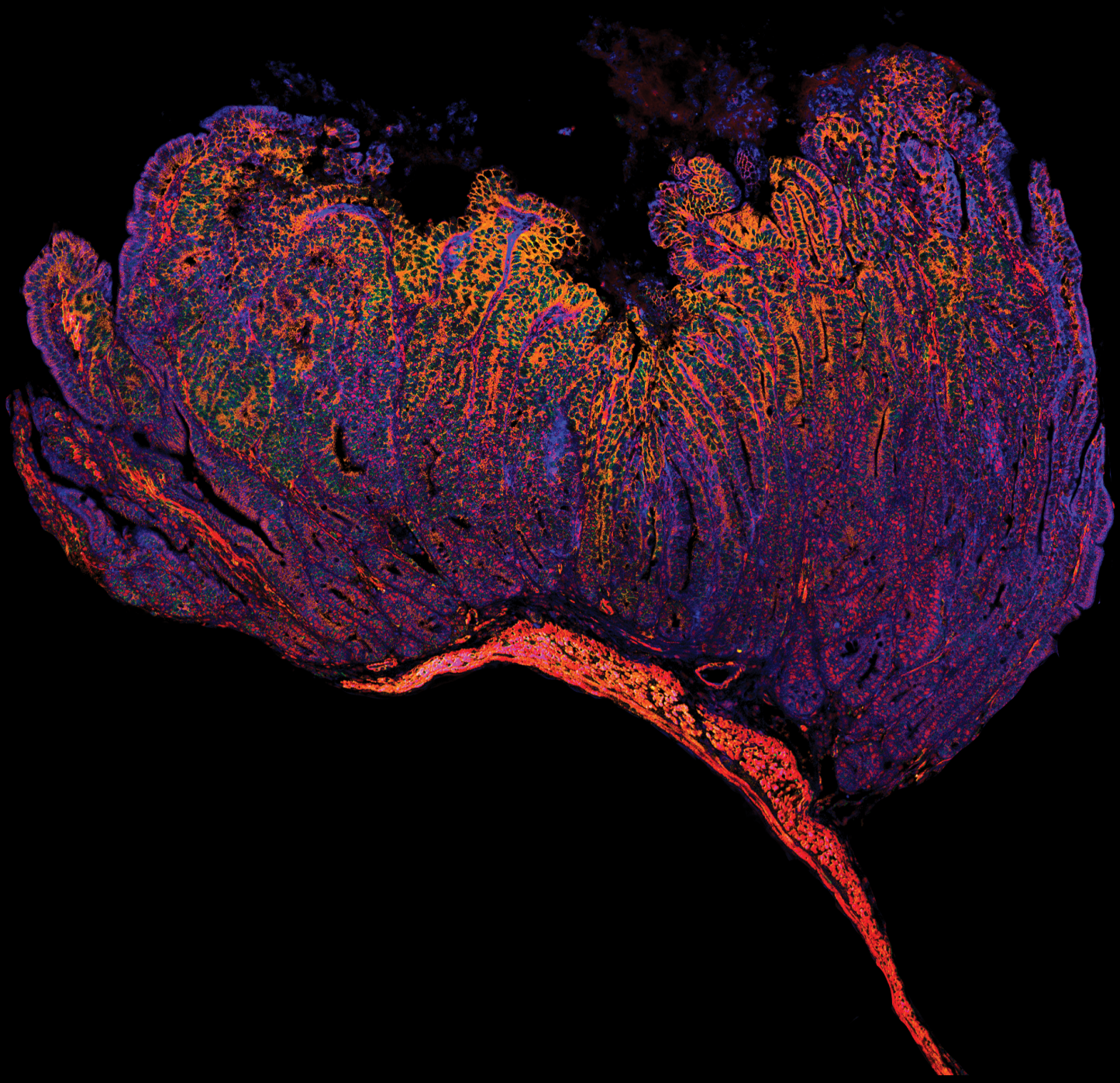
NORWEGIAN BIOSCIENCE SOCIETY

60th Contact Meeting

RØROS, NORWAY
23-26 January 2025



N:B:S
Norwegian Bioscience Society

Front Cover Image by Lilith Sian Lee, Martin-Alonso Group, NTNU.

A fluorescent image showing the structure of an intestinal adenoma from a mouse model bearing multiple intestinal neoplasia; f-actin (blue), ß-catenin (pale orange), MYH11 (yellow), αSMA (green), nuclei (red).

The image was taken with the Zeiss confocal microscope LSM880 at the Cellular & Molecular Imaging Core Facility (CMIC), Norweigan University of Science and Technology (NTNU).

Contents

Welcome to Røros and the 60th NBS Contact Meeting

Dear fellow researcher!

