin activity on tumor cell behavior remains poorly defined, which is a hindrance to understanding the molecular heterogeneity of WT and to the development of targeted therapies aimed at modulating Wnt/ß-catenin signaling.

To investigate the dose-dependent effects of ß-catenin, we treated multiple adherent patient-derived short-term cell cultures with increasing concentrations of CHIR99021, a GSK3ß inhibitor that activates Wnt signaling. We analyzed changes in ß-catenin localization and expression of transcriptional partners and developmental markers associated with ß-catenin signaling (LEF1, TCF7L2, CITED1, SIX2) using immunofluorescence and RT-qPCR. Cellular metabolic activity was assessed via luminescent viability assays.

Our results reveal that graded ß-catenin activation induces distinct transcriptional responses. At lower CHIR concentrations, expression of the stemness-associated marker *CITED1* peaked, while higher levels led to upregulation of *LEF1* and downregulation of *TCF7L2* and *SIX2* – which are implicated in the differentiation of nephron progenitor cells during kidney development. As the balance between stemness and differentiation is thought to influence tumor heterogeneity and treatment response, understanding how ß-catenin signaling governs this transition may offer insights into disease progression and therapeutic targeting. This molecular shift was accompanied by changes in metabolic function, indicating a transition toward aerobic glycolysis, suggesting that ß-catenin signaling may influence the cellular metabolic state alongside identity.

These findings support a model in which ß-catenin activity fine-tunes the balance between stemness and differentiated cell states in WT. By defining the transcriptional and functional consequences of ß-catenin dosage in several WT-derived cell models, we aim to better understand how signaling dynamics shape tumor heterogeneity and identify potential entry points for therapeutic intervention.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

Poster Session 2

NOTE: The Science Flash poster abstracts from Poster Session 2 are listed in the Science Flash Session 2
S3: The multifaceted world of lipids
S7: Organelle and membrane biology
S8: Advances in toxicology and risk assessment
S9: RNA in gene regulation
S10: Unveiling protein and cell dynamics

PS2-S3-PP01 Integrative analysis of multi-omics data to elucidate potential antitumor mechanisms of a ketogenic diet in melanoma

Rohit Dnyansagar[1], Natalie Bordag[2], Rodolphe Poupardin[3], Julia Tevini[1,], Victoria E Stefan[1,4], Sophia Derdak[5], Martin Bilban[5,6], Nikolaus Fortelny[7], Barbara Kofler[1], Roland Lang[8], **Daniela D Weber[1]**

[1] Research Program for Receptor Biochemistry and Tumor Metabolism, Department of Pediatrics, University Hospital of the Paracelsus Medical University, Austria
[2] Department of Dermatology and Venereology, Medical University of Graz, Graz, Austria
[3] Cell Therapy Institute, Paracelsus Medical University, Salzburg, Austria
[4] Department of Biosciences and Medical Biology, Paris Lodron University Salzburg, Salzburg, Austria
[5] Core Facilities, Medical University of Vienna, Vienna, Austria
[6] Department of Laboratory Medicine, Medical University of Vienna, Vienna, Austria
[7] Center for Tumor Biology and Immunology, Department of Biosciences and Medical Biology, Paris Lodron University Salzburg, Salzburg, Austria
[8] Department of Dermatology and Allergology, University Hospital of the Paracelsus Medical University, Salzburg, Austria

The ketogenic diet (KD) is a highly attractive approach to target metabolic vulnerabilities of tumor cells. Using metabolic profiling, we recently showed that different human melanoma cell lines engrafted into mice exhibit distinct metabolomes, partially independent of genetic driver mutations. Moreover, we demonstrated that treatment of these genetically and metabolically heterogeneous melanoma xenografts with a KD effectively reduced tumor growth. Targeted metabolomics of plasma and tumor samples revealed significant changes in amino acid and lipid metabolism induced by the KD.

To further elucidate antitumor mechanisms of the KD, bulk RNA sequencing was performed on xenograft tissue from mice bearing BRAF-mutant, NRAS-mutant or BRAF/NRAS wild-type melanoma treated with either KD or control diet. Transcriptomics and metabolomics data integration was conducted using mixOmics DIABLO, correlation analysis as well as joint pathway analysis.

Correlation analysis between KD-regulated metabolites and the transcriptome identified several metabolite-gene pairs, which were subjected to joint pathway analysis. Joint pathway analysis showed enrichment of lipid-related pathways, such as sphingolipid metabolism and phosphatidylcholine catabolism, across all xenografts. Moreover, mixOmics DIABLO analysis revealed good correlation between metabolites and genes in the different xenograft models. The discriminatory analysis on the combined dataset of all xenografts helped to identify the latent component that separates KD from control samples. Joint pathway analysis based on component loadings recovered several pathways detected in the correlation-based analysis.

Integrative metabolomic–transcriptomic analysis revealed key pathway-level insights that were shared across xenografts, as well as xenograft-specific patterns. Using a latent variable approach, we identified a principal component that discriminated KD- from control diet-treated mice.

PS2-S3-PP02 Functional analysis of Lcb1 and Lcb2 phosphorylation sites in *S. cerevisiae*

Sophia Pichler[1], Brigitta Seifert[1], Niklas Schomisch[1], Carolin Körner[2], Bianca Esch[2], Florian Fröhlich[2], Oliver Schmidt[1]

[1] Cellbiology, Medical University Innsbruck, Austria
[2] Bioanalytical Chemistry Section, Department of Biology/Chemistry, Osnabrück University, 49076 Osnabrück, Germany

Sphingolipids (SL) play a crucial role as major structural components of cellular membranes and as signalling molecules. The initiation and at the same time also the rate-limiting step of sphingolipid-biosynthesis happens in the ER by the enzyme serine-palmitoyl-coenzym A transferase (SPT), which in *S. cerevisiae* consist of Lcb1, Lcb2 and the accessory factors Tsc3 and Sac1. Regulation of enzyme activity is achieved by the Orm proteins, Orm1 and Orm2 in yeast, which together with the SPT form the SPOTS complex. In the SPOTS complex the SPT is inactive, but is activated when Orm1 and Orm2 become phosphorylated and dissociate from the complex [1, 2].
A possible further regulation mechanism for the SPT is the phosphorylation of Lcb1 and Lcb2. Several phosphorylation sites for Lcb1 and Lcb2 are annotated in databases from high-throughput phospho-proteomics studies. These have the potential to regulate SPT enzymatic activity, complex assembly or Lcb1 turnover independently from the canonical phospho-regulation via the Orm proteins, which we assessed by mutating novel phosphorylation sites to either non-phosphorylatable or phospho-mimetic residues.

The Lcb1 T121 phosphorylation site was measured independently in two previous studies [3, 4] and we confirmed phosphorylation of this residue in isolated SPOTS complexes. A mutant strain containing phospho-mimetic Lcb1 T121D has lower Lcb1 protein levels and is myriocin-hypersensitive [5]. Interestingly, however, Lcb1 turnover and SPOTS complex formation are largely unaffected by the phospho-mimetic mutation, which suggests a reduced SPT activity when T121 is phosphorylated.

Our results suggest that T121 in Lcb1 is the first regulatory SPT phosphorylation site not located on the Orm proteins. The human ortholog SPTLC1 has a tyrosine phosphorylation site (Y82) at the equivalent position, indicating that this regulatory mechanism could be conserved from yeast to humans.

[1] D.K. Breslow et al., "Orm family proteins mediate sphingolipid homeostasis", *Nature*, *463*(7284), pp. 1048–1053, 2010

[2] O. Schmidt et al., "Endosome and Golgi-associated degradation (EGAD) of membrane proteins regulates sphingolipid metabolism", *The EMBO Journal*, *38*(15), 2019

[3] M. C. Lanz et al., "In-depth and 3-dimensional exploration of the budding yeast phosphoproteome", *EMBO Reports*, *22*(2), 2021

[4] M. Leutert et al., "The regulatory landscape of the yeast phosphoproteome", *Nature Structural and Molecular Biology*, *30*(11), 1761–1773, 2023

[5] Y. Miyake et al., "Serine Palmitoyltransferase Is the Primary Target of a Sphingosine-like Immunosuppressant, ISP-1/Myriocin", *Biochemical and Biophysical Research Communications*, *211*(2), 396–403, 1995

PS2-S3-PP03 Lipids and their role in membrane protein degradation pathways.

Konstantin Adrian Siegmann

Molecular Biochemistry, Medical University Innsbruck, Austria

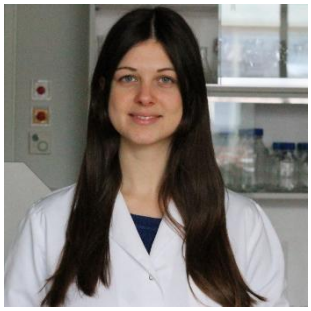
Membrane proteins constitute approximately 30% of the proteome and most membrane proteins are co-translationally inserted into the lipid bilayer of the ER. While membrane protein quality control mechanism at the ER are well characterized, there is only limited knowledge about membrane protein quality control procress in post-ER compartments.

We have recently identified in *S. cerevisiae* a membrane protein quality control (QC) system, that leverages the biophysical properties of lipid bilayers and transmembrane domains to identify and degrade orphaned proteins at the Golgi. At the heart of this Golgi quality control process operates the “Defective in SREBP-cleavage” (Dsc) ubiquitin ligase complex. The Dsc complex uses its rhomboid pseudo-protease subunit Dsc2 to locally thin the lipid bilayer at the Golgi to promote substrate detection via hydrophobic matching. The ensuing interaction promotes substrate poly-ubiquitination, extraction of the TMDs from the lipid bilayer via the mechanoenzyme Cdc48, and proteasomal degradation. We termed this pathway Endosome- and Golgi-associated degradation (EGAD) (Schmidt et al., 2019; Weyer & Schwabl & Tang, 2024).

Hence we speculate that the Dsc complex exploits for membrane protein quality control at the Golgi the transition from an ER lipid territory (shorter and more desaturated acyl chain) to a plasma membrane lipid territory (longer and more saturated acyl chains). To test this idea, we focus on the role of lipids in Golgi QC. Torward this goal we plan to alter the yeast lipidome to investigate *in vivo*whether the membrane lipid composition is crucial for the function of the Dsc complex. Towards this goal, I will inhibit fatty acid synthase and provide defined exogenous lipids thereby establishing conditions that allow the manipulation of lipid bilayer properties. I will present preliminary results indicating that the function of the Dsc complex might be sensitive to the lipid environment.

Overall, the results of my work will lead to a better understanding of how lipids contribute to protein quality control at the Golgi.

PS2-S3-PP04 Plasmalogen catabolism: a new fluorescent HPLC-based Assay



Denise Kummer, Ilaria Dorigatti, Theresia Dunzendorfer-Matt, Georg Golderer, Ernst R. Werner, Katrin Watschinger

Institute of Molecular Biochemistry, Medical University of Innsbruck, Austria

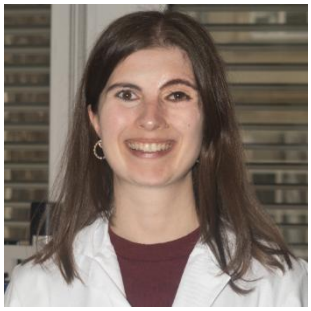
Plasmalogens are a prominent class of glycerophospholipids distinguished by their characteristic 1-*O*-alk-1'-enyl double bond. Accounting for about 20% of the mammalian phospholipid pool, they have been linked to various human disorders, including Zellweger syndrome, Rhizomelic Chondrodysplasia Punctata, as well as neurodegenerative diseases such as Alzheimer's. While their biosynthesis in peroxisomes and the endoplasmic reticulum has been thoroughly studied, their catabolic processes remain less understood. Plasmalogen degradation involves conversion to 2'-lyso forms, catalyzed by lysoplasmalogenase. TMEM86B, expressed and purified from bacteria, has been confirmed to encode lysoplasmalogenase activity using a coupled optical assay. TMEM86A, although not yet purified, was also suspected to function as a lysoplasmalogenase, supported by indirect lipidomic data from tissues exhibiting altered TMEM86A levels and results near the detection limit of the optical assay.

We developed a novel assay to measure lysoplasmalogenase activity, involving substrate incubation, aldehyde product derivatization, and hydrazone quantification through reversed-phase HPLC with fluorescence detection. Optimization steps included the reaction buffer and time, as well as the substrate and sample concentration.

This method is sufficiently sensitive to detect lysoplasmalogenase activity in cells expressing TMEM86A or TMEM86B and to distinguish their responses to the substrates lysoplasmenylethanolamine and lysoplasmenylcholine. The less studied TMEM86A was confirmed to exhibit lysoplasmalogenase activity. To investigate key enzymatic regions, mutations were introduced into putative active-site residues of both TMEM86A and TMEM86B. Analysis of enzyme activity relative to protein expression revealed that seven of the eight mutants showed a significant reduction in activity, highlighting critical residues required for function. Additionally, the assay effectively measured lysoplasmalogenase activity in various mouse tissues.

Our assay provides a robust and versatile tool for studying lysoplasmalogenase activity in cells and mouse tissues, advancing research into plasmalogen catabolism and plasmalogen-related disorders.

PS2-S3-PP05 Isotopic tracing of enzyme-mediated regulation of cardiolipin biosynthesis and remodeling



Nina Weidacher, Markus A. Keller, Johannes Zschocke

Medical University of Innsbruck, Austria

Cardiolipins are phospholipids exclusively located in mitochondrial membranes where their specific acyl chain diversity is essential for mitochondrial function, such as stabilizing the electron transport chain. Thereby, cardiolipins are the frontline defense against reactive oxygen species, sacrificing their unsaturated acyl chains in order to protect the integrity of membrane functions. To maintain cardiolipin homeostasis, mitochondria can either replace damaged cardiolipins through *de novo* biosynthesis, or by selectively exchanging oxidized side chains. The transacylase tafazzin typically involved in cardiolipin remodeling, a process responsible for establishing cardiolipin acyl chain specificity, likely also plays a major role in the side chain repair mechanism of oxidized cardiolipins.

However, the individual quantitative contributions of these processes under physiological conditions remain unexplored. We take advantage of three different inherited disease that are supposed to affect the cardiolipin metabolism, namely MEGD(H)EL syndrome, Sengers syndrome and Barth syndrome, which are caused by impairment of the enzymes SERAC1, AGK, and tafazzin, respectively.

We developed a steady-state isotopic labeled incorporation assay using either ^{13}C-glucose or ^{13}C-fatty acids to track *de novo* biosynthesis or remodeling in cultured cells in a time-dependent manner by LC-MS/MS analysis. ^{13}C-Glucose incorporation using different fatty acid supplementations revealed biosynthetic rates of newly synthesized cardiolipins in various lipid environments and proofed the necessity of more biosynthesis in tafazzin deficient cells. Furthermore, the incorporation of either ^{13}C-palmitic acid or ^{13}C-linoleic acid highlighted the impact of different lipid environments in remodeling. The latter not only significantly changes the cardiolipin profile as it is highly favored by remodeling, but also decrease the amount of free reactive oxygen species. This resulted in different requirements for remodeling.

The established incorporation assay studying these inherited diseases affecting cardiolipin metabolism demonstrated the demand for more biosynthesis in tafazzin deficient cells lacking remodeling capability and further showed the requirements for remodeling in different lipid environments.

PS2-S3-PP06 PPARα- links mitochondrial β-oxidation disorders with membrane lipid remodeling

Viktorija Juric[1], Jessica Patricia Popottnigg[2], Sabrina Sailer[3], Jakob Koch[3], Yvonne Wohlfarter[3], Antonia Aileen Degen[4], Heinz Zoller[5], Daniela Karall[6], Sabine Scholl-Bürgi[6], Judith Hagenbuchner[7], Johannes Zschocke[3], Markus Andreas Keller[3]

[1] Institute of Human Genetics, Medical University Innsbruck, Austria
[2] Institute of Human Genetics, Medical University of Innsbruck, Innsbruck, Austria. Department of Internal Medicine I, Medical University of Innsbruck, Innsbruck, Austria.
[3] Institute of Human Genetics, Medical University of Innsbruck, Innsbruck, Austria.
[4] Department of Child and Adolescence Health, Pediatrics I, Medical University of Innsbruck, Innsbruck, Austria. Bioprinting Lab, Medical University of Innsbruck, Innsbruck, Austria.
[5] Department of Internal Medicine I, Medical University of Innsbruck, Innsbruck, Austria.
[6] Department of Paediatrics I (Inherited Metabolic Disorders, Medical University of Innsbruck), Innsbruck, Austria
[7] Department of Child and Adolescence Health, Pediatrics I, Medical University of Innsbruck, Innsbruck, Austria. Bioprinting Lab, Medical University of Innsbruck, Innsbruck, Austria

The central pathway for degrading fatty acids into acetyl-CoA is mitochondrial β-oxidation. Failure in function of enzymes involved in this process can lead to accumulation of unusual fatty acid intermediates, along with energy depletion and organ dysfunction in affected patients. Two well-known inherited mitochondrial β-oxidation disorders are Very-Long-Chain Acyl-CoA Dehydrogenase Deficiency (VLCADD) and Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHADD). The effects of disturbance in fatty acid metabolism on rest of the lipidome are so far largely unexplored. In this study, we utilized two model systems for VLCADD and LCHADD: patient-derived fibroblasts and CRISPR/Cas9 knockouts in HEK-293T cells. Functional impairment of mitochondrial β-oxidation was confirmed by analysing acylcarnitine phenotypes. Additionally, we validated previously described increase of reactive oxygen species (ROS) levels in both models. Next, we performed untargeted lipidomics analysis by LC-MS/MS and observed an accumulation of odd-chain lipids (OCLs) in beta-oxidation defective cell lines compared to controls. This finding was unexpected, as elevated levels of odd-chain lipids are uncommon in healthy human cells. Thus, we investigated which metabolic processes could be responsible for accumulation of OCLs. Several scenarios where experimentally tested, of which over-activation of peroxisomal α-oxidation, driven by activation PPARα signaling emerged as one of the most likely possibilities. To test this hypothesis, we investigated origin of the OCLs by analyzing PPARα activity - a transcriptional regulator of lipid metabolism and enzymes involved in the peroxisomal α-oxidation. Specifically, we performed western blot analysis to assess PPARα phosphorylation, which is indicator of its activation status. Indeed, we found PPARalpha to be upregulated in cultured models for VLCADD and LCHADD. In summary, our current mechanistic understanding is that mitochondrial β-oxidation disorders intracellularly accumulate unusual fatty-acid intermediates that induce PPAR-α, triggering the activation of peroxisomal lipid metabolism, including α-oxidation. Although cells might be able to partially compensates for some regulatory changes, they do increase production of odd-chain fatty acids which are subsequently incorporated into complex lipids. Elucidating the biochemical origin of the OCLs intermediates and their involvement in the regulation of PPARα is essential to understand the pathomechanisms of disorders and their impact on the health of patients with VLCADD and LCHADD.

PS2-S7-PP01 Delineating hepatocytic apical trafficking defects in MyoVb associated liver disease

Doris Stepic[1], Stephan Geley[2], Lukas A. Huber[1], Georg F. Vogel[3]

[1] Medical University Innsbruck, Austria
[2] Institute of Pathophysiology, Medical University of Innsbruck, Innsbruck, Austria
[3] Institute for Cell Biology, Medical University of Innsbruck, Innsbruck, Austria; Department of Paediatrics I, Medical University of Innsbruck, Innsbruck, Austria

The existence of apical, lateral and basal domains of the plasma membrane in polarized epithelial cells, each with distinct functions and protein composition necessitates targeted protein trafficking. Therefore, disturbed polarized trafficking might result in disease. One example is the intestinal microvillus inclusion disease (MVID) which is characterized by defects in enterocyte polarity and mislocalization of apical proteins. MVID is caused by mutations in the MYO5B, STX3, and STXBP2 genes, which encode the proteins MyosinVb (Myo5b), Syntaxin3 (Stx3), and Munc18-2, respectively. Myo5b is a motor protein that carries apically destined vesicles, while Stx3 and Munc18-2 facilitate the fusion of vesicles with the apical membrane. Interestingly, some patients with MVID develop cholestatic liver disease (CLD) characterized by mislocalization of the apical membrane proteins in hepatocytes. The question is how apical trafficking functions in hepatocytes, particularly given that only dominant-negative missense mutations, but not nonsense mutations of Myo5b result in CLD and that Stx3 is not present. To investigate this, we are using polarized hepatocytic HepG2 cells, from which basis we developed transgenic lines to identify key players in apical protein trafficking in hepatocytes using protein interaction studies. MYO5B knockout cells will allow to identify a possible compensation in the apical trafficking machinery observed in patients. We found that Stx2 resides apically and may substitute for Stx3 in hepatocytes. Generating a STX2 knockout will enable us to test this hypothesis. Additionally, apical surface proteome studies in various knockout backgrounds will allow us to find out which apical proteins are trafficked via said machineries.

PS2-S7-PP02 Effects of mechanical stress on the lipid homeostasis of the endoplasmic reticulum

Alexander Plesche[1], Nina Weidacher[2], Markus Keller[2], Hesso Farhan[1]

[1] Institut für Pathophysiologie, Medizinische Universität Innsbruck, Austria
[2] Medial University of Innsbruck / Institute of Human Genetics

In living organisms, mechanical stimuli and stresses affect cells at every given moment. The cellular response and its adaptations to these mechanical cues are only beginning to be unraveled. Particular knowledge gaps exist in how intracellular organelles other than the nucleus experience and react to mechanical forces. Our study investigates changes in the lipidome following mechanical stress, with a special focus the endoplasmic reticulum (ER) as the main synthesis and transport hub for lipids. Our model for mechanical stress is confinement, effectively restricting cellular height to only 3µm.

Following confinement, the morphological appearance of the ER changes, characterized by an increase in sheet-like structures at the expense of the peripheral tubular network. This alteration effectively reduces the amount of membranes with a high curvature. Accompanying these changes is a shift in the ratio between phosphatidylcholine (PC) and phosphatidylethanolamine (PE) species, with a relative increase of PC species. The PC:PE shift is likely a direct conversion of PE to PC species by the phosphatidylethanolamine-N-methyltransferase (PEMT) enzyme. Given the cylindrical geometry of PC lipids, their enrichment likely facilitates the formation of the extended planar sheet structures. Supporting this, RNA interference-mediated knockdown of PEMT prevents the sheet expansion under confinement.

Lipid transport between intracellular organelles is largely mediated by non-vesicular trafficking at membrane contact sites. Following confinement, we found a reduction of contact sites between the ER and mitochondria. At the same time, mitochondria fragment, raising the question whether lipid exchange between the two organelles is altered or even responsible for the observed morphological changes.

Future work on the project aims to understand a possible direct mechanical regulation of PEMT, as well as to understand the interplay between mitochondrial fragmentation and lipid homeostasis at the ER under confinement.

PS2-S7-PP03 Advanced modeling of LCHADD/VLCADD with 3D-bioprinting and induced-pluripotent stem cell technology

Antonia Degen[0], Christian Ploner[1], Leopold von Balthazar[2], Jack Rohrer[2], Daniela Karall[3], Thomas Müller[3], Michael Ausserlechner[0], Judith Hagenbuchner[0]

[1] Department of Plastic, Reconstructive and Aesthetic Surgery, Medical University of Innsbruck
[2] Institute of Chemistry and Biotechnology, Zurich University of Applied Sciences (ZHAW), Wädenswil, Switzerland
[3] Department of Pediatrics I, Medical University Innsbruck, Innsbruck, Austria
[0] 3D Bioprinting Core Facility, Medical University of Innsbruck, Austria

Background: Long-chain-3-hydroxy-acyl-CoA-dehydrogenase-deficiency (LCHADD) and Very-long-chain-acyl-CoA-dehydrogenase-deficiency (VLCADD) are rare disorders of the oxidation of long-chain fatty acids (LC-FA). These conditions often lead to severe cardiac complications, such as cardiomyopathy and arrhythmia, which are major causes of early and sudden death in affected patients.

Methods: This study investigates mitochondrial rearrangement in β-oxidation-defective fibroblasts exposed to various rescuers in 2D. Mitochondrial morphology was assessed via live cell fluorescence microscopy, quantifying branches and dots. A 3D-bioprinted, vascularized tissue model with healthy and patient-derived fibroblasts was established to mimic tissue physiology. To model cardiac complications in LCHADD/VLCADD, patient-derived fibroblasts were reprogrammed into iPSCs and differentiated into cardiomyocytes for analysis of cardiac markers by immunochemistry.

Findings: Analysis of mitochondrial morphology in patient fibroblasts revealed significant alterations and increased intracellular ROS levels due to NOX2. NOX2 inhibitors and other rescuers restored mitochondrial network integrity. 3D-bioprinted tissue models with patient fibroblasts exhibited impaired vessel formation. Functional characterization of patient-derived iPSCs revealed a profibrotic phenotype, with osteogenic and chondrogenic, but not adipogenic, differentiation, along with increased stress fiber levels. Cardiomyocyte differentiation showed morphological differences and altered beating activity between healthy and patient-derived cells.

Interpretation: Our findings will enhance the understanding and treatment of LCHADD/VLCADD, addressing the lack of therapies for elevated ROS levels and mitochondrial dysfunction. Additionally, this model, using human iPSC technology, will enable the study of cardiac complications and patient-specific differences, as well as the effects of various treatment modalities.

PS2-S7-PP04 Alpha-arrestin mediated control of cellular nutrient uptake and its role in metabolic signaling

Nikolas Marchet, Jennifer Kahlhofer, Kristian Zubak, Brigitta Seifert, Sabine Scholl-Bürgi, Daniela Karall, David Teis

Molecular Biochemistry, Medical University of Innsbruck, Austria

Entry and exit from cellular quiescence require dynamic adjustments in nutrient acquisition, yet the mechanisms by which quiescent cells downregulate amino acid (AA) transport remain poorly understood. We now demonstrate that cells entering quiescence select plasma membrane-resident amino acid (AA) transporters for endocytosis and lysosomal degradation, to match AA uptake with reduced translation. The endocytic degradation of the heterodimeric AA transporter SLC7A5-SLC3A2 (LAT1-4F2hc) requires the α-arrestin TXNIP. A novel TXNIP loss-of-function mutation in a patient with severe metabolic disease further supports its role in nutrient homeostasis and human health. These findings highlight TXNIP's role in controlling SLC7A5-SLC3A2 mediated AA acquisition with implications for metabolism and human health (Kahlhofer J., Marchet N., EMBO J in revision). Mechanistically, we show that a single PPCY motif in TXNIP is required for the downregulation of SLC7A5-SLC3A2 and demonstrate its importance for protein-protein interaction of TXNIP with members of the HECT-type ubiquitin ligase family in an in vitro approach. During growth, active AKT phosphorylates TXNIP on S308, rendering it thereby inactive. In quiescence, reduced AKT signaling licenses TXNIP dependent endocytosis of SLC7A5-SLC3A2 to decrease AA uptake. TXNIP deficiency results in dysregulated AA uptake, enhanced mTORC1 signaling, increased translation, accelerated quiescence exit, and proliferation. Conversely, during extened periods of quiescence, TXNIP and the endocytic removal of SLC7A5-SLC3A2 become essential for cell survival.

PS2-S7-PP05 Evolutionary conservation and structural flexibility in BORC and BLOC-1

Mariana E.G. de Araujo[1], Sascha Amann[2], Taras Stasyk[1], Alexander Schleiffer[2], Paula Flümann[1], Isabel Singer[1], Leopold Kremser[3], Vojtech Dostal[1], Thanida Laopanupong[1], Nikolaus Obojes[4], Moritz H. Wallnöfer[1], Caroline Krebiehl[1], Georg F. Vogel[5], Michael W. Hess[6], Bettina Sarg[3], Tim Clausen[2], David Haselbach[2], Lukas A. Huber[1]

[1] Institute of Cell Biology,, Medical University Innsbruck, Austria
[2] Research Institute of Molecular Pathology, Vienna BioCenter, 1030 Vienna, Austria.
[3] Institute of Medical Biochemistry, Protein Core Facility, Biocenter, Innsbruck Medical University, 6020 Innsbruck, Austria.
[4] Institute for Alpine Environment, Eurac Research, 39100 Bolzano, Italy
[5] Department of Paediatrics I, Medical University of Innsbruck, 6020 Innsbruck, Austria.
[6] Institute of Histology and Embryology, Medical University of Innsbruck, 6020 Innsbruck, Austria

BORC and BLOC1 are evolutionarily related complexes that emerged at the time of the last eukaryotic common ancestor and are essential for endocytic trafficking. Here, we show that BORC's 3D-fold is conserved across distantly related species, assembling as two tetrads of intertwined α-helices, with N-termini converging at the core and C-termini extending outward. Using integrative structural biology, we validated this architecture, identified residues essential for assembly, and confirmed the effects of disease-associated mutations. Strikingly, conservation analysis reveals that several vertebrates likely possess only six BORC components. Both octameric and hexameric BORC assemble similarly, with subunits occupying equivalent positions and our data support their coexistence in cells. We further uncover the integration of BORC and BLOC1 specific components in the same complex and observed that mutations disrupting BORC assembly also impaired the interactions with BLOC1-specific subunits. Additionally, we found EARP components interact with certain BORC and BLOC1 subunits, suggesting that mixed complexes may regulate recycling pathways. Together, these findings challenge the view of BORC and BLOC1 as distinct entities. We propose a dynamic model in which modular assemblies form on demand to carry out specific cellular functions.

PS2-S7-PP06 The Dsc ubiquitin ligase complex identifies transmembrane degrons to degrade orphaned proteins at the Golgi

Yannick Weyer[0], Sinead I. Schwabl[0], Xuechen Tang[1], Astha Purwar[0], Konstantin Siegmann[0], Angela Ruepp[0], Theresia Dunzendorfer-Matt[0], Bettina Sarg[2], Leopold Kremser[2], Klaus R. Liedl[1], Oliver Schmidt[3], David Teis[0]

[1] Department of General, Inorganic and Theoretical Chemistry, Center for Molecular Biosciences Innsbruck, University of Innsbruck, Innsbruck, Austria
[2] Institute of Medical Biochemistry, Protein Core Facility, Medical University of Innsbruck, Innsbruck, Austria
[3] Institute of Cell Biology, Medical University of Innsbruck, Innsbruck, Austria
[0] Institute of Molecular Biochemistry, Medical University of Innsbruck, CCB, Austria

The Golgi apparatus is essential for protein sorting, yet its quality control mechanisms are poorly understood. Here we show that the Dsc ubiquitin ligase complex uses its rhomboid pseudo-protease subunit, Dsc2, to assess the hydrophobic length of α-helical transmembrane domains (TMDs) at the Golgi. Thereby the Dsc complex likely interacts with orphaned ER and Golgi proteins that have shorter TMDs and ubiquitinates them for targeted degradation. Some Dsc substrates will be extracted by Cdc48 for endosome and Golgi associated proteasomal degradation (EGAD), while others will undergo ESCRT dependent vacuolar degradation. Some substrates are degraded by both, EGAD- or ESCRT pathways. The accumulation of Dsc substrates entails a specific increase in glycerophospholipids with shorter and asymmetric fatty acyl chains. Hence, the Dsc complex mediates the selective degradation of orphaned proteins at the sorting center of cells, which prevents their spreading across other organelles and thereby preserves cellular membrane protein and lipid composition.

PS2-S7-PP07 BORC segregates synaptic vesicle and lysosomal proteins through motors UNC-104/KIF1A and UNC-116/KIF5

Anal Mathew, Sohan Seal, Aditee Dandekar, Badal Singh Chauhan, Sruthi Sivadasan, Michael L. Nonet, Sandhya P. Koushika

Department of Biological Sciences, Tata Institute of Fundamental Research, Mumbai, India

Synaptic vesicle proteins (SVPs) and lysosomal proteins can be present together in neurons and these compartments are thought to segregate further to SVPs and lysosomal proteins. In this study, we identify genes and characterize a genetic pathway involved in the segregation of SVPs and lysosomal proteins in the neuronal cell body. We show that BORC (BLOC-1-related complex) plays a role in segregating SVPs and lysosomal proteins in the cell body. BORC subunit SAM-4/Myrlysin acts through ARL-8 and Kinesin motor proteins UNC-116/KIF5 and UNC-104/KIF1A in segregating SVPs and lysosomal proteins. Additionally, we also show that LRK-1/LRRK2 and APB-3/AP-3 (β3), involved in pre-SV biogenesis, regulate the segregation of SVPs and lysosomal proteins in the neuronal cell body. LRK-1 recruits SAM-4 that in turn governs the localization of APB-3 suggesting a hierarchical pathway of LRK-1-SAM-4-APB-3 for the segregation of SVPs and lysosomal proteins. Additionally, we also observe that the size of lysosomal protein-containing compartments (LPCCs) is smaller in SAM-4 and LRK-1. This size regulation depends on UNC-116. Together, we show that BORC recruited by LRK-1, via motors and AP-3 mediates the segregation of SVPs and lysosomal proteins in the neuronal cell body.

PS2-S8-PP01 Effects of azole antifungals on immunobiochemical pathways

Aldrien Ryan Naces Reynaldo[1,2], Lucia Parráková[1], Michael Zwerger[1], Pablo Monfort-Lanzas[1,3], Michaela Lackner[2,4], Johanna M Gostner[1,2,5]

[1] Institute of Medical Biochemistry, Biocenter, Medical University of Innsbruck, Innsbruck, Austria
[2] MYCOS consortium, Medical University of Innsbruck, Innsbruck, Austria
[3] Institute of Bioinformatics, Biocenter, Medical University of Innsbruck, Innsbruck, Austria
[4] Institute for Hygiene and Medical Microbiology, Medical University of Innsbruck, Innsbruck, Austria
[5] Core Facility Metabolomics II, Biocenter, Medical University of Innsbruck, Innsbruck, Austria

In recent decades, fungal infections have emerged as a significant public health concern. Among the most widely used antifungal agents are azoles — five-membered aromatic heterocycles characterized by the presence of at least one nitrogen atom and two double bonds. They exert their antifungal effects by binding to the heme group of the cytochrome P450 enzyme lanosterol 14α-demethylase (CYP51), thereby blocking ergosterol production which is essential for the fungal cell wall.Adverse effects associated with human health include hepatotoxicity, endocrine disruption, and there are notable drug-drug interactions that are of clinical importance. The dual use of azoles in the environment and in the clinic is discussed as a driving force for the development of resistance and requires further consideration.Very little is known about the interaction of azoles with immunobiochemical pathways in humans. For example, miconazole-induced oxidative stress has already been studied in cancer cells, but a more comprehensive comparison of reactive oxygen species generation capacities and interference with redox signaling mechanisms of other azoles is still lacking.In our in vitro study, we compare the effects of different azoles on key metabolic pathways of the cellular immune response, such as tryptophan breakdown along the kynurenine axis. More knowledge about such interactions is important to better understand immunomodulation and resistance development by azoles.