We would like to welcome you to the 60th Annual Contact Meeting of the Norwegian Bioscience Society (NBS) at Røros! This year's meeting is organized by the Norwegian University of Science and Technology. The meeting hosts more than 150 delegates from universities, research institutions and biotech companies in Norway. We are very happy to welcome internationally renowned speakers within plant- and human developmental biology, neuroscience, cancer, infection and inflammatory disease, cell biology, nano-/biomaterials, and innovations in biosciences. We look forward to thought-provoking talks and lively discussions!

Our winter meeting has established as a major social event, a melting pot of different disciplines, a place to introduce new undergraduate and graduate students to the collegium, to meet old and make new friends. One of our ambitions for the meeting is to continue the focus on excellent science presented by young scientists at the minisymposia and the poster sessions. We suggest that you read the abstracts presented in this book to plan which minisymposia and posters you would like to visit.

The NBS Annual Contact Meeting started in 1963 as a happy skiing event for a few enthusiasts and despite its growth, has kept its informal and vibrant nature as well as the time slots allocated for skiing or other outdoors/leisure activities. We have carried this practice further and hope for the traditional vigor in the bar, on the dance floor and in the lecture and the exhibition halls!

Many commercial companies, as well as the Norwegian Research council, support the meeting. The companies that supply us with instruments and reagents for our research also have exhibitions and superb competitions at their stands; this is one of the reasons that the NBS contact meeting is unlike all other meetings you will attend. Pay them all a visit and get to know the latest developments regarding technologies and instruments that may greatly aid your research.

Welcome and enjoy!

The Organizing committee:

Trude Helen Flo	Tore Brembu
Elisabeth Hyldbakk	Magnar Bjørås
Bjørnar Sporsheim	Thorsten Hamann
Vidar Beisvåg	Therese Standal
Liv Ryan	Berit L Strand
Lars Hagen	Nathalie Jurisch-Yaksi

Practical information

The venue

Surrounded by mountains in the UNESCO-protected town of Røros, Røros Hotel offers rooms with free Wi-Fi and a flat-screen TV. Røros town center is an 8-minute walk away. The hotel restaurant Bergrosa uses fresh, local products in its traditional Norwegian dishes. Activities in the surrounding area include hiking and historical tours in Røros. Røros Hotell also has a children's playroom and a pool free to use for guests at the conference. The Røros Museum is a 10-minute walk away, and Røros Central Station is just over 1 km from the hotel.

Meeting Schedule

The scientific part of the meeting starts at 15:00 Thursday (23rd of January), with lunch at 13.00. Registration is possible from 11:00 and onwards. The meeting ends after the banquet Saturday evening (25th of January).

Check-in/Check-out

Check-in possible from 13:00 Thursday 23rd (guaranteed from 15.00). Check-out before 11:00 Sunday 26th. Delayed check-out is possible (additional fee, contact the reception for more details).

Meals

Breakfast is served at the hotel 07:00-10:00 each morning. All meals, except the Saturday Banquet are served in the dining room located at the ground floor at Røros Hotel. The times for lunch and dinner are indicated in the meeting program. Thursday and Saturday we will have a buffet lunch. On Friday there will be a set dish course, served at the table. Thursday dinner will have a set menu and will be served at the table. Friday we will have a buffet dinner. The Saturday Banquet dinner will be arranged in "Falkbergetsalen". Drinks for lunch and dinner are not covered by the conference fee except for the wine served at the banquet dinner on Saturday. Your badge will serve as your meal ticket.

Reception and banquet

On Saturday, a reception will be held at 19.30, in the pit/"Gropa" outside the "Falkbergetsalen" plenary hall (where the posters were presented). Following the reception, the banquet will be held in "Falkbergetsalen" from 20.00. Your badge will serve as your meal ticket.

Secretariat/Technical room

The secretariat is located at the reception of the conference area. The secretariat will be staffed prior to plenary and minisymposium sessions and during the exhibition/poster sessions. You can download your presentations for plenary sessions and minisymposia here.

Wireless Internet

Wireless Internet is available throughout the hotel (Konferanse Wifi) and conference rooms (Røros Hotell Wifi). No PW necessary.

Website

The meeting website is available at: https://www.biokjemisk.no/contact-meeting-2025/

Exhibition

The exhibition takes place in the area outside "Falkbergetsalen" and is open as indicated in the program. We strongly encourage all participants to visit the exhibition.

Plenary sessions

All plenary lectures will take place in "Falkbergetsalen".

Minisymposia

Minisymposia will be held in parallel at 3 different locations at the conference area (Falkbergetsalen, Christianus and Sextus). Each talk should last a maximum of 12 minutes. In addition, there will be 3 minutes available for discussion. Files with the presentations should be handed in to the meeting organizers on a memory stick at the Secretariat/Technical room as early as possible on the day of presentation.

Posters session

The posters should be mounted on Thursday soon after arrival, in pit/"Gropa" outside the plenary hall "Falkbergetsalen". All posters will be displayed until Friday evening. Authors should present their posters on:

Thursday 18:15-19:30 odd numbers (P1, P3…)
Friday 18:00-19:15 even numbers (P2, P4…)

The posters must be removed Saturday morning before 10.00 as the poster walls will be demounted at 10.00 and the poster area will be cleared and used for a social event.
It will be served one glass of beer/wine or soft drink, per person at poster sessions.

The poster awards will be announced during the Banquet on Saturday.

Power breakfast

There will be 2 dedicated power breakfast sessions organized on Friday and Saturday morning during breakfast (08:00-09:00). During these sessions, trainees will have the opportunity to interact with invited speakers, organization committee members and sales representatives from different companies. The discussion will be on various topics, including career development, networking, resilience in science, and innovation.

It will be possible to register for the power breakfast at the registration desk on Thursday when participants pick up their badge. More information will be provided about the topics and attendees at the desk. There will be limited availability, and it will be first come-first served.

Social program at the Hotel

Røros Hotell offers several opportunities for social interactions. Make sure that you find your way to the dancing room and the many bars/pub. All nights there will be a DJ (DJ Janus4K). On Friday night, there will be Silent Disco in addition.

Outdoor activities

In the program for Saturday, there is time for outdoor activities and relaxation.

Guided tour in Olavs`s Mine (Olavsgruva) with underground concert

Guided tour through the mines Nyberget and Olavsgruva, 50 m underground and 500 m into the mountain, ending in Bergmannshallen where musician Bendik Qvam will give a concert, playing with the amazing acoustics in the mines! https://rorosmuseet.no/olavsgruva
Time: Saturday 25th, 10:00 at the Hotel reception for departure by bus. Return for lunch at 12:30.
Price: Kr 250 per person.
Deadline for registration: Thursday 23rd at 20:00 (registration list at the reception of Røros Hotell).
The temperature in the mines is a constant +4 C. Remember warm clothes and suitable footwear!

Cross country skiing

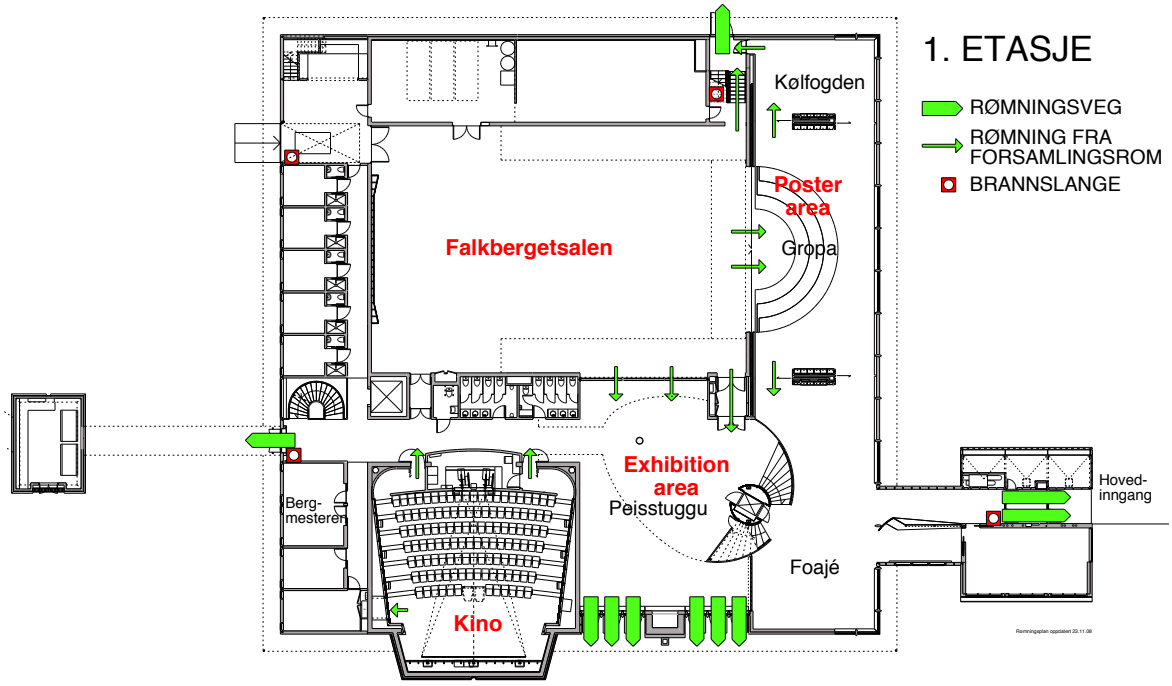
Røros is the perfect location for cross-country skiing. The ski trail starts right outside the hotel. Trail map is available in the hotel reception. If you don't bring your own, it may be possible to borrow some winter equipment from "BUA" (Open Thursday 14:00-16:00).