PS2-S8-PP02 Evolving regulatory frameworks through case studies focused on uncertainty characterization for the assessment of developmental neurotoxicity

Martin Paparella[1], Ishita Virmani[1], Melanie Ort[1], Ellen Fritsche[2]

[1] Medical Biochemistry, Medical University Innsbruck, Austria
[2] University of Basel

In vitro methodology for developmental neurotoxicity (DNT) [1] may significantly reduce the practical limitations of in vivo approaches in terms of ethical conflicts, costs and required time for testing. These practical advantages of in vitro methodology can also facilitate their standardization and validation process, which in turn may reduce the uncertainty in the experimental data variability. Yet, appreciating the conceptually similar uncertainty in the relevance of the experimental data from in vitro versus in vivo methodology requires reflection on basic assumptions and concepts in regulatory toxicology. Uncertainty for extrapolation from experimental models to the real world human population variability needs due consideration. Ultimately, we may recognize in vitro cellular level data as risk factors for organism level effects, similar to genetic predispositions that may represent a risk factor, which translates to a disease in probabilistic terms. Building on what is known about uncertainties for in vivo and in vitro data based DNT assessment [2] a possible evolution of the current regulatory classification towards a probabilistic, potency and fully human in vitro data based classification will be outlined. The latter does not intend to predict current Globally Harmonized System (GHS) classes. It was proposed as one possible solution to the Designathon challenge [3] and is being further developed via case studies conducted within the European Horizons projects CHIASMA [4] and INSIGHT [5]. The approach will be demonstrated using available in vitro DNT data.

[1] OECD, Initial Recommendations on Evaluation of Data from the Developmental Neurotoxicity (DNT) In-Vitro Testing Battery, in: OECD (Ed.) Series on Testing and Assessment No. 377, 2023.

[2] M. Paparella, S.H. Bennekou, A. Bal-Price, An analysis of the limitations and uncertainties of in vivo developmental neurotoxicity testing and assessment to identify the potential for alternative approaches, Reprod Toxicol 96 (2020).

[3] https://single-market-economy.ec.europa.eu/calls-expression-interest/epaa-launches-designathon-human-systemic-toxicity_en (accessed 17.05.2025)

[4] https://chiasma-project.eu/ (accessed 17.05.2025)

[5] https://insight-project.org/ (accessed 17.05.2025)

PS2-S9-PP01 tRNA superwobbling - the decoding of valine codons in M. capricolum and E. coli

Isabell Gonnella[0], Raphael Plangger[1], Christoph Kreutz[1], Matthias Erlacher[0]

[1] Institute of Organic Chemistry and Center for Molecular Biosciences Innsbruck (CMBI), University of Innsbruck
[0] Medical University of Innsbruck, Austria

Transfer RNAs (tRNAs) are crucial adapter molecules decoding the genetic code during the process of protein synthesis. Although similar in their characteristic L-shaped structure, they are variable in their sequences and modifications. tRNAs are highly modified molecules harboring about 100 different RNA derivatives at different sequence positions. Depending on the type and location of the modifications, ranging from simple methylations to highly complex modifications, they influence structure and stability of the tRNA molecule as well as decoding. To determine and to study the impact of the tRNA sequence and their modifications on aminoacylation and decoding, tRNAs can be generated by splinted ligation of chemically synthesized RNA oligonucleotides. Thereby, tRNAs from different organisms with defined tRNA sequence and defined modifications are characterized. A recombinant translation system combined with different reporter messenger RNAs (mRNAs) provide a suitable setting to test decoding of these individually modified tRNAs. In this project we will compare the decoding capacity of the "standard" *E. coli* $tRNA^{Val}$UAC with the superwobbling $tRNA^{Val}$ UAC from *M. mycoides.* By introducing modifications into the each tRNAs individually, we aim to assess the impact of the modification on both tRNAs and determine to what extend the modifications contribute to the potential differences in the decoding capacity of a standard or superwobbling tRNA.

PS2-S9-PP02 Expanding the genetic code via novel codon–anticodon pairs

Mara Gortan[0], Filip Sebest[1], Christoph Kreutz[1], Matthias Erlacher[0]

[1] Institute of Organic Chemistry and Center for Molecular Biosciences Innsbruck (CMBI), University of Innsbruck
[0] Universität Innsbruck, Austria

The natural genetic code—comprising 4 nucleotides and 20 (or 21) standard amino acids—enables the generation of a vast array of functional proteins and peptides. However, by expanding the genetic code also site-specific incorporations of non-canonical amino acids (ncAAs) into proteins is possible. This opens up possibilities for designing proteins with novel properties, allowing precise control over protein structure and function. In the past, various strategies have been developed, including the use of suppressor tRNAs, quadruplet codons, and the creation of novel codon/anticodon pairs. While these novel codon/anticodon systems rely on altered hydrogen-bonding patterns or hydrophobic interactions, our approach takes a fundamentally different route. We will employ mRNA modifications that work not through specific molecular interactions, but through steric blockages. These blockages can only be bypassed by tRNAs engineered with complementary structural features designed to accommodate these steric hindrances. Previous experiments with the RNA^{Gly} UCC from *Mycoplasma mycoides* demonstrated that a ribose abasic at position 34 still allows the decoding of purine-ending glycine codons (GGG, GGA). This provides the opportunity of combining these rab-sites with bulky inhibitory modifications. As a proof of principle, we showed that translation is blocked by the modification isobutyl-guanosine, and that protein synthesis can be restored upon addition of the rab-tRNA. Building on this concept, our goal is to test whether a similar codon–anticodon interaction can be applied to other tRNAs as well. Ultimately, we will establish and experimental setup based on rab-tRNAs for the incorporation of an ncAA into proteins.

PS2-S9-PP03 mRNA modifications in translation and RNA stability

Jennifer Wuggenig[0], Valentin Tumler[0], Elena Mayer[0], Ronald Micura[1], Matthias Erlacher[0]

[1] Institute for Organic Chemistry
[0] Medizinische Universität Innsbruck, Austria

RNA modifications have been identified in almost all types of RNA molecules, non-coding RNAs as well as messenger RNAs (mRNAs), and these modifications influence essential functions such as transcription, processing, splicing, translation and stability. Modifications within mRNAs have recently gained attention as they can significantly impact their localisation, translation as well as their stability. This depends not only on the type of modifications, but also on their locations. By introducing different natural and non-natural modifications to different parts of reporter mRNAs, we aim for a better understanding of their affect protein synthesis and mRNA stability, as well as how these processes are linked by modifications. The ribose abasic (rab) modification within the coding sequence (CDS) completely blocked translation while only minimally affecting RNA stability. In contrast, 6-methyladenosine (m6A) reduced protein output in a codon position–dependent manner, with comparable effects on mRNA stability across positions. Current experiments also including other modifications aim to determine whether RNA stability is influenced directly by these modifications or indirectly through ribosome stalling.

Since these experiments were all conducted in HEK293T cells, we aimed to determine whether selected modifications exert the same effect in other cell types such as Hela, N2A or SH-SYS5. For instance, the serotonin receptor 5-HT2c is one of the most prominent examples for A-to-I editing and has been shown to be important to modulate the receptor activity. However, the edited mRNAs are not translated in HEK293T cells, suggesting differences in the translation machinery of neuronal cells. By using different variants of the edited 5-HT2c mRNAs and transfecting them in different cell types we will try to determine to what extend the modifications differ in their effect and what the reason for this is.

PS2-S10-PP01 Investigating the reaction mechanism of coproheme decarboxylase from *Bacillus subtilis* reacting with FMN

Ela Zdenković, Nikolaus Falb, Stefan Hofbauer

Protein Biochemistry, The University of Natural Resources and Life Sciences (BOKU), Austria

Gram-positive bacteria utilize the coproporphyrin dependent (CPD) pathway for heme biosynthesis in which coproheme decarboxylase (ChdC) is a key enzyme. It is responsible for catalyzing a two-step oxidative decarboxylation of coproheme into heme *b* - a two-step reaction mechanism consisting of the formation a porphyrin radical species (Compound I) which is subsequently transferred onto a nearby tyrosine residue, yielding a tyrosyl radical of a crucial catalytic role. Hydrogen peroxide (H_2O_2) is an already known co-substrate and electron acceptor for the reaction catalyzed by ChdC. However, due to the toxic effects H_2O_2 can exert on the cell, alternative co-substrates are an important research target for further deconvoluting the reaction mechanism of ChdC.

FMN is known for its role in redox reactions in cells. Unlike other established electron carriers NAD or FAD, which were previously shown to be unable to mediate this reaction, prior studies have shown that the reaction of ChdC can be mediated by FMN under both aerobic and anaerobic conditions. This study focuses on further investigating the reaction of ChdC with FMN in depth, since the key question about how the tyrosyl radical essential for the reaction is formed is still unanswered in this case.

To mechanistically characterize the reaction of ChdC mediated by FMN the following methods were used: spin trapping, mass spectrometry, and spectroscopic measurements. Spin trapping was used to investigate tyrosyl radical formation during the aerobic and anaerobic reaction of ChdC and FMN: 2-methyl-2-nitrosopropane (MNP) was used to trap tyrosine radicals in the form of MNP-tyrosyl spin adducts during the reaction. Sample analysis was then performed by mass spectroscopy, where the mass of peptides containing tyrosines were compared to assess tyrosyl radical formation, with the goal to screen for other catalytically relevant tyrosine residues mediating electron transfer to FMN.

Together these results provide insight into the mechanistic properties of an alternative oxidative mechanism for heme biosynthesis, deepening our understanding of the role of FMN as an electron acceptor for ChdC.

Literature:

A. Dailey, S. Gerdes, T. A. Dailey, J. S. Burch, J. D. Phillips, Noncanonical coproporphyrin-dependent bacterial heme biosynthesis pathway that does not use protoporphyrin. Proc. Natl. Acad. Sci. 112, 2210–2215 (2015). Milazzo, T. Gabler, D. Pühringer, Z. Jandová, D. Maresch, H. Michlits, V. Pfanzagl, K. Djinović-Carugo, C. Oostenbrink, P. G. Furtmüller, C. Obinger, G. Smulevich & S. Hofbauer**,** *Redox Cofactor Rotates during Its Stepwise Decarboxylation: Molecular Mechanism of Conversion of Coproheme to Heme b*, ACS Catalysis 9, 6766–6782 (2019).

PS2-S10-PP02 Ligand shuffling – comparison of different porphyrins in complex with chlorite dismutase from *Dechloromonas aromatica.*

Annalena Habeler, Thomas Gabler, Stefan Hofbauer

Protein biochemistry, University of Natural Resources and Life Sciences Vienna (BOKU), Austria

Chlorite dismutase (Cld) is a heme *b* dependent oxidoreductase that catalyzes the decomposition of chlorite into chloride and dioxygen, providing an essential detoxification mechanism in bacteria and archaea capable of (per)chlorate respiration. Interestingly, Cld shares structural homology with coproheme decarboxylases (ChdCs), which utilize coproheme as a substrate in the terminal step of the coproporphyrin-dependent heme biosynthesis pathway. This raises the question as to whether Cld can accommodate alternative, presumably non-native porphyrin cofactors such as coproheme. Since chlorite dismutase of *Dechloromonas aromatica* (*Da*Cld) can be recombinantly expressed and the heme cofactor extracted to obtain the apo form, it serves as a suitable model system to test the enzyme's ability to coordinate coproheme in place of its native ligand heme *b*. This study thus aims to provide proof of concept for cofactor flexibility in Cld-type enzymes by comparing the structural and functional properties of heme *b*- and coproheme-bound forms.

After successful apo-*Da*Cld purification, electronic absorption spectroscopy was used to characterize bound porphyrin spectra and binding kinetics were analyzed with stopped-flow spectroscopy to validate coproheme binding to the enzyme and the corresponding stoichiometric ratio. Notably, the binding of heme *b* was too rapid to be resolved under experimental conditions, highlighting its superior affinity. For subsequent assays, the enzyme was reconstituted with either heme *b* or coproheme. Substrate conversion was confirmed via dioxygen production measured using Clark electrode measurements. These results demonstrate that the coproheme-bound enzyme retains catalytic activity, albeit at lower efficiency relative to the native cofactor as reflected by K_M, k_{cat} and specificity constant values. Cyanide-binding assays, monitored by UV-vis and stopped-flow spectroscopy, verified active site accessibility for both cofactors. However, association was significantly faster for the heme *b*-bound enzyme, evident from determined kinetic parameters.

To further explore coproheme interaction with *Da*Cld, crystallization trials and mutant strains targeting the cofactor-binding region are being conducted. In addition, Cld from *Candidatus Nitrospira defluvii* (*Nd*Cld), an organism harboring the genetic potential for the coproporphyrin-dependent heme biosynthesis pathway, is currently investigated to assess potential physiological relevance.

PS2-S10-PP03 Structural analysis of TPO oligomerization and the functional role of its domains

Isabella Fegerl, Vera Pfanzagl

Natural Sciences and Sustainable Resources, BOKU University, Austria

The thyroid gland is an important endocrine gland that secretes hormones essential for growth, development and metabolism. The oxidoreductase thyroid peroxidase (TPO) is a crucial heme-containing enzyme for thyroid hormone biosynthesis. It is a multidomain transmembrane protein, embedded in the apical membrane of thyrocytes. TPO catalyses iodide oxidation for tyrosine iodination and phenolic coupling of iodotyrosine residues in thyroglobulin. TPO is associated with autoimmune diseases like Graves' and Hashimoto's disease, leading to hyper- or hypothyroidism. Hashimoto's thyroiditis affects nearly 2% of the world's population, where the thyroid degrades, because patients develop autoantibodies against the TPO ectodomain. Patients with Graves' disease have dysregulated thyroid hormone biosynthesis, causing TPO overactivity. TPO's domain architecture and oligomerization state are so far unknown. TPO is thought to be active as covalently linked dimer. However, biochemical evidence suggests TPO can also exist as monomer, as autoantibodies recognizing its monomeric form in Hashimoto's patients.

We investigated TPO's structure, oligomerization, stability and domain functionality. Using a recombinant split luciferase assay, we found that TPO dimerizes in the cell membrane. We further tested different TPO domain variants *in vivo* in a thyroidal epithelial cell line to gain more insights into the putative dimerization site. The thermal stability of purified TPO ectodomain variants were analyzed by circular dichroism and differential scanning calorimetry and showed one major unfolding process with a small stabilizing effect of the heme. These data deepen our understanding of TPO's biochemical and structural aspects and its role in autoimmune diseases.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

S5: Infection and immunity

Chairs:

Guenter Weiss
Innsbruck Medical University, AT

Michaela Lackner
Medical University of Innsbruck, AT

S5-IT01 Programmed Cells? Epigenetics and Cell Engineering for Immunity and Cancer

Christoph Bock

CeMM & Medical University of Vienna, Austria

Cell engineering is becoming widely useful for fundamental biology (e.g., cells as probes and recorders) and for therapy (e.g., CAR T cells). Our research combines biotechnology and bioinformatics to genetically program human and mouse cells, in order to execute complex biological functions *in vitro* and *in vivo*. We specifically focus on the many roles of epigenetic mechanisms as mediators of cellular memory and plasticity, connecting the developmental history of individual human cells to their future potential.

Our goal is to understand cells by programming them based on a quantitative understanding of epigenetic cell states. We pursue three synergistic directions: To map and analyze cell states by multi-omics, single-cell, and spatial profiling (READ), to model regulatory circuitries with deep learning (LEARN), and to build artificial biological programs into cells by genome engineering (WRITE). We develop wet-lab and computational methods for all three directions and pursue initial applications for cancer and immunity.

READ: We analyzed the single-cell and spatial landscape of autoimmune granulomas (Krausgruber et al. 2023 Immunity), epigenetic heterogeneity in solid tumors (Klughammer et al. 2018 Nature Medicine; Sheffield et al. 2017 Nature Medicine), the role of structural cells in immune regulation (Krausgruber et al. 2020 Nature), and organoids in the Human Cell Atlas (Bock et al. 2021 Nature Biotechnology).

LEARN: We inferred regulatory circuits from single-cell data using “knowledge-primed neural networks” (Fortelny et al. 2020 Genome Biology), used knockout collections for JAK-STAT signaling in mouse (Fortelny et al. Nature Immunology) to test for causality, demonstrated the use of GPT-4 as a biomedical simulator (Schaefer et al. 2024 CBM) and developed a joint multimodal embedding model of transcriptomes and text for natural language based analysis of scRNA-seq data (https://cellwhisperer.cemm.at).

WRITE: We developed concepts and assays for high-content CRISPR screening (Bock et al. 2022 Nature Reviews Methods Primers), including the CROP-seq method for pooled CRISPR screening with single-cell RNA sequencing readout (Datlinger et al. 2017 Nature Methods) and the scifi-RNA-seq method cost-effective single-cell RNA-seq in 100,000s or millions of cells (Datlinger et al. 2021 Nature Methods).

Combining these three directions, we developed a platform for epigenetic and gene-regulatory optimization of CAR T cells using high-content screens in human primary cells (*ex vivo*) and in mice (*in vivo*). We identified several regulators that boost the performance of CAR T cells in these screens, and we systematically validated the *in vivo* effects of these boosted CAR T cells in systemic *in vivo* tumor models.

In conclusion, the combination of high-throughput profiling (READ), deep neural networks (LEARN), and genome editing at scale (WRITE) enables rapid functional dissection of epigenetic cell states and gene-regulatory networks in human cells, and their rational programming for biological research and therapy.

Funding: C.B. is supported by an ERC Consolidator Grant (n° 101001971) of the European Union.

Competing interests: C.B. is a co-founder and scientific advisor of Myllia Biotechnology (CRISPR screening technology and service) and Neurolentech (precision medicine for neurodevelopmental disorders).

S5-ST01 High-Definition Spatial Profiling of the Skin Microenvironment in Post-COVID Small Fiber Neuropathy

Yelyzaveta Miller-Michlits[0], Irina Poverennaya[1], Alexander Miller-Michlits[0], Michael Stingl[2], Ida Weiss[0], Paulus Rommer[3], Wolfgang Bauer[4], Martin Komenda-Lett[5], Elisabeth Lindeck-Pozza[5], Sigrid Klotz[6], Martin Bilban[7], Julia Wanschitz[8], Igor Adameyko[1], Adelheid Wöhrer[0]

[1] Department of Neuroimmunology, Center for Brain Research, Medical University of Vienna, Spitalgasse 4, 1090 Vienna, Austria
[2] Medical Practice Neurostingl, Garnisongasse 7/13, 1090 Vienna, Austria
[3] Department of Neurology, Medical University of Vienna, Währinger Gürtel 18-20, 1090 Vienna, Austria
[4] Department of Dermatology, Medical University of Vienna, Währinger Gürtel 18-20, 1090 Vienna, Austria
[5] Department of Neurology, Vienna Health Association Clinic Favoriten, Kundratstraße 3, 1100 Vienna, Austria
[6] Division of Neuropathology and Neurochemistry, Department of Neurology, Medical University of Vienna, Währinger Gürtel 18-20, 1090 Vienna, Austria
[7] Core Facility Genomics, Anna Spiegel Research Center, Medical University of Vienna, Lazarettgasse 14, 1090 Vienna, Austria
[8] Department of Neurology, Medical University of Innsbruck, Anichstraße 35, 6020 Innsbruck, Tirol, Austria
[0] Institute of Neuropathology and Neuromolecular Pathology, Medical University of Innsbruck, Austria

Post-viral small fiber neuropathy (SFN) is a severe disabling complication of SARS-CoV-2 infection, marked by sensory-autonomic dysfunction and selective Aδ/C-fiber loss months after acute infection. While axonal pathology is recognized, the cellular mechanisms driving nerve fiber de- and regeneration remain poorly defined. We hypothesized that Schwann cells (SCs), as mediators of axonal support and neuroimmune communication, may be critically involved in post-COVID SFN. Skin punch biopsies were collected from affected individuals and age- and sex-matched controls (6 to 12 months post acute COVID infection), and Intraepidermal nerve fiber density (IENFD) was quantified via PGP9.5 immunofluorescence. Spatial transcriptomics (Visium HD, 10X Genomics) was performed on 13 skin sections (6 SFN, 7 controls), with downstream analyses including cell type deconvolution (RCTD), SC-specific differential expression, and pathway enrichment (clusterProfiler, MSigDB). Protein-level spatial mapping was initiated using multiplex immunofluorescence (Opal, Akoya Biosciences) targeting axonal, glial, immune, vascular, and autonomic markers. The cohort comprised 47 individuals (F:M=2.6:1, mean age 42.5 years), of whom 80.9% showed reduced IENFD. Older age (p=0.003, Mann–Whitney) and non-length-dependent SFN (p=0.0172, Kruskal–Wallis) were associated with more pronounced axonal loss. Spatial transcriptomics revealed focal depletion of SCs and dermal macrophages in cases. SCs upregulated galanin (GAL) and translocase of inner mitochondrial membrane 10B (TIMM10B), consistent with nociceptive sensitization and mitochondrial stress. In contrast to controls, cases showed diminished expression of sodium voltage-gated channel alpha subunit 7 (SCN7A) expression in macrophages within SC-rich spatial bins, indicating disrupted glial–immune interaction. Female cases showed altered expression of hormone-responsive genes (NR3C1, IGF1, ESR1). Inflammatory, hypoxic, or mast cell signatures were not enriched in post-viral SFN. Multiplex immunofluorescence staining confirmed robust marker detection across compartments with image analysis being ongoing, which will help corroborate the neuroimmune and glial–vascular interactions. Taken together, these findings implicate Schwann cell dysfunction and loss of local neuroimmune homeostasis as key mechanisms in post-COVID SFN, independent of canonical inflammatory pathways.

S5-ST02 Clinical relevance of circulating blood microaggregates and reactivation of Epstein-Barr virus in long-term Post-COVID patients

Martin Hermann[1], Christoph Lisch[2], Regine Gerth[3], Georg Wick[4], Eva Untersmayr-Elsenhuber[5], Tatjana Marth[6], Mirjam Bachler[1], Dietmar Fries[1], Nikolaus Wick[3]

[1] Medical University Innsbruck, Austria
[2] Sanatorium Hochrum, Austria
[3] Specialized Laboratories Wick, Innsbruck Austria
[4] Division of Pathophysiology, Biocenter, Medical University Innsbruck, Austria
[5] Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Austria
[6] Fachhochschule für Gesundheit, Innsbruck

Chronic persistence of systemic symptoms after recovery from active COVID-19 has become a significant disease burden, named post-COVID. The underlying nature of this illness still remains well hidden behind it´s plethora of signs and symptoms, making it difficult to find a specific treatment option. Herein we introduce a novel diagnostic morphological approach for visualizing microaggregates circulating in peripheral venous blood, which are large enough to impede capillary blood flow.

Among many pathophysiological hypotheses we focus on impaired hemostasis as well as reactivation of latent Epstein-Barr virus. In addition, secretion of interferon gamma by mononuclear leukocytes in response to peptides of Epstein-Barr virus (EBV) is increased in these patients. As a promising therapeutic approach, we provide retrospective data on the effect of anti-thrombotic and virostatic drugs, respectively. In a large number of patients, clinical improvement was observed after platelet inhibition, particularly when EBV was also treated with antiviral therapy.

S5-ST03 Identification of highly suppressive human regulatory T cells in old age

Rocamora Reverte Lourdes, Sapper Tobias, Weinberger Birgit

Immunosenescence and Vaccination, Institute for Biomedical Aging Research, Universität Innsbruck, Austria

The immune system is a tightly regulated network that defends the body against foreign antigens while maintaining tolerance to self. Regulatory T (Treg) cells are key mediators of immune tolerance and homeostasis, and their integrity is critical for maintaining the balance between health and disease. Aging leads to immune dysregulation, increasing susceptibility to various pathologies. It is well established that aging affects T lymphocytes (both $CD4^+$ and $CD8^+$), which often acquire a pro-inflammatory profile and exhibit signs of functional exhaustion. Senescent T cells typically downregulate co-stimulatory molecules like CD28, while upregulating inhibitory receptors such as PD-1 and CTLA-4. Interestingly, well-functioning Treg cells express some markers related to aged T cells, and their age-associated changes are not well defined. In addition, whether Treg functionality declines or is enhanced with age remains debated.

In our study, we compared $CD4^+$ Treg cells from young and older donors. While the expression of classical Treg markers remained stable, Tregs from older individuals showed significantly higher levels of CD28. Notably, $CD28^{high}$ Tregs expressed more Foxp3, CTLA-4 and PD-1 than $CD28^{low}$ Tregs. Importanly, $CD28^{high}$ Tregs also exhibited a $CD45RO^+$ memory/effector phenotype and showed accumulated DNA damage upon apoptotic stimuli. To investigate the functional role of CD28 levels on Treg suppressive capacity, we sorted $CD4^+CD25^+CD127^{low}$ Tregs based on CD28 expression and co-cultured them with proliferating PBMCs. Regardless of donor age, $CD28^{high}$ Tregs displayed superior suppressive activity compared to their $CD28^{low}$ counterparts.

Our findings suggest that elevated CD28 expression identifies a highly suppressive Treg subset in the elderly, potentially contributing to the dampened immune responses observed in the elderly.

S5-ST04 Loss of NR2F6 reduces tissue-resident macrophages and protects from *Salmonella* Typhimurium infection.

Johannes Woelk[6], Christa Pfeifhofer-Obermair[1], Julia Benz[2], Natascha Brigo[3], Milena Bamberger[6], Alexeja Kleiter[4], Martin Hermann[5], Günter Weiss[1], **Natascha Hermann-Kleiter[6]**

[1] Medical University of Innsbruck, Department of Internal Medicine, Innsbruck, Austria
[2] Friedrich-Alexander-University Erlangen-Nuremberg, Clinical Microbiology, Immunology and Hygiene, Erlangen, Germany
[3] Department of Internal Medicine, Innsbruck, Austria
[4] Medical University of Innsbruck, Department of Dermatology, Venereology & Allergology and 3D Bioprinting Laboratory, Innsbruck, Austria
[5] Medical University of Innsbruck, Department of Anaesthesia and Intensive Care Medicine, Innsbruck, Austria
[6] Genetics and Pharmacology, Medical University Innsbruck, Austria

Introduction*:* Mononuclear phagocytes are critical components of the innate immune system, which have emerged as a key rheostat regulating the balance between organ health and disease. Nuclear receptors (NR) control essential aspects of macrophage and monocyte biology. Our previous research identified the nuclear receptor NR2F6 as a regulator of T and NK cell responses.

Objectives: Define the functional role of NR2F6 in tissue-resident macrophages in homeostasis and bacterial infection.

Methods: We analyzed mononuclear phagocytes in various tissues from both healthy and *Salmonella Typhimurium*-infected germline *Nr2f6*-deficient mice using flow cytometry, bulk RNA sequencing, western blots, legendplex assays, metabolic assays, confocal microscopy, phagocytosis assays, and congenic adoptive transfer experiments.

Results: In healthy mice, NR2F6 deficiency alters tissue-resident macrophage populations in the liver, lung, and spleen. In response to *Salmonella* Typhimurium infection, mice deficient in the nuclear receptor NR2F6 exhibit improved clinical outcomes, characterized by reduced weight loss, bacterial loads in the spleen and liver, and decreased plasma pro-inflammatory cytokines. Despite unchanged basal iron metabolism in the spleen and liver, iron regulatory proteins and the IL-6-hepcidin axis are altered in *Nr2f6*-deficient mice during *Salmonella* infection, reducing hypoferremia. Transcriptomic analysis of splenic red pulp macrophages reveals significant alterations of phagocytosis-related genes, including upregulation of *Sirpa*. *In vitro,* phagocytosis of red blood cells, regulated by the inhibitory CD47-Sirpα axis, and *Salmonella* Typhimurium phagocytosis is significantly impaired in *Nr2f6*-deficient splenic macrophages. Blocking Sirpα *in vitro* restores the phagocytic activity of *Nr2f6*-deficient macrophages to wild-type levels. *In vivo, Salmonella* Typhimurium loads are partially increased post-infection in anti-Sirpα-treated *Nr2f6*-deficient mice.

Conclusions: These findings uncover a previously unrecognized role of NR2F6 in host-pathogen interactions, positioning it as a potential therapeutic target for infectious diseases.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

S6: Mechanical aspects of cell adhesion and migration

Chairs:

Francesco Baschieri
Medical University
Innsbruck, AT

Francois Tyckaert
MUI, AT

S6-IT01 Forces in receptor-mediated cell adhesion

Elisabetta Ada Cavalcanti-Adam

Cellular Biomechanics, University of Bayreuth, Germany

Cell adhesion receptors such as integrins and cadherins are central to how cells sense, generate, and respond to mechanical cues. In this talk, I will present how spatial patterning of ligands and nanoscale modulation of substrate stiffness affect integrin clustering and the dynamics of force transmission at adhesion sites. Using molecular tension sensors, traction force microscopy, and tunable nanoengineered substrates, we explore how the molecular clutch mechanism governs adhesion reinforcement, rigidity sensing, and cell spreading. Furthermore, I will discuss how specific integrin subtypes and growth factor co-presentation at the nanoscale regulate collective migration and differentiation. Finally, we show that mechanical remodeling driven by RAB5A overexpression—through integrin upregulation and spheroid softening—enables a transition to coordinated, supra-cellular spreading modes, offering insights into the mechanobiology of epithelial invasion.

S6-ST01 Topographically driven migration of cancer cells

Pere Patón González, Elias Moser, Maria Reichhold, Francesco Baschieri

Molecular Pathophysiology, University of Innsbruck, Austria

Metastases are the leading cause of cancer-related mortality, yet no therapies specifically target cancer cell dissemination. Metastatic tumors often exhibit aligned collagen fibers, which cancer cells use for invasion—a process known as contact guidance. In vitro, cells similarly align and migrate along structured topographies, but the underlying mechanism remains unclear.

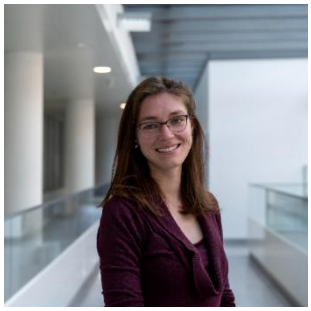
To investigate contact guidance, we developed a soft lithography method to generate transparent nanocurvatures. We then optimized an automated workflow to track cell migration using phase contrast imaging. This allowed us to observe that metastatic breast cancer cells (MDA-MB-231) migrate along nanocurvatures, exhibiting strong contact guidance.

We reasoned that adhesion and force transmission are key for contact guidance.

Focal adhesions (FAs) typically mediate adhesive migration by connecting the extracellular matrix to the cytoskeleton enabling force transmission. Talin1 is a key protein for FA assembly. To assess the role of FA in contact guidance, we generated cells Talin1-deficient clones (MDA dTLN1). Surprisingly, dTLN1 cells retained their ability to undergo contact guidance, suggesting an alternative mechanism for topographic sensing. We hypothesized that Endocytosis-Related Adhesions (ERAs), which form when endocytosis stalls on oversized cargo like collagen fibers, may mediate adhesion. Indeed, ERA markers accumulated on nanocurvatures.

To explore force transmission in contact guidance, we performed a small-scale drug screen targeting the actin and microtubule cytoskeleton using topographical migration as readout. Preliminary results indicate a role for microtubules in contact guidance. Future studies will focus on defining ERA and microtubules function in topography sensing. Unraveling this mechanism enable to design new anti-metastatic therapies.

S6-ST02 Unraveling the YAP1-TGFb1 axis: a key driver of androgen receptor loss in prostate cancer-associated fibroblasts



Elena Brunner[0], Elisabeth Damisch[0], **Melanie Emma Groninger[0]**, Lukas Nommensen[0], Lucy Neumann[0], Georgios Fotakis[1], Zlatko Trajanoski[2], Georg Schäfer[3], Christian Ploner[4], Sofia Karkampouna[5], Francesco Bonollo[6], Marianna Kruithof-de Julio[5], Natalie Sampson[0]

[1] Department of Internal Medicine V, Medical University of Innsbruck, 6020 Innsbruck, Austria
[2] Institute of Bioinformatics, Medical University of Innsbruck, 6020 Innsbruck, Austria
[3] Institute of Pathology, Neuropathology and Molecular Pathology, Medical University of Innsbruck, 6020 Innsbruck, Austria
[4] Department of Plastic, Reconstructive and Aesthetic Surgery, Medical University of Innsbruck, 6020 Innsbruck, Austria
[5] Department for BioMedical Research, Urology Research Laboratory & Department of Urology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland
[6] Department for BioMedical Research, Urology Research Laboratory, University of Bern, Bern, Switzerland
[0] Department of Experimental Urology, Medical University of Innsbruck, Austria

Due to their pivotal roles in tumor progression and therapy resistance, cancer-associated fibroblasts (CAF) are considered key therapeutic targets with loss of stromal androgen receptor (AR) a poorly understood hallmark of aggressive prostate cancer (PCa). A paucity of pre-clinical models however has hampered functional studies of CAF heterogeneity. We demonstrate that our newly-generated CAF biobank contains three FAP^{+}-fibroblast subtypes, each with unique molecular and functional traits. Cultures with an early-activated phenotype expressed the highest levels of AR and exhibited AR-dependent growth. Consistently, stromal cells expressing early-activation markers co-expressed nuclear AR in clinical specimens and were enriched in pre-neoplastic lesions/low-grade PCa. Conversely, myofibroblastic CAF (myCAF), which expressed low AR levels *in vitro* and *in vivo* and were proliferatively-insensitive to AR signaling modulation, constituted the predominant CAF subpopulation in stromogenic high-grade PCa and castration-resistant LACP9 patient-derived xenografts. Exacerbation of the myCAF state upon castration of LAPC9-bearing hosts underscored these findings. Mechanistically, AR loss in myCAF was driven by an NFkB-TGFb1-YAP1 axis, whose combined targeting synergistically repressed myofibroblastic hallmarks and impaired autophagic flux, effects that were potentiated by enzalutamide resulting in myCAF cell death. Collectively, these findings provide a mechanistic rationale for adjuvant targeting of the YAP1-TGFb signaling axis to improve patient outcomes.

S6-ST03 Spatial engineering of collagen ligand nanopatterns to study integrin-dependent migration in cancer

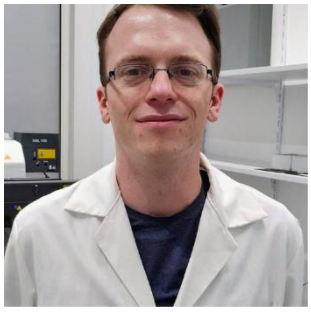
Mateo Ceballos Giraldo[1], **Victoria Levario Diaz[1]**, Abhishek Anan Jalan[2], Matthias Weiss[3], Elisabetta Ada Cavalcanti-Adam[1]

[1] Cellular Biomechanics, University of Bayreuth, Germany
[2] Department of Biochemistry, University of Bayreuth, Bayreuth, Germany
[3] Experimental Physics I, University of Bayreuth, Universitätsstraße 30, D-95447 Bayreuth, Germany

The ability of cancer cells to migrate through the extracellular matrix (ECM) is a hallmark of metastasis and is tightly regulated by integrin-mediated adhesion.[1,2] Invasive breast cancer cells, such as MDA-MB-231, adopt a mesenchymal migration mode that relies on dynamic interactions with collagen GFOGER-like sequences via integrins α1β1, α2β1, α10β1, and α11β1.[3] These collagen-binding integrins are associated with tumor progression, epithelial-to-mesenchymal transition, and matrix remodeling,[5] yet how their nanoscale organization influences front–back coordination during migration remains poorly understood. To investigate this, we engineered defined 1D micro-nanopatterned stripes using block-copolymer micelle nanolithography, functionalized with collagen-mimetic peptides specific to the above integrins. The 10 µm-wide stripes feature a quasi-hexagonal arrangement of 8 nm gold nanoparticles spaced at 50 nm and 100 nm, enabling precise control over integrin clustering and focal adhesion assembly. This setup allows the engagement of single integrin heterodimers at each ligand-presenting site. Using time-lapse microscopy and immunostaining, we studied the migratory behavior of MDA-MB-231 cells on these ligand-presenting nanopatterns. We observed that variations in ligand spacing significantly affected stick–slip dynamics, front–rear coordination and migration speed. Notably, GFOGER-like sequence, GLOGEN in 100 nm ligand spacing promoted more coordinated and persistent migration, suggesting a critical role for integrin spatial organization in regulating invasive behavior. Our findings demonstrate that the nanoscale presentation of collagen-derived ligands modulates cancer cell migration via integrin-mediated signaling. This approach provides a powerful platform for dissecting the mechanistic role of specific integrin subtypes in cancer progression and may inform future strategies for targeting metastatic dissemination.