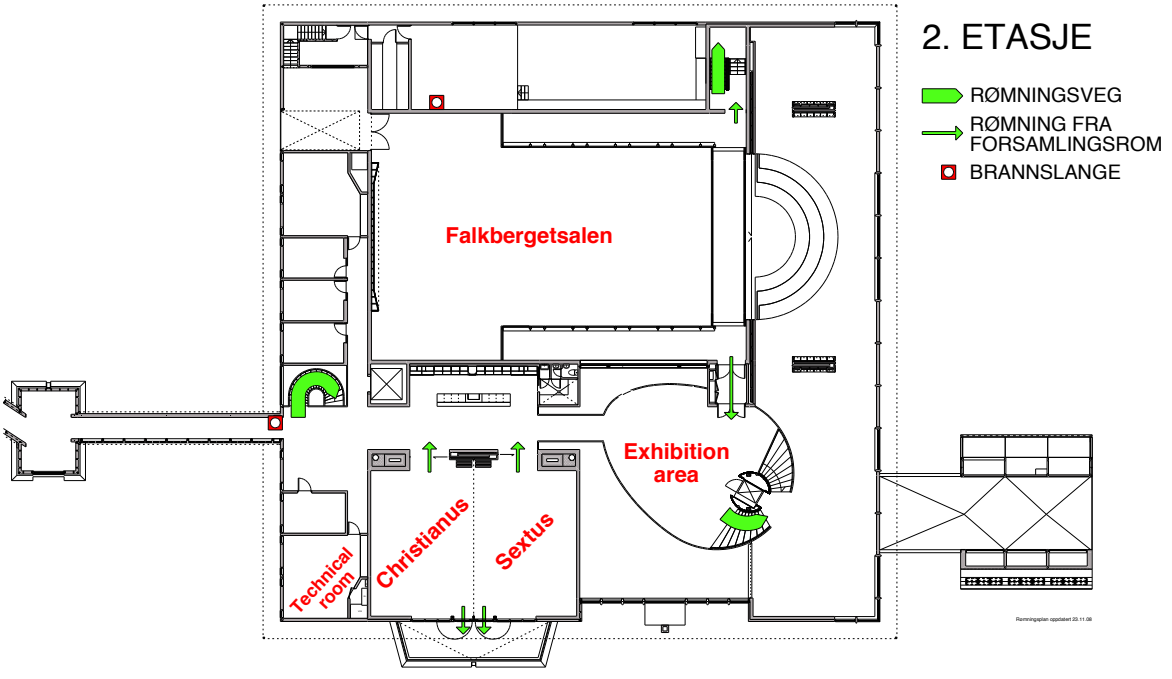
A walk in the city centre
Røros is on the UNESCO list of World Heritage sites. Experience the old mining town by foot. Take the opportunity to go shopping in the many small, charming shops offering unique handcrafted items.

Dog sledging and horse sledge ride
Information regarding booking etc can be found at the web page: https://www.biokjemisk.no/contact-meeting-2025/outdoor-activities/

For more info about things to do in Røros: https://www.roros.no/en/ or contact the hotel reception.

Transportation
If you need help with transport, please contact the hotel reception desk. Taxis can be ordered at the hotel reception desk.





Organizing committee

The meeting is organized by Norwegian University of Science and Technology (NTNU).

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Scientific, Power breakfast

Norwegian Bioscience Society

Invitation to the general assembly of the Norwegian Bioscience Society (NBS).

Time: Saturday 25. January 2024 17.30-18.30
Place: Røros hotell

Agenda:

A. Opening of the general assembly (President).
B. Approval of the invitation and agenda.
C. Election of chairperson, 2 minutes secretaries and 2 persons to approve that the report for the general assembly is correct.
D. Approval of the board report.
E. Approval of the revised accounts of NBS, NBS-nytt and Contact Meeting
F. Election of president and/or general secretary.
G. Matters proposed by the board:
H. Other matters received:
I. Approval of the proposed budget

Orientations

J. NBS-nytt: the editor informs about NBS Nytt 2024.
K. Report from NBS local branches.
    - Oslo
    - Bergen
    - Trondheim
    - Tromsø
    - Ås
M. NBS Contact meeting 2026: Bergen
N. NBS Contact meeting 2027: Tromsø

Trondheim December 15th., 2024

Magnus Steigedal, secretary general NBS

Tannlege Olaf Aase
og frues minneforelesning

Ping-Chih Ho

Tannlege Olaf Aase og frues legat

The FEBS National Lecturer

Dagmar Wachten


HOUM


BIO-RAD


ThermoFisher
SCIENTIFIC


SAVEEN
WERNER


TRIOLAB


Novogene


METTLER TOLEDO


The Research
Council of Norway


BioNordika
YOUR SCIENTIFIC SUPPLIER


SARSTEDT


QIAGEN


Teknolab as


PARSE
BIOSCIENCES

Program overview

Thursday, 23rd of January

11.00 – 15.00	**Registration**	
13.00 – 15.00	**Lunch**	
15.00 – 15.15	**Welcome: Trude Flo (Falkberget)**	
15.15 – 16.00	**PL1:** ***Mysteries of multicellularity - a green perspective.*** **Dolf Weijers**, Wageningen University and Research, Netherlands. Chaired by Thorsen Hamann **(Falkberget)**	
16.00 – 16.45	**PL2:** ***From deterministic cardiac development to regulative whole heart regeneration*****. Lionel Christiaen**, Michael Sars institute, UiB, Norway. Chaired by Vidar Beisvåg **(Falkberget)**	
16.45 – 17.15	**Exhibition/Break**	
17.15 – 18.15	**Paralell Minisymposium Session 1 (1-2)**	
	1. Genetics / Structural Biology (Falkberget) Chair: Pål Falnes, Thorsten Hamann.	**2. Microbiology / Physiology (Sextus)** Chair: Trygve Brautaset, Marte Dragset.
17.15 – 17.30	**M01.** ***Decoding transcriptional regulation of cell wall integrity in Arabidopsis.*** Tereza Ticha.	**M05.** ***Omics-based profiling of a microbial community able to metabolize an oxidized polyethylene-like wax.*** Ronja M. Sandholm.
17.30 – 17.45	**M02.** ***A Na^+/H^+ exchanger with potential.*** Valeriia Kalienkova.	**M06.** ***Identification of enzymes involved in degradation of a novel exopolysaccharide from Lactiplantibacillus pentosus.*** Victor Daisuke Kietzmann
17.45 – 18.00	**M03.** ***CARNMT1-meditated histidine methylation of C3H zinc fingers – identifying novel substrates and exploring sequence requirements.*** Jedrzej Malecki.	**M07.** ***The role of lytic polysaccharide monooxygenases as virulence factors.*** Gustav Vaaje-Kolstad.
18.00 – 18.15	**M04.** ***Nanoscale 3D DNA tracing reveals the mechanism of self-organization of mitotic chromosomes.*** Kai Sandvold Beckwith.	**M08.**
18.15 – 19.30	**Exhibition / Poster Session 1 (odd numbered posters are presented)**	
19.30 – 20.00	**Break**	
20.00 –	**Dinner**	

Friday, 24th of January

07.00 – 09.00	**Breakfast**	
08.00 – 09.00	**Power Breakfast**	
09.00 – 09.45	**PL3*: What about all those other mycobacteria?,* Eric Rubin**, Harvard T.H. Chan School of Public Health, US. Chaired by Magnus Steigedal **(Falkberget)**	
09.45 – 10.30	**PL4: *Dentist Olaf Aase and Wife Memorial Lecture: Reprogramming HCC tumor microenvironment from bench to bedside.* Ping-Chih Ho**, Ludwig Institute for Cancer Research, Switzerland. Chaired by Therese Standal (**Falkberget)**	
10.30 – 11.00	**Exhibition/Break**	
11.00 – 12.30	**Innovation session** Chaired by Magnar Bjørås (**Falkberget)**	
11.00 – 11.35	**IS1: *Bridging groundbreaking research with research-driven innovation - the value of industrial collaboration*. Jan Terje Andersen,** University of Oslo and Oslo University Hospital of Oslo, Norway	
11.35 – 12.10	**IS2: *Development of antibacterial peptides targeting the β-clamp and AMR*. Marit Otterlei,** APIM Therapeutics, Norway	
12.10 – 12.30	**IS3: *From corona to salmon diseases – a story of basic research and market needs*. Tonje Steigedal,** Lybe Scientific, Norway.	
12.30 – 14.00	**Lunch**	
14.00 – 14.45	**PL5: *Designing and translating next generation biomaterials for early disease detection and treatment.* Dame Molly Stevens**, Kavli Institute for Nanoscience Discovery, Univ. of Oxford, UK. Chaired by Berit Strand **(Falkberget)**	
14.45 – 15.30	**PL6: *Inflammasomes in health and disease*. Eicke Latz,** DRFZ Berlin, Germany. Chaired by Trude Flo **(Falkberget)**	
15.30 – 16.00	**Exhibition/Break**	
16.00 – 17.45	**Paralell Minisymposium Session 2 (3-4)**	
	3. Cell Biology / Neuroscience (Falkberget) Chair: Barbara van Loon, Helene Knævelsrud.	**4. Cancer (Sextus)** Chair: Inger Øynebråten, Tereza Ticha.
16.00 – 16.15	**M09. *Rab11-FIP2 controls NLRP3 inflammasome activation through Rab11b.*** *Harald Husebye.*	**M17. *Toll-like receptor agonists and interferons synergize to render human macrophages cytotoxic to cancer cells.*** Inger Øynebråten.
16.15 – 16.30	**M10. *Function of DNA glycosylase coordination in neurodevelopment.*** Barbara Van Loon.	**M18. *A multi-omic approach to genetic variants in breast cancer: Insights from the Norwegian Breast Cancer Study.*** Ina Skaara Brorson.
16.30 – 16.45	**M11. *Exploring autophagy termination in Drosophila.*** Helene Knævelsrud.	**M19. *Blocking S100A9-signaling is detrimental to the initiation of anti-tumor immunity.*** Elisabeth Müller.