Hanahan, D., & Weinberg, R. A. (2011) *Cell*, 144(5), 646–674; Pickup, M. W., Mouw, J. K., & Weaver, V. M. (2014) *EMBO rep*, 15, 1243-1253; Popova, S. N., et al (2007). *Acta Physiol*. 190, 179-187; Zelt, C., & Gullberg, D. (2016) *Journal of Cell Science*, 129(4), 653-664; Niland, S., & Eble, J. A. (2020) *Int J Mol Sci*, 22(1), 238.

S6-ST04 Metabolic modulation and mechanotransduction in T24 bladder cancer cells



Maximilian Jobst, Giorgia Del Favero

Department of Food Chemistry and Toxicology, University of Vienna, Austria

Bladder tissue is exposed to chemical and physical cues: urine accumulates multiple potentially bioactive xenobiotics, this is accompanied by urine flow, as well as expansion and contraction of the organ. In response biomolecular processes of cells can be adapted to enable growth and functional stability despite these challenging conditions. Yet, adjusting to one cue might change the sensitivity to another as was demonstrated before, for instance autophagy modulation may alter the cells response profile to shear stress [1,2].

This work aims at elucidating if a similar interplay exists between metabolic modulation and response capacity to shear stress. For this, two model substances were selected: 2-Desoxy-Glucose (2DG, 2 mM), an inhibitor of glycolysis and MitoTEMPOL (MT, 1 µM), a mitochondrial antioxidant supporting OXPHOS. Even at non-cytotoxic concentrations the compounds altered T24 cell's motility, increasing migration upon MT incubation and decreasing it with 2DG. AFM measurements revealed an increase in cell stiffness upon incubation with the metabolic modulators (2DG nuclear, perinuclear and cytoplasmic area; MT cytoplasmic area). In control condition, mechanical preconditioning with shear stress returned an increase in stiffness in all subcellular compartments. Yet, this response was mitigated by the metabolic modulators, especially 2DG in the nuclear and perinuclear area. Exploring elements of the mechanosensory apparatus, incubation with 2DG and MT altered actin signal intensity and morphometric appearance of the network. Further the (re-)organization of the cytoskeleton depends on PTMs of its building blocks, for instance actin acetylation[3]. Both compounds increased the pan-acetylation in the nuclear area. Yet the cytoplasmic signal, reflective of cytoskeletal modifications, aligned with diverging biophysical changes observed in the cells. Namely, increasing in cells treated with 2DG and decreasing following MT incubation.

In sum, the current work describes how metabolic modulation triggers biomolecular changes, connected to impaired motility and biomechanical responses to shear stress. Importantly this connects two major components present in the *in vivo* bladder environment in a combined model. Further research is needed to fully understand the interplay between chemical and physical cues, aiming to improve the predictability of *in vitro* systems.

1, Jobst, M. et al., 2024; 2, Jobst, M. et al., 2023; 3, Latario A, M., 2020.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

S7: Organelle and membrane biology

Chairs:

Oliver Schmidt
Medical University of Innsbruck, AT

Hesso Farhan
Medical University of Innsbruck, AT

S7-IT01 Lipid storage and interorganelle communication

Abdou Rachid Thiam

CNRS/ENS, France

Cells depend on the precise coordination of lipid metabolism and organelle communication to maintain homeostasis in response to fluctuating metabolic demands. At the center of this network is the endoplasmic reticulum (ER), where lipids are synthesized, sorted, and directed toward storage or functional use. Lipid droplets (LDs), dynamic organelles that store neutral lipids, emerge from the ER in a tightly regulated process driven by protein machinery. Among these, the ER membrane protein seipin plays a crucial role in nucleating LDs and coordinating the local lipid environment. Recent studies, including our reconstitution-based biophysical work, highlight how seipin regulates the local balance between glycerolipids and sphingolipids, thereby influencing LD formation and broader organelle homeostasis. In parallel, lipid transfer proteins (LTPs) facilitate non-vesicular lipid transport at membrane contact sites, thereby enabling communication between organelles such as the ER, mitochondria, and lysosomes. Our integrative approach, combining reconstitution assays and live-cell imaging, demonstrates how regulated protein-lipid interactions orchestrate interorganelle communication and ensure lipid storage is dynamically controlled. These insights enhance our understanding of lipid homeostasis and the physical principles underlying organelle function.

S7-ST01 The role of the Retriever in polarized plasma membrane recycling

Luca Szabó[1], Bettina Sarg[2], Leopold Kremser[2], Klaus Faserl[2], Hesso Farhan[3], Lukas A. Huber[1], Georg-Friedrich Vogel[4]

[1] Medizinische Universität Innsbruck, Austria
[2] Institute of Medical Biochemistry, Protein Core Facility, Biocenter, Medical University of Innsbruck, Innsbruck, Austria
[3] Institute of Pathophysiology, Biocenter, Medical University of Innsbruck, Innsbruck, Austria
[4] Institute of Cell Biology, Biocenter, Medical University of Innsbruck, Innsbruck, Austria & Paediatrics I, Medical University of Innsbruck, Innsbruck, Austria

In a CRISPR-knock-out-screen on apical trafficking of DPPIV in Caco2 cells, we found the Retriever subunit dscr3 among the hits, which controls recycling together with mtmr2 (also found among the hits) through the CCC complex.

The Retriever complex, a trimeric assembly of vps29, vps35l and dscr3, shares a similar structure and function with the Retromer as they have a common subunit (vps29) and both recycle proteins from endosomes towards the plasma membrane (PM) or Golgi. Crucial difference, however, is that they recognize a different subset of cargoes through different adaptor proteins. It was shown in non-polarized cells that the cargo adaptor of the Retriever is snx17. Up to date, the Retriever complex has not been studied in the context of epithelial polarity, in particular apical and basolateral Retriever cargo segregation.

To address this, we used the epithelial polarity model Madin-Darby Canine Kidney (MDCK) cells and generated WT, VPS35L knock-out (KO), SNX17 KO, MTMR2 KO and CCDC22 KO lines. To study PM cargo recycling, we implemented an unbiased approach where we compared polarized WT and KO clones by selectively biotinylating apical and basolateral PM proteins and identified Retriever-dependent PM cargoes by quantitative mass spectrometry in combination with tandem mass tag (TMT)-labeling.

We have found previously established snx17 cargoes as well as several others among the proteins that appeared to be regulated in our KO clones based on the mass spectrometry measurements. The ongoing experiments aim to confirm that the Retriever regulates the chosen new cargo candidates and thus has a role in basolateral and apical sorting. This will include imaging of fluorescently tagged cargoes and the characterization of the altered endosomal/exocytic system.

Overall, the project aims to provide a comprehensive understanding of Retriever-dependent plasma membrane cargo recycling in polarized epithelial cells.

S7-ST02 Characterizing a protective function of the ESCRT machinery at the stressed plasma membrane

Astha Purwar[1], Simon Sprenger[2], Oliver Schmidt[2], David Teis[1]

[1] Molecular Biochemistry, Medical University Innsbruck, Austria
[2] Institute of Cell Biology, Medical University of Innsbruck, Austria

The endosomal-sorting complexes required for transport (ESCRT) were identified in budding yeast (*S. cerevisiae*) for their role in directing ubiquitinated transmembrane proteins into the vacuolar lumen for degradation via the multivesicular body (MVB) pathway. Beyond this function, ESCRTs have now been implicated in other cellular processes, such as cytokinesis, viral budding, and autophagy. These seemingly unrelated processes require the assembly of ESCRT-III filaments and their interaction with Vps4 (AAA-ATPase) to drive membrane remodeling with similar topological features. Typically, ESCRT machinery catalyzes negative membrane curvature, such as during the MVB pathway, exosome formation, or membrane repair processes.

Interestingly, we observed that plasma membrane stress (PM) induced by inhibition of TORC2 or hyperosmotic shock in *S. cerevisiae* recruits Snf7 (an ESCRT-III subunit) to PM structures invaginating into the cytosol (positive curvature) to preserve PM integrity. These findings raise two important questions: (1) How do ESCRT-III assemblies preserve PM integrity in response to TORC2 inhibition, and (2) how do ESCRT-III polymers assemble at the membranes with positive curvature. More broadly, does ESCRT-III filament formation follow a set of general rules, or is adapted to perform varying biological tasks, which would imply organelle-specific ESCRT-III assembly reactions.

Our first objective aims to understand how ESCRT-III assembly is initiated at the stressed (but possibly unruptured) PM. Thereby we aim to identify the physicochemical cues that trigger ESCRT-III/Vps4 recruitment to the stressed PM. Furthermore, we will investigate whether the ESCRT-III assembly at the PM and endosomes follows similar or different biochemical principles, particularly the interaction surfaces between ESCRT-III subunits and their stoichiometries. Finally, we seek to dissect how ESCRT-III assemblies alleviate PM stress.

Our work will expand the understanding of how ESCRT-III is recruited to stressed membranes and delineate either universal or organelle-specific adaptations for ESCRT-III assembly.

S7-ST03 Mechanistic dissection of the ER export of the sphingolipid biosynthesis regulator Orm2

Niklas Schomisch[1], Brigitta Seifert[1], Sinead Iduna Schwabl[2], Barış Bekdaş[1], Bellmunt Blanco[1], Natascha Noé[1], Jana Bleher[1], Bianca M. Esch[3], Florian Fröhlich[3], David Teis[2], Oliver Schmidt[1]

[1] Zellbiologie, Austria
[2] Institute of Biochemistry, Biocenter, Medical University of Innsbruck, Austria
[3] Department of Biology/Chemistry, Bioanalytical Chemistry Section, Osnabrück, Germany

ORMDL family proteins are conserved regulators of the sphingolipid biosynthesis, with the main function to inhibit the rate-limiting enzyme serine-palmitoyl transferase (SPT) in the ER [1]. In humans, dysregulation of SPT activity causes a form of amyotrophic lateral sclerosis (ALS), and is genetically linked to several inflammatory diseases [2,3]. In budding yeast the ORMDL family consists of two proteins, Orm1 and Orm2. Both are are embedded in a homeostatic system that adjusts sphingolipid levels to cellular demands [1]. Although Orm1 and Orm2 share about 70% sequence identity, the two proteins inhibit the SPT with different potency, Orm2 being the stronger inhibitor [4]. To date little is known about specific interactors and functions beyond SPT inhibition. Yet, their regulation is different, with Orm2 being subject to regulated ER export and proteolytic turnover via the EGAD pathway, which is not observed for Orm1 [5]. How the specificity of ER export vs. retention of these highly homologous proteins is achieved is unknown. Here, we identified a mechanism which might be responsible for retaining Orm2 in the ER membrane, until it becomes released and primed for export by phosphorylation. In an Orm2-interactome we found two p24 proteins, which are known substrate adaptors of COPII vesicles and hence could mediate ER export specificity. Moreover, we found that Orm1 is strongly retained in the ER by intrinsic sequence motifs that can be transplanted onto Orm2.

[1] Schomisch and Schmidt, 2024, Biospektrum

[2] Mohassel et al., 2021, Nat. Med.

[3] Moffatt et al., 2007, Nature

[4] Körner; Schäfer et al., 2024, Cell Rep

[5] Schmidt et al., 2019, EMBO J.

S7-ST04 LAMTOR1 phosphorylation orchestrates protein interactions and metabolic signalling at the lysosome

Isabel I. Singer[1], Flora S. Gradl[1], Caroline Krebiehl[1], Taras Stasyk[1], Nikolaus Obojes[2], Eva Rauch[1], Mariana E.G. de Araujo[1], Lukas A. Huber[1]

[1] Cell Biology, Medical University Innsbruck, Austria
[2] Institute for Alpine Environment, Eurac Bozen, Italy

Lysosomes house a sophisticated nutrient-sensing machinery that integrates information about the cell's energy levels, extra- and intracellular nutrient availability, as well as the presence of stress factors and hormones. The LAMTOR-complex serves a central hub in regulating some of these processes by recruiting and/or activating AMPK, MAPK and mTOR on the lysosomal surface. Signalling to and from lysosomes can be of catabolic or anabolic nature, cooperative or mutually exclusive, depending on the associations LAMTOR establishes with other proteins- or protein complexes.

Given that LAMTOR1, the membrane anchor of the LAMTOR-complex, is highly phosphorylated, we decided to explore posttranslational modifications as a regulatory mechanism in this context.

Using recombinant LAMTOR-complex, we confirmed *in-vitro*, that AMPK phosphorylates LAMTOR1 at S63. While it is well established how anabolic signaling is coordinated by the LAMTOR complex, very little is known about LAMTOR's role in catabolism. Given the role of AMPK as a catabolic master regulator, this result prompted us to further investigate the effects of this phosphorylation on binding partner interactions and signaling downstream of LAMTOR.

To this end, we performed a mass spectrometry-based interactome analysis under AMPK activating conditions using mutations at the 63 site to evaluate the dependence of changes in binding partner interactions on phosphorylation. The interactome revealed not only that S63 critically influences the binding affinity to key components of the lysosomal mTORC1 signaling complex, but also uncovered previously unrecognized functions of the LAMTOR complex in catabolism control, that operate independent of mTOR.

The current phase of research is dedicated to validating the interactome data and exploring the *in vivo* effects of the aforementioned phosphorylation site. Through this analysis we expect to improve our understanding of lysosomal signaling pathways and how they are regulated.

This work is funded by the FWF funded PhD program Cellular Basis of Diseases: Molecular Control of Metabolism and Inflammation (DOC 82 doc.fund)

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

S8: Advances in toxicology and risk assessment

Chairs:

Johanna Gostner
Medical University of Innsbruck, AT

Giorgia Del Favero
University of Vienna - Faculty of Chemistry, AT

Session sponsored by

ASTOX
Austrian Society of Toxicology
Österreichische Gesellschaft für Toxikologie

S8-IT01 NAMs in risk assessment – challenges and perspectives

Philip Marx-Stölting

BfR, Germany

There have been several projects developing new approach methods (NAM, in vitro or in silico methods) in the past. However, regulatory uptake of these methods is still limited, especially for more complex endpoints like systemic toxicity, carcinogenicity or endocrine disruption. To accelerate uptake of NAM into a next generation risk assessment (NGRA) it is therefore needed to link regulatory needs and perspectives closer to NAM development.

In the European Partnership for the Assessment of Risks from Chemicals (PARC) the concept of co-design of NAM as well beta testing of NAM has been explored. Co-design means that regulators priorities different endpoints and projects based on regulatory needs and monitor projects closely by frequent peer review. In contrast beta testing refers to use of selected NAMs in combination for regulatory decision making (if allowed by regulation) prior to their full regulatory implementation, e.g. when closing data gaps of concern for data-poor compounds.

Additionally, a roadmap is under construction in the EU that aims at outlining a strategy for phasing out animal testing.

The presentation will give an overview on challenges in the implementation of NAM and NGRA but also show how recent EU initiatives aim at overcoming these challenges.

S8-ST01 Dose-response modeling from omics data in toxicology

Pablo Monfort-Lanzas[1], Hubert Hackl[2], Johanna M. Gostner[3]

[1] Institute of Medical Biochemistry, Medical University of Innsbruck, Austria
[2] 2. Institute of Bioinformatics, Biocenter, Medical University of Innsbruck, Innsbruck, Austria
[3] 1. Institute of Medical Biochemistry, Biocenter, Medical University of Innsbruck, Innsbruck, Austria

Understanding the molecular effects of chemical exposures requires methods that can model complex biological responses and capture nonlinear patterns. Omics datasets are widely generated in toxicologic and pharmacologic research to obtain quantitative and mechanistic information. However, interpreting these data remains difficult, especially when considering dose- or concentration-dependent effects. Traditional dose-response models assume monotonicity and focus on single features. This limits their ability to capture the complexity of biological responses.

Dose-response relationships in biological systems are frequently non-monotonic, reflecting the influence of adaptive or feedback processes. Meanwhile it is well recognized that several substances induce such patterns, including hormetic responses and threshold-dependent transitions, which are not well represented by classical modeling approaches. Pathway-level dose responses offer a more mechanistic perspective and are essential for understanding modes of action.

Most existing tools rely on mathematical models that fit a limited set of predefined functions to each gene individually. Pathway-level responses are then inferred by aggregating benchmark doses, typically using confidence intervals. While the BMD is widely used, it captures only part of the response and may overlook early or subtle changes. Furthermore, many available tools are complex and require bioinformatics skills, and few offer user-friendly web applications. To address these challenges, we developed DoseRider, a web tool (https://doserider.i-med.ac.at/) for pathway-level dose-response modeling using mixed models with splines. It supports multiple omics types and introduces trend change doses (TCDs) as early indicators of pathway perturbation.

In conclusion, pathway-level modeling is essential for interpreting omics data and uncovering mechanisms of action, and DoseRider supports this by effectively capturing non-linear responses and identifying biologically relevant thresholds.

S8-ST02 Describing the role of shape-dependent toxicity for foodborne contaminants in a human Intestinal cell model

Janice Bergen[1], Claudia Iriarte-Mesa[2], Francesco Crudo[3], Doris Marko[3], Freddy Kleitz[2], Giorgia Del Favero[4]

[1] Food Chemistry and Toxicology/ Core Facility Multimodal Imaging, University of Vienna, Austria
[2] Department of Functional Materials and Catalysis, Faculty of Chemistry, University of Vienna, Vienna, Austria
[3] Department of Food Chemistry and Toxicology, Faculty of Chemistry, University of Vienna, Vienna, Austria
[4] Department of Food Chemistry and Toxicology, Faculty of Chemistry, University of Vienna, Vienna, Austria; Core Facility Multimodal Imaging, Faculty of Chemistry, University of Vienna, Vienna, Austria

Developing models for toxicological profiling based on advanced cell culture systems is substantial to bridge the gap between *in vivo* and *in vitro* testing and ultimately reduce the need of animal-based testing. Depicting the complexity of the gut, basic knowledge on the capacity of intestinal cells to interact with differentially shaped materials can find application in several fields, including design of cargoes for drug delivery[1,2], integration of nanostructure-based models for toxicological profiling[3] or for the evaluation of the potential impact of foodborne nano-micro fragments resulting from the degradation of food contact materials or contaminants[4]. Building on the knowledge gained studying the interaction of synthesized silica nanoparticles (NPs) displaying spherical, rod, and virus-like morphology with the human intestinal model Caco2/HT29-MTX-E12[5], supported the development of a novel model to probe intestinal barrier function at the nanoscale using tailored mesoporous silica-based nanorods[3]. Furthermore, complementary functionalization of spherical SiO_2-based NPs proved effective in modulating movement through the mucosal lining and interaction with the cells depending on hydrophobicity/hydrophilicity and/or surface charge[6]. Here, SiO_2-based rod-shaped mesoporous NPs of different dimensions (small rods; 35 nm x 160 nm and bacteria-like rods; 200 nm x 450 nm) were synthesized and combined with chemical surface modifications to obtain tailored passage through the mucus layer and cell interactions. Particles methylation or phosphonation significantly modified cell-cell contact (i.e. intercellular distances) and penetration depth. This demonstrates that cell-particle interaction depends on both shape and surface chemistry, with great implications for the study of polymeric contaminants such as micro- and nanoplastics[7,8,9].

DOIs:

[1]10.1021/acs.molpharmaceut.3c00017, [2]10.1039/c7nr05762h, [3]10.1016/j.foodres.2025.116206, [4]10.1016/j.fct.2025.115280, [5]10.1021/acs.nanolett.3c00835, [6]10.1002/smsc.202400112, [7]10.2903/j.efsa.2016.4501, [8]10.1016/j.envpol.2024.123473, [9]10.1016/j.envint.2023.107968

S8-ST03 Unraveling AKT isoform-specific activity and drug responses using cell-based assays

Sophie Strich[1], Selina Schwaighofer[2], Nileeka Balasuriya[3], David Moser[2], Alina Huber[2], Ludger Hengst[4], Alexandra Newton[3], Eduard Stefan[1]

[1] Medical University of Innsbruck, Austria
[2] Tyrolean Cancer Research Institute (TKFI), Innrain 66, 6020 Innsbruck, Austria
[3] Department of Pharmacology, University of California San Diego, Gilmann Drive 9500, La Jolla, CA 92093-0721, USA
[4] Division of Medical Biochemistry, Medical University of Innsbruck, Innrain 80/82, 6020 Innsbruck, Austria

Protein kinases play a crucial role in pathophysiological signal transduction, acting as molecular switches that regulate essential cellular processes, and are regulated by various mechanisms, making them prime targets for drug development. Dysregulation of central kinases such as AKT are linked to a wide range of diseases, including cancer, diabetes, and neurodegenerative conditions. Understanding AKT's involvement in cellular signaling and its isoform-specific functions is crucial for developing targeted therapies that can precisely address specific AKT isoforms and cancer hot spot mutations such as AKT1-E17K [Craven et al., *Nature 2025*]. Yet, more effective methods for screening and validating new drug candidates are needed. In this project, we first assessed the conformational states of the isoforms AKT1, AKT2, and AKT3 using the cell-based Kinase Conformation (KinCon) reporter system [Kugler et al., *eLife 2024*]. We discovered major isoform-specific conformation changes of the full-length kinases upon exposure with preclinical and FDA-approved small molecule kinase inhibitors (AKTi). Secondly, the phosphotransferase activity profile of all three AKT isoforms was benchmarked alongside conventional phosphorylation readouts, utilizing FRET reporters [Kunkel et al., JBC 2005] and the newly engineered luciferase protein-fragment complementation assays. We have first evidence that allosteric AKTi alter AKT conformations and activities in an isoform-dependent manner. These cell-based reporter systems will pave the way to systematically analyze further kinase drug candidates. Currently we are evaluating isoform-specific profiles of AKT inhibitors, for predicting their efficacy, potency and specificity in the context of cancer patient-specific AKT mutations.

S8-ST04 Combination of lenvatinib and antibiotics: A new strategy to overcome resistance in differentiated thyroid cancer?

Celina Ablinger[1], Petra Huber-Cantonati[1], Daniela D. Weber[2], Sarah Pichler[1], Georg Schischkow[1], Marta Garcia-Miralles[1], Christian Pirich[3], Teresa Kiener[3], Gundula Rendl[3], Barbara Kofler[2], Johanna Pachmayr[1]

[1] Institute of Pharmacy, Paracelsus Medical University Salzburg, Austria
[2] Research Program for Receptor Biochemistry and Tumor Metabolism, Department of Pediatrics, University Hospital of the Paracelsus Medical University, Salzburg, Austria
[3] Division of Molecular Imaging and Theranostics, Department of Nuclear Medicine, University Hospital, Paracelsus Medical University, Salzburg, Austria

Objective

Thyroid cancer is the eighth most frequent cancer worldwide with differentiated thyroid cancer (DTC) accounting for over 90% of all cases (1). Current standard treatment options include thyroidectomy, and radioiodine leading to mostly very good overall survival rates. However, prognosis is poor in radioiodine-refractory disease treated with lenvatinib. Resistance to lenvatinib and severe side effects highlight the need for new therapeutic strategies (2). One promising approach to overcome lenvatinib resistance involves the use of antibiotics, which have shown anti-tumor activity in various tumor entities *in vitro* (3). Therefore, we hypothesize that combination therapy with lenvatinib and selected antibiotics may represent a novel strategy to improve treatment outcomes in DTC.

Methods

To assess the combination effects of lenvatinib and tigecycline or eravacycline, lenvatinib-resistant K1 cells were treated for 72 h and cell viability was analyzed using the CCK-8 assay. To better mimic the *in vivo* tumor situation, viability of 3D spheroids was determined with the CellTiter-Glo® 3D assay (Promega, Madison, US). Cellular bioenergetic measurements following treatment were performed using the Seahorse XFe96 Analyzer (Agilent Technologies, Santa Clara, California). Apoptosis induction was evaluated with the caspase 3/7 activity assay (Promega). Changes in apoptosis related proteins were analyzed with immunoblots.

Results

The combination of lenvatinib with either tigecycline or eravacycline synergistically reduced 2D and 3D cell viability. Metabolic analyses revealed impaired mitochondrial function, characterized by reduced basal and maximal respiration, along with a shift toward a quiescent energetic state. Apoptosis was indicated by a significant increase of caspase 3/7 activity. Furthermore, the combinations reduced the expression of anti-apoptotic proteins and induced cleavage of apoptosis related proteins.

Conclusion

Our findings demonstrate that combining lenvatinib with tigecycline or eravacycline enhances anti-tumor efficacy compared to monotherapy by reducing cell viability, impairing mitochondrial function, inducing apoptosis and modulating key regulators of cell survival. These results underscore the therapeutic potential to improve treatment outcomes in DTC.

Acknowledgements

This project is supported by the PMU-FFF research fund (R-19/03/120 ARD), Salzburger Krebshilfe Stipendium and the Salzburger Kinderkrebshilfe.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

S9: RNA in Gene Regulation

Chairs:

Sebastian Herzog
Medical University Innsbruck, AT

Matthias Erlacher
Medical University of Innsbruck, AT

S9-IT01 DEAD-box ATPases are global regulators of membraneless organelles

Maria Hondele

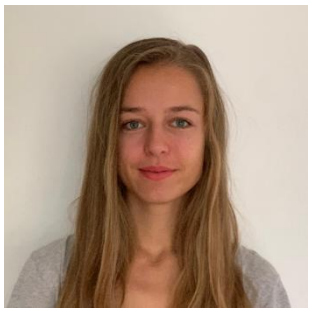
Biozentrum, University of Basel, Switzerland

The ability of proteins and nucleic acids to form biomolecular condensates enables cells to rapidly and reversibly compartmentalize components into membraneless organelles such as nucleoli, P-bodies, and stress granules. Yet, the principles governing their assembly, turnover, and selectivity remain unclear.

We show that RNA-dependent DEAD-box ATPases (DDXs), a large and conserved family, act as global regulators of RNA-containing condensates in both prokaryotes and eukaryotes. Using *in vitro* reconstitution and cellular assays, we find that the ATPase activity of many DDXs dynamically regulates the turnover of major membraneless organelles, and that several DDXs can themselves form biochemically selective condensates.

Briefly, I will also touch a frequently overlooked variable in condensate studies: many fluorescent protein and peptide tags strongly affect condensation, highlighting the importance of careful experimental design.

S9-ST01 Experimental identification of preQ$_1$-binding RNAs in the pathogenic bacterium *Listeria monocytogenes*



Malou Hanisch[1], Laurin Flemmich[2], Christoph Mitteregger[2], Ingo Bauer[1], Cristian A. Velandia-Huerto[3], Ivo Hofacker[3], Ronald Micura[2], Alexandra Lusser[1]

[1] Molecular Biology, Medical University of Innsbruck, Austria
[2] Institute of Organic Chemistry, Center for Molecular Biosciences Innsbruck, University of Innsbruck, Innrain 80-82 6020 Innsbruck, Austria.
[3] Department of Theoretical Chemistry, University of Vienna, Währinger Straße 17, 1090 Vienna, Austria

Riboswitches are widespread regulatory RNA modules in bacteria, with many different classes already identified and even more yet to be discovered. Traditionally, the identification of riboswitches has relied on bioinformatic analyses and genetic screens. In our laboratory, we explored the possibility of identifying and characterizing predicted and novel riboswitches using an affinity purification-based approach with a functionalized preQ$_1$ ligand. We successfully enriched a predicted preQ$_1$ riboswitch from *L. monocytogenes* total RNA. Biophysical characterization revealed that this riboswitch can simultaneously bind two ligand molecules and functions as a regulator of translation *in vivo*. Based on our pull-down approach, we generated a transcriptome-wide pull-down library that showed strong preQ$_1$-dependent enrichment of several candidate sequences. Characterization of one of these candidate mRNAs revealed a preQ$_1$ riboswitch-like sequence in its 5' untranslated region. This potential riboswitch candidate showed a novel way of controlling gene expression upon ligand binding by allowing translation from an alternative start codon located in this region by promoting stop codon readthrough.

S9-ST02 The interplay between RNA chemical probes and RNA binding proteins: cautionary tale or new opportunity?

David Klingler, Lucy Fallon, Daniel Cohn, Amy Crawford, Liza Marcus, Alisha N. Jones

Chemistry, New York University, United States of America

Chemical probing experiments are powerful tools to investigate secondary structures of RNA *in vivo* and *in vitro*. These studies have also been used to identify binding sites based on changes in reactivity profiles in presence or absence of a ligand. This proved especially useful for the identification of protein binding sites. So far, however, little thought has been given to the fact that the proteins binding to their target RNA are also susceptible to modification by the highly reactive chemical probes. In this work, we employ a powerful combination of matrix-assisted laser desorption ionization mass spectrometry (MALDI-MS), nuclear magnetic resonance (NMR) spectroscopy, and molecular dynamics (MD) simulations to investigate the interplay between commonly used chemical probing reagents and RNA binding proteins (RBP). Indeed, we find that RBPs are readily modified by the highly electrophilic compounds used in chemical probing. NMR spectroscopy and MD simulations reveal a site-selectivity for these off-target effects that can affect the RNA binding interface of proteins. If critical residues are modified, proteins can even lose their binding affinity altogether, which we demonstrate using an example from our lab. We discuss the implications in the context of chemical probing experiments of RNA-protein complexes and explore ways to use this feature to our advantage in future studies of RNA-protein interactions.

S9-ST03 The impact of Nsun2-mediated 5-methylcytosine on mRNA dynamics during mESC differentiation

Magdalena Fickl[1], Isabel Delazer[1], Ingo Bauer[1], Theresa Rummel[2], Dietmar Rieder[3], Kamila Nykiel[1], Valentin Tumler[1], Lukas Trixl[1], Anna Razkova[4], Matthias Schäfer[5], Florian Erhard[2], Ronald Micura[4], Alexandra Lusser[1]

[1] Medical University of Innsbruck, Austria
[2] Institute of Virology and Immunobiology, Würzburg University, Germany
[3] Institute of Bioinformatics, Biocenter, Medical University of Innsbruck, Austria
[4] Institute of Organic Chemistry, University of Innsbruck, Austria
[5] Division of Cell and Developmental Biology, Medical University of Innsbruck, Austria

RNA modifications are present in all domains of life and their relevance in many cellular functions is becoming more and more clear. The RNA methyltransferase Nsun2 deposits 5-methylcytosine (m^5C) modifications onto different classes of RNA. Apart from tRNAs and other ncRNAs, Nsun2 is one of only three enzymes that targets mRNAs. While its role in tRNAs has been studied to a greater extent, far less is known about the functional significance of Nsun2-dependent cytosine methylation of mRNA. At the molecular level, several reports have suggested that m^5C affects mRNA stability in positive and negative ways. At the organismal level, Nsun2 was shown to be involved in neuronal development. In this study, we examined if and how Nsun2 affects mRNA dynamics, i.e. synthesis and degradation during cell differentiation. To this end, we differentiated $Nsun2^{-/-}$ and wild type mouse embryonic stem cells (mESC) into the neuroectodermal lineage and studied mRNA turnover using TUC-seq. We found substantial global dysregulation of mRNA dynamics in differentiating but not in pluripotent stem cells and we report on the potential molecular mechanisms responsible for the observed effects.

S9-ST04 The stability of RNA G-quadruplexes in the gas phase

Anna Ploner[0], Sarah Viola Heel[1], Kathrin Breuker[1]

[1] Universität Innsbruck
[0] Institute of Organic Chemistry, Austria

G-quadruplexes are stable, four-stranded secondary structure motifs of ribonucleic acids (RNA) that form in the presence of alkali metal cations. The presence of G-quadruplexes in regulatory regions of the transcriptome can influence post-transcriptional gene regulation and RNA metabolism, with implications for cellular processes and human disease.[1] To further develop native mass spectrometry (MS) for structural studies of RNA, we have investigated the stability of tetramolecular G-quadruplexes of telomeric RNA repeats[2] with the sequences UAGGGU (ORN-1) and UUAGGG (ORN-2)[3] in the gas phase.

Native MS using electrospray ionization (ESI) produced tetramolecular quadruplexes of ORN-1 with at least three K^+ or up to three NH_4^+ ions, consistent with these cations being sandwiched between the three G-quartets and the stabilizing U-tetrad. In contrast, the gaseous quadruplex of ORN-2, which lacks the U-tetrad of ORN-1, showed incorporation of only two K^+ or NH_4^+ ions, in agreement with solution studies. The stability of the quadruplex ions in the gas phase was probed by energy-resolved collisionally activated dissociation (CAD). RNA monomer, dimer and trimer ions were detected as major products, the ratio of which was found to depend on the quadruplex net charge. RNA sequence and the type of cation (K^+ or NH_4^+) did not affect the dissociation pattern. However, the energy required to dissociate the quadruplexes was found to depend on net charge, sequence, and the type of cation. In agreement with their stabilities in solution, the quadruplexes of ORN-1 were found to be more stable in the gas phase than those of ORN-2. Furthermore, the quadruplexes with K^+ are more stable than those with NH_4^+, consistent with proton transfer from NH_4^+ to the RNA followed by loss of NH_3. Importantly, we found that in the gas phase, the noncovalent interactions stabilizing the G-quadruplex structure can be stronger than the covalent RNA phosphodiester backbone bonds, highlighting the potential of native MS for the identification and localization of G-quadruplexes in RNAs involved in cellular processes.

1 Kharel et al. Nat Commun **2023**, 14, 205

2 Azzalin et al. Science **2007**, 318, 798

3 Xu et al. J Am Chem Soc **2010**, 132, 7231

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

S10: Unveiling protein and cell dynamics

Chairs:

Theresia Dunzendorfer-Matt
Medizinische Universität Innsbruck, AT

Eduard STEFAN
University of innsbruck, AT

S10-IT01 Organelle mechano-signalling and error correction in the early embryo

Verena Ruprecht

University Innsbruck, Austria

The body plan and shape of an organism emerges from dynamic processes at the single cell level. To robustly build multicellular structures and tissues of defined form and function, cells need to efficiently process both biochemical and physical signals and adapt to noise and stress factors. We employ an interdisciplinary approach that comprises live cell in vivo imaging and bottom-up in vitro methods to identify mechanisms that control morphodynamic processes in development and regulate functional plasticity at the cell and tissue level. We previously identified that the nucleus is an intracellular mechanosensing hub and the activation of cell mechano-transduction pathways at the nuclear envelope controls cell mechanics and migration plasticity. By this mechanisms cells can rapidly adapt to mechanical forces in their tissue environment. I will present our recent progress in the quantitative mapping of intracellular organelle structures in vitro and in vivo and discuss our work on mechanical stress protection. We identified a rapid remodelling of nucleus-mitochondrial organisation, associated with mechano-metabolic changes in the nucleus to promote DNA damage repair and cell fitness. I will further discuss the role of mechano-signalling pathways in regulating actin cytoskeleton dynamics and cellular error correction in vivo. Our work supports that ‘mechano-plasticity’ at the cellular and tissue level confers stress adaptability relevant for robust development and tissue homeostasis.