16.45 – 17.00	**M12.** ***Unravelling the role of nuclear membrane complex ESCRT-III in DNA damage after ionizing radiation.*** Marie-Catherine Drigeard Desgarnier.	**M20.** ***Spatial metabolic profiling of bone marrow niches in multiple myeloma patients using imaging mass cytometry.*** Ingrid Aass Roseth.
17.00 – 17.15	**M13.** ***Morphological profiling of mammalian macrophages.*** Torkild Visnes.	**M21.** ***Achieving Spatial Transcriptomic Data from Colonic Mucosal Compartments using FFPE Tissue and Laser Capture Microdissection.*** Lusie Frostvoll Kuraas.
17.15 – 17.30	**M14.** ***The roles of the choroid plexus: from cerebrospinal fluid secretion to regulation of brain physiology and animal behavior.*** Inyoung Jeong.	**M22.** ***CDK12/CDK13 inhibition disrupt transcriptional elongation and replication fork progression critical for glioblastoma survival.*** Deo Prakash Pandey.
17.30 – 17.45	**M15.** ***The evolutionary origins of vesicle fusion in synapses - insights from our closest relatives.*** Aishwarya Ravi.	**M23.** ***Smashing the Limits of Single Cell Transcriptomics - Introducing Evercode*****.** Anne Helness. Parse Biosciences.
17.45 – 18.00	**M16.** ***Tankyrase inhibition demonstrates anti-fibrotic effects in vitro, ex vivo, and in vivo in preclinical pulmonary fibrosis models.*** Shoshy Brinch.	**M24.**
18.00 – 19.15	**Exhibition / Poster Session 2 (even numbered posters are presented)**	
19.00 – 20.00	**Break**	
20.00 –	**Dinner**	

Saturday, 25th of January

07.00 – 09.00	**Breakfast**	
08.00 – 09.00	**Power Breakfast**	
09.00 – 12.00	**Outdoor Activities**	
12.00 – 13.30	**Lunch**	
13.30 – 14.15	**PL7:** ***The FEBS National Lecture: Shedding light on ciliary signaling and function.*** **Dagmar Wachten**, Univ. of Bonn, Germany. Chaired by Nathalie Jurisch-Yaksi **(Falkberget)**	
14.15 – 15.00	**PL8:** ***The Role of Astroglia-Neuron Interactions in Network Hyperexcitability and Seizures.*** **Emre Yaksi**, Kavli Institute for Systems Neuroscience, NTNU, Norway. Chaired by Magnar Bjørås (**Falkberget)**	
15.00 – 15.30	**Exhibition/Break**	
15.30 – 17.30	**Paralell Minisymposium Session 3 (5-6)**	
	5. Biotechnology /Technology Development (Christianus) Chair: Dirk Linke, Tage Thorstensen.	**6. Immunity / Stress Biology (Sextus)** Chair: Shirin Kappelhoff, Alexandre Corthay.
15.30 – 15.45	**M25.** ***Miniaturization of T cell cultivation and utilization for process development.*** Hanne Haslene-Hox.	**M33.** ***Exploring NINJ1 in Mtb-induced cell death using genetically modified induced pluripotent stem cell (iPSC)-derived macrophages.*** Mathilde Hansen.
15.45 – 16.00	**M26.** ***Cell Encapsulation in Sulfated Alginate Beads for Therapeutic Applications in Type 1 Diabetes and Acute Liver Failure.*** Joachim S. Kjesbu.	**M34.** ***Dissecting the regulation, structural dynamics, and physiological role of human Ninj1 activity during Mtb-induced cell death on a molecular scale.*** Shirin Kappelhoff.
16.00 – 16.15	**M27.** ***Functional Analysis of LPA2 and LPA3 Reveals Their Essential Role in Photosynthetic performance in Diatoms.*** Marthe Hafskjold.	**M35.** ***Understanding the association between viral etiology, immune dysregulations, clinical and environmental factors in development of chronic lung disease in children in Nepal: Children's Lung Study in Dhulikhel, Nepal.*** Nishan Katuwal.
16.15 – 16.30	**M28.** ***Can CRISPR-Cas9 mediated knockout of susceptibility genes in lettuce reduce the need for chemical pesticides against white mold in Norway?*** Tage Thorstensen.	**M36.** ***Investigating the effects of JAK-inhibitors on inflammatory responses in intestinal epithelial cells using IBD patient-derived colonoids.*** Arun Sridhar.
16.30 – 16.45	**M29.** ***A trimeric coiled-coil motif binds bacterial lipopolysaccharides with picomolar affinity - and can be used in LPS detection and removal applications.*** Dirk Linke.	**M37.** ***Decoding the intracellular complement system in human macrophages.*** Stine Kristensen.

16.45 – 17.00	**M30.** ***RGD-alginate microbeads as scaffolds for structuring human pulmonary fibroblasts.*** Margrethe Cecilie Stahl.	**M38.** ***STING-ing CD4+ T cells to Death: The Role of the Innate Immune Receptor STING in Human CD4+ T.*** Chan Ha You.
17.00 – 17.15	**M31.** ***Preparation of defined gellan oligosaccharides by a combined chemical and enzymatic depolymerization.*** Pascal Mrozek.	**M39.** ***Targeting Glutamate Transporters: A Translational Approach to Seizure Therapeutics.*** Ahmed Jamali.
17.15 – 17.30	**M32.** ***Enzymatic production of long-chain aliphatic diacids as monomers for future plastics.*** Esteban López-Tavera.	**M40.** ***Exploring PCNAs regulatory role in stress.*** Jana Scheffold.
17.30 – 18.30	**NBS General Assembly (Christianus)**	
18.30 – 19.30	**Break**	
19.30 – 20.00	**Reception (the Pit/"Gropa")**	
20.00 –	**Banquet** (**Falkberget)**	

Plenary Speakers

Dolf Weijers **PL1**

Wageningen University and Research – NETHERLANDS
https://www.wur.nl/en/persons/dolf-weijers.htm

Dolf Weijers started his lab at Wageningen University in 2006 — Netherland.

His research program focuses on two areas: principles underlying multicellular plant development and mechanisms in auxin biology. A general strategy is to (1) use simple models (such as the Arabidopsis embryo) to address complex questions, (2) integrate methodologies from multiple fields (e.g., microscopy, transcriptomics, genetics, biochemistry, modelling) and (3) focus on major, unresolved questions of fundamental origin.

In past years, his team has made seminal discoveries, including the identification of genes and mechanisms controlling root, vascular tissue, ground tissue and stem cell identity in the Arabidopsis embryo. His team has more recently included evolutionary approaches, and adopted Bryophyte model systems that now allow comparative evolutionary studies, and discovery of ancestral system properties.

Weijers is theme chair for Developmental Biology at the graduate school Experimental Plant Sciences, he is secretary general of the International Association for Sexual Plant Reproduction Research and board member of the International Plant Growth Substances Association and the Dutch Society for Developmental Biology. He is an elected member of the Royal Netherlands Academy of Sciences (KNAW; 2021) and EMBO (2020) and founded the Wageningen Young Academy and Science Café Wageningen. He is senior editor at the Plant Cell, was editor in chief of Plant Reproduction, and acts on the editorial advisory board of Science Signaling

Lionel Christiaen **PL2**

Michel Sars institute, UiB, Bergen — NORWAY
https://www.uib.no/en/michaelsarscentre/141681/christiaen-group

Lionel Christiaen is Director of the Michael Sars Centre in Bergen (Norway) and Professor at New York University (USA) – Norway

His research aims at understanding how tissue-specific regulatory programs and cell-cell communication coordinate cellular behavior in the context of animal development, regeneration and evolution. His laboratory focuses on cardiopharyngeal lineages, which produce the heart and head muscles, using the ascidian Ciona as model. His laboratory has contributed seminal findings in developmental and evolutionary biology, identifying key processes contributing to human congenital disorders.