S10-ST01 Unraveling the MuSK Network: A Time-Resolved Proteomic Map of Neuromuscular Signaling

Cinzia Barresi[0], Eleonora Maino[1], Weiqiang Chen[2], Markus Hartl[3], Markus Ruegg[1], **Ruth Herbst[0]**

[1] Biozentrum, University of Basel, Basel, Switzerland
[2] Mass Spectrometry Facility, Max Perutz Labs, Vienna BioCenter (VBC), Vienna, Austria.
[3] Mass Spectrometry Facility, Max Perutz Labs, Vienna BioCenter (VBC), Vienna, Austria
[0] MedUni Vienna, Austria

The exchange of signals between motor neurons and skeletal muscle plays a crucial role in shaping the neuromuscular junction (NMJ), which in turn governs skeletal muscle movement. Disruptions in NMJ development can severely impair muscle function and lead to neuromuscular disorders.

Muscle-specific kinase (MuSK), a receptor tyrosine kinase located at the postsynaptic NMJ, is essential for proper NMJ formation. Its activity is precisely regulated by the nerve-derived proteoglycan Agrin, its co-receptor Lrp4, and the adaptor protein Dok-7. The coordinated interaction among these proteins is necessary to sustain MuSK activation and relay signals to downstream effectors. While proteomics studies have advanced our understanding of MuSK signaling, many details—particularly those related to the timing and regulation of events following MuSK activation—remain unclear.

In this study, we present the MuSK proximity proteome using proximity-dependent biotin identification combined with mass spectrometry. We developed a muscle cell line expressing MuSK fused to TurboID, a highly active biotin ligase, enabling high temporal resolution. Muscle cells were stimulated with Agrin for 2, 4, and 8 hours to capture temporal aspects of MuSK signaling. Through this approach, we identified 74 proteins, including established MuSK substrates and novel interacting partners, which we grouped based on their temporal regulation. Among proteins enriched during early signaling, CrkL emerged as a central signaling hub, potentially activating or modulating various signaling molecules—most of which are involved in small GTPase-mediated pathways. Within this group, we identified Rapgef1 (Rap guanine nucleotide exchange factor 1), a known CrkL binding partner. Strikingly, we discovered that Rapgef1 is essential for Agrin-dependent acetylcholine receptor (AChR) cluster formation. Knockdown of Rapgef1 led to reduced AChR phosphorylation and impaired the formation of full-sized AChR clusters in Agrin-stimulated myotubes. More recently, we demonstrated that knocking out Rapgef1 in skeletal muscle of adult mice leads to fragmentation of existing NMJs, further underscoring Rapgef1's crucial role in MuSK signaling and NMJ development.

In summary, our proteomic analysis offers new insights into the MuSK-associated proximity network, highlights a previously unrecognized role for Rapgef1 in MuSK downstream signaling, and advances our understanding of the intricate processes underlying NMJ formation.

S10-ST02 The AID2 system offers a potent tool for rapid, reversible, or sustained degradation of essential proteins in live mice

Valentina Sladky, Margaret Strong, Daniel Tapias-Gomez, Andrew Holland

Institute of Developmental Immunology, Medical University Innsbruck, Austria

Studying essential genes involved in fast dynamic processes such as cell division in live animals is challenging as genetic perturbations are irreversible, limited by slow protein depletion kinetics, or cause adaption and viability issues. The original auxin-inducible-degron (AID) system can overcome these limitations but is partially toxic in mice. Here, we use the optimized, high affinity AID2 system to degrade an essential protein in vivo. The centrosomal protein CEP192 is required for centriole duplication, centrosome maturation and microtubule nucleation. Since it is an essential gene, experiments have been limited to cultured cells and investigating potential roles in specialized tissues such as multiciliated epithelia was not possible. We generated a conditional mouse model appying the AID2 system for degradation of endogenous CEP192 in live animals. We found that the auxin derivative 5-Ph-IAA is well tolerated over 14 days and achieved near-complete CEP192 degradation in less than one hour. Long-term CEP192 depletion resulted in weight loss due cell division errors and massive cell death in proliferative tissues. In summary, we show that the second-generation AID system is well suited for rapid and/or sustained protein depletion in live mice, offering a new tool for interrogating protein function *in vivo*.

S10-ST03 Empowering the identification and validation of drug candidates targeting oncoproteins and E3 ligase functions

Alexandra Fritz[1], Jakob Fleischmann[2], Sophie Strich[1], Valentina Kugler[1], Selina Schwaighofer[1], Thomas Nuener[3], Andreas Feichtner[2], Philipp Tschaikner[2], Eduard Stefan[2]

[1] Molecular Biology, University of Innsbruck, Austria
[2] KinCon biolabs GmbH, Innsbruck, Austria
[3] Tyrolean Cancer Research Institute (TKFI), Innsbruck, Austria

Protein kinases act as spatiotemporal molecular switches that regulate essential cellular processes, with their dysregulation driving oncogenic transformation and therapy resistance. Despite their central role in cancer biology, targeting mutationally activated kinases and notoriously undruggable oncoproteins remains challenging due to context-dependent interactions and unique scaffolding functions. To address this, we employed the Kinase Conformation (KinCon) reporter system, enabling real-time tracking of kinase conformations and direct visualization of target engagement using allosteric and competitive small molecules in living cells and high-content formats**.** Here, we demonstrate the unique sensitivities of the KinCon reporter system, particularly in tracking BRAF-kinase activity conformations upon melanoma drug binding. The effects of several FDA-approved BRAF inhibitors were validated and compared to next-generation compounds such as Plixorafenib (Röck et al., Sci.Adv. 2019, Mayrhofer et al., PNAS 2020, Kugler et al., eLife 2024). In this context, also MEK1 mutations induce open, active conformations that are reversible upon inhibitor binding (Fleischmann et al., PNAS Nexus 2023), while dual BRAF/MEK1 inhibition synergistically enforcing inactive MEK1 states, providing molecular information on interrelated kinase activity states in cell culture model systems (Fleischmann et al., PNAS Nexus 2023; Biomolecules 2021). Expanding beyond kinases, we recently integrated hard-to-target proteins such as the tumor suppressor p53 and the E3 ligase MDM2. This advancement enables the analysis of small molecule interactions—including PROTACs and molecular glues—and facilitates systemic validation of drug efficacies and specificities. Our findings underscore the critical role of conformational dynamics in cancer-driving enzymes and the persistent challenge of targeting proteins like mutant p53 and MDM2. The protein conformation reporter system provides a powerful approach for real-time analysis of conformational states and drug engagement of both established and hard-to-target cancer proteins within living cells.

S10-ST04 Unravelling dopamine receptor selectivity: Combining in vitro studies with molecular dynamics to gain mechanistic insights

Veronika Temml, Moritz Connor Schulte, Lukas Zell, Daniela Schuster

Pharmaceutical and Medicinal Chemistry, Paracelsus Medical University Salzburg, Austria

The dopamine receptors (DR) represent key targets in Parkinson's Disease, schizophrenia and depression, with several approved drugs on the market. However, subtype selectivity remains challenging and many drugs suffer from a poor side effect profile. In this study novel DR ligands were discovered in a pharmacophore-based virtual screening. Virtual hits were then tested in a cell based in vitro assay and active scaffolds were also investigated for their subtype selectivity. The structures were then submitted to docking studies and molecular dynamics simulations on subtypes D2-3R to elucidate the molecular interaction patterns responsible for selective binding.

Experimental evaluation of Ki values for DRs was performed in a Homogenous Time-Resolved Fluorescence (HTRF) assay on D1-3R subtype expressing cells, acquired from PerkinElmer/cisbio [1,2]. Pharmacophore modelling was conducted in Ligandscout (inte:ligand) and Discovery Studio (Biovia) [1]. Molecular Docking was executed in GOLD (CCDC)[2]. For MD simulations each ligand protein complex from the docking simulations was embedded in a membrane within a water box with 0.15M NaCl to mimic the cellular environment. The MD simulation was conducted with Desmond (Schrödinger) using the OPLS5 force field for 100ns at 310K to enable the observation of conformational changes of the receptor.

Among 90 hits from four pharmacophore models, six novel D2R ligands were discovered. Compound 14 displayed the highest binding affinity (Ki=4.1nM). Nine compounds from the virtual screening and apomorphine were investigated in D1-3R expressing cells. Eight displayed subtype selectivity to varying degrees. The most pronounced selectivity was observed for compound 10 with nanomolar D3R activity (Ki=2.3nM) and 264-fold D2R/D3R selectivity. Subsequent docking and MD simulations revealed a relationship between ligand selectivity and a so far undescribed π-stacking interaction with a conserved tyrosine residue. Higher interaction counts over the course of the trajectory indicate D3R selectivity.

The successful in silico prediction of DR ligands and the MD supported elucidation of key interactions responsible for subtype selectivity enables the rational design of D3R subtype selective ligands that could act as drugs or valuable biochemical tools to investigate the physiological role of the different DR subtypes.

[1] Zell et al, Molecules 27(14), 4435, 2022**.** [2] Zell et al, Biomedicines 11(5), 1468, 2023.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

Abstracts – Day 3, Fri, 26.9

.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

Plenary 3

Chair:

Lukas A. Huber
Medical University of Innsbruck, AT

Plenary Lecture

P3-PL01 Protein covariation advances functional annotation of the human proteome

Georg Kustatscher

University of Edinburgh, United Kingdom

Most research aiming to understand the molecular foundations of life and disease has focused on a limited set of increasingly well-known proteins. By contrast, thousands of human proteins remain 'understudied': their biological function is poorly understood and annotation of their molecular properties is scarce. This annotation inequality hinders biomedical progress because mechanistic investigations of gene–disease associations typically focus on proteins that are already well known, a phenomenon also known as the street-light effect (Kustatscher et al, Nat Methods 2022).

We have previously shown that protein covariation (coexpression) analysis is a powerful proteomics approach to link uncharacterised proteins to known cellular processes (Messner et al, Cell 2023; Kustatscher et al, Nat Biotechnol 2019). Here, we present a new covariation map of the human proteome. To assemble it, we developed a proteomics data processing pipeline that is fast, scalable, and includes appropriate FDR control for very large datasets. Based on the Fragpipe platform, this pipeline enabled us to re-process 23,000 previously published MS runs in less than two weeks. This resulted in the ProteomeHD.2 dataset, which covers the abundance changes of 16,000 proteins in response to 2,500 biological perturbations, quantified using SILAC labelling (Kourtis et al, in preparation).

To determine which proteins have similar covariation patterns across ProteomeHD.2, and might thus be functionally related, we developed a machine-learning-based strategy. The resulting proteome covariation map reveals functional associations for about 10,000 human proteins. We show that it captures functional associations as well as more established techniques, such as affinity-purification MS experiments, allowing us to make predictions on the potential biological functions of many previously unidentified and understudied human proteins.

Finally, we use our pipeline to provide novel evidence for the existence of many HUPO missing proteins and amino acid substitution variants (but not microproteins).

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

Science Flashes 3

Chair:

Lukas A. Huber
Medical University of Innsbruck, AT

PS3-S11-SF01 Therapeutic targeting of thyroid hormone pathway in prostate cancer

Aleksandra Fesiuk[1], Nicolas Blavet[2], Vojtech Bystry[2], Boris Tichý[2], Cécile Philippe[3], Daniel Pölöske[1], Brigitte Hantusch[1], Lukas Kenner[1]

[1] Department of Pathology, Medical University of Vienna, Austria
[2] Central European Institute of Technology, Masaryk University, Brno 62500, Czech Republic
[3] Department of Biomedical Imaging and Image Guided Therapy, Division of Nuclear Medicine, Medical University Vienna, Vienna, Austria

Prostate cancer (PCa) is the second most frequently diagnosed malignancy in men and is largely driven by androgen receptor (AR) signaling. However, approximately 20% of patients develop resistance to AR-targeted therapies, underscoring the urgent need for alternative therapeutic approaches. Emerging evidence suggests a link between hyperthyroidism and an increased risk of PCa, with thyroid hormone receptors (THRs) implicated in cancer progression. Notably, sequencing analyses of PCa samples from an in-house cohort revealed an enrichment of mutations in genes associated with thyroid hormone (TH) signaling. In this project we aim to investigate the role of TH signaling in PCa pathogenesis. We observed, that pharmacological inhibition of TRβ using the selective antagonist NH-3 significantly reduced tumor volume and mass in 22Rv1 and LNCaP xenograft models. *In vitro*, NH-3 effectively suppressed PCa cell proliferation. RNA sequencing revealed transcriptomic changes in TH-related pathways, as well as androgen (AR) signaling, cell cycle regulation, and lipid metabolism. These effects were confirmed by decreased expression of AR and AR-regulated genes, as well as reduced fatty acid synthase (FASN) protein levels. Increased uptake of the radiolabeled fatty acid analog [^{18}F]FTHA suggested a compensatory response to impaired de novo lipid synthesis. Our findings support the therapeutic potential of targeting TH signaling in PCa by disrupting AR signaling, altering lipid metabolism, and inducing cell cycle arrest. Given the observed alterations of genes affected by TH signaling, further investigation is needed to clarify its role in PCa progression and to evaluate its therapeutic potential.

PS3-S11-SF02 Modelling Batten Disease employing iPSC-derived organoids reveals early progenitor loss and accelerated neuronal differentiation

Sofia Angelini[1], Elisa Gabassi[1], Marcel Tisch[1], Yvonne Klingl[2], Christian Grimm[2], Frank Edenhofer[1]

[1] Department of Genomics, Stem Cell Biology and Regenerative Medicine, University of Innsbruck, Austria
[2] Walther-Straub-Institute for Pharmacology and Toxicology, Medical Faculty, Ludwig-Maximilians-University (LMU) Munich, 80336 Munich, Germany

Juvenile neuronal ceroid lipofuscinosis (JNCL), or Batten disease, is a rare and severe pediatric neurodegenerative disorder caused by mutations in the CLN3 gene. It is characterised by progressive vision loss, cognitive and motor decline, and premature death. It currently lacks effective therapies. Despite advances in understanding lysosomal storage disorders (LSDs), the early molecular and developmental mechanisms underlying CLN3-related neurodegeneration remain poorly understood, also due to the lack of human-relevant models.

In this study, we used iPSC-derived cerebral organoids generated from four variant lines: WT, CLN3 KO, and two mutants carrying the D416G (severe) and R405W (mild, only causing vision loss) mutations. Organoids were analysed at days 25, 30, and 60 of differentiation. Day 30 organoids, both of D416G and R405W genotypes, showed reduced expression of PAX6, a neural progenitor marker, and smaller rosette-like structures. D416G, in particular, showed a significant 40% reduction in rosette area and size, despite displaying a similar number of rosettes compared to WT, suggesting impaired progenitor expansion. MAP2 staining, marking post-mitotic neurons, was also reduced in both mutated samples, indicating a delay in early neuronal differentiation.

By day 60, MAP2 expression increased in D416G and R405W, pointing to a shift toward accelerated maturation. In parallel, SATB2 (an upper-layer neuronal marker) was 50% upregulated in D416G and KO organoids, while CTIP2 (deep-layer marker) remained unchanged. These results suggest a dysregulated cortical differentiation, particularly resulting in premature specification in the D416G variant.

PAX6 remained low only in D416G at day 60, reflecting a persistent progenitor imbalance. All mutant lines displayed smaller rosette sizes, and both KO and D416G showed reduced rosette numbers compared to the WT. In addition, approximately 50% of KO organoids failed to develop between days 30 and 60, and the remaining organoids were significantly smaller. This suggests that early compensatory mechanisms are not maintained over time.

Overall, these findings highlight distinct neurodevelopmental patterns depending on CLN3 mutation type. D416G shows early progenitor loss and accelerated differentiation, consistent with a severe phenotype. The second mutation, R405W, behaves more similarly to WT, whereas the KO initially compensates but then fails to maintain normal development. In conclusion, our data underscore the role of early neurodevelopmental disruptions in JNCL pathogenesis and demonstrate the value of iPSC-derived organoids for modelling mutation-specific disease mechanisms.

PS3-S12-SF01 The antibacterial activity and therapeutic potential of an amphibian derived peptide

Cristina Schöpf[1], Jakob Scheler[2], Débora Cristina Coraça-Huber[3], Alessandra Romanelli[4], Ulrike Binder[2], Reinhard Würzner[2], Florentine Marx[1]

[1] Molecular Biology, Medizinische Universität Innsbruck, Biocenter Innsbruck (CCB), Austria
[2] Institute of Hygiene and Medical Microbiology, Medical University Innsbruck, Innsbruck, Austria
[3] Research Laboratory for Biofilms and Implant Associated Infections (BIOFILM LAB), Experimental Orthopedics, Department of Orthopedic Surgery, Medical University of Innsbruck, Innsbruck, Austria
[4] Department of Pharmaceutical Sciences, University of Milan, Milan, Italy

Antimicrobial peptides (AMPs) have been identified as promising candidates for the development of topical treatments for microbial skin infections, including those caused by the Gram-positive human pathogen *Staphylococcus aureus*. Among the AMPs, Temporin B (TB) is of particular interest. This 13-amino-acid-long cationic peptide, secreted by the granular glands of the European frog *Rana temporaria*, serves as a primary line of defense against invading pathogens.

The objective of this study was to evaluate the topical antibacterial efficacy and tolerance of a synthetic analog of TB (TBA) against *S. aureus*. The kinetics of bacterial killing were assessed through the employment of microbiological methods, revealing that TBA exhibited potent bactericidal activity at low micromolar concentrations. The peptide demonstrated a high level of tolerance when applied to *in vitro* three-dimensional (3D) human epidermis equivalents (HEEs), with no detectable tissue defects. *In vivo* testing using the invertebrate mini-host model *Galleria mellonella* confirmed the peptide's lack of toxicity.

The therapeutic potential of TBA was further supported by experiments involving HEEs infected with *S. aureus*. Topical application of TBA significantly reduced the bacterial load and also led to a measurable decrease in the pro-inflammatory response compared to infected, untreated controls. These findings underscore the strong antibacterial activity and therapeutic promise of TBA in the treatment of *S. aureus*-associated skin infections.

Future research will focus on elucidating the species-specific mode of action of TBA, particularly in mixed infection models. Furthermore, the development of smart drug delivery systems will be essential to optimize the efficacy of topical formulations, advancing TBA toward clinical application.

PS3-S12-SF02 MAA analytics Analytical considerations in the purification of mycosporine-like amino acids from marine organisms

Armin Oberosler[1], Fabian Hammerle[1], Cornelia Karg[1], Michael Zwerger[2], Ignacio Zegri[3], Ulf Karsten[4], Thomas Werner[3], Johanna M. Gostner[2], Markus Ganzera[1]

[1] Pharmacognosy, University of Innsbruck, Austria
[2] Institute of Medical Biochemistry, Medical University of Innsbruck, Innsbruck, Austria
[3] Leibniz Institute for Catalysis, University of Paderborn, Paderborn, Germany
[4] Department of Applied Ecology and Phycology, University of Rostock, Rostock, Germany

Mycosporine-like amino acids (MAAs) are compounds with extraordinary UV-absorbing properties, produced by lichens, fungi, algae, and cyanobacteria, providing protection against UV radiation and oxidative stress. However, limited attention has been paid to this substance class due to several analytical challenges. Their high polarity, low natural abundance, structural similarity, and the frequent overestimation of purity due to strong UV absorption complicate the extraction, isolation, and biological evaluation of MAAs.

In this study, commercially available *Porphyra* sp. (commonly known as Nori) material was investigated as a natural source of MAAs. A Design of Experiments (DoE) approach was used in combination with analytical HPLC to identify optimal purification strategies.

The detection of common MAAs such as shinorine and porphyra-334 confirms that *Porphyra* sp. is not only a rich natural source but also a promising starting material for further research on these interesting natural products. Given their photoprotective and antioxidant potential, MAAs are promising candidates for applications in cosmetics, nutraceuticals, and pharmaceuticals.

Thus, this work contributes to the ongoing exploration of marine natural products and emphasizes the need for harmonized analytical workflows tailored to complex algal matrices.

PS3-S13-SF01 The PIDDosome - between ploidy control and cell death

Felix Eichin[1], Valentina C Sladky[1], Matthäus A Reiner[1], Marina Leone[1], Ernesto Abila[2], André F Rendeiro[2], Ralph Böttcher[3], Thomas Kolbe[4], Andreas Villunger[1]

[1] Medical University of Innsbruck, Austria
[2] CeMM, Research Center for Molecular Medicine of the Austrian Academy of Sciences, 1090 Vienna, Austria
[3] Max Planck Institute of Biochemistry, 82152 Martinsried, Germany
[4] Institute of In vivo and In vitro Models, Department of Biological Sciences and Pathobiology, University of Veterinary Medicine, 1210 Vienna, Austria

The PIDDosome is the key activation platform of caspase-2 and was originally reported to induce apoptosis upon DNA damage. More recently, however, it became clear that PIDDosome-dependent caspase-2 activation is also involved in cellular functions unrelated to cell death. The presence of extra centrosomes was shown to be sufficient to activate the PIDDosome and induce stabilization of p53, as MDM2 is cleaved by active caspase-2, subsequently leading to p21-mediated cell cycle arrest. By this, the PIDDosome limits hepatic polyploidy during development and regeneration. Interestingly, full-length PIDD1 undergoes auto-processing leading to different protein fragments, PIDD1-C, PIDD1-CC and PIDD1-N, active in different molecular complexes, such as the NEMO-PIDDosome, implicated in sterile inflammation, involving PIDD1-C, RIPK1 and NEMO. In order to expand our current knowledge we generated new *in vivo* models in which the auto-processing of endogenous PIDD1 is impaired by specific point mutations, which should allow us to investigate the function of the different PIDD1 fragments and related complexes *in vivo*.

Preliminary data of these mice indicate that sequential processing of full-length PIDD1 is crucial for the ability of the PIDDosome to limit hepatocyte ploidy *in vivo.* Impairing the first processing step, creating PIDD1-C, abrogates formation of PIDD1-CC, contrasting published findings. As a consequence, Pidd1S451A mutant mice display increases in hepatic ploidy, similar to *Pidd1* knockout mice or mice expressing Pidd1S593A or Pidd1mut/mut. In addition, mouse embryonic fibroblasts isolated from E14.5 embryos from these mice confirm impaired auto-processing and impaired caspase-2 activation upon cytokinesis failure. Interestingly, in hematopoietic precursor cells the PIDDosome induces cell death rather than cell cycle arrest. Together, these findings document that rapid auto-processing of PIDD1 in a sequential manner is critical for its function in ploidy control.

PS3-S13-SF02 Discovering new players in inflammatory cell death

Marlene Lochner, Joel S. Riley

Medical University of Innsbruck, Austria

Mitochondrial permeabilisation during cell death can, under certain circumstances, be highly inflammatory. The release of mitochondrial DNA from the mitochondrial matrix contributes to inflammation during cell death via an interferon response during caspase inhibition. Furthermore, chains of ubiquitin decorate mitochondrial membranes after their permeabilisation, resulting in an NF-kB inflammatory response. These mechanisms parallel a cell's response to bacterial infections. Guanylate binding proteins (GBPs) are known to be highly upregulated in an IFNγ-dependent manner and bind to bacterial membranes forming a large multimeric platform. These GBP platforms have a myriad of roles, including co-ordinating the cells anti-pathogen response and destroying the pathogen itself.

We now show that GBPs are recruited to permeabilised mitochondria during inflammatory cell death. Thus, we aim to understand the role of GBPs at these mitochondria, starting at mitochondrial membrane binding partners, membrane disruption and signaling. With these goals we want to further uncover how mitochondria are inflammatory during cell death.

Using super-resolution imaging we show that all members of the GBP family are recruited to permeabilised mitochondria. We also show that this is a general feature of mitochondrial permeabilisation, independent of the activation of BAX/BAK. Additionally, we have determined that ubiquitination of mitochondria is not required for GBP recruitment or assembly. By employing a range of biochemical, imaging and proteomics approaches, we aim to uncover the role of GBPs mitochondrial recruitment during cell death and how this impacts the inflammatory outcomes of cell death.

PS3-S14-SF01 Myeloid checkpoints as targets for combination immunotherapy in ovarian cancer

Leonie Madersbacher[1], Katja Rungger[1], Raphael Gronauer[1], Konstantin Wilhelmy[1], Pablo Monfort-Lanzas[2], Johanna Gostner[3], Alain Zeimet[4], Christian Marth[4], Heidelinde Fiegl[4], Hubert Hackl[1]

[1] Institut für Bioinformatik, Medizinische Universität Innsbruck, Austria
[2] Institute of Bioinformatics, Biocenter, Medical University of Innsbruck, Institute of Medical Biochemistry, Biocenter, Medical University of Innsbruck
[3] Institute of Medical Biochemistry, Biocenter, Medical University of Innsbruck
[4] Department of Obstetrics and Gynecology, Medical University of Innsbruck

Immunotherapy has shown only limited benefit for ovarian cancer patients leading to increased efforts to develop combination immunotherapy strategies. We could demonstrate that for combination immunotherapy with PARPi and immune checkpoint blockers the tumor-associated macrophages (TAMs) expressing TREM2, LILRB4, SIGLEC9, might be critical for therapy response. We developed a computational workflow to systematically investigate ovarian cancer intrinsic factors affecting the tumor microenvironment. Using bulk and single-cell RNA sequencing analyses, and spatial transcriptomics from various cohorts including a cohort from the Medical University in Innsbruck we could pinpoint that myeloid immune checkpoints such as non-canonical HLA molecules could be interesting drug targets. Using Perturb-seq screens, a single cell atlas for drug perturbation (Tahoe~100M), and reversal of transcriptional phenotypes such as M2 macrophage polarization or the immunosuppressive tryptophan pathway, a number of drugs for repurposing have been identified. These drugs together with knock-out of specific factors will be tested in an *in vitro* co-culture system consisting of a human 3D ovarian cancer model, T lymphocytes and M2-like macrophages.

PS3-S14-SF02 The intratumoral microbiome and their effects on AHR-driven immune responses in pancreatic adenocarcinoma

Katja Rungger[1], Leonie Madersbacher[2], Pablo Monfort-Lanzas[3], Raphael Gronauer[2], Gabriel Floriani[2], Cornelia Speth[4], Ruben Bellotti[5], Manuel Maglione[5], Hubert Hackl[2]

[1] Institute of Bioinformatics, Medical University of Innsbruck, Austria
[2] Institute of Bioinformatics, Biocenter, Medical University of Innsbruck, Innsbruck, Austria
[3] Institute of Bioinformatics, Biocenter, Medical University of Innsbruck, Innsbruck, Austria AND Institute of Medical Biochemistry, Biocenter, Medical University of Innsbruck, Innsbruck, Austria
[4] Institute of Hygiene and Medical Microbiology, Medical University of Innsbruck, Innsbruck, Austria
[5] Department of Visceral, Transplant and Thoracic Surgery, Medical University of Innsbruck, Innsbruck, Austria

The role of intratumoral microbiota in tumor biology and cancer immunity is increasingly recognized and may have applications in diagnosis and treatment. However, their species-specific effects are still largely unclear. To enable scalable and reproducible analyses of the tumor microbiome we have developed an automated analysis pipeline using the Nextflow system. Here, we investigated the intratumoral microbiome in pancreatic adenocarcinoma (PAAD), focusing on the genus *Malassezia* and its potential to activate the aryl hydrocarbon receptor (AHR), a transcription factor that regulates immune responses and cell differentiation. Using raw RNA sequencing data from The Cancer Genome Atlas, we identified microbial species by filtering out human reads and taxonomically classifying the remaining sequences using kraken2. Alignment quality and decontamination procedures were conducted with Recentrifuge. Analyses of microbial diversity showed that bacterial species richness was highest compared to fungal and viral richness. Among the fungal taxa identified were *M. globosa* and *M. restricta*, consistent with previous reports and validated on FFPE tumor blocks with in situ hybridization and sequencing methods. Notably, tumor samples containing *Malassezia* reads exhibited a significant enrichment of a previously characterized pan-tissue AHR gene signature compared to samples lacking *Malassezia*. This enrichment was not observed in comparisons between tumor and normal pancreatic tissue, suggesting that *Malassezia*-derived metabolites may contribute to AHR pathway activation within the tumor microenvironment. Furthermore, survival analysis showed a significant reduction in overall survival in patients whose tumors were positive for *Malassezia* and had high AHR signature levels compared to patients without *Malassezia* and with low AHR activity. The pan-tissue AHR signature correlates with several estimated immune cell fractions, including a negative correlation with natural killer cells.

In summary, this work has provided a basis for how intratumoral bacteria, fungi and viruses can be assessed based on RNA sequencing data. It highlights potential interactions between the tumor microbiome, host immunity, and AHR signaling in PAAD.

PS3-PhD-SF01 Identification of a Golgi quality control network in mammalian cells

Lucija Kucej[1], Klaus Faserl[2], Bettina Sarg[2], David Teis[1]

[1] Molecular Biochemistry, Medical University of Innsbruck, Austria
[2] Medical University of Innsbruck, Protein Core Facility

Protein homeostasis or proteostasis is essential for maintaining healthy cellular function. It involves a tightly regulated balance of protein synthesis, folding, modification, sorting, and degradation. Disruption at any stage of this process can lead to the accumulation of misfolded or mislocalized proteins, contributing to the development of various diseases, including neurodegenerative disorders and cancer.

To prevent these issues, cells rely on proteostasis networks that detect and eliminate misfolded or orphaned membrane proteins (i.e., proteins that fail to assemble into complexes or reach their intended destinations). While the protein quality control functions of the ER, lysosomes, and mitochondria are well characterized, the Golgi apparatus is often overlooked, despite its crucial role in protein sorting and modification. Given its sorting capabilities, the Golgi presents an ideal site for detecting misfolded proteins that have escaped the ER, or orphaned proteins.

Previous research in Teis lab has identified RER1 as a key component of the Golgi quality control system in budding yeast. RER1 retrieves orphaned membrane proteins often unassembled subunits of multimeric complexes from the early Golgi and returns them to the ER. Dysregulation of this pathway has been implicated in diseases such as Alzheimer's and Parkinson's, as well as in tumor progression.

This project aims to further investigate the role of RER1 in the Golgi quality control network in mammalian cells and to characterize additional proteins that contribute to this system. By combining proteomic approaches, genetic manipulation, and advanced imaging, the study seeks to identify another proteins that cooperate with RER1 to maintain proteostasis and prevent the accumulation of orphaned proteins.

PS3-PhD-SF02 Optimisation of an XL-MS workflow to investigate the architecture of native lysosomal LAMTOR assemblies

Eva Rauch[0], Martina Höllwarth[0], Vincenza Vigorito[1], Luca Fava[1], Lukas A. Huber[0], Taras Stasyk[0]

[1] Armenise-Harvard Laboratory of Cell Division, Department of Cellular, Computational and Integrative Biology - CIBIO, University of Trento, Trento, Italy
[0] Cell Biology, Medical University of Innsbruck, Austria

The late endosomal and lysosomal adaptor and MAPK and mTOR activator (LAMTOR) scaffolding complex resides at the lysosomes, where it mediates catabolic and anabolic signalling. Anchored onto the lysosomal membrane by the lipid-modified N-terminal domain of LAMTOR1, the complex further includes subunits LAMTOR2-5. Previous studies have identified the presence of at least four different LAMTOR assemblies on the lysosome associated with catabolic or anabolic signalling mediated by its association with Rag-GTPases, SLC38A9, the v-ATPase or AXIN with LKB1. Furthermore, LAMTOR is a negative regulator of BORC, a protein complex involved in lysosomal biogenesis and cellular positioning.

The goal of the project is to elucidate the structural organization of native LAMTOR assemblies under various stimuli, providing insight into how a single scaffolding complex orchestrates these diverse biological functions. We are applying state-of-the-art cross-linking mass-spectrometry (XL-MS) methods to capture endogenous protein-protein interactions.

We have developed a robust affinity purification protocol for SH-tagged bait proteins via Strep-Tactin columns. Notably, the approach is fully compatible with downstream cross-linking and LC-MS analysis. Preliminary PPIs were generated by applying our protocol to SH-LAMTOR3 and SH-BORCS7 baits treated with the MS-cleavable cross-linkers DSBU and DSSO. Further optimizations including integrating the IMAC-enrichable cross-linker PhoX into the workflow enabled the detection of over 300 cross-links in a single LC-MS run.

Ultimately, to investigate native LAMTOR assemblies, we have generated hTERT-RPE1 cells endogenously expressing ALFA-tagged LAMTOR4. We are currently optimizing an AP-XL-MS approach using DSSO and PhoX in combination with ALFA-tagged endogenously expressed baits to achieve the high sensitivity needed to detect endogenous interactions. As a complementary tag-free approach, we are working on intact organelle cross-linking of the lysosome enabled by the membrane permeability of the tBu-PhoX cross-linking reagent and our expertise in lysosomal isolation.

In summary, we have established two complementary affinity-purification workflows for commonly used protein tags, fully compatible with chemical cross-linking, enrichment and downstream LC-MS analysis. These novel pipelines can serve as powerful tools to dissect structural dynamics, complex topologies and direct protein-protein interactions in vivo.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

Poster Session 3

NOTE: The Science Flash poster abstracts from Poster Session 3 are listed in the Science Flash Session 3
S11: Stem cells, cell cycle and cancer
S12: Natural products in life science research
S13: Cell death in health and disease
S14: Machine learning and perturbation in cellular systems
Poster Session 3: PhD Session

PS3-S11-PP01 Extracellular matrix signalling pathway crosstalk in primary human mesenchymal stromal cells

Anju Kombara, Alexandra Petric, Janina Burk

Veterinärmedizinische Universität Wien, Austria

Multipotent mesenchymal stromal cells (MSCs) are well-known for their cellular plasticity and can differentiate into various cell types including tenocytes. They are known to actively produce and remodel extracellular matrix (ECM) components and are, thus, an ideal model to study ECM-related signalling pathways *in vitro*. Understanding the key ECM signalling pathways and their interplay is essential for elucidating mechanisms that drive MSC fate and maladaptation. In this regard, the ERK and ROCK pathways are likely to play crucial roles, yet there are no consistent data on their possible interplay. We hypothesised that inhibition of ROCK together with non-canonical TGF-β signalling leads to increased ERK pathway activation.

Primary adipose-derived MSCs, isolated and cultured from three human donors, were treated with either 10µM Y-27632 (ROCK inhibitor), 10ng/ml TGF-β3 or a combination of both. In order to observe the dynamic changes in ERK pathway activation, a time course experiment was set up. Cells were analysed after 0.5h, 1h, 4h and 24h, at which phospho- and total ERK expression were quantified by western blot.

Our results indicate that ERK phosphorylation increases substantially upon inhibition of ROCK. In part of the donors, this was further pronounced by induction of MSCs with TGF-β3. No effect on ERK phosphorylation was seen when cells were treated with TGF-β3 alone. Data from the time course experiment showed that ERK phosphorylation and dephosphorylation occurs in less than 24h. Our results also clearly indicate pathway activation and not just a change in overall ERK expression. This suggests a possible non-canonical crosstalk between the three pathways – TGF-β, ROCK and ERK.

Our data demonstrates a crosstalk between ROCK and ERK pathways in primary human MSCs. Thereby, they help towards understanding pathway interactions, compensation mechanisms as well as feedback mechanisms emerging from the interplay of ROCK, ERK and TGF-β pathways. Ultimately, this aids in better understanding mechanisms behind ECM remodelling by MSCs.

PS3-S11-PP02 Transcriptional trajectory and single cell gene expression analysis reveal barriers of iPSC reprogramming

Niklas Schweiger[1], Katharina Günther[1], Francesca Finotello[2], Angeliki Spathopoulou[1], Frank Edenhofer[1]

[1] University of Innsbruck, Austria
[2] Digital Science Center (DiSC), University of Innsbruck, Austria

The reprogramming of somatic cells to induced pluripotent stem cells (iPSCs) can be accomplished through the transient expression of a combination of transcription factors. This achievement has led to significant advancements in disease modelling, tissue engineering and drug screening. Nevertheless, reprogramming efficiency remains low and insights into the molecular mechanism of reprogramming remains scarce. Due to the heterogeneous nature of somatic cells undergoing reprogramming and their capacity for divergent cell fates, it is imperative to identify pivotal bifurcation events and to focus on the trajectory to pluripotency. Here we present the gene expression and transcriptional trajectory data from a time-resolved single-nuclei transcriptomics investigation, spanning the transition from fibroblasts to iPSCs. Fibroblasts were previously transduced employing CellTagging, a lentivirus-based approach that allows the unique labeling of individual cells with heritable barcode combinations (Biddy et al., 2018). Cells were collected for sequencing at 4 timepoints after the infection with Sendai virus, which introduced the Yamanaka factors. We observed one discrete trajectory which is resolved over the process of reprogramming, with one trajectory converging towards clusters associated with pluripotency and another towards non-reprogrammed clusters. Gene expression analysis of cells from the reprogrammed trajectory revealed a decrease in fibroblast markers and a mesenchymal-to-endothelial transition (MET). This transition subsequently led to the expression of pluripotency-associated marker genes. Furthermore, an analysis of transcription factors revealed elevated levels of activity of transcription factors associated with pluripotency, as well as regulators of MET/EMT in the reprogrammed trajectory. We identified GRHL2 as a potential target to enhance reprogramming efficiency. Previous studies by Cieply et al. demonstrated that GRHL2 increased the expression of miRNAs belonging to the miR-200 family. These miRNAs subsequently suppressed ZEB1, a pivotal regulator of EMT. The present study aims to validate this hypothesis through experimental validation in a laboratory setting, employing GRHL2 overexpressing experiments. Our study will provide deeper insight into reprogramming mechanisms and enable enhanced cell conversion protocols.

PS3-S11-PP03 The protein interaction network of p27 in prometaphase

Miriam Unterkofler, Martin Taschler, Bettina Sarg, Klaus Faserl, Michael Kullmann, Ludger Hengst, Heidelinde Jäkel

Medical Biochemistry, Biocenter Innsbruck, Austria

$p27^{Kip1}$ is a member of the CIP/KIP Cyclin-dependent kinase (CDK) inhibitors that regulates cell proliferation especially in G0/G1 phases and G1 to S phase transition. In these cell cycle stages, p27 can efficiently inhibit cyclin D-CDK4/6 and cyclin A/E-CDK2 activity. However, phosphorylation of p27 on tyrosines reduces its inhibitory capacity thereby promoting cell proliferation. While the molecular and functional effects of p27 tyrosine phosphorylation have been extensively characterized in G1 and S phases, its role in mitosis remains unclear.

To investigate the effect of p27 tyrosine-phosphorylation across different cell cycle stages, we have generated HeLa Flp-In T-Rex cells with inducible expression of either wild-type p27 or p27 mutants mimicking tyrosine phosphorylation by substituting tyrosines (Y) with glutamic acid (E). Immunoblot analysis of cells synchronised at various cell cycle phases revealed a marked increase in p27 protein in M-phase, when specifically the two tyrosines, Y74 and Y88, were mutated to mimic phosphorylation. To elucidate the functional significance of elevated p27-Y74,88E levels during his critical final phase of the cell cycle, we aimed to characterize the interactomes of p27-Y74,88E and wild-type p27 in Paclitaxel-arrested prometaphase cells. Mass spectrometry combined with bioinformatic analysis of immunoprecipitates revealed distinct interaction partners dependent on the presence of the tyrosine-phosphorylation mimicking mutations. Interestingly, the p27-Y74,88E mutant predominantly diminished interactions when compared to p27 wild-type, rather than enabling new ones.

Based on this comprehensive profiling of the p27 interactome, we aim to uncover the molecular mechanism by which p27 tyrosine phosphorylation modulates its protein degradation in mitosis and to explore the functional implications of p27 in the cellular response to the widely used anticancer drug Taxol.

PS3-S11-PP04 Single-cell profiling of striatal organoids derived from Leigh syndrome patients highlights gene network dysregulated in neurodevelopment

Martina Podlesnic[1], Marta Suárez-Cubero[1], Stephanie Le[2], Antonio delSol[3], Satoshi Okawa[3], Alessandro Prigione[2], Frank Edenhofer[1]

[1] Genomics, Stem Cell Biology and Regenerative Medicine, University of Innsbruck, Austria
[2] Department of General Pediatrics, Neonatology and Pediatric Cardiology, Heinrich Heine University Düsseldorf
[3] Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg

Leigh syndrome (LS), a severe neurodevelopmental disease, is caused by mutations in mitochondrial genes leading to dysregulated ATP production. The nuclear DNA-encoded gene *NDUFS4* encoding a subunit of mitochondrial complex I is frequently mutated in patients causing alterations in various brain regions including the striatum. The underlying pathophysiological mechanisms driving this rare disease remain elusive. Here, we aimed to investigate transcriptomic alterations in early development of striatal organoids derived from LS patient induced pluripotent stem cells carrying a *NDUFS4* mutation and their matched isogenic controls. Single cell RNA sequencing (scRNA seq) revealed a slight dorsalisation of LS patient-derived organoids. In particular, the fraction of dorsal telencephalic glutamatergic neurons expanded at the expense of ventral telencephalic GABAergic neurons. Differential expression analysis confirmed downregulation of genes involved in mitochondrial complex I and OXPHOS with ventral telencephalic GABAergic neurons being highly susceptible to these changes. Across the vast majority of cell types, 7 upregulated and 16 downregulated genes were found to be shared. Lastly, leveraging STRING analysis for network construction allowed us to further narrow down the DEG candidates to *NR2F1*, *FOXP2*, and *ETV1.* These are implicated in neural differentiation by PAX6 regulation, neurite outgrowth of striatal medium spiny neurons in mouse and regulation of GABAergic subunit in developing cerebellar neurons, respectively, and by that could mediate the disease mechanism. In conclusion, our study revealed gene candidates involved in the distinct neuronal phenotypes paving a way for further understanding of LS and establishing novel intervention paradigms.

PS3-S11-PP05 Development of a 3D-bioprinted Mesothelium-on-Chip system to study Ovarian Cancer

Verena Sturmlehner[1], Juliane Rettenwender[1], Heidelinde Fiegl[2], Michael Ausserlechner[1], Judith Hagenbuchner[1]

[1] Pediatrics I - 3D Bioprinting Core Facility, Medical University Innsbruck, Austria
[2] Obstetrics and Gynecology, Medical University Innsbruck, Austria

Ovarian cancer (OvCa) is the fifth-common cause of cancer death in females and has a 5-year survival rate of about 50%. Reasons for its high mortality are nonspecific symptoms, the lack of useful biomarkers and therapeutic limitations. Furthermore, over 75% of high-grade serous ovarian cancer patients, the most common subtype of ovarian cancer, are presenting with ascites containing multicellular aggregates, which are linked to metastasis and relapse of the cancer. However, currently used models lack the ability to directly investigate the OvCa-spheroid invasion into the peritoneal mesothelium. Therefore, we are in need of a more complex, animal-free model that mimics the peritoneal mesothelium, to get a better understanding of the invasion of OvCa into the mesothelium and to identify the role of mesothelium and tumor spheroids for OvCa disease progression.

Using 3D-bioprinting, we developed a unique in vitro system for studying OvCa-spheroid mesothelium interaction. The tissue equivalent is 3D-bioprinted using micro-valve jetting into a custom-made small laser-cut acryl chip. The artificial mesothelium consists of three layers of fibroblasts covered by a monolayer of peritoneal mesothelium cells.
Using this newly developed Mesothelium-on-Chip system, we investigated the invasion process of two ovarian cancer cell lines, HTB77 and SKOV6. Furthermore, we showed that a treatment with anti-TGF-beta antibody, Resveratrol and Metformin leads to an inhibition of the invasion of the OvCa spheroids.

This model allows us to study OvCa-spheroid adhesion, invasion and drug resistance in a 3D-bioprinted, animal free model. Furthermore, it will give us the opportunity to predict patient's therapy response using ascites-derived multicellular aggregates to improve patient-tailored therapy.

PS3-S11-PP06 A novel isoform of Skp2 generated by alternative translational initiation

Betül SARI, Omar TORRES-QUESADA, Ludger HENGST

CCB Biocenter, Austria

The eukaryotic cell cycle can be subdivided four phases: G1 (Gap 1), S (DNA Synthesis), G2 (Gap 2), and M (Mitosis and cytokinesis). Each cell cycle phase transition is regulated by the activation or inactivation of specific cyclin-dependent kinase (CDK)/cyclin complexes. The kinase activity of Cdk/cyclin complexes is controlled by multiple mechanisms including regulation by CDK inhibitors (CKIs). The protein levels of CKIs, such as p27, are regulated by the ubiquitin-proteasome system. SCF-Skp2 is a E3 ubiquitin ligase complex that targets CKIs. As substrate recognition subunit of SCF-Skp2, the Skp2 (S-phase kinase-associated protein 2) protein can bind to other SCF (Skp, Cullin, F-box containing complex) subunits and phosphorylated CKIs, inducing K48 polyubiquitylation of these CKIs, which causes their proteasomal degradation.

Skp2 is an oncoprotein, which is often deregulated in cancer. In human cell lines, Skp2 protein can be detected as two bands in the Western Blot, with a size of app. 47kDa and 43kDa. The smaller, faster migrating band has been considered as a degradation product. We observed that the smaller isoform is translated from an alternative translation initiation codon, methionine-36. Importantly, the shorter isoform is more stable than the full-length isoform during the G1-phase, due to a missing “destruction box”, which has been shown to be targeted by another E3 ubiquitin ligase, APC-Cdh1. Using CRISPR-Cas9 edited cell lines, we demonstrate that both Skp2 isoforms are able to downregulate the Skp2 substrates p27, p21 or p57. Interestingly, cyclin D1 accumulates not only in cells lacking Skp2 expression, but also in cells only expressing the smaller Skp2 isoform. Interestingly, in immunoprecipitation experiments, both isoforms of Skp2 can interact with cyclin D1. Re-expression of Skp2 isoforms in a CRISPR-Cas9 edited cell line that does not express Skp2 could rescue p27 degradation but not the cyclin D1 accumulation. The physiological relevance of cyclin D1 binding to Skp2 and the molecular mechanism for the cyclin D1 accumulation in cells lacking full length Skp2 remain to be determined.

PS3-S11-PP07 Identification of Novel p57^{Kip2} Phosphorylation Sites: A Key Tyrosine Modification Blocks Cyclin-CDK Binding

Michael Keith Kullmann[1], Heidelinde Jäkel[1], Martin Dvorak[1], Taras Stasyk[2], Leopold Kremser[3], Bettina Sarg[3], Ludger Hengst[1]

[1] Medical Biochemistry, Medical University of Innsbruck, Austria
[2] Medical University of Innsbruck, Institute of Cell Biology
[3] Medical University of Innsbruck, Institute of Medical Biochemistry/Protein Core Facility

p57^{Kip2} (p57) is a member of the Cip/Kip family of cell cycle inhibitors. It binds to and inhibits the enzymatic activity of cyclin/CDK complexes, the drivers of the eukaryotic cell cycle.

Biochemical studies have characterized p57 as a highly phosphorylated protein in cells with only a minor portion being unphosphorylated. At least five distinct mono-phosphorylated and additional di- and poly-phosphorylated isoforms exist in human cells. At present, only serine 282 (S282) and threonine 310 (T310) have been identified as phospho-acceptor sites in human p57. Both regulate the subcellular localization and proteasomal degradation of p57.

To fill the gap of knowledge about the phosphorylation sites in p57, we performed a phosphosite analysis using mass spectrometry (MS). Human p57 was exogenously expressed in mammalian cells, isolated and enriched by immunoprecipitation, and processed for the analysis by MS.

We identified nine distinct phospho-acceptor sites, of which eight have not been described before. Phosphorylated S268 of p57 was recently identified in G2/M arrested cells and proposed as a potential Aurora kinase A (AURKA) target site.

We aimed to identify additional S268-kinases to get a hint where S268 phosphorylated p57 might fulfill its cellular function.

By applying a kinase prediction tool to a 20 amino acid sequence containing S268 of human p57, we obtained potential candidates for S268 kinases. From the Top 30 kinases we were able to generate and express 19 kinases of which 9 phosphorylate p57 by co-expression in cells. The majority of the S268 kinases belong to the Ca2+/calmodulin-dependent protein kinase (CAMK) class of enzymes. Interestingly, most of these kinases phosphorylated S268 much more efficiently than AURKA.

In our MS analysis we also identified two phosphorylated peptides containing tyrosine 63 (Y63) or tyrosine 91 (Y91). Interestingly, both tyrosines reside in the cyclin/CDK binding region of p57 and should not be accessible by kinases in a cyclin/CDK/p57 trimeric complex. In vitro and in vivo studies revealed, however, that p57 is readily phosphorylated by SRC-kinases, with Y63 being the preferred target. When Y63 is changed to glutamic acid this "phospho-mimetic" variant of p57 no longer binds to Cyclin-CDKs, indicating a regulatory function of these modification.

We are currently analyzing the contribution of phosphorylated Y63 and S268 to physiological differentiation processes and the pathological proliferation of cancer cells with high SRC kinase activities.

PS3-S11-PP08 Role of the CDK-Inhibitor $p27^{Kip1}$ on Myeloid/Lymphoid Neoplasm with rearrangement of PDGFRα

Carlos Castillo Giron, Heidelinde Jaekel, Ludger Hengst

Medical University of Innsbruck, Austria

Introduction

Myeloid/lymphoid neoplasms with eosinophilia that harbour the *FIP1L1–PDGFRA* fusion constitute a molecularly defined subgroup of haematologic malignancies. The fusion product is a cytoplasmic, constitutively active tyrosine kinase that drives uncontrolled proliferation and survival. Progression through G_1 requires active CDK–cyclin complexes, whose activity is regulated by the CDK inhibitor $p27^{Kip1}$. p27 neutralises CDKs by inserting a 3_{10}-helix into the kinase catalytic cleft; phosphorylation of p27 at Tyr-88 (pY88) ejects this helix, permitting ATP binding and partial CDK re-activation.

Methods and Results

We demonstrate that oncogenic *FIP1L1–PDGFRA* colocalizes with p27 in the nucleus, can physically associate with it and phosphorylates p27 at residues Tyr-74 and Tyr-88. These modifications were confirmed *in vitro* and *in vivo*, and observed at endogenous levels in the *FIP1L1–PDGFRA*-positive EOL-1 patient derived cell line. Phosphorylation at these sites impairs CDK inhibition of p27, converts it into an assembly factor of CDK4,6 and leads to its increased ubiquitin-mediated degradation. Pharmacological inhibition of *FIP1L1-PDGFRA* with the tyrosine kinase inhibitor imatinib markedly reduced p27 tyrosine phosphorylation, restores p27 expression and induced a pronounced G_1 arrest, as quantified by propidium-iodide FACS analysis. These data suggest that phosphorylation pf p27 by *FIP1L1–PDGFRA* may be one important mechanism leading to enhanced proliferation of *FIP1L1–PDGFRA* transformed cells.

Conclusion

Tyrosine phosphorylation–mediated neutralisation of p27 is a previously unrecognised mechanism by which *FIP1L1–PDGFRA* promotes cell-cycle entry. Clinically, most patients achieve durable remission with imatinib; however, kinase-domain point mutations can drive relapse, and ponatinib—while effective against many resistant variants—does not fully prevent additional relapses. Our data suggest a testable therapeutic strategy: after emergence of ponatinib resistance, co-administration of a CDK4/6 inhibitor such as palbociclib could mimic p27's brake on CDK activity and maintain resistant clones in G_1 arrest, thereby deepening and prolonging clinical responses.

PS3-S11-PP09 Taming the Double-Edged Sword: How FoxM1 Regulates Its Own Power in Senescence and Cancer

Sem Peijnenborgh, Anastasia Rakhimbekova, Tobias Madl

Medicinal Chemistry, Medical University Graz, Austria

Cellular senescence—a hallmark of aging—is characterized by irreversible cell cycle arrest and the development of a senescence-associated secretory phenotype (SASP), defined by the release of pro-inflammatory cytokines, growth factors, and proteases. While senescence initially suppresses tumorigenesis, it can later contribute to chronic inflammation, tumor progression, and stem cell exhaustion. FoxM1, a transcription factor that promotes cell proliferation, survival, and metastasis, inhibits senescence but is frequently overexpressed in cancers such as colorectal and breast cancer, where it drives tumor growth and spread. Therefore, tight regulation of FoxM1 is essential for balancing tumor suppression and aging. In this study, we examine the autoregulatory mechanism of FoxM1 by investigating interactions between its intrinsically disordered N-terminal negative regulatory domain (NRD) and its C-terminal transactivation domain (TAD).

These interactions were analyzed using nuclear magnetic resonance spectroscopy and isothermal titration calorimetry. Our findings reveal that the NRD binds not only to the TAD but also to the forkhead DNA-binding domain, suggesting an autoinhibitory mechanism that may regulate FoxM1's transcriptional activity and DNA binding. This structural flexibility could be key to modulating FoxM1's dual roles in cancer and aging.

PS3-S12-PP01 Establishing a screening protocol for the detection of antitumoral photosensitizers in *Penicillium* spp., *Talaromyces* spp. and *Hamigera* spp.

Vanessa Kern[0], **Carmen Bendetta**[0], Angelika Seeber[1], Pamela Vrabl[0], Bianka Siewert[1]

[1] Institute of Pharmacy/Pharmacognosy, Center for Molecular Biosciences Innsbruck (CMBI), Center for Chemistry and Biomedicine, University of Innsbruck, Innrain 80-82, 6020 Innsbruck, Austria.
[0] Microbiology, University of Innsbruck, Austria

Introduction

Cancer remains a major cause of death; however, standard therapies often lack specificity and cause side effects [1]. A more targeted approach is Photodynamic therapy (PDT), which uses photosensitizers to destroy tumor cells upon light activation [2]. Fungi of the genera *Talaromyces*, *Penicillium* and *Hamigera* produce diverse secondary metabolites and are promising sources of novel photosensitizers [3-5].

Aim

This study aimed to establish a screening protocol for fungal photosensitizers with antitumoral activity. Their efficacy was compared to reference compounds to assess their potential as antitumor agents.

Materials and Methods

Nine fungal species from the genera *Talaromyces*, *Penicillium* and *Hamigera* were cultivated under varying conditions (media composition, light, temperature, incubation time, submerged and agar plate cultures). The fungal cultures were harvested and extracted with a solvent mix. Crude extracts were evaluated for their ability to selectively induce cancer cell death upon blue light irradiation (λ = 478 nm, H = 5.3 J/cm^2), while sparing cells remaining in the dark. Cell lines were derived from lung, bladder and nasopharynx, as those tissue types can be irradiated minimally invasive.

Results

T. islandicus, *T. stipitatus and P. restrictum* showed notable photocytotoxicity. Blue-light exposure resulted in EC_{50} values of >0,5 µg/mL for *T. islandicus,* >14 µg/mL for *T. stipitatus,* >5 µg/ml for *P. restrictum*. Activity depended on cultivation conditions, especially the medium. *T. islandicus* and *P. restrictum* extracts showed activity against various cancer cell lines with even higher potency than the benchmark photosensitizers skyrin and emodin, approaching the potency of doxorubicin.

Conclusio

A screening protocol for fungal photosensitizers against cancer cells was successfully established, identifying three fungal species producing photocytotoxic metabolites. Their efficacy matched, or even surpassed that of reference photosensitizers.

This research was supported by the Austrian Science Fund (P37163).

[1] Schirrmacher, V. (2018). DOI: 10.3892/ijo.2018.4661

[2] Agostinis, P., et al. (2011). DOI: 10.3322/caac.20114

[3] Lei, L., et al. (2022). DOI: 10.3389/fmicb.2022.984801

[4] Assaf, C. E. H., et al. (2020). DOI: 10.3390/ijms21249462

[5] Igarashi, Y., et al. (2014). DOI: 10.1080/21501203.2014.917736

PS3-S12-PP02 Triggering photosensitizer production in *Talaromyces islandicus*

Niccolò Mariani[1], Markus Meitinger[1], Angelika Seeber[2], Christoph W. Schinagl[1], Desiree Artmann-Pabst[1], Bianka Siewert[2], Pamela Vrabl[1]

[1] University of Innsbruck, Austria
[2] Institute of Pharmacy/Pharmacognosy, University of Innsbruck, Austria

Filamentous fungi are a prolific source of bioactive secondary metabolites (SM), including photosensitizers (PS). PS are light-absorbing molecules which transfer the absorbed energy to other molecules, often generating reactive oxygen species (ROS) that can induce chemical or biological effects. These compounds play a critical role in photodynamic therapy (PDT), a promising, minimally invasive approach for cancer treatment [1]. With the demand for anti-cancer medications constantly increasing [2], the development of new PS is crucial for improving the efficacy and selectivity of PDT. However, the biosynthetic gene clusters responsible for SM and thus PS production are often silent under standard laboratory conditions and require specific environmental or physiological cues for activation.

Talaromyces islandicus has drawn attention due to its metabolic capacity to produce a plethora of structurally diverse SM, including polyene-like and quinoid pigments (e.g., islandicin, skyrin, emodin) and halogenated peptides such as cyclochlorotine, with hepatotoxic and carcinogenic properties [3]. In an ongoing screening for fungal PS, several light-activable candidates were identified in *T. islandicus*, while the conditions triggering their production remain uncharacterized. The present work aims to explore the environmental and physiological conditions that promote the biosynthesis of these photosensitizing compounds. The fungus was therefore cultivated under various growth conditions (e.g., changes in medium composition, temperature, light) and using different cultivation techniques (e.g., agar plates, Erlenmeyer flasks, bioreactor batch cultivation). The metabolites were then characterized through targeted analysis using TLC, HPLC, HR-MS/MS, and NMR.

The findings suggest that the PS production is significantly influenced by culture conditions, particularly the growth medium, which affect both PS quantity and variety. The successful production of these metabolites in bioreactor batch cultures, albeit at still low yields, paves the way for future biotechnological and therapeutic applications.

This work was supported by the Austrian Science Fund P37163.

1. Agostinis, P., et al.,2011 DOI: 10.3322/caac.20114

2. Soerjomataram, I. and F. Bray, 2021 DOI: 10.1038/s41571-021-00514-z

3. Yilmaz, N., et al., 2014 DOI: 10.1016/j.simyco.2014.08

.001

PS3-S12-PP03 UVISION - from sea to cell: translating marine Mycosporine-like amino acids into biomedical UV filters

Cornelia A. Karg[1], Michael J. Zwerger[2], Fabian Hammerle[1], Stefanie Hofer[2], Armin Oberosler[1], Ignacio Zegri Perez de la Torre[3], Thomas Werner[3], Ulf Karsten[4], Markus Ganzera[1], Johanna M. Gostner[5]

[1] Universität Innsbruck, Austria
[2] Institute of Medical Biochemistry, Medical University of Innsbruck, Innsbruck, Austria
[3] Department of Chemistry and Center for Sustainable Systems Design (CSSD), University of Paderborn, Paderborn, Germany
[4] Department of Applied Ecology and Phycology, University of Rostock, Rostock, Germany
[5] Institute of Medical Biochemistry, Medical University of Innsbruck, Innsbruck, Austria / Core Facility Metabolomics II, Medical University of Innsbruck, Innsbruck, Austria

Mycosporine-like amino acids (MAAs) are naturally occurring compounds synthesized or accumulated by a wide range of marine organisms, including microorganisms, algae, and invertebrates. Their biosynthesis is primarily stimulated by exposure to intense solar radiation. MAAs are notable for their strong ultraviolet (UV) absorption properties, enabling them to effectively attenuate harmful UV radiation. In marine organisms, these compounds function as natural sunscreens, protecting tissues from UV-induced damage. However, their biological roles extend beyond photoprotection. Despite their promising bioactivity, detailed knowledge of MAAs remains limited, partly due to the scarcity of available material for research.

The UVISION project follows a “from sea to cell” approach, aiming to explore the chemical diversity of marine-derived MAAs and translate their protective potential into biomedical contexts. Building upon methodological advances from previous FWF-funded projects, UVISION integrates multidisciplinary expertise ranging from marine biology, phycology, pharmacognosy, phytochemistry, medical biochemistry, toxicology, to chemical synthesis.

Our objectives are (1) to identify and characterize novel MAAs from underexplored marine sources; (2) to elucidate their UV-protective mechanisms using human cell line models; and (3) to develop synthetic and purification protocols that enable their broader application.

This interdisciplinary framework reflects the full pipeline from marine biodiversity to human cell-based testing, supporting the development of MAAs as potent natural UV filters for pharmaceutical and biomedical use.

PS3-S12-PP04 Investigating the effect of immobilising α-galactosidase onto magnetic, CMD-coated iron oxide nanoparticles on its activity and storage, for ease of separation in blood samples

Satinee Loh[1], Marco Eigenfeld[2], Sebastian Schwaminger[2]

[1] Medical University of Graz, Austria
[2] Division of Medicinal Chemistry, Otto-Loewi Institute, Medical University of Graz, Graz, Austria; BioTechMed-Graz, Graz, Austria

Alpha-galactosidase catalyses the hydrolysis of terminal, non-reducing α-D-galactose residues from oligosaccharides, galactomannans, and glycoproteins. They are also known to have transglycosylation activity, which provides an enzymatic approach to the synthesis of disaccharides. Its function makes it relevant to the sugar, pulp and paper, as well as food industries. Furthermore, some α-galactosidases have the ability to remove the terminal α1à3 linked galactosyl residue on type B erythrocyte antigens, converting blood group B to O. This is of interest to the medical field as blood type O is often in demand, being a universal donor for the other blood groups.

Alpha-galactosidase was cloned into pPICZα, and transformed into *K. phaffii*. The yeast was cultured in BMMY media for 72 hours. The supernatant was loaded onto an immobilised metal affinity chromatography column to purify the protein, utilising its histidine-tag. Its activity was determined by an enzymatic assay with 4-methylumbelliferyl-α-D-galactopyronaside as substrate and measuring the product's fluorescence. Different substrate concentrations were investigated for free α-galactosidase to obtain the K_m and V_{max}. Different reaction temperatures were also investigated. Iron oxide nanoparticles coated with carboxymethyl-dextran (ION@CMD) were synthesised and characterised. Different buffers and pH conditions are being investigated to optimise the immobilisation procedure of α-galactosidase. Subsequently, enzymatic activity assays that were conducted for the free-enzyme will be repeated for the immobilised one to determine the effect of immobilisation to ION@CMD.

The nanoparticle-coating was checked with FT-IR, and their size was determined with DLS. The coating was successful and the size of the particles was 116 nm. Preliminary results show that α-galactosidase adsorbs onto the ION@CMD particles up to 7×10^{-6} g/g and 2×10^{-5} g/g, in 50 mM Tris buffer pH 7 and 7.6, respectively, before the enzyme begins to precipitate. From the adsorption isotherms, it appears the ION@CMD is precipitating the enzyme when immobilised in Tris buffer. Thus, the need to optimise the immobilisation conditions and trial other buffers and pH values.

The ongoing research on immobilising α-galactosidase to ION@CMD aims to allow for magnetic separation of the enzyme from blood samples, prolong the storage-life of the enzyme, and determine any benefits of its activity at lower-than-body temperatures.

PS3-S12-PP05 The light of us: Photoantimicrobial activity of extracts from selected *Talaromyces* and *Penicillium* species

Friederike Luise Glauch[1], Markus Meitinger[1], Angelika Seeber[2], Bianka Siewert[2], Pamela Vrabl[1]

[1] Universität Innsbruck, Austria
[2] Institute of Pharmacy/Pharmacognosy, Center for Molecular Biosciences Innsbruck (CMBI), Center for Chemistry and Biomedicine, University of Innsbruck, Innrain 80-82, 6020 Innsbruck, Austria

Background: The global overuse of antibiotics has driven a resistance crisis, with projections of up to 40 million deaths by 2050[1]. Alternative therapies such as photodynamic antimicrobial chemotherapy (PACT), which uses light-activated photosensitizers (e.g., anthraquinones) are under investigation[2]. Fungi from *Penicillium* and *Talaromyces* spp. show promise as sources of such compounds[3].

Aims: This study aims to characterize fungal extracts and their biological activities using the PhotoMIC technique.

Material and Methods: Selected strains of *Talaromyces* and *Penicillium* spp. were cultivated on various media to trigger intra- and extracellular pigmentations. Crude extracts were tested at different concentrations for (photo)antimicrobial activity against *Candida albicans*, *Escherichia coli*, and *Staphylococcus aureus* in 96-well plates (450 nm, 30 J/cm², ~15 min) as described earlier[4].

Results: The culture medium had a significant impact on the light and dark toxicity of the fungal extracts. Notably, extracts of *T. islandicus* from MEA -grown cultures showed strong antimicrobial and phototoxic activity with minimal inhibitory concentrations (MICs) of 1.8 mg/L (*S. aureus*), 15 mg/L (*C. albicans*), and 30 mg/L (*E. coli*). *T. stipitatus* extracts from cultures grown on S2G medium were phototoxic against *S. aureus* (MIC: 15 mg/L), as well as *P. restrictum* extracts from a rice-grown culture (MICs of 3.75 mg/L against *S. aureus* and 60 mg/L against *E. coli*).

Conclusion: *Talaromyces* and *Penicillium* species exhibited (photo)antimicrobial activity, sometimes even at low concentrations, highlighting the potential of filamentous fungi as sources of novel agents for photodynamic therapy.

Refrences:

[1]Naddaf, M. (2024). https://doi.org/10.1038/d41586-024-03033-w

[2]Siewert, B. (2021). https://doi.org/10.1007/s43630-021-00034

[3]Igarashi, Y. et al. (2014). https://doi.org/10.1080/21501203.2014.917736

[4]Fiala J. et al. (2021). https://doi.org/10.3389/fmicb.2021.703544

This work was supported by the Austrian Science Fund (FWF) project P37163.

PS3-S12-PP06 Chitin and glycan-binding proteins in *Hydra's* adhesive system: unveiling potential for future biomimetic applications

Matthias Achrainer[1], Julia Ofer[0], Nick Aldred[2], Kevin Grüner[0], Stefan Redl[3], Bert Hobmayer[0], **Birgit Lengerer[0]**

[1] Institute of Zoology and Center for Molecular Biosciences, University of Innsbruck, Austria
[2] School of Life Sciences, University of Essex, Colchester, United Kingdom
[3] Institute of Neuroanatomy, Medical University of Innsbruck, Austria
[0] Zoology, University Innsbruck, Austria

Hydra, a freshwater cnidarian, utilizes a reversible adhesive system for surface attachment, providing a compelling model for studying temporary adhesion. Our research identifies chitin as a critical structural component of *Hydra's* adhesive, forming a fibrinous meshwork synthesized by a basal disc-specific chitin synthase (Chs2). Functional knockdown of Chs2 significantly reduces adhesive strength, highlighting chitin's essential role in maintaining the structural integrity of the adhesive matrix. Furthermore, we identify an arabinose-binding domain-containing protein (Ab2) as a key mediator of adhesive organization. Knockdown of Ab2 disrupts the adhesive structure and severely impairs attachment ability, suggesting its role in glycan interactions within the adhesive matrix. Unlike other reversible adhesive systems that rely on large multidomain proteins, *Hydra's* adhesive is primarily glycan-based, with chitin and glycan-binding proteins playing central roles. This unique composition offers a simpler, glycan-driven mechanism for reversible adhesion, distinct from protein-dominated systems. Our findings not only provide new insights into the molecular underpinnings of *Hydra's* adhesive system but also highlight its potential as a model for developing innovative, scalable adhesive technologies inspired by nature.

PS3-S12-PP07 Merged with PS3-S12-PP01

PS3-S12-PP08 Discovery of a novel pieicidin-family metabolite through activation of a cryptic biosynthetic gene cluster in *Nocardia terpnica*

Annelies Oismüller, Sacha Pidot, Marion Herisse, Napawit Nonthakaew

University of Graz, Austria

Antimicrobial resistance (AMR) is a growing global health crisis, with incidence and associated mortality continuing to rise. A proven strategy to counter AMR is the discovery of novel antimicrobial agents, many of which are derived from microbial secondary metabolites—non-essential molecules conferring ecological advantages such as defence and competitive fitness. Filamentous actinomycetes, particularly *Streptomyces* species, are among the most prolific producers of these compounds, accounting for the majority of antibiotic classes in current clinical use. Closely related to *Streptomyces*, *Nocardia* species also harbour numerous biosynthetic gene clusters (BGCs), yet many are cryptic and remain silent under standard laboratory conditions. Unlocking these silent pathways offers significant potential for the discovery of structurally novel and biologically potent metabolites.

Previous work has shown that inactivation of genes in a diverse range of loci can lead to the activation of silent BGCs, as can the growth of bacteria on different media types. Yet the combined impact of these approaches has not been evaluated. Here, a comprehensive screen of ~8,500 *Nocardia terpenica* transposon mutants grown on diverse media was performed to identify altered secondary metabolism, assessed by colony morphology. High-performance liquid chromatography (HPLC) revealed novel peaks in multiple mutants, indicating altered secondary metabolite production. Genome sequencing and proteomic analysis of one such mutant demonstrated that a transposon insertion upstream of an AfsR/SARP family transcriptional regulator resulted in significant upregulation of a type I polyketide synthase/non-ribosomal peptide synthetase encoding BGC (known as BGC 39), responsible for the production of a novel member of the piericidin-family of molecules. This finding represents a clear demonstration that transposon mutagenesis, coupled with environmental modulation, can successfully activate silent BGCs in *Nocardia*.

This approach shows strong potential for uncovering silent BGCs in *Nocardia*. Future work will focus on purification and structural elucidation of the novel compound, evaluation of its antimicrobial and other bioactivities, and genetic dissection of the regulatory network controlling BGC 39. While regulatory perturbation is strongly implicated in the observed activation, the precise molecular mechanism remains to be determined.

PS3-S12-PP09 The natural product Nostatin A inhibits V-ATPase activity and gives novel insights into consequences of lysosomal perturbations

Filip M. Gallob[0], Dominika Tuckova[1], Severin Lechner[0], Georg Winter[0], Pavel Hrouzek[1], Andreas Villunger[2]

[1] Centre Algatech, Institute of Microbiology, Czech Academy of Sciences, Novohradská 237, Centre Algatech, Institute of Microbiology, Czech Academy of Sciences, 379 01 Třeboň, Czech Republic
[2] Institute for Developmental Immunology, Biocenter, Medical University of Innsbruck, Innsbruck, Austria
[0] CeMM Research Center for Molecular Medicine, Austria

Natural products (NPs) and their structural derivatives have greatly contributed to the current shape of our therapeutic landscape. NPs and NP-inspired compounds are used as standard of care treatments for a wide range of indications, ranging from cardiovascular diseases to cancers. The recently discovered cyanobacterial secondary metabolite Nostatin A (NoA) has been shown to possess unique structural properties as well as high bioactivity, making it an attractive option for drug development efforts. In this study we aimed to deconvolute the molecular mode of action of NoA and characterize its molecular interaction partners. Through characterizing the cellular stress pathways in response to NoA exposure, we discovered that NoA leads to the activation of GCN2, which ultimately promotes high rates of cell death through the Integrated Stress Response (ISR). GCN2 activation is followed by eIF2α phosphorylation, 5'cap independent translation of the stress transcription factor ATF4 and the induction of apoptosis across a range of cell types. However, we discovered that NoA-induced apoptosis is not solely driven by the ISR but receives pro-apoptotic signaling input from the JNK mitogen-activated protein kinase (MAPK). We can show that the ribotoxic stress response MAPK ZAKα reduced early pJNK signaling, while the endoplasmic reticulum associated factor IRE1α reduced late phosphorylation of JNK. Using a chemoproteomic competition assay we identified multiple V-ATPase components as putative interaction partners of NoA. While target validation is ongoing, we were able to establish that Nostatin A inhibits V-ATPase activity with similar kinetics to established V-ATPase inhibitors such as Bafilomycin A1. We found that analogous to NoA, Bafilomycin A1 also leads to GCN2 dependent ATF4 upregulation as well as ZAKα and IRE1α dependent JNK phosphorylation with comparable kinetics. Counterintuitively, we found that both compounds also lead to an early hyperactivation of mTORC1. This body of work highlights the relative contributions of different pro-apoptotic pathways to cell death in response to V-ATPase inhibition. In addition, we can show that mTORC1 hyperactivation is an early response to v-ATPase inhibition.

PS3-S13-PP01 Stress Pathway Activation Induced-Macropinocytosis in p53-Deficient Cells Following Fine Dust Exposure

Tamara Lang, Christian Wechselberger

Department of Pathophysiology, Johannes Kepler University, Austria

Fine dust, or particulate matter (PM), is a pervasive environmental pollutant with profound implications for human health. Due to their small size, particles such as PM2.5 can penetrate deep into the respiratory tract, translocate into the bloodstream, and evade innate defense mechanisms, thereby initiating cascades of oxidative stress, inflammation, and genotoxic damage — all of which are key contributors to tumorigenesis. In this study, we investigated the molecular and cellular responses to PM2.5 exposure in an in vitro model using wild-type (WT) cells and p53-deficient cells. Cells were subjected to short-term and chronic exposure, followed by assessments of viability, morphology, and gene expression. Reporter assays revealed robust activation of oxidative stress (ARE) and xenobiotic response (XRE) pathways, alongside p53-associated signaling in WT cells. p53-deficient cells exhibited a distinct phenotype characterized by prominent intracellular macropinosomes and pronounced morphological alterations, which were absent in WT cells and became apparent upon exposure to PM2.5.

These findings indicate that p53 status not only modulates stress pathway activation but also alters cellular uptake mechanisms such as macropinocytosis in response to environmental particulate matter. Together, our results highlight potential links between fine dust exposure, defective tumor suppressor function, and cellular processes relevant to early cancer development.

PS3-S14-PP01 Scaling immune-cell receptor analysis with Scirpy to millions of single cells

Felix Petschko, Mario Kanetscheider, Tobias Ganzenhuber, Antonio Rodríguez-Sánchez, Gregor Sturm, Francesca Finotello

University of Innsbruck, Austria

Scirpy is a popular Python tool for single-cell analysis of adaptive immune receptor repertoires, used in large-scale studies like the Tabula Sapiens. With the rapid growth of data size driven by advancements in sequencing technologies, scalability has become a central challenge. The analysis of larger datasets enables more detailed and robust insights into immune repertoires. More performant solutions reduce hardware cost and accelerate the discovery of biological insights.

A key functionality of Scirpy is clonotype analysis, which identifies T or B cells likely to recognize the same antigen or share a common ancestor. This analysis consists of two crucial steps: 1) computing distances between complementarity-determining region 3 (CDR3) sequences based on a similarity metric; 2) identifying cell clusters based on the computed CDR3 similarity and V/J gene usage. These two major steps proved to be performance bottlenecks for Scirpy analysis of large datasets, alongside secondary limitations like result graph visualization and result storage.

We focused on two metrics that are most commonly used: a sequence distance based on a substitution matrix for TCRs, and Hamming distance for BCRs. We integrated tcrdist3, an accelerated CPU implementation of the TCRdist metric and further optimized it by supporting sparse matrices. For the Hamming distance, we created a CPU implementation with Numba and a GPU version with CuPy. For the clustering step, we reimplemented existing algorithms optimizing sparse matrix operations. We added result graph filtering for better readability and efficiency, and changed the output data format to accelerate result storage.

For 1.5 million T cells with 64 CPU cores, the improved CPU version of the Hamming distance calculation achieved a speedup of ~15.6 (92.5s vs. 1440.3s). This calculation took 468.2s with the TCRdist method. The Hamming distance GPU implementation achieved an additional speedup of 9.2 (43.7s vs. 402.2s) over the improved CPU version on a laptop. The improved CPU version of the cluster identification achieved a speedup of ~127.7 (57.5s vs. 7345.4s) for 1 million cells with 64 CPU cores. We successfully tested the improved CPU versions on up to 8 million T cells, which was previously infeasible due to memory or runtime constraints.

These enhancements significantly improve Scirpy's capability to analyze growing single-cell RNA sequencing data, facilitating continued usability in large-scale immune repertoire analysis.

PS3-S14-PP02 spacedeconv: deconvolution of tissue architecture from spatial transcriptomics

Constantin Zackl[1], Maria Zopoglou[1], Reto Stauffer[2], Markus Ausserhofer[1], Marieke E. Ijsselsteijn[3], Gregor Sturm[4], Noel Filipe da Cunha Carvalho de Miranda[3], Francesca Finotello[1]

[1] Molecular Biology, University of Innsbruck, Austria
[2] Department of Statistics, Digital Science Center (DiSC), University of Innsbruck, 6020 Innsbruck, Austria
[3] Department of Pathology, Leiden University Medical Centre, 2333ZA Leiden, the Netherlands
[4] Boehringer Ingelheim International Pharma GmbH & Co KG, Biberach, Germany

Background. Understanding tissue architecture through the study of cellular organization and its underlying molecular mechanisms is crucial for revealing how tissues function and how they become dysfunctional in disease. The emergence of spatial omics technologies has enabled the investigation of cell transcriptomes within their native tissue context, although not all platforms offer single-cell resolution. To date, several cell-type deconvolution methods have been proposed to computationally infer the cellular composition of complex tissues profiled with RNA sequencing. However, deconvolution methods differ in programming languages, input data types, and range of applicability, which complicate their execution, comparison, and selection for specific investigations.

Results. We developed the spacedeconv R package as a unified interface for the deconvolution of spatial transcriptomics data. It offers streamlined access to a variety of deconvolution methods and further supports data preprocessing and normalization, quantitative analysis of intra- and inter-cellular communication, and flexible visualization of spatial quantifications. Via the analysis of data from different organisms and tissues, we demonstrated how spacedeconv can be used to investigate the cellular and molecular underpinnings of tissue architecture, and showed how the peculiarities of specific methods can be preferred depending on the application. spacedeconv can further complement deconvolution results with different data modalities, as we exemplified by leveraging spatial T-cell receptor information to investigate the distribution of bystander and tumor-reactive T cells in brain metastases, or digital pathology information to elucidate features associated with the presence of tertiary-lymphoid structures in renal cancer.

Conclusions. spacedeconv is a comprehensive tool that streamlines deconvolution analysis of spatial transcriptomics data, further bridging tissue cellular composition with the underlying molecular machinery. spacedeconv can advance our understanding of tissue complexity in different organisms, tissues, and disease contexts. Furthermore, it provides a unified platform that will facilitate the access, assessment, and comparison of deconvolution tools.

PS3-PhD-PP01 A tale of two TOLs: *PIN*-pointing the issue for high temperature adaptation

Nils Leibrock, Jeanette Moulinier-Anzola, Rebecca Lugsteiner, Simone Colucci, Barbara Korbei

BOKU Vienna, Austria

Here, we present how sessile plants leverage developed targeted protein degradation strategies to adapt to their ever-changing environmental conditions. A key strategy plants use to maintain cellular homeostasis involves protein degradation and translocation through endosomal trafficking. The ESCRT (endosomal sorting complex required for transport) is responsible for recognition of ubiquitinated cargo and sorting it into intraluminal vesicles for degradation in the vacuole. While mammals can rely on the functionality of ESCRT-0 subunits for cargo recognition and sorting, plants only possess the remaining ESCRT-I, -II and -III subunits. In plants, TOL- (TOM1-like) proteins are fundamental in the initial recognition and sorting of ubiquitin-tagged proteins. In the absence of ESCRT-0, TOLs assume its role and show significant influence on plant morphology. In this study, we investigate how TOLs function in intracellular trafficking of phytohormone transporters, which are critical for plant adaptation and could open up agricultural opportunities.

PS3-PhD-PP02 SZT2 in ER/Lysosome Crosstalk and the maintenance of proteostasis

Thanida Laopanupong[1], Martina Mari[1], Utku Horzum[2], Taras Stasyk[1], Hesso Farhan[2], Lukas A. Huber[1], Mariana Eca Guimaraes de Araujo[1]

[1] Cell biology, Medical University of Innsbruck, Austria
[2] Institut für Pathophysiology, Medizinische Universität, Innsbruck, Austria

Seizure Threshold 2 (SZT2) is highly expressed in the brain, especially in parietal and frontal cortex, and is implicated in epileptogenesis in mice and humans. Biallelic SZT2 variants have been linked to Developmental and Epileptic Encephalopathy 18 (DEE18).

SZT2 is a core subunit of the KICSTOR complex, a negative regulator of lysosomal mTORC1 signaling. The complex suppresses mTORC1 activity in amino acids, glucose, and cholesterol deprivation, but not in the absence of growth factors. In SZT2KO cells, mTORC1 remains active under catabolic conditions, as shown by persistent activation of P70S6K and 4EBP1. These cells also exhibit increased size, reduced mitochondria abundance and impaired mitochondrial function (basal respiration and ATP production).

The sustained activation of protein synthesis regulators under amino acids (AA) starvation raises the question of how SZT2KO cells adapt to this stress condition. Our main objective is therefore to determine how proteostasis and vialibity are maintained in SZT2 ablated cells.

Puromycin-labeling assay revealed no increase in protein synthesis in SZT2KO cells compared to wild-type controls (WT) under amino acid starvation. Cell size analysis showed that while SZT2KO cells are larger than WT and rescued cells, they can shrink during AA starvation and expand upon re-stimulation, indicating SZT2KO cells can react and adjust their cell size in response to environmental changes.

We analysed the 3D Golgi body volume and ER-exit site (ERES) number under steady state, starvation and re-stimulation. SZT2KO cells showed larger and more fragmented Golgi and increased ERES counts under steady state. Under AA starvation and re-stimulation, their Golgi volume became more heterogeneous. Moreover, they failed to adjust ERES numbers under AA starvation. These findings suggest that SZT2 depletion affects the biosynthetic pathway.

In summary, SZT2KO cells exhibit persistent mTORC1 signalling, altered cell size, disrupted Golgi structure, and ERES dysregulation. Future work will examine the balance between protein synthesis and degradation using specific inhibitors, assessing trafficking efficiency via the RUSH assay and protein crowding using GEMs. Special attention will be given to autophagy and ER-lysosome contact sites to understand how crosstalk between these organelles influences proteostasis in SZT2-deficient cells.

PS3-PhD-PP03 Radiation-induced calcific aortic valve disease: a viral mimicry disorder?

Dominik Hau[0], Michael Graber[0], Lynn Muller[0], Elke Kirchmair[0], Lara Usko[0], Manuel Fiegl[1], Veronika Niedrist[0], Can Gollmann-Tepeköylü[0], Michael Grimm[0], Johannes Holfeld[0]

[1] EMBL Barcelona
[0] Cardiac research laboratory, Medical university of Innsbruck, Austria

Aortic valve calcification is a common late complication of thoracic radiotherapy, yet its molecular drivers remain insufficiently understood. Recent findings suggest that ionizing radiation can reactivate silenced genomic elements such as human endogenous retroviruses (HERVs), and has been associated with the re-expression of retroelements. We hypothesized that radiation-induced HERVK re-expression promotes calcification in valvular interstitial cells (VICs), and that RVLPs (retrovirus like particles) generated from reactivated elements are sufficient to trigger similar effects in non-irradiated cells.

Primary human VICs were exposed to 10 Gy irradiation and analyzed via RNA sequencing, RT-qPCR, droplet digital PCR (ddPCR), dsRNA-specific ELISA, immunoblotting, and transmission electron microscopy. Functional calcification was assessed by Alizarin Red S staining. To test causality, HERVK knockdown and overexpression experiments were performed. Additionally, we generated RVLPs exogenously by transfecting HEK293T cells with plasmids encoding a reconstructed HERVK consensus sequence. The resulting particles were applied to naïve VICs in the absence of radiation.

Radiation led to a robust upregulation of HERVK transcripts, increased intracellular dsRNA, and the formation of RVLPs in VICs. We further detected HERV-derived RNA and Env protein in the supernatant of irradiated cells, indicating the extracellular release of retroviral components. Conditioned medium from irradiated cells induced pro-inflammatory and pro-calcific gene expression in untreated VICs. Strikingly, RVLPs generated via plasmid-based expression of a reconstructed HERVK consensus sequence elicited comparable inflammatory activation and calcification, mimicking the effects of irradiation. These responses were broadly suppressed by pharmacological inhibition using Abacavir, which reduced calcification induced by both irradiation and RVLP treatment, and concomitantly diminished HERV expression as well as pro-inflammatory cytokine and osteogenic factor levels.

Our findings suggest that radiation triggers a retroelement-driven cascade that promotes VIC calcification via HERVK activation and RVLP formation. The ability of synthetic RVLPs to reproduce these effects in the absence of radiation highlights a self-sustaining pathological loop. While pattern recognition receptors such as TLR3 may mediate this response, further mechanistic work is needed. Targeting HERV-derived products may represent a promising strategy to prevent radiation-induced cardiovascular damage.

PS3-PhD-PP04 Characterization of the Axl/Gas6 signaling pathway following receptor inhibition by peptide ligands and siRNAs.

Alexandra Tsal-Tsalko[0], Hans Peter Weizenböck[0], Christian Klein[0], Rita Seeböck[1], Mario Mikula[2], Florian Eibensteiner[0], Harald Hundsberger[0]

[1] Institute of Clinical Pathology and Molecular Pathology of the Lower Austria Central Region (University Hospital St. Pölten)
[2] Institute of Medical Genetics, Center for Pathobiochemistry and Genetics, Medical University of Vienna, Vienna, 1090, Austria
[0] IMC Fachhochschule Krems, Austria

Melanoma, which arises from melanocytes in the basal epidermis, represents the most lethal form of skin cancer. While early-stage melanoma can often be cured by surgical resection, once the cancer spreads into the dermis, the relative 5-year survival rate drops considerably. Targeted therapies, particularly BRAF inhibitors, have improved outcomes. However, resistance to these therapies remains a major challenge, limiting long-term survival in advanced stages. Axl, a receptor tyrosine kinase, belonging to the TAM (Tyro3, Axl, MER) receptor family, plays an important role in such resistance mechanisms. Upon binding of its ligand Gas6, Axl activates downstream signaling pathways such as PI3K/Akt and ERK/MAPK, which promote invasion, metastasis, and proliferation of cancer cells.

The aim of our project is to investigate the activation of the Gas6/Axl signaling pathway in melanoma cells. This helps us to identify novel target proteins and develop new approaches to overcome therapy resistance. Our work focuses on characterizing the proteome and interactome of Axl in isogenic melanoma cell lines (WM793b and 1205Lu). To investigate the Axl proteome, Axl is silenced using siRNAs, followed by mass spectrometry analysis of whole cell protein isolates. This approach allows for identification of novel targets involved in Axl signalling. A proximity-dependent biotin identification assay (BioID) is used to analyze the Axl interactome. Proteins in close proximity to Axl are selectively biotinylated, isolated, and identified using mass spectrometry. This approach provides a deeper insight into Axl's interaction partners and their potential roles in melanoma progression. In parallel, we are developing several variants of the Axl ligand Gas6, that are designed to bind Axl without activating downstream signaling.

Our results reveal that Axl silencing leads to significant downregulation of proteins involved in cell migration and stress response, while upregulating factors that are linked to differentiation, protein homeostasis and oxidative stress defense. In parallel, recombinant Gas6 ligand variants were successfully expressed in Pichia pastoris cells. These Gas6 variants will be tested for their ability to bind Axl without triggering receptor activation. The findings provide a foundation for targeting Axl-mediated signaling in melanoma and suggest new strategies to overcome therapy resistance.

PS3-PhD-PP05 REGIMOPROT: Identification and Characterization of Extracellular Matrix Components involved in Bone Regeneration

Adrian Lendvai[1], Hans Peter Weitzenböck[1], Christian Klein[1], Andreas Kogler[2], Monika Pichler[2], Andrea De Luna[3], Stefan Nehrer[3], Harald Hundsberger[1]

[1] IMC Krems, Austria
[2] Cells+Tissuebank Austria gemeinnützige GmbH
[3] University for Continuing Education Krems

Bone allograft implants are essential in orthopedic and dental surgery, facilitating bone reconstruction and repair while avoiding the need for autografts, which require harvesting the patient's bone. This minimizes surgical risks and recovery time. Allografts act as scaffolds, supporting new bone growth and promoting natural healing and integration within the body. They are used in various forms such as powders, chips, or complete bone segments, depending on clinical needs. Bone allografts improve patient outcomes by accelerating recovery, restoring structural integrity, and enhancing function. The extracellular matrix (ECM) in bone allografts plays a crucial role in osteogenesis by providing structural support and bioactive signals that regulate cell adhesion, proliferation, and differentiation. Rich in collagen, glycoproteins, and growth factors, the ECM influences osteoblast activity and enhances new bone formation. Decellularization techniques aim to preserve these key components while minimizing immune response. Retaining ECM integrity in allografts can improve graft integration, vascularization, and bone remodeling, making it a vital factor in regenerative medicine. Characterizing ECM dynamics may lead to improved allograft designs and enhanced bone healing outcomes. In collaboration with Cells + Tissuebank Austria gemeinnützige GmbH, we conduct advanced research on protein extraction from bone tissue to enhance the biological functionality of allografts. During the manufacturing process, fresh bone material undergoes multiple cleaning and processing steps, which may lead to the loss of bioactive proteins essential for bone regeneration. To address this, we employ mass spectrometry and various extraction techniques to systematically analyze the protein composition at each stage of processing. By characterizing these extracellular matrix components, we aim to identify key osteoinductive factors that may contribute to improved bone healing. Ultimately, our findings will be integrated into novel cell activity assays, enabling a deeper understanding of the regenerative potential of allograft materials along with the development of more effective bone grafting solutions.

PS3-PhD-PP06 Unravelling Tendon Degeneration: Cellular and Metabolic Insights from SPARC-Deficient Model

Nevra Pelin Cesur[1], Andrea Wagner[1], Daniela D. Weber[2], Christopher Gerner[3], Thomas Lettner[1], Renate Gehwolf[1], Andreas Traweger[1]

[1] tendon&bone regeneration /Paracelsus Medical University, Austria
[2] Research Program for Receptor Biochemistry and Tumor Metabolism, Department of Pediatrics,University Hospital of the Paracelsus Medical University, Salzburg, Austira
[3] University of Vienna, Institute of Analytical Chemistry, Vienna, Austria

Injured tendons often heal with impaired structural and functional properties, leading to scar tissue formation and disrupted extracellular matrix (ECM) organization. These alterations can initiate deleterious cellular responses, contributing to chronic tendon disorders. Our research has identified the matricellular protein SPARC (Secreted Protein Acidic and Rich in Cysteine; also known as BM-40 or osteonectin) as a critical regulator of tendon integrity and homeostasis (1,2). Global SPARC knockout (SPARC−/−) mice exhibit significantly thinner, biomechanically compromised tendons with features of spontaneous rupture and pathological remodeling. These tendons show ECM disorganization, abnormal mechanical stress responses, and increased lipid accumulation—hallmarks of tendon degeneration. However, due to the systemic nature of the knockout model, potential secondary effects from SPARC loss in associated tissues (e.g., bone or muscle) could not be excluded.

To address this limitation, we generated a tendon-specific SPARC knockout mouse (Sparc^fl/fl:Scx-Cre^+), using the tendon-lineage Scleraxis-Cre driver. Efficient deletion of SPARC in tendon tissues was confirmed via genotyping, mRNA analysis, and Western blotting. Histological, immunohistochemical, and biomechanical assessments (including nanoindentation) confirmed substantial structural and functional alterations in the Achilles, flexor, and tail tendons of knockout mice. Multi-omics analyses were conducted to gain mechanistic insight. Single-nucleus RNA sequencing (snRNA-seq) revealed eight cell clusters in control tendons versus seven in the knockout, with shifts in fibroblast and macrophage-like populations. Metabolomic profiling identified 461 significantly dysregulated metabolites—most notably phosphatidylcholines, amino acids, acylcarnitines, sphingomyelins, triglycerides, and others—suggesting metabolic imbalance and possible ER stress. These findings were supported by whole transcriptomic analyses, which are underway to further characterize gene expression changes.

Altogether, the Sparc^fl/fl:Scx-Cre^+ model offers a powerful platform for dissecting the cellular, molecular, and metabolic underpinnings of tendinopathy. It reinforces the central role of SPARC in maintaining tendon health and provides critical insights for therapeutic development.

(1) Gehwolf R. et al; 2016

(2) Wang T, Wagner A, Gehwolf R et al. 2021

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

S11: Stem cells, cell cycle and cancer

Chairs:

Heidelinde Jäkel
Medical University of Innsbruck, AT

Frank Edenhofer
University Innabruck, AT

S11-IT01 Structural studies of chromosome segregation.

Jun Yu[0], Sophia Schmidt[0], Margherita Botto[0], Andrew Howe[1], Chloe Gent[2], David Morgan[2], **Andreas Boland[0]**

[1] 4Bioimaging Center, University of Geneva, Geneva, Switzerland
[2] Department of Physiology, University of California, San Francisco, San Francisco, CA 94143, USA
[0] Molecular and Cellular Biology, University of Geneva, Switzerland

During mitosis, the cohesin complex holds together sister chromatids until anaphase, when the cysteine protease separase get activated and cleaves the cohesin subunit SCC1 or RAD21, thus triggering chromosome separation. We recently employed a multidisciplinary approach including cryoEM, biochemical analysis, and cross-linking mass spectrometry to elucidate the regulation and activation of separase, providing novel insights into the intricate regulatory network of chromosome segregation.

The first study reveals how separase cleaves SCC1 at two distinct sites and why cleavage is enhanced upon phosphorylation of substrate residues. CryoEM structures of human separase, in apo- or substrate-bound forms, confirm the first cleavage site, reassign the second, and identify multiple docking sites, including four phosphate-binding pockets. Interestingly, the cohesin subunit SA1/SA2 promotes cleavage at the second site, and a model based on cryoEM and mass spectrometry explains how separase targets the cohesin ring complex, providing insights into the mechanics of sister chromatid separation.

The second study investigates separase inhibition by securin and/or the CDK1-cyclin B1-CKS1 (CCC) complex, which block its activity until anaphase. CryoEM structures show that both inhibitors use specific motifs to obstruct separase's catalytic and docking sites. However, securin employs its own motifs, while CDK1-cyclin B1 uses separase's disordered loops, including one blocking both separase and CDK1 catalytic sites and another obstructing a docking cleft. A phosphoserine in separase binds to a phosphate-binding pocket in cyclin B1, crucially stabilizing the interaction between CCC and separase.

Together, these findings provides insights into one of the most fundamental events in the life of a eukaryotic cell, the separation of sister chromatids. We show how human separase recognises its substrates and is inhibited by two mutual exclusive inhibitors until anaphase onset. Our studies provide a framework for structure-guided development of novel cancer pharmaceuticals.

S11-ST01 Adaptive CDK Pathways Underpinning Therapy Resistance

Alessia Schirripa[0], Helge Schoeppe[1], Elisabeth Gamper[0], Mark Steinlechner[0], Thorsten Klampfl[0], Veronika Sexl[1], Eduard Stefan[1], Ulrich Stelzl[2], Teresa Kaserer[1], Karoline Kollmann[0]

[1] University of Innsbruck, Innsbruck, Austria
[2] University of Graz, Graz, Austria
[0] University of Veterinary Medicine Vienna, Austria

Cyclin-dependent kinases (CDKs) are master regulators of cell-cycle progression and transcriptional control, with CDK6 playing a role in both processes. Unlike other cell-cycle CDKs, CDK6 possesses an unusually long and structurally unresolved C-terminus. To study its function, we reconstituted CDK6-deficient leukemic cells with either full-length CDK6 or a C-terminally truncated variant (CDK6 ΔC, lacking the last 32 amino acids). Our results revealed that the C-terminus is essential for nuclear localization, chromatin binding, and interaction with canonical regulators such as Cyclin D, INK4 inhibitors, and $p27^{Kip1}$. Structural computational modeling confirmed reduced protein flexibility due to truncation, disrupting conformational dynamics critical for partner binding. Surprisingly, interaction with Cyclin B1 remained intact, an unexpected finding suggesting a distinct, C-terminal-independent interaction mode, potentially linking CDK6 to later cell-cycle phases or alternative functional pathways.

Preliminary data suggest that CDK8 represents another example of a CDK that bridges transcriptional regulation and cell cycle control. The combination of CDK8 mutant mouse models, RNA-seq analysis and CDK8 Co-IP-MS data of $p185^{BCR\text{-}ABL+}$ cells, revealed a direct involvement of CDK8 during mitosis, suggesting a novel potential combinatorial strategy: pairing CDK8 inhibition with agents targeting mitotic progression to enhance anti-leukemic efficacy.

These data highlight the need to explore cell-cycle-phase specific atypical CDK complexes which might contribute to resistance against CDK inhibitors, like CDK4/6 inhibitors, particularly in breast cancer and leukemia.

S11-ST02 Novel functions of the small p27^{KIP1} uORF-encoded peptide

Omar Torres-Quesada[1], Martin Dvorak[1], Klaus Faserl[2], Bettina Sarg[2], Leopold Kremser[2], Ludger Hengst[1]

[1] Medical Biochemistry Institute, Medical University Innsbruck, Austria
[2] Protein Core Facility, Institute of Medical Biochemistry, CCB-Biocenter, Medical University of Innsbruck, Austria

Cyclin-dependent kinase (CDK) inhibitor 1B (p27^{Kip1}) is encoded in humans by the *CDKN1B* gene and it plays a critical role in regulating cell proliferation, cell cycle progression, and differentiation. It controls the G1-to-S phase transition by negatively regulating CDK2/Cyclin E and CDK2/Cyclin A complexes. Although *CDKN1B* mutations are relatively rare in human cancers, p27^{KIP1} is frequently downregulated or mislocalized, contributing to tumorigenesis through its role as a tumor suppressor.

The CDKN1B mRNA contains a highly structured 5' untranslated region (5'UTR) that harbors several translational regulatory elements, including an internal ribosome entry site (IRES) and an upstream open reading frame (uORF) encoding a 29-amino acid peptide. This uORF can influence translation during ribosomal scanning, thereby modulating the expression of the main p27 ORF by enabling reinitiation downstream or inducing ribosomal stalling, which reduces downstream translation. However, many questions remain about the full spectrum of regulatory functions the uORF may exert and the specific structural elements involved.

Sequence analysis and structural predictions have revealed that the p27^{KIP1} uORF-encoded peptide is highly hydrophobic and more evolutionarily conserved than the p27 protein itself. This suggests strong evolutionary pressure to preserve not only the uORF as a structural regulator of p27 translation but also its amino acid sequence. Interestingly, the uORF peptide exhibits distinct protein expression, stability, and subcellular localization patterns compared to the p27 protein, and it is stabilized in response to DNA damage signaling. Our data indicate that the p27^{KIP1} uORF may regulate additional key cellular functions, potentially acting as an independent trans-regulatory peptide.

S11-ST03 A novel ERAD-to-mTORC1 signaling axis constitutes a vulnerability of multiple myeloma cells to targeting secretory proteostasis

Utku Horzum[1], Herbert Oberacher[2], Margot Haun[1], Monica Roman-Trufero[3], Holger Auner[3], Agnieszka Martowicz[4], Gerold Untergasser[4], Eberhard Gunsilius[4], Wolfgang Willenbacher[4], Dominik Wolf[4], Hesso Farhan[1]

[1] Institute of Pathophysiology, Medical University of Innsbruck, Austria
[2] Institute of Legal Medicine, Medical University of Innsbruck, Innsbruck, Austria
[3] Division of Hematology, Lausanne University Hospital, Lausanne, Switzerland
[4] Department of Hematology and Oncology, Internal Medicine V, Comprehensive Cancer Center Innsbruck (CCCI), Tyrolean Cancer Research Institute (TKFI), Medical University of Innsbruck, Innsbruck, Austria

Multiple myeloma (MM), the second most common hematological malignancy, results from the clonal proliferation of malignant plasma cells in the bone marrow. MM cells produce and secrete vast amounts of immunoglobulins, requiring major adaptive changes of the endoplasmic reticulum (ER) proteostasis machinery. Our study aims to identify vulnerabilities within the ER-export machinery as therapeutic targets for MM.

Secretory proteins leave the ER in a COPII-dependent manner at ER exit sites (ERES). The four SEC24 paralogs (A-D) are the part of the COPII coat responsible for capturing secretory cargo. Notably, the machinery controlling immunoglobulin trafficking from the ER are poorly investigated, and the impact of disrupting this process on myeloma cell survival remains unclear. We performed single and combined siRNA knockdowns of SEC24 paralogs in non-secretory MM cells (KMS-12PE) and secretory MM cells (AMO-1, and NCI-H929). While the non-secretory KMS-12PE cells were unsensitive, both secretory cells lines were highly sensitive to silencing SEC24 paralogs, particularly SEC24A&B. Accordingly, immunoglobulins exhibited stronger colocalization with SEC24A&B-positive ERES. Interestingly, although knockdown of SEC24A&B increased misfolded protein levels, we did not observe a major increase of the UPR, indicating that ER stress is not responsible for sensitizing secretory MM cells to death. Instead, SEC24A&B silenced cells exhibited higher mTORC1 activity, and inhibition of mTORC1 rescued these cells from death. This indicates a link between ER-export disruption and mTORC1 signaling.

Silencing SEC24A&B increased the level of misfolded proteins in the ER, inducing ERAD-mediated proteasomal protein degradation, thereby increasing cytosolic amino acid levels. Inhibiting ERAD rescued SEC24A&B knockdown MM cells from death. Notably, despite higher mTORC1 activity, the translation rate was significantly lower in SEC24A&B depleted cells, indicative of metabolic imbalance, where a higher energetic demand cannot be met. Altering ER-export resulted in swelling of mitochondria, reduced the spare respiratory capacity and a reduced ability to produce ATP, thus explaining why the higher energetic demand cannot be met.

Altogether, our work reveals an unprecedented link between ERAD and mTORC1 signaling that can be exploited a potential therapeutic strategy in multiple myeloma.

S11-ST04 Novel stem cells from the human brain - cellular and epigenetic plasticity of eNSPCs

Amelie Schurer[1], Angeliki Spathopoulou[1], Marcel Tisch[1], Katharina Günther[1], Marc-Christian Thier[2], Marta Suarez Cubero[1], Theresa Lindlbauer[1], Louisa Dury[1], Li Li[3], Tanja Schlaiß[4], Simone Liebscher[5], Francesca Finotello[6], Gunnar Schotta[3], Christopher Esk[1], Oliver Brüstle[7], Katja Schenke-Layland[8], Andreas Trumpp[2], Frank Edenhofer[1]

[1] Molecular Biology, University of Innsbruck, Austria
[2] German Cancer Research Center - HI-STEM, Heidelberg, Germany
[3] Biomedical Centre (BMC), Ludwig-Maximilians-University, Munich, Germany
[4] Department of Gynecology and Obstetrics, University Hospital Würzburg, Würzburg, Germany
[5] Institute of Biomedical Engineering, Department for Medical Technologies and Regenerative Medicine, Faculty of Medicine, Eberhard Karls University Tübingen, Germany
[6] Institute of Molecular Biology, Department Genomics, Stem Cell Biology & Regenerative Medicine, Leopold-Franzens-University Innsbruck, Innsbruck, Austria; Digital Science Center (DiSC), University of Innsbruck, Innsbruck, Austria
[7] Institute of Reconstructive Neurobiology, University of Bonn Medical Faculty and University Hospital Bonn, Bonn, Germany
[8] Institute of Biomedical Engineering, Department for Medical Technologies and Regenerative Medicine, Faculty of Medicine, Eberhard Karls University Tübingen, Germany; NMI Natural and Medical Sciences Institute at the University Tübingen, Reutlingen, G

To fully understand the earliest human specific neurodevelopmental processes remains a significant challenge in the field of developmental biology. In the past, primarily animal models were employed to model early events during neurodevelopment, however in the context of human neurodevelopment they often lack complexity and similarities to the human organism. Previous studies described rosette-like progenitors and PSC-derived neuroepithelial cells (Cattaneo and Conti, 2010) as alternative model systems, yet the establishment of a stable, tissue-derived human neural progenitor cell (NPC) line has remained elusive. Recently, we established a long-term *in vitro* maintained embryonic neuroepithelial stem/progenitor cell (eNSPC) line, stabilized in chemically defined medium (CSPFL). These cells exhibit a naïve, non-polarized phenotype and as confirmed by single-cell RNA sequencing, represent a homogeneous population of multipotent stem cells, throughout different monoclonal lines with individual genetic backgrounds. eNSPCs are highly plastic, demonstrated by their broad differentiation potential, generating forebrain, midbrain, and hindbrain identities as well as neural crest lineages and sensory neurons. This highlights their capacity to not only produce diverse central but also peripheral nervous system derivatives. Here, we present the analysis of their regional identity along the anterior-posterior and dorsal-ventral axes, indicating that eNSPCs originate from the midbrain-hindbrain border (MHB) region. Moreover, we found changes in the eNSPCs chromatin accessibility profile over prolonged culturing and a distinct epigenetic landscape compared to other NPC populations. Principal component analysis revealed distinct clustering of eNSPCs high and low passage, separated from induced neural stem cell (iNSCs) and small molecule NPC (smNPCs) populations. On a single-locus level, high-passage eNSPCs exhibited increased chromatin accessibility at the regulatory region of the *SOX2*, while accessibility of neurogenic markers such as *ASCL1* remained unchanged. This suggests a reinforced stem cell identity and stabilization of an early multipotent neural progenitor state upon prolonged culture in CSPFL medium. Taken together, the establishment and comprehensive characterization of eNSPCs provides a robust platform to study human specific processes in early neurodevelopment and potentially serves as a novel tool for disease modelling and advancing regenerative therapies.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

S12: Natural products in life science research

Chairs:

Cornelia Karg
Universität Innsbruck, AT

Simone Moser
University of Innsbruck, AT

S12-IT01 Synthesis of phyllobilins and bacteriochlorophylls – valuable phytochemicals

Nguyen, Duy T. M. Chung, Thao Luu, and **Jonathan S. Lindsey**

Department of Chemistry, North Carolina State University, Raleigh, NC 27695 USAJulia-Thu

The advent of synthetic routes to the native photosynthetic pigments (e.g., chlorophyll *a*, bacteriochlorophyll *a*) and native derivatives (e.g., phyllobilins) – somewhat neglected classes of compounds (1) – is expected to open a portal for addressing diverse scientific questions. An approach to the macrocycles relies on joining distinct halves via (i) Knoevenagel condensation followed by (ii) Nazarov cyclization, S_EAr, and MeOH elimination (2). The *trans*-dialkyl substituents of each ring are introduced via asymmetric methods at an early stage of the synthesis. Access to phyllobilins proceeds similarly (3), but with lesser demands on chirality and without final macrocyclization. Key targets include isotopologues for studies of energy flow in photosynthetic assemblies (^{13}C-labeled bacteriochlorophylls) and biodistribution upon oral consumption (^{18}F-labeled phylloxanthobilins). This research is supported by the NSF (CHE-2348052).

S12-ST01 Heme biosynthesis in prokaryotes - enzyme mechanisms, interactions and more

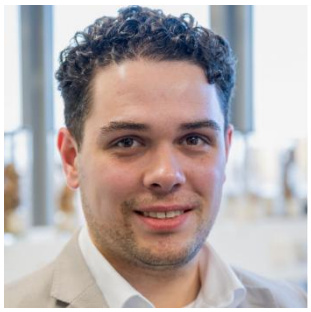
Stefan Hofbauer, Thomas Gabler, Gaurav Patil, Nikolaus Falb, Alice Cassiani, Jakob Ender, Paul Furtmüller

BOKU University, Austria

Nature has evolved three heme biosynthesis pathways, which consist of seven to eight enzymatic steps. They all share a common precursor (5-aminolevulinic acid) and core processing steps leading to uroporphyrinogen III, and are divided into the protoporphyrin-dependent, the coproporphyrin-dependent and the siroheme-dependent pathways thereafter. We have focused our research interests on the so-called coproporphyrin dependent heme biosynthesis pathway, which is almost exclusively utilized by Gram-positive bacteria. This pathway is substantially different to the protoporphyrin-dependent pathway, used by eukaryotes and Gram-negative bacteria, and the siroheme-dependent pathway employed mainly by Archaea. The coproporphyrin-dependent pathway was the last one to be identified only ten years ago, and exhibits unique intermediate porphyrins and enzymes, that do not occur in the others. This makes this biosynthetic route a promising target for the development of novel substances for antibacterial treatments, as many Gram-positive pathogens are showing multiple antibiotic resistances and rely on the coproporphyrin heme biosynthesis pathway.

We have set out to investigate the mode of action of each enzymatic step by performing in-depth kinetic, structural and functional studies using biochemical and biophysical techniques. Understanding mechanistic details that drive catalysis is a pre-requisite for future endeavors to find potential inhibitors targeting prokaryotic heme biosynthesis as drug-lead compounds. Furthermore, each product within this biosynthetic pathway is the substrate for the next enzymes and protein-protein interactions are crucial for regulation and finally heme production. Two enzymes have been in the focus of our research until now, coproheme decarboxylase, which catalyzes the final step yielding the product heme *b*, and coproporphyrin ferrochelatase, which facilitates iron incorporation into the porphyrin in the second last step of the pathway. We have investigated several representatives of these enzymes from various Gram-positive organisms of different phylae. All findings will be discussed in context of the overall heme biosynthesis pathway and shed light on mechanistic peculiarities of involved enzymes.

S12-ST02 The alkaloid derivative 2-Desaza-annomontine (C81) impedes angiogenesis through inhibition of CDC2-like kinases (CLKs) and β-catenin activity.



Thomas Josef Zech[1,3], Anne Wolf[2,6], Mandy Hector[2], Iris Bischoff-Kont[3], Güzin Melissa Krishnathas[3], Silvia Kuntschar[4], Tobias Schmid[4], Franz Bracher[5], Thomas Langmann[2,6], Robert Fürst[1,3]

[1] Pharmacy, Ludwig-Maximilians-Universität, Germany
[2] Laboratory for Experimental Immunology of the Eye, Department of Ophthalmology, University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Germany
[3] Institute for Pharmaceutical Biology, Faculty of Biochemistry, Chemistry and Pharmacy, Goethe University, Frankfurt, Germany
[4] Institute of Biochemistry I, Faculty of Medicine, Goethe University, Frankfurt, Germany
[5] Pharmaceutical Chemistry, Department of Pharmacy – Center for Drug Research, Ludwig-Maximilians-Universität, Munich, Germany
[6] Centre for Molecular Medicine Cologne (CMMC), University of Cologne, Cologne, Germany

Angiogenesis is the creation of blood-vessels from pre-existing ones. In multiple pathologies, such as cancer or chronic inflammation, angiogenesis contributes to the progression of the underlying condition. While therapies have been developed and applied, their efficacy is still not adequate, especially in the treatment of aberrant angiogenesis in inflammation-related diseases.

C81 is a derivative of the alkaloid annomontine and impedes inflammatory processes in the endothelium[1]. Accordingly, the initial aim was to evaluate if C81 also impairs angiogenesis and thus possesses a dual mechanism. Moreover, C81 inhibits the kinases DYRK1B, DYRK2, PIM3, and the splicing kinases CLK1-4. Therefore, a further aim was to relate the targeted proteins to the effects of C81.

Indeed, in an *in vivo* laser-induced choroidal neovascularization (CNV) model we observed that C81 inhibited angiogenesis. Functionally, this was caused by C81 reducing the VEGF-induced angiogenic activity of endothelial cells (ECs), which was derived from decreased VEGFR2 expression.

To find the responsible targets, we used inhibitors of the addressed kinases, of which only CLK inhibition phenocopied C81-derived effects in ECs. Moreover, knockdowns of the individual CLK isoforms were also able to phenocopy C81-derived effects, proving the involvement of these kinases.

Mechanistically, RNA-seq revealed that CLK inhibition does not affect the splicing of VEGFR2. However, a following GO-term analysis and reporter gene assay confirmed that CLK inhibitors are potent inhibitors of β-catenin activity, which is known to induce VEGFR2 expression and angiogenesis[2]. Finally, the relevance of this pathway was confirmed, as the knockdown of β-catenin decreased VEGFR2 expression.

(1) Krishnathas, G. M.; Strödke, B.; Mittmann, L.; Zech, T.; Berger, L. M.; Reichel, C. A.; Rösser, S.; Schmid, T.; Knapp, S.; Müller, S.; Bracher, F.; Fürst, R.; Bischoff-Kont, I. C81-Evoked Inhibition of the TNFR1-NFκB Pathway during Inflammatory Processes for Stabilization of the Impaired Vascular Endothelial Barrier for Leukocytes. *FASEB J.* **2021**, *35* (6), e21656. https://doi.org/10.1096/fj.202100037R.

(2) Skurk, C.; Maatz, H.; Rocnik, E.; Bialik, A.; Force, T.; Walsh, K. Glycogen-Synthase Kinase3beta/Beta-Catenin Axis Promotes Angiogenesis through Activation of Vascular Endothelial Growth Factor Signaling in Endothelial Cells. *Circ. Res.* **2005**, *96* (3), 308–318. https://doi.org/10.1161/01.RES.0000156273.30274.f7.

S12-ST03 From Molecule to Mechanism: Understanding Benzylated Dihydrochalcones in Breast Cancer Therapy

Petra Huber-Cantonati[1], Marta Garcia-Miralles[1], Celina Ablinger[1], Andrea Ghidini[2], Guillaume Viault[2], Jean-Jacques Helesbeux[2], Daniela Schuster[3], Johanna Pachmayr[1], Veronika Temml[3]

[1] Paracelsus Medical University Salzburg, Austria
[2] Univ. Angers, SONAS, F-49000 Angers, France
[3] Institute of Pharmacy/Department of Pharmaceutical and Medical Chemistry, Paracelsus Medical University Salzburg, 5020 Salzburg, Austria, Research and Innovation Center for Novel Therapies and Regenerative Medicine, Austria

Objective: Breast cancer (BC) remains a major global health burden and the leading cause of cancer-related mortality. While therapeutic advances have improved outcomes in hormone receptor-positive subtypes, triple-negative breast cancer (TNBC) remains a clinical challenge due to the absence of targetable biomarkers and frequent therapeutic resistance. Recent evidence suggests that nuclear receptors such as estrogen receptor beta (ERβ) and androgen receptor (AR), expressed in up to 43% of TNBC cases, may serve as novel therapeutic targets.

In this context, benzylated dihydrochalcones (bnDHCs), as derivatives of natural products, present a promising scaffold for the development of receptor modulators with anticancer potential. Kafka et al. already showed that MF-15, firstly isolated from the leaves of *Melodorum siamensis*, has anti-proliferative and anti-neoplastic impacts on resistant prostate cancer cells by targeting among others the AR. Thus, the underlying study explores the effects of MF-15 and its derivatives on nuclear receptor signalling in BC models, with a focus on TNBC.

Methods: Cell viability (Resazurin, CellTiter-Glo® 2.0), colony formation (crystal violet), and migration (wound healing assay) were assessed in two BC cell lines with different receptor status (MCF-7 – ER/progesterone receptor positive, MDA-MB468 – triple-negative) and the non-tumorigenic MCF10A cell line. To get first insights into the underlying mode of action, the impact on mitochondrial membrane potential (MMP) was analysed using the JC-10 assay.

Results: Treatment with bnDHCs, including the lead compound MF-15, results in a concentration-dependent reduction of cell viability and ATP levels (IC_{50} in the low micromolar range) with stronger effects in the triple-negative MDA-MB468 cell line. Colony formation is markedly impaired across BC cell lines, while migration is only moderately affected. Notably, MMP drops below 25% of control levels following treatment, suggesting a strong impact on mitochondrial function.

Conclusion: These findings support bnDHCs as promising candidates for further investigation in BC, particularly TNBC. Future studies should focus on elucidating their precise molecular mechanisms and potential synergistic effects with standard chemotherapeutics.

Acknowledgments: This project is funded by Österreichische Krebshilfe Salzburg.

S12-ST04 Harnessing *Penicillium* and *Talaromyces* species for scalable production of potent photoantimicrobials and photoanticancer agents

Pamela Vrabl[0], Markus Meitinger[0], Angelika Seeber[1], Vanessa Kern[0], Carmen Bendetta[0], Friederike Glauch[0], Niccolo Mariani[0], Magdalena Hintner[1], Fabian Klotz[0], Desiree Artmann-Pabst[0], Christoph Walter Schinagl[0], Martin Kirchmair[0], Simone Moser[1], Bianka Siewert[2]

[1] Institute of Pharmacy/Pharmacognosy University of Innsbruck
[2] Institute of Pharmacy/Pharmacognosy University of Innsbruck AND Pharmaceutical Biology, University of Hamburg
[0] Institute of Microbiology, University of Innsbruck, Austria

Photodynamic therapy (PDT) has emerged as a promising strategy to address multidrug-resistant microorganisms and cancer by leveraging light-activated photosensitizers that generate reactive oxygen species, which in turn can selectively kill pathogens and cancer cells. While plant-derived photosensitizers have dominated the field, recent evidence suggests that fungi represent an underexplored reservoir of potent natural photosensitizers. Harnessing fungal photosensitizers could expand the arsenal against cancer and drug-resistant microorganisms, especially if scalable production methods are established.

This study explores *Penicillium* and *Talaromyces* species, known for anthraquinone biosynthesis, for their potential to produce photosensitizers with selective activity against cancer cells and microorganisms. Additionally, we aim to optimize the cultivation conditions to enable large-scale production of these metabolites. Using the OSMAC (One Strain, Many Compounds) approach, strains were cultivated under diverse conditions (e.g., variations in media, temperature, light, co-cultivation) in solid and submerged cultures. Crude extracts were screened for photocytotoxicity against cancer cell lines (i.e., nasopharynx, bladder, hypopharynx, esophageal, and nasal septum) and for photoantimicrobial activity against *Candida albicans*, *Escherichia coli*, and *Staphylococcus aureus*. UHPLC-HRMS/MS analysis enabled dereplication and putative annotation of bioactive metabolites.

Notably, extracts from *Talaromyces islandicus*, *T. stipitatus,* and *Penicillium restrictum* exhibited under blue light (λ = 478 nm, H = 5.3 J cm^{-2}, 15 min) strong photocytotoxic effects at 0.625 µg mL^{-1}, and 12.6 µg mL^{-1}, respectively. Ongoing bioactivity-guided fractionation has led to the putative annotation of iridoskyrin as the active metabolite in *T. islandicus*. Efforts to enhance photosensitizer yields in submerged cultivations, including bioreactor batch cultivation, have been successful, supporting the feasibility of scalable production.

In summary, our findings underscore the potential of *Penicillium* and *Talaromyces* species as sources of effective photoantimicrobial and photoanticancer agents. The ability to produce these photosensitizers in bioreactor batch cultivations is a crucial step toward a future industrial scale-up, offering new means in the fight against resistant microorganisms and cancer.

This work was supported by the Austrian Science Fund (P37163).

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

S13: Cell death in health and disease

Chairs:

Joel Riley
Medical University of Innsbruck, AT

Verena Labi
Medical University of Innsbruck, AT

S13-IT01 Membrane pores in cell death at the nanoscale: assembly, structure and regulation

Katia Cosentino

Department of Biomedical, Metabolic and Neural Sciences, UNIMORE-University of Modena and Reggio Emilia, Italy

Membrane permeabilization is a critical step in the execution of cell death programs such as apoptosis and pyroptosis, with profound physiological and pathological consequences related to infection, immunity, cancer, and neurodegeneration.

Gasdermins (GSDMs) orchestrate the inflammatory cell death pyroptosis by assembling into oligomers that permeabilize the plasma membrane and other subcellular membranes through a mechanism that remains incompletely understood.

Using biophysical methods and single-molecule imaging, we unraveled the assembly sequence of Gasdermin D (GSDMD) oligomers, identifying a key role for specific cysteine residues in mediating palmitoylation-dependent membrane targeting and interactions between subunits.

To directly resolve GSDMD pore formation at the plasma membrane, we combined DNA-PAINT super-resolution microscopy with polymer-supported plasma membranes (PSPMs), a novel approach that makes isolated, intact PM sheets accessible to high-resolution imaging. This strategy revealed a diversity of GSDMD oligomeric structures, including arcs, rings, and smaller assemblies. We also identified a critical role for the lipid $PI(3,4,5)P_3$ in regulating pore size and stability.

Finally, we tracked the dynamic localization of GSDMs to different cellular membranes and correlated these patterns with their lipid-binding preferences.

Together, our findings reveal a tightly regulated process of GSDM pore formation during pyroptosis and provide new insights into the molecular control of inflammatory cell death.

S13-ST01 The BASP1 protein interferes with WNT pathway signaling

Leonie I. Weber, Lea E. Timpen, Anna-Sophia Egger, José Ramos-Pittol, Marcel Kwiatkowski, Markus Hartl

Biochemistry, University of Innsbruck, Austria

MYC is a transcription factor with oncogenic potential controlling fundamental cellular processes like proliferation, metabolism, differentiation, or apoptosis. While MYC activities in normal cells are essential and tightly regulated, MYC is frequently found to be deregulated in most human tumors, in which this oncoprotein represents both a major cancer driver and a challenging drug target.

The transcriptional MYC target *BASP1* (brain acid-soluble protein 1) is downregulated in MYC-dependent cancer cells and ectopic BASP1 expression interferes with MYC-induced cell transformation.

Using human colon cancer cells (SW480) featured by high MYC expression and a silenced *BASP1* gene, we generated cell lines overexpressing BASP1.

BASP1-expressing SW480 display a strongly diminished transformed phenotype accompanied by significant reduction of *MYC* expression at mRNA and protein level.

Transcriptome, proteome, and interactome comparison of SW480 with our BASP1-overexpressing cell lines was performed using RNA-Seq, Immunoprecipitation, and Liquid chromatography coupled to Mass spectrometry (LC-MS).

Genes and proteins downregulated in BASP1- expressing cells are the MYC-associated factor X (MAX) and the metastasis-associated protein 1 (MTA1). Upregulated genes include the metastasis suppressor KISS1 and the kinase STK4, that is known to promote β-catenin degradation. Since the WNT signalling pathway plays a crucial role in cancer development in colorectal cancers we further investigated key proteins of this pathway. The WNT signalling protein β-catenin (CTNNB1), TCF4, or the TCF4-specific kinase TNIK are downregulated upon BASP1 activation. Furthermore, a TCF4 reporter assay confirms that BASP1 expression significantly lowers WNT pathway activity, suggesting that BASP1 directly interferes with established WNT-triggered *MYC* activation.

S13-ST02 Transcriptomic and functional characterization of patient-derived PRPF31- retinal organoids of retinitis pigmentosa

Ahmad Salti[0], Alessandro Bellapianta[0], Jingjing Qi[1], Michele Giugliano[2], Matthias Bolz[0]

[1] Tumor Epigenetics Laboratory, Johannes Kepler University Linz, Linz, Austria.
[2] Department of Biomedical Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy
[0] Cellular and Molecular Ophthalmology, Johannes Kepler University Linz, Austria

Retinitis Pigmentosa (RP) encompasses a heterogeneous group of genetic disorders leading to progressive photoreceptor degeneration and eventual blindness. Among these, mutations in the PRPF31 gene represent a common cause of autosomal dominant RP (RP11). While significant research has focused on photoreceptor pathology, the effects on other retinal cells remain less explored. This study aims to elucidate functional deficits and transcriptomic alterations specific within retinal organoids (ROs) derived from PRPF31-mutant patient-specific induced pluripotent stem cells (iPSCs), employing advanced multielectrode array (MEA) recordings and comprehensive single-cell RNA sequencing (scRNA-seq). Organoids were characterized at both early (day 85) and late (day 285) stages to capture dynamic developmental and degenerative processes. Electrophysiological functionality of neuronal networks, particularly RGC activity, was assessed using 2D and Mesh MEA technologies, allowing detailed analysis of spontaneous spike activity, spike amplitude, firing frequency, and network synchronization. Concurrently, scRNA-seq was conducted to profile population-specific transcriptomic changes. MEA analyses revealed profound functional impairments in PRPF31-ROs as early as day 60. Mutant organoids exhibited significantly decreased spontaneous electrophysiological activity, characterized by reduced spike amplitudes, lowered firing rates, and impaired synchronization, indicative of disrupted network connectivity. Transcriptomic profiling revealed substantial upregulation of oxidative stress-related genes (e.g., HMOX1), apoptosis mediators (e.g., BAX), and neuronal stress markers (e.g., SNAP25, GAP43). Pathway enrichment analyses underscored significant dysregulation in cell specific pathways governing axon guidance, neuronal differentiation, synaptic transmission, and oxidative stress responses. These early transcriptomic alterations preceded notable photoreceptor degeneration observed at later stages, suggesting an initial neuronal vulnerability that potentially exacerbates subsequent retinal pathology. Our integrative approach, combining advanced electrophysiological assessments with comprehensive single-cell transcriptomic analyses, delineates critical insights into the functional and molecular disruptions affecting retinal cells in PRPF31-associated Retinitis Pigmentosa.

S13-ST03 The PIDDosome-p53 axis dictates cell fate after cell-cell fusion

Paul Petermann[0], Vincent Braun[0], Felix Eichin[0], Alexandra Boegli[1], Petr Broz[1], Andreas Villunger[0]

[1] Department of Immunobiology, University of Lausanne
[0] Institute of Developmental Immunology, Medical University of Innsbruck, Austria

In pathological cell-cell fusion events induced by viral or bacterial infections, asynchronous cells form multinucleated syncytia. These fusion events may contribute to pathogenesis and induce chromosomal instability, potentially promoting tumorigenesis. The cellular mechanisms preventing this are incompletely understood. Exploiting the ability of the vesicular stomatitis virus glycoprotein (VSV-G) to induce cell fusion of VSV-G-expressing cells in a pH-dependent manner, we provide evidence that the fusion of asynchronous cells triggers the activation of the PIDDosome multiprotein complex, resulting in caspase-2-mediated cleavage of MDM2, stabilization of p53, and upregulation of p21, which contributes to a reduced syncytial cell cycle progression. This process depends mainly on the recruitment of PIDD1 to clustered mature centrioles present after cell fusion, as both, centriole depletion and knockout of the centrosomal distal appendage protein ANKRD26 abrogate PIDDosome activation in this context. Moreover, the majority of multinucleated cells die within 60 h post-fusion, which is significantly delayed upon pan-caspase inhibition. As caspase-9 deficiency and BCL2 overexpression display only slight improvement in syncytial viability, syncytial death may be induced by a pathway alternative to MOMP-driven apoptosis. Interestingly, PIDDosome-deficient syncytia exhibit reduced survival rates, indicating a partially protective effect for PIDDosome signaling. In a second model, we studied infection events of *Burkholderia thailandensis*, a gram-negative bacteria that after invasion hijacks the host actin machinery to spread into neighboring cells, thereby inducing cell-cell fusion. By impairing bacterial growth using the bacteriostatic chloramphenicol to promote syncytial endurance, we could confirm the clustering of centrosomes, activation of the PIDDosome, and PIDDosome-dependent reduction in syncytial cell cycle progression also in *B. thailandensis*-mediated fusion events. Taken together, our results indicate that PIDDosome signaling can act as an important player in shaping the cellular fate after pathological cell-cell fusion events, allowing cells to arrest instead of die.

S13-ST04 The role of sub-lethal mitochondrial permeabilization in B cell mutagenesis and oncogenic transformation

Nadine Kinz[1], Sarah Spoeck[1], Johannes Weiss[1], Andreas Villunger[1], Verena Labi[1], Francesca Finotello[2], Joel S. Riley[1]

[1] Developmental Immunology, University of Innsbruck, Austria
[2] Institute of Molecular Biology, Digital Science Center, University of Innsbruck, Innsbruck, Austria

Mitochondrial outer membrane permeabilisation (MOMP) commits a cell to undergo apoptosis. Despite the dogma that MOMP is the point-of-no-return and occurs in every mitochondria in a cell, recent studies have shown that in cells which encounter a sub-lethal stress, only a limited number of mitochondria undergo permeabilisation, resulting in sub-lethal caspase activation, a phenomenon termed “minority-MOMP”. Nevertheless, this caspase activation is sufficient to induce caspase-activated-DNAse (CAD)-dependent DNA damage and oncogenic transformation. Minority-MOMP has mostly been studied in the setting of solid tumors - however, whether minority-MOMP occurs in hematopoietic cells is unclear.

Using *in vitro* culture systems and pre-clinical mouse models of pre-malignant and malignant B-cell lymphomas, we establish that minority-MOMP and its downstream CAD-dependent effects occur in progenitor B-cells as well as in human B-cell lymphoma cell lines. Exploiting these mouse models, we ask whether minority-MOMP plays a role in B-cell lymphomagenesis.

Employing BH3-profiling, we have classified human lymphoma cells as either apoptosis-primed or unprimed, revealing intricate BCL-2 family relationships. We have correlated sensitivity to chemotherapy to these BCL-2 family member dependencies and also determined whether cancer treatment-induced minority-MOMP generates vulnerabilities which might explain the high relapse rates (~40%) in B-cell lymphoma patients.

Altogether, understanding the underlying molecular mechanisms, as well as survival strategies employed by cancer cells that undergo minority-MOMP, will pave new paths for therapeutic intervention.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

S14: Machine learning and perturbation in cellular systems

Chairs:

Heidi Fiegl
Medical University Innsbruck, AT

Hubert Hackl
Medical University of Innsbruck, AT

S14-IT01 Multi-modal Spatial and Single-cell Profiling of Metastatic Breast Cancer and Integrated Computational Analysis

Johanna Klughammer

Genecenter LMU, Germany

Metastatic breast cancer (MBC) remains the leading cause of breast cancer–related mortality, yet its tumor microenvironment (TME) is poorly characterized, particularly across metastatic sites and receptor subtypes. In our recent study (Klughammer et al., Nat Med, 2024), we present a comprehensive atlas of MBC, combining single-cell and spatial transcriptomic profiling across 67 biopsies from 60 patients, spanning four molecular subtypes and nine anatomical locations.

Each sample was analyzed using scRNA-seq or snRNA-seq, together with up to four spatial modalities (Slide-seq, MERFISH, Expansion Sequencing, and CODEX). To integrate and interpret this multi-modal data, we employed a suite of computational methods implemented in the TACCO framework (Mages et al., 2023), enabling robust, reference-based cell type decomposition and spatial mapping across modalities and patients.

Our analysis reveals substantial heterogeneity in cell type composition, EMT states, and immune exclusion across both clinical subtypes and anatomical sites. Spatial profiling uncovered recurrent patterns of T cell exclusion, myeloid cell enrichment, and tumor–stromal compartmentalization.

This atlas serves as both a biological and computational resource for the community. It highlights the power of integrated, multi-resolution spatial analysis using interpretable computational tools to resolve complex tissue architecture in metastatic cancer.

S14-ST01 Spatial profiling of cell niches to uncover mechanisms of immune evasion in cancer

Alexander Kirchmair[1], Niloofar Nemati[1], Alessia Rossi[1], Valentin Marteau[1], Michela Carlet[1], Dietmar Rieder[1], Arno Amann[2], Andreas Seeber[2], Elisabeth Gasser[3], Michael Günther[4], Steffen Ormanns[4], Anne Krogsdam[1], Stefan Salcher[2], Zlatko Trajanoski[1]

[1] Institute of Bioinformatics, Medical University of Innsbruck, Austria
[2] Department of Internal Medicine V, Haematology & Oncology, Comprehensive Cancer Center Innsbruck and Tyrolean Cancer Research Institute, Medical University of Innsbruck, Austria
[3] Department of Visceral, Transplant and Thoracic Surgery, Medical University Innsbruck, Austria
[4] Innpath, Tirol Kliniken, Medical University Innsbruck, Austria

Immune cell density and localization play critical roles in shaping anti-tumor immune responses and influence the efficacy of therapies in solid cancers. To investigate the spatial determinants of immune suppression, we collected pathologically annotated tumor cores, invasive margins and adjacent normal tissues from 15 colorectal cancer patients and performed high-resolution spatial profiling with Xenium in situ transcriptomics. We developed a computational workflow for the integrative analysis of spatial and single-cell RNA sequencing data, and applied deep learning methods to delineate tissue domains and distinct cell niches. Further in-depth analysis revealed the spatial organization and interactions of immune cells, and the underlying signaling cues that establish an immunosuppressive tumor microenvironment. These findings provide novel insights into the mechanisms of immune evasion in cancer and offer a spatial framework to inform the design of targeted immunotherapies.

S14-ST02 omnideconv: a unifying framework for single-cell-informed deconvolution of transcriptomic data

Lorenzo Merotto[0], Alexander Dietrich[1], Konstantin Pelz[1], Bernhard Eder[0], Constantin Zackl[0], Katharina Reinisch[2], Frank Edenhofer[3], Federico Marini[4], Gregor Sturm[5], Markus List[1], Francesca Finotello[0]

[1] Data Science in Systems Biology, TUM School of Life Sciences, Technical University of Munich
[2] Institute for Informatics, Ludwig-Maximilians-Universität München
[3] Department of Molecular Biology, Center for Molecular Biosciences Innsbruck (CMBI)
[4] nstitute of Medical Biostatistics, Epidemiology and Informatics (IMBEI), University Medical Center of the Johannes Gutenberg University Mainz
[5] Biocenter, Institute of Bioinformatics, Medical University of Innsbruck
[0] Dept. of Molecular Biology / Digital Science Centre (DiSC), Austria

Computational deconvolution techniques enable the estimation of cell-type proportions from bulk RNA-seq data by leveraging cell-type reference transcriptomic profiles. Recently, a new generation of deconvolution methods has emerged, extending these capabilities by learning from annotated single-cell RNA-seq (scRNA-seq) datasets, allowing for a broader applicability across cell types, tissues, and organisms. However, this flexibility complicates their applicability and evaluation of their performance.

To support the development, application, and assessment of single-cell-informed deconvolution methods, we introduce omnideconv (omnideconv.org), a comprehensive ecosystem of tools and resources designed to unify tool access, enhance usability, and streamline method benchmarking and optimization.

The ecosystem includes: (1) omnideconv, an R package providing a unified interface for tool applicability; (2) deconvExplorer, an interactive app for visualizing deconvolution results; (3) deconvData, a curated collection of validation datasets from different tissues and organisms; (4) SimBu, a simulator for pseudo-bulk RNA-seq generation to be used for method assessment; and (5) deconvBench, a Nextflow-based reproducible benchmarking pipeline. Using these components, we conducted a systematic evaluation of eight state-of-the-art deconvolution methods across multiple scenarios, systematically investigating the impact on deconvolution performance of factors such as RNA bias, resolution of cell-type annotation, unknown cellular content, and batch effects in the training data. Our comprehensive benchmarking revealed major differences in methods' performance depending on the testing scenario, , and helps identify the most suitable approaches for different deconvolution challenges and data types. By facilitating access, comparison, and optimization, omnideconv supports the refinement and adoption of deconvolution methods across a wide range of biological contexts.

S14-ST03 Deciphering the role of the healthy tissue microenvironment in early-stage NSCLC

Mieke Nicolaï, Martina Sykora, Gabriele Gamerith, Dominik Wolf, Sieghart Sopper

Internal Medicine V, Medical University of Innsbruck, Austria

Non-small cell lung cancer (NSCLC) is one of the most lethal cancers worldwide with curative surgery being the first line treatment for early-stage NSCLC. Despite complete tumor resection, recurrence occurs in 30 to 55% of the patients. Differences in the immune response within the tumor microenvironment (TME) have been suggested as major factor explaining the differences in outcome for patients after surgery. Paradoxically, the TME is removed at surgery, raising the question of whether critical immune components that influence recurrence exist elsewhere, particularly in the adjacent lung tissue. This is supported by anecdotal evidence in the literature but also by our own preliminary results based on our big biobank of early-stage NSCLC with samples from more than 400 patients and deep clinical annotation over an observation period of up to eight years.

To investigate the role of the normal adjacent lung tissue on recurrence, we aim to delineate the differences in the immune system composition between early-stage NSCLC patients that relapsed and those that did not relapse within two years. We apply single-cell RNA sequencing with simultaneous surface protein profiling (CITE-seq) on samples of 6 patients (3 relapse, 3 non-relapse) and bulk RNA-seq deconvolution on samples of 18 patients (9 relapse, 9 non-relapse) to delineate immune composition differences between relapsed and non-relapsed patients, focusing on normal adjacent lung tissue. In parallel, we characterize T-cell and B-cell receptor repertoires across tumor, adjacent lung, and peripheral blood to infer immune clonality, expansion, and migratory dynamics associated with clinical outcomes. Our preliminary findings show that the cell composition and the transcriptional profile of the T cell compartment in adjacent tissue differs between relapse and non-relapse patients. A higher clonal expansion can be found in non-relapse compared to relapse patients. These findings suggest that immunological changes within adjacent lung tissue may influence disease outcome after surgery. In the future, we will expand our multi-omics sequencing cohort and validate our findings in a spatial context through multiplex imaging.

S14-ST04 Rectangle: robust cell-type deconvolution informed by single-cell RNA sequencing data

Bernhard Eder[1], Lorenzo Merotto[1], Irene Rigatto[1], Alexander Dietrich[2], Constantin Zackl[1], Markus List[2], Gregor Sturm[3], Francesca Finotello[1]

[1] Computational Biomedicine Group, University of Innsbruck, Austria
[2] Data Science in Systems Biology, TUM School of Life Sciences, Technical University of Munich, 85354 Freising, Germany
[3] Boehringer Ingelheim International Pharma GmbH & Co KG, 88397 Biberach, Germany

Understanding the cellular composition of biological tissues is central to both basic research and clinical applications. While single-cell RNA sequencing (scRNA-seq) offers detailed insights into tissues at the level of individual cells, it remains expensive and technically challenging, limiting its use in biological research. Bulk RNA sequencing (RNA-seq) offers a more accessible alternative when coupled with in silico cell type *deconvolution*. Deconvolution methods can computationally infer the composition of tissue samples profiled with bulk RNA-seq data by leveraging cell-type-specific signatures derived from purified or scRNA-seq data. Despite their promise, existing methods for single-cell-informed cell-type deconvolution present several limitations, including limited computational scalability, difficulty disentangling closely related cell-type profiles (i.e. 'multicollinearity'), and inability to correctly handle mRNA bias and unknown cellular content.

To overcome these limitations, we developed *Rectangle*, a new computational method for the deconvolution of bulk and spatial RNA-seq informed by single-cell RNA-seq data. *Rectangle* extracts reliable cell-type-specific expression signatures from annotated scRNA-seq data and predicts cell-type proportions using a hierarchical divide-and-conquer approach. In contrast to existing approaches, Rectangle explicitly accounts for mRNA abundance bias and estimates unknown cellular content. The latter is crucial for real-world applications, where the available single-cell reference used for signature extraction might not cover all cell types present in the data to be deconvoluted.

We performed an extensive benchmarking across different organisms and datasets, demonstrating *Rectangle's* high estimation accuracy, computational efficiency, and robustness to multicollinearity and unknown content. *Rectangle's* deconvolution performance is in line with or superior to that of other established methods in diverse bulk transcriptomics contexts, and further requires minimal hardware and memory overhead for data analysis. Notably, *Rectangle* also adapts seamlessly to spatial transcriptomics through minor parameter adjustments, achieving accurate results on different gold-standard spatial datasets. By addressing both biological and computational challenges, Rectangle provides a versatile and scalable solution for transcriptomic deconvolution, designed to meet the needs of diverse research applications.

17th ÖGMBT Annual Meeting "From Molecules to Organisms - Interactions and Interventions", Sept. 24-26 2025, Innsbruck, Austria

Plenary 4

Chair:

Johanna Gostner
Medical University of Innsbruck, AT

Plenary Lecture

P4-PL01 Immunometabolic circuits that control cell viability

Peter Murray

Max-Planck-Institute of Biochemistry, Germany

Activated immune cells are programmed to express enzymes that selectively degrade amino acids such as arginine, tryptophan and tyrosine. This process elicits multiple signaling pathways via the effect of essential amino acid depletion (e.g., GCN2) coincident with the generation of specific metabolites that regulate stress signaling pathways such as NRF2 and AHR. As programmed amino acid metabolism is species specific, we have focused on two enzymes whose expression is conserved in humans and rodents: IDO1 and IL4i1. IDO1 is a cytoplasmic tryptophan oxidoreductase regulated by interferons, while IL4i1 is a secreted oxidoreductase. Both IDO1 and IL4i1 generate metabolites that are powerful suppressors of ferroptosis via free radical scavenging and NRF2 activation but independent of AHR signaling. Recently, we have made inroads into understanding the molecular basis of immune-mediated anti-ferroptosis controlled by IL4i1 and IDO1 in addition to linking the pathways to cancer cell survival. Overall, our hypothesis is that immunological anti-ferroptosis is a pathway necessary for normal resolution of inflammation and tissue restoration that becomes hijacked in cancer. Thus, the metabolites generated byIL4i1 and IDO1 are oncometabolites in settings of malignancy as they support the ability of stressed tumor cells to escape ferroptosis.

Author Index

E

F

G

H

I

J

K

L

M

N

O

P

Q

R

S

T

Ü

U

V

W

Y

Z

Participant Index

TIP: Click on a social media Icon to open the corresponding link

Ablinger Celina
Institute of Pharmacy
Paracelsus Medical University
Salzburg
Austria
E: celina.ablinger@pmu.ac.at

Angelini Sofia
Department of Genomics, Stem Cell Biology and Regenerative Medicine
University of Innsbruck
Austria
E: sofia.angelini@student.uibk.ac.at

Arapovic Julia
Nutrition
University of Vienna
Austria
E: julia.arapovic@univie.ac.at

Auricht Hannah-Sophie
Molecular Systems Biology (MOSYS)
University of Vienna
Austria
E: a12320753@unet.univie.ac.at

Baschieri Francesco
Inst. of pathophysiology
Medical University Innsbruck
Austria
E: francesco.baschieri@i-med.ac.at

Baumbach Christina-Marie
Dpt. Physiology and Pathophysiology
University of Veterinary Medicine Vienna
Austria
E: christina-marie.baumbach@vetmeduni.ac.at

Beiden Ivan
Clinical Centre for Equine Health and Research
University of Veterinary Medicine, Vienna
Austria
E: beidenivanuni1@gmail.com

Beil-Peter Manuela
SLAS European Ambassador
SLAS
United States of America
E: mbeilpeter@slas.org

Bekdas Baris
Cell Biology
Medical University Innsbruck
Austria
E: baris.bekdas@i-med.ac.at

Bendetta Carmen
University of Innsbruck
Austria
E: carmen.bendetta@student.uibk.ac.at

Bergen Janice
Food Chemistry and Toxicology/ Core Facility Multimodal Imaging
University of Vienna
Austria
E: janice.bergen@univie.ac.at

Bhattarai Marcel
Bioanalytik
Macherey-Nagel
Germany
E: mbhattarai@mn-net.com

Blum Florian
Institute of Virology
Medical University Innsbruck
Austria
E: florian.blum@student.i-med.ac.at

Bock Christoph
CeMM & Medical University of Vienna
Austria
E: cbock@cemm.oeaw.ac.at

Boland Andreas
Molecular and Cellular Biology
University of Geneva
Switzerland
E: Andreas.Boland@unige.ch

Brandl Sarah
Medical University of Innsbruck
Austria
E: sarah.brandl@i-med.ac.at

Bressin Annkatrin
Max-Planck-Institute for Molecular Genetics
Germany
E: bressin@molgen.mpg.de

Brezina Stefanie
Center of Cancer Research, Medical University of Vienna
Austria
E: stefanie.brezina@meduniwien.ac.at

Brueller Werner
Health risk assessment and toxicology consultant
Austria
E: werner.brueller@a1.net

Burtscher Johannes
University of Innsbruck
Austria
E: joh.burtscher@gmail.com

Busato Gianluca
Management Center Innsbruck
Austria
E: bg3752@mci4me.at

Camilleri Julia
Sales Department
Novogene Europe
Germany
E: julia.camilleri@novogene-europe.com

Carlsson Jonas
Organic Chemistry
University of Innsbruck
Austria
E: jonas.carlsson@uibk.ac.at

Cassiani Alice
Department of Natural Sciences and Sustainable Resources
BOKU University
Austria
E: alice.cassiani@boku.ac.at

Castillo Giron Carlos
Medical University of Innsbruck
Austria
E: carlos.castillo@i-med.ac.at

Cavalcanti-Adam E. Ada
Cellular Biomechanics
University of Bayreuth
Germany
E: eacavalcanti@uni-bayreuth.de

Cebula Hannah Marie
Developmental Cancer Genomics
St. Anna's Children's Cancer Research Institute
Austria
E: marie.cebula@ccri.at

cesur nevra pelin
tendon&bone regeneration /Paracelsus Medical University
Austria
E: nevra.cesur@pmu.ac.at

Chen-Wacker Chen
e-BLOT Life sciences
Germany
E: chen-wacker@e-blot.com

Cloos Elizabeth
BOKU University Vienna
Austria
E: elizabeth.cloos@boku.ac.at

Collingro Astrid
Centre for Microbiology and Environmental Systems Science
University of Vienna
Austria
E: astrid.collingro@univie.ac.at

Cont Denisa
Department for Biomedical Research
University for Continuing Education Krems
Austria
E: denisa.cont@donau-uni.ac.at

Cosentino Katia
Department of Biomedical, Metabolic and Neural Sciences
UNIMORE-University of Modena and Reggio Emilia
Italy
E: katia.cosentino@unimore.it

Dahms Sven O.
Biosciences and Medical Biology
University of Salzburg
Austria
E: sven.dahms@plus.ac.at

Dall Elfriede
Universität Salzburg
Austria
E: elfriede.dall@plus.ac.at

Degen Antonia
3D Bioprinting Core Facility
Medical University of Innsbruck
Austria
E: antonia.degen@i-med.ac.at

Del Favero Giorgia
University of Vienna - Faculty of Chemistry
Austria
E: giorgia.del.favero@univie.ac.at

Deneke Victoria
Research Institute of Molecular Pathology
Austria
E: victoria.deneke@imp.ac.at

Dorigatti Ilaria
Medical University Innsbruck
Austria
E: ilaria.dorigatti@i-med.ac.at

Dunzendorfer-Matt Theresia
Biozentrum
Medizinische Universität Innsbruck
Austria
E: theresia.dunzendorfer-matt@i-med.ac.at

Eca Guimaraes de Araujo Mariana
Institute of Cell Biology,
Medical University Innsbruck
Austria
E: mariana.araujo@i-med.ac.at

Edenhofer Frank
Molecular Biology
University Innabruck
Austria
E: Frank.edenhofer@uibk.ac.at

Eder Bernhard
Computational Biomedicine Group
University of Innsbruck
Austria
E: bernhard.eder@student.uibk.ac.at

Eder Marlies
Biochemie und molekulare Biomedizin
Institut für molekulare Biowissenschaften
Austria
E: marlies.eder@edu.uni-graz.at

Egger Valeria
University of Innsbruck
Austria
E: valeria.egger@student.uibk.ac.at

Eichin Felix
Medical University of Innsbruck
Austria
E: felix.eichin@i-med.ac.at

Elvert Christian
Department of Pharmacognosy
University of Innsbruck
Austria
E: Christian.Elvert@uibk.ac.at

Ender Jakob
Department of Natural Sciences and Sustainable Resources, Institute of Biochemistry
Boku University
Austria
E: jakob.ender@boku.ac.at

Englisch Rainer
THP Medical Products VertriebsGmbH
Austria
E: r.englisch@thp.at

Erlacher Matthias
Institute of Genomics and RNomics
Medical University of Innsbruck
Austria
E: Matthias.Erlacher@i-med.ac.at

Eschlböck Alexander
Department of Microbiology
Universität Innsbruck
Austria
E: alexander.eschlboeck@uibk.ac.at

Fahringer Lukas
VWR International GmbH
Austria
E:
lukas.fahringer@avantorsciences.com

Falb Nikolaus
Department of Natural Sciences and Sustainable Resources, Biochemistry
BOKU University Vienna
Austria
E: nikolaus.falb@boku.ac.at

Fallmann Rupert
LabService GmbH
Austria
E: office@labservice.at

Farhan Hesso
Medical University of Innsbruck
Austria
E: hesso.farhan@i-med.ac.at

Farina Silvia
biotechnology
MCI / university of Padova
Italy
E: fs8977@mci4me.at

Fegerl Isabella
Natural Sciences and Sustainable Resources
BOKU University
Austria
E: isabella.fegerl@boku.ac.at

Felder Thomas
Department of Laboratory Medicine
Paracelsus Medical University
Austria
E: t.felder@salk.at

Fernandez Collado Javier
FEI Deutschland GmbH
Germany
E:
javier.fernandezcollado@thermofisher.com

Fesiuk Aleksandra
Department of Pathology
Medical University of Vienna
Austria
E:
aleksandra.fesiuk@meduniwien.ac.at

Fickl Magdalena
Medical University of Innsbruck
Austria
E: magdalena.fickl@i-med.ac.at

Fiegl Heidi
Medical University Innsbruck
Austria
E: Heidelinde.Fiegl@i-med.ac.at

Finotello Francesca
Department of Molceular Biology and Digital Science Center (DiSC)
University of Innsbruck
Austria
E: francesca.finotello@uibk.ac.at

Fontaine Jackson
Systems Neuroscience
Medical University of Innsbruck
Austria
E: jackson.fontaine@i-med.ac.at

Fritz Alexandra
Molecular Biology
University of Innsbruck
Austria
E: Alexandra.Fritz@uibk.ac.at

Furumaya Charita
LabBuddy
Netherlands
E: charita.furumaya@labbuddy.net

Gabler Thomas
BOKU University
Austria
E: tgabler@groupwise.boku.ac.at

Gallob Filip
CeMM Research Center for Molecular Medicine
Austria
E: fgallob@cemm.at

Garvetto Andrea
Microbiology
Universität Innsbruck
Austria
E: andrea.garvetto@uibk.ac.at

Gautsch Christof
Sales LSB Detection
Tecan Sales Austria GmbH
Austria
E: christof.gautsch@tecan.com

Geismann Mary
SLAS
United States of America
E: mgeismann@slas.org

Gerold Gisa
Institute of Virology
Medical University of Innsbruck
Austria
E: gisa.gerold@i-med.ac.at

Gitzl Jochen
BTLW
Boku University
Austria
E: jochen.gitzl@boku.ac.at

Glaser Walter
ÖGMBT
Austria
E: walter.glaser@oegmbt.at

Glauch Friederike Luise
Universität Innsbruck
Austria
E:
friederike.glauch@student.uibk.ac.at

Gortan Mara
Universität Innsbruck
Austria
E: maragortan1@gmail.com

Gostner Johanna
Institute of Medical Biochemistry
Medical University of Innsbruck
Austria
E: johanna.gostner@i-med.ac.at

Grimm Matthias
Bartelt GmbH
Austria
E: matthias.grimm@bartelt.at

Groninger Melanie Emma
Department of Experimental Urology
Medical University of Innsbruck
Austria
E: melanie.groninger@i-med.ac.at

Großkinsky Dominik K.
Center for Health and Bioresources
AIT Austrian Institute of Technology
Austria
E: dominik.grosskinsky@ait.ac.at

Großmann Sonja
University Innsbruck
Austria
E: Sonja.Grossmann@uibk.ac.at

Gsur Andrea
Center for Cancer Research
Medical University of Vienna
Austria
E: andrea.gsur@gmx.at

Guerrero Navarro Lena
Institute for Biomedical Aging Research
University of Innsbruck
Austria
E: lena.guerrero-navarro@uibk.ac.at

Guglielmotti Victoria
Max Planck Zentrum für Physik und Medizin (Erlangen, Germany) / Institut Jacques Monod (Paris, France)
France
E: victoria.guglielmotti@fau.de

Guo Li
e-Blot Life Science Co. Ltd.
China
E: li.guo@e-blot.com

Habeler Annalena
Protein biochemistry
University of Natural Resources and Life Sciences Vienna (BOKU)
Austria
E: annalena@groupwise.boku.ac.at

Hackl Hubert
Institute of Bioinformatics, Biocenter
Medical University of Innsbruck
Austria
E: hubert.hackl@i-med.ac.at

Hagen Lisa Marie
"NAWI Graz Austria" iGEM Team 2025
University of Graz
Austria
E: lisamariehagen2002@yahoo.com

Hagmann Lisa
University of Innsbruck
Austria
E: lisa.hagmann@student.uibk.ac.at

Hallama Rainer
Genscript Biotech (Netherlands) B.V.
Austria
E: rainer.hallama@genscript.com

Handle Florian
XPseq Analytics GmbH
Austria
E: florian.handle@xpseq-analytics.com

Hanisch Malou
Molecular Biology
Medical University of Innsbruck
Austria
E: malou.hanisch@i-med.ac.at

Hartl Lukas
Microsynth Austria GmbH
Austria
E: lukas.hartl@microsynth.at

Hattinger Eva
Takara Bio Europe
France
E: eva_hattinger@takarabio.com

Hatzmann Florian
Institute of Biochemistry
University of Innsbruck
Austria
E: Florian.Hatzmann@uibk.ac.at

Hau Dominik
Cardiac research laboratory
Medical university of Innsbruck
Austria
E: dominik.hau@i-med.ac.at

Heisig Kilian
Nutritional Sciences
University of Vienna
Austria
E: kilian.heisig@gmx.at

Hengst Ludger
Medical University of Innsbruck
Austria
E: ludger.hengst@i-med.ac.at

Herbst Ruth
MedUni Vienna
Austria
E: ruth.herbst@meduniwien.ac.at

Hermann Martin
Medical University Innsbruck
Austria
E: martin.hermann@tirol-kliniken.at

Herrmann Timo
Takara Bio Europe
Germany
E: timo_herrmann@takarabio.com

Herzog Sebastian
Developmental Immunology
Medical University Innsbruck
Austria
E: sebastian.herzog@i-med.ac.at

Heuböck Elisabeth
Abteilung für Pathophysiologie
Johannes Kepler Universität Linz - Zentrum für medizinische Forschung
Austria
E: elisabeth.heuboeck@jku.at

Hnaien Sara
Microbiology
Universität Innsbruck
Austria
E: sara.hnaien@student.uibk.ac.at

Hocq Rémi
Institute of Chemical, Environmental and Bioscience Engineering
TU Wien
Austria
E: remi.hocq@tuwien.ac.at

Hofbauer Stefan
BOKU University
Austria
E: stefan.hofbauer@boku.ac.at

Höllwarth Martina A.
Cell Biology
Medical University of Innsbruck
Austria
E: martina.hoellwarth@i-med.ac.at

Hondele Maria
Biozentrum
University of Basel
Switzerland
E: maria.hondele@unibas.ch

Hörhold Clemens
Universität Innsbruck
Austria
E: c.hoerhold@outlook.de

Horzum Utku
Institute of Pathophysiology
Medical University of Innsbruck
Austria
E: utku.horzum@i-med.ac.at

Hu Zoe
Genscript Biotech (Netherlands) B.V.
Netherlands
E: zoe.hu@genscript.com

Huber Katharina
Universität Innsbruck
Austria
E: csas1347@student.uibk.ac.at

Huber Sophie
BOKU University
Austria
E: sophie.huber@boku.ac.at

Huber, Dr. Lukas A.
Medical University of Innsbruck
Austria
E: lukas.a.huber@i-med.ac.at

Huber-Cantonati Petra
Paracelsus Medical University
Salzburg
Austria
E: petra.cantonati@pmu.ac.at

Huberts Tobias
Medicinal Chemistry
Medical University Graz
Austria
E: tobias.huberts@medunigraz.at

Hüfner Katharina
Department of Psychiatry, Psychotherapy, Psychosomatics and Medical Psychology
Medical University Innsbruck
Austria
E: katharina.huefner@tirol-kliniken.at

Jäkel Heidelinde
Medical Biocheminstry
Medical University of Innsbruck
Austria
E: heidelinde.jaekel@i-med.ac.at

Jiang Shenyi
Ludwig Maximilian University of Munich
Germany
E: Shenyi.Jiang@lmu.de

Jobst Maximilian
Department of Food Chemistry and Toxicology
University of Vienna
Austria
E: maximilian.jobst@univie.ac.at

Jungwirth Linda
Proteintech Germany GmbH
Germany
E: linda.jungwirth@ptglab.com

Juric Viktorija
Institute of Human Genetics
Medical University Innsbruck
Austria
E: viktorija.juric@i-med.ac.at

Kalcher Karoline
TU Graz
Austria
E: kalcherkaroline@gmail.com

Kanetscheider Mario
University of Innsbruck
Austria
E: mario.kanetscheider@student.uibk.ac.at

Karg Cornelia
Universität Innsbruck
Austria
E: Cornelia.Karg@uibk.ac.at

Kellner Max Josef
Helmholtz Zentrum für Infektionsforschung
Germany
E: maxjosef.kellner@helmholtz-hzi.de

Kern Vanessa
Microbiology
University of Innsbruck
Austria
E: vanessa.kern@student.uibk.ac.at

Khassidov Alexandra
ÖGMBT
Austria
E: alexandra.khassidov@oegmbt.at

Kinz Nadine
Developmental Immunology
University of Innsbruck
Austria
E: nadine.kinz@i-med.ac.at

Kirchmair Alexander
Institute of Bioinformatics
Medical University of Innsbruck
Austria
E: alexander.kirchmair@i-med.ac.at

Kirchmair Thomas
University of Innsbruck
Austria
E: thokirchmair04@gmail.com

Kleiter Natascha
Genetics and Pharmacology
Medical University Innsbruck
Austria
E: natascha.kleiter@i-med.ac.at

Klingler David
Chemistry
New York University
United States of America
E: david.klingler@gmx.at

Klughammer Johanna
Genecenter LMU
Germany
E: klughammer@genzentrum.lmu.de

Koeberle Andreas
Institute of Pharmaceutical Sciences
University of Graz
Austria
E: andreas.koeberle@uni-graz.at

Kokot Janik
Institute of Human Genetics
Medical University of Innsbruck
Austria
E: janik.kokot@i-med.ac.at

Kreczko Karol
Department of Biomolecular & Self-Organizing Matter
Johannes Kepler University Linz
Austria
E: Karol_Kreczko@wp.pl

Kreuzer Natalie
VWR International GmbH
Austria
E: natalie.kreuzer@avantorsciences.com

Kucej Lucija
Molecular Biochemistry
Medical University of Innsbruck
Austria
E: lucija.kucej@i-med.ac.at

Kuen Tatjana
Institute of Neuroscience
Autonomous University of Barcelona
Spain
E: tatjana.kuen1@gmail.com

Kullmann Michael
Medical Biochemistry
Medical University of Innsbruck
Austria
E: michael.kullmann@i-med.ac.at

Kumar Mukesh
Ritter GmbH
Germany
E: mukesh.kumar@avantorsciences.com

Kummer Denise
Institute of Molecular Biochemistry
Medical University of Innsbruck
Austria
E: denise.kummer@i-med.ac.at

Kustatscher Georg
University of Edinburgh
United Kingdom
E: georg.kustatscher@ed.ac.uk

Labi Verena
Inst. for Developmental Immunology
Medical University of Innsbruck
Austria
E: verena.labi@i-med.ac.at

Lackner Michaela
Hygiene and Medical Microbiology
Medical University of Innsbruck
Austria
E: michaela.lackner@i-med.ac.at

Lang Tamara
Department of Pathophysiology
Johannes Kepler University
Austria
E: tamara.lang@jku.at

Laopanupong Thanida
Cell biology
Medical University of Innsbruck
Austria
E: Thanida.Laopanupong@student.i-med.ac.at

Leibrock Nils
BOKU Vienna
Austria
E: nils.leibrock@boku.ac.at

Leitgeb Urban
Biochemistry
BOKU University
Austria
E: urban.leitgeb@boku.ac.at

Lendvai Adrian
IMC Krems
Austria
E: adrian.lendvai@imc.ac.at

Lengerer Birgit
Zoology
University Innsbruck
Austria
E: birgit.lengerer@uibk.ac.at

Levario Diaz Victoria
Cellular Biomechanics
University of Bayreuth
Germany
E: Victoria.Levario-Diaz@uni-bayreuth.de

Liebscher Sabine
Institute of Neurobiochemistry
Austria
E: sabine.liebscher@i-med.ac.at

Lindsey Jonathan
Chemistry
North Carolina State University
United States of America
E: jlindsey@ncsu.edu

Lochner Marlene
Medical University of Innsbruck
Austria
E: marlene.lochner@i-med.ac.at

Loh Satinee
Medical University of Graz
Austria
E: satinee.loh@medunigraz.at

Madersbacher Leonie
Institut für Bioinformatik
Medizinische Universität Innsbruck
Austria
E: leonie.madersbacher@i-med.ac.at

Mair Georg
SZABO-SCANDIC
Austria
E: g.mair@szabo-scandic.at

Mandl Markus
Department of Pathophysiology
JKU Medical Faculty
Austria
E: markus.mandl@jku.at

Mara Elisabeth
FH Kärnten
Austria
E: e.mara@fh-kaernten.at

Marchet Nikolas
Molecular Biochemistry
Medical University of Innsbruck
Austria
E: nikolas.marchet@i-med.ac.at

Mariani Niccolò
University of Innsbruck
Austria
E: Niccolo.mariani@student.uibk.ac.at

Marx-Ladurner Florentine
Institute of Molecular Biology
Medical University of Innsbruck
Austria
E: florentine.marx@i-med.ac.at

Marx-Stölting Philip
BfR
Germany
E: philip.marx-stoelting@bfr.bund.de

Mathew Amal
Department of Biological Sciences
Tata Institute of Fundamental Research, Mumbai
India
E: amalmathewkkt@gmail.com

Mattes Erwin
Privat
Austria
E: erwin.mattes@hotmail.com

Mayer Andreas
Otto-Warburg-Laboratory
MPI for Molecular Genetics
Germany
E: mayer@molgen.mpg.de

Meilinger Yara
Ecomedicine
PMU Salzburg
Austria
E: yara.meilinger@pmu.ac.at

Melo Santos Natalia Regina
Institute of Pathophysiology
Medical University of Innsbruck
Austria
E: natalia.melo@i-med.ac.at

Memic Alma
LabConsulting GmbH
Austria
E: alma.memic@labconsulting.at

Merotto Lorenzo
Dept. of Molecular Biology / Digital Science Centre (DiSC)
Austria
E: lorenzo.merotto@uibk.ac.at

Miller-Michlits Yelyzaveta
Institute of Neuropathology and Neuromolecular Pathology
Medical University of Innsbruck
Austria
E: yelyzaveta.miller-michlits@i-med.ac.at

Monfort-Lanzas Pablo
Institute of Medical Biochemistry
Medical University of Innsbruck
Austria
E: pablo.monfort@i-med.ac.at

Montalbo Kristy
SZABO-SCANDIC
Austria
E: k.montalbo@szabo-scandic.at

Moser Simone
University of Innsbruck
Austria
E: simone.moser@uibk.ac.at

Muller Lynn
Cardiac Surgery Dept.
Medical University Innsbruck
Austria
E: lynn.muller@i-med.ac.at

Murray Peter
Max-Planck-Institute of Biochemistry
Germany
E: murray@biochem.mpg.de

NACES REYNALDO ALDRIEN RYAN
Institute of Medical Biochemistry
Medical University of Innsbruck
Austria
E: aldrien.naces@i-med.ac.at

Nachbaur Imke
ÖGMBT
Austria
E: imke.nachbaur@oegmbt.at

Nagl Markus
Institute of Hygiene and Medical Microbiology
Medical University of Innsbruck
Austria
E: m.nagl@i-med.ac.at

Neuhauser Sigrid
Institut of Microbiology
University of Innsbruck
Austria
E: Sigrid.neuhauser@uibk.ac.at

Nicolaï Mieke
Internal Medicine V
Medical University of Innsbruck
Austria
E: mieke.nicolai@i-med.ac.at

Nigsch Lena Sophia
Department of Organic Chemistry
University of Innsbruck
Austria
E: lena.nigsch@uibk.ac.at

Nykiel Kamila
Molecular Biology
Medical University Innsbruck
Austria
E: kamila.nykiel@i-med.ac.at

O'Donnell Valerie
Cardiff University
United Kingdom
E: o-donnellvb@cardiff.ac.uk

Oberosler Armin
Pharmacognosy
University of Innsbruck
Austria
E: Armin.Oberosler@uibk.ac.at

Oismüller Annelies
University of Graz
Austria
E: annelies.oismueller@edu.uni-graz.at

Oleksyshyn Khrystyna
University of Innsbruck
Austria
E: khrystyna.oleksyshyn@student.uibk.ac.at

Olson William
Institute for Biomedical Aging Research
Austria
E: william.olson@uibk.ac.at

Pallua Johannes
Universitätsklinik für Orthopädie und Traumatologie
Medizinische Universität Innsbruck
Austria
E: johannes.pallua@i-med.ac.at

Pankevich Eugenia
CeMM Research Center for Molecular Medicine
Austria
E: epankevich@cemm.at

Papadopoulos Sofia
Promega GmbH
Germany
E: sofia.papadopoulos@promega.com

Paparella Martin
Medical Biochemistry
Medical University Innsbruck
Austria
E: martin.paparella@i-med.ac.at

Parráková Lucia
Medical Biochemistry
Medical University of Innsbruck
Austria
E: lucia.parrakova@i-med.ac.at

Passecker Johannes
Medical University Innsbruck
Austria
E: johannes.passecker@i-med.ac.at

Patón González Pere
Molecular Pathophysiology
University of Innsbruck
Austria
E: pere.paton@i-med.ac.at

Peijnenborgh Sem
Medicinal Chemistry
Medical University Graz
Austria
E: sem.peijnenborgh@medunigraz.at

Petermann Paul
Institute of Developmental Immunology
Medical University of Innsbruck
Austria
E: paul.petermann@i-med.ac.at

Petschko Felix
University of Innsbruck
Austria
E: felixpetschko@gmail.com

Pichler Harald
Molecular Biotechnology
Graz University of Technology
Austria
E: harald.pichler@tugraz.at

Pichler Sophia
Cellbiology
Medical University Innsbruck
Austria
E: sophia.pichler25@icloud.com

Plesche Alexander
Institut für Pathophysiologie
Medizinische Universität Innsbruck
Austria
E: alexander.plesche@student.i-med.ac.at

Ploner Anna
Institute of Organic Chemistry
Austria
E: anna.ploner@uibk.ac.at

Podlesnic Martina
Genomics, Stem Cell Biology and Regenerative Medicine
University of Innsbruck
Austria
E: martina.podlesnic@uibk.ac.at

Pollio Adam
Zellbiologie
Medical University of Innsbruck
Austria
E: adam.pollio@i-med.ac.at

Prömer Jakob
Institute for Specific Prophylaxis and Tropical Medicine
Medical University of Vienna
Austria
E: jakob.proemer@meduniwien.ac.at

Ramel Daniel
"NAWI Graz Austria" iGEM-Team 2025, Institute for Molecular Biosciences
University of Graz
Austria
E: daniel.ramel@edu.uni-graz.at

Ramos Pittol Jose Miguel
Institute of Biochemistry
University of Innsbruck
Austria
E: Jose.Ramos-Pittol@uibk.ac.at

Rauch Eva
Cell Biology
Medical University of Innsbruck
Austria
E: eva.rauch@i-med.ac.at

Rausch Linda K.
Department of Sport Science
University of Innsbruck
Austria
E: linda.rausch@uibk.ac.at

Reindl Marco
Nano Lab, Division of Medicinal Chemistry
Medical University of Graz
Austria
E: marco.reindl@medunigraz.at

Reiterer-Farhan Veronika
Medical University of Innsbruck
Austria
E: veronika.reiterer-farhan@i-med.ac.at

Rendeiro André
CeMM Research Center for Molecular Medicine
Austria
E: arendeiro@cemm.oeaw.ac.at

RIGATO IRENE
UNIVERSITY OF INNSBRUCK
Austria
E: irene.rigato@uibk.ac.at

Riley Joel
Institute of Developmental Immunology
Medical University of Innsbruck
Austria
E: joel.riley@i-med.ac.at

Rocamora Reverte Lourdes
Immunosenescence and Vaccination
Institute for Biomedical Aging Research, Universität Innsbruck
Austria
E: lourdes.rocamora@uibk.ac.at

Rodgarkia Chantal
THP Medical Products VertriebsGmbH
Austria
E: c.rodgarkia@thp.at

Rungger Katja
Institute of Bioinformatics
Medical University of Innsbruck
Austria
E: katja.rungger@i-med.ac.at

Ruprecht Verena
University Innsbruck
Austria
E: Verena.Ruprecht@uibk.ac.at

Russ Katharina
Department of Microbiology
University of Innsbruck
Austria
E: katharina.russ@uibk.ac.at

Rytchenko Yana
University of Innsbruck
Austria
E: yanarytchenko@gmail.com

Sailer Sabrina
Institute of Human Genetics
Medical University of Innsbruck
Austria
E: sabrina.sailer@i-med.ac.at

Salcher Lino
University of Innsbruck
Austria
E: lino.salcher@student.uibk.ac.at

Salti Ahmad
Cellular and Molecular Ophthalmology
Johannes Kepler University Linz
Austria
E: AHMAD.SALTI@JKU.AT

Sammarco Laura
Pathophysiology
Medicine University of Innsbruck
Austria
E: laura.sammarco@i-med.ac.at

Sampson Natalie
Medical University of Innsbruck
Austria
E: natalie.sampson@i-med.ac.at

Santer Hannah
Medical Biochemistry
Medical University of Innsbruck
Austria
E: Hannah.Santer@student.i-med.ac.at

Santhosh Anagha
Department of Microbiology
University Of Innsbruck
Austria
E: Anagha.Santhosh@uibk.ac.at

Sari Betul
CCB Biocenter
Austria
E: betuel.sari@i-med.ac.at

Sauer Michael
OMV AG
Austria
E: michael-sauer@posteo.at

Schaller Hubert
Institut de biologie moléculaire des plantes
IBMP CNRS
France
E: hubert.schaller@ibmp-cnrs.unistra.fr

Schirripa Alessia
University of Veterinary Medicine Vienna
Austria
E: alessia.schirripa@vetmeduni.ac.at

Schmack Katharina
Francis Crick Institute
United Kingdom
E: katharina.schmack@crick.ac.uk

Schmidt Oliver
Institute of Cell Biology
Medical University of Innsbruck
Austria
E: oliver.schmidt@i-med.ac.at

Schomisch Niklas
Zellbiologie
Austria
E: niklas.schomisch@i-med.ac.at

Schurer Amelie
Molecular Biology
University of Innsbruck
Austria
E: amelie.schurer@uibk.ac.at

Schwaiger Elke
University of Innsbruck
Austria
E: elke.schwaiger@student.uibk.ac.at

Schwarz Johannes
Sales Department
Novogene Europe
Germany
E: johannes.schwarz@novogene-europe.com

Schweiger Niklas
University of Innsbruck
Austria
E: niklas.schweiger@student.uibk.ac.at

Seeber Angelika
Pharmacognosy
University of Innsbruck
Austria
E: Angelika.Seeber@uibk.ac.at

Seipelt Joachim
Nuvonis Technologies
Austria
E: joachim.seipelt@icloud.com

Sexl Veronika
Universität Innsbruck
Austria
E: rektorin@uibk.ac.at

Siegmann Konstantin Adrian
Molecular Biochemistry
Medical University Innsbruck
Austria
E: Konstantin.Siegmann@i-med.ac.at

Simonsen Anne
Molecular Cell Biology
Oslo University Hospital
Norway
E: anne.simonsen@medisin.uio.no

Singer Isabel
Cell Biology
Medical University Innsbruck
Austria
E: isabel.singer@i-med.ac.at

Sladky Valentina
Institute of Developmental Immunology
Medical University Innsbruck
Austria
E: Valentina.sladky@i-med.ac.at

Sokolova Polina
Universität Wien
Austria
E: basilika18@gmail.com

Spetea Mariana
Institute of Pharmacy
Universität Innsbruck
Austria
E: mariana.spetea@uibk.ac.at

STEFAN Eduard
University of innsbruck
Austria
E: eduard.stefan@uibk.ac.at

Stefan Victoria
Department of Pediatrics
University Hospital of the Paracelsus Medical University Salzburg
Austria
E: v.stefan@salk.at

Stepic Doris
Medical University Innsbruck
Austria
E: doris.stepic@i-med.ac.at

Sternberg Felix
University of Vienna
Austria
E: felixlocker@yahoo.de

Strich Sophie
Medical University of Innsbruck
Austria
E: sophie.strich@student.i-med.ac.at

Strobl Victoria
Cell Metabolism and Differentiation Research (CMDR)
Research Institute for Biomedical Ageing Research (IBA), Leopold-Franzens-University Innsbruck
Austria
E: victoria.strobl@uibk.ac.at

Teis David
Biocenter - Institute of Molecular Biochemistry
Medical University Innsbruck
Austria
E: david.teis@i-med.ac.at

Temml Veronika
Pharmaceutical and Medicinal Chemistry
Paracelsus Medical University Salzburg
Austria
E: Veronika.Temml@pmu.ac.at

Thallinger Gerhard
Institute of Biomedical Informatics
Graz University of Technology
Austria
E: gerhard.thallinger@tugraz.at

Thiam Abdou Rachid
CNRS/ENS
France
E: thiam@ens.fr

Timpen Lea Emmy
Biochemistry
University of Innsbruck
Austria
E: lea.timpen@uibk.ac.at

Torres-Quesada Omar
Medical Biochemistry Institute
Medical University Innsbruck
Austria
E: omar.torres-quesada@i-med.ac.at

Toth Maria
BOKU University
Austria
E: maria.toth@boku.ac.at

Trajanoski Zlatko
Biocenter
Medical University of Innsbruck,
Institut für Bioinformatik
Austria
E: zlatko.trajanoski@i-med.ac.at

Trifonova Iuliia
PLUS Salzburg
Austria
E: iuliia.trifonova@stud.plus.ac.at

Tsal-Tsalko Alexandra
IMC Fachhochschule Krems
Austria
E: alexandra.tsal@imc.ac.at

Tyckaert Francois
Pathophysiology
MUI
Austria
E: francois.tyckaert@i-med.ac.at

Unterkofler Miriam
Medical Biochemistry
Biocenter Innsbruck
Austria
E: miriam.unterkofler@gmail.com

van Wingerden Rens
LabBuddy (Kryt BV)
Netherlands
E: rens.vanwingerden@labbuddy.net

Vitale Nicolas
INCI CNRS UPR3212
France
E: vitalen@unistra.fr

Völk Thomas
Promega GmbH
Germany
E: thomas.voelk@promega.com

von Gregory Martin
Promega GmbH
Germany
E: martin.von.gregory@promega.com

Vrabl Pamela
Institute of Microbiology
University of Innsbruck
Austria
E: Pamela.Vrabl@uibk.ac.at

Wagner Katharina
Medizinische Universität Innsbruck
Austria
E: katharina.wagner@i-med.ac.at

Wagner Simon
Account Manager Austria and Switzerland
Thermo Fisher Scientific
Austria
E: simon.wagner@thermofisher.com

Wallerus Alexander
Institute of Systems Neuroscience
Medical University of Innsbruck
Austria
E: alexander.wallerus@i-med.ac.at

Watschinger Katrin
Biocenter
Medical University of Innsbruck
Austria
E: katrin.watschinger@i-med.ac.at

Weber Daniela
Research Program for Receptor Biochemistry and Tumor Metabolism, Department of Pediatrics
University Hospital of the Paracelsus Medical University
Austria
E: d.weber@salk.at

Weber Leonie
Biochemistry
University of Innsbruck
Austria
E: leonie.weber@uibk.ac.at

Weidacher Nina
Medical University of Innsbruck
Austria
E: Nina.Weidacher@i-med.ac.at

Weiss Guenter
Dept. Internal Medicine II
Innsbruck Medical University
Austria
E: guenter.weiss@i-med.ac.at

Weiss Ida
University of Vienna
Austria
E: weiss.ida@gmx.at

Weyer Yannick
Institute of Molecular Biochemistry
Medical University of Innsbruck
Austria
E: weyeryan@gmail.com

Weyer Yannick
Institute of Molecular Biochemistry
Medical University of Innsbruck, CCB
Austria
E: yannick.weyer@i-med.ac.at

Zdenkovic Ela
Protein Biochemistry
The University of Natural Resources and Life Sciences (BOKU)
Austria
E: ela_zdenkovic@groupwise.boku.ac.at

Zech Thomas Josef
Pharmacy
Ludwig-Maximilians-Universität
Germany
E: Thomas.Zech@cup.lmu.de

Attribution

Cover image of CCB: MUI/Lackner

Imprint

Austrian Association of Molecular Life Sciences and Biotechnology (ÖGMBT)
ZVR: 031344888
Editor & Layout: Walter Glaser, Alexandra Khassidov, Imke Nachbaur and Verena Mats
Content as per August, 2025

The ÖGMBT gratefully acknowledges the support of:

MEDIA PARTNER