Eric Rubin PL3

Harvard T.H. Chan School of Public Health — USA
https://www.hsph.harvard.edu/rubin-lab/

Eric J. Rubin, M.D., Ph.D., is a Professor in the Department of Immunology and Infectious Diseases at the Harvard T.H. Chan School of Public Health, an Associate Physician specializing in infectious disease at Brigham and Women's Hospital, and Editor-in-Chief of the New England Journal of Medicine (NEJM) — USA.

Dr. Rubin is an esteemed microbiologist, recognized for pioneering bacterial genetic tools used to create the next generation of anti-tuberculosis (TB) drugs. His career at Harvard Chan School spans more than 20 years, during which he has primarily focused on Mycobacterium tuberculosis, the pathogen that causes human TB and is the second leading infectious killer of adults worldwide. Rubin, who grew up in Brockton, Massachusetts, and earned MD and PhD degrees at Tufts University, was previously chair of the Department of Immunology and Infectious Diseases and the Irene Heinz Given Professor of Immunology and Infectious Diseases.

He was elected Fellow of the American Academy of Microbiology in 2012. In 2019, he was named editor-in-chief of NEJM and in 2021 he was elected to the National Academy of Medicine, USA.

Ping-Chih Ho PL4

Ludwig Institute for Cancer Research, Lausanne — SWITZERLAND
https://www.ludwigcancerresearch.org/scientist/ping-chih-ho/

Professor Ping-Chih Ho is a cancer immunologist at the Ludwig Institute for Cancer Research, Lausanne — Switzerland

His research focuses on immunometabolism in T cells and macrophages. He has made substantial contributions to our understanding of how tumor cells evade immunosurveillance through their metabolism, and how it may be possible to preprogram the metabolic machinery of immune cells to improve immunotherapy. His work is also delineating links between metabolic processes, signaling cascades and epigenetic programming in the activation and differentiation of T cells and macrophages. Ho did his undergraduate and postgraduate training at National Taiwan University and obtained his PhD at the University of Minnesota. He was a post doc at Susan Kaech laboratory at Yale University, before being recruited as an adjunct Ludwig scientist and tenure-track assistant professor in the Department of Oncology at the University of Lausanne.

He became a full member of the Ludwig Institute in 2023 and is currently a full professor at the University of Lausanne. Ho has received several prestigious awards, including the Swiss Bridge Award, Anna Fuller Award, Cancer Research Institute-CLIP investigator award, Melanoma Research Alliance-SITC Young investigator Award, a European Research Council Starting Grant and a Swiss National Science Foundation Consolidator Grant. He is a member of the European Molecular Biology Organization's Young Investigator Programme. Ho also recently became an elected member of the Henry Kunkel Society which acknowledges scientists who has made substantial impacts for immunology and immunopathology.

Dame Molly Stevens PL5

Oxford University — UK
https://eng.ox.ac.uk/people/molly-stevens/

Professor Dame Molly Stevens FREng FRS joined Univeristy of Oxford and the Institute for Biomedical Engineering as the John Black Professor of Bionanoscience in April 2023, where she is also Deputy Director of the Kavli Institute for Nanoscience Discovery — UK.

Prof Stevens obtained her PhD at the University of Nottingham, did her postdoctoral research at the Massachusetts Institute of Technology, and led a highly interdisciplinary research programme at Imperial College London from 2004-2023 where she still holds a part-time position. Since 2015, she has also been part-time Professor of Biomaterials and Regenerative Medicine in the Department of Medical Biochemistry and Biophysics at the Karolinska Institutet, Sweden. Professor Dame Stevens is an international leader in ground-breaking biosensing technologies, transformative regenerative medicine and advanced therapeutics approaches The Stevens Group's biomaterial innovations are also applied to soft robotics, and to the interface between living and non-living matter, and are underpinned by collaborations with molecular dynamics experts and data scientists in the digital health field. This work is inherently interdisciplinary, so the Stevens Group is made up of a diverse cast of materials scientists, engineers, chemists, biologists, physicists and surgeons.

Professor Dame Stevens has published extensively in leading journals such as Science, Nature, Nature Nanotechnology and Nature Materials; and has won >40 awards. She is a serial entrepreneur and has significant expertise and experience in commercialization of devices, with numerous patents filed and 4 spin-out companies based on her research.

Eicke Latz **PL6**

DRFZ, Bonn — GERMANY
https://www.iiibonn.de/eicke-latz-lab/science

Prof. Dr. (med.) Eicke Latz is the Scientific Director of the German Rheumatism Research Centre Berlin, a Leibniz Institute, and Professor of Experimental Rheumatology at the Charité Universitätsmedizin Berlin — Germany

Prof. Latz studied medicine at the Georg-August University in Göttingen and the Freie Universität Berlin, following which, he worked as an intensive care physician at the Charité Universitätsmedizin in Berlin. In 2001, he moved to the USA, working as a postdoctoral researcher at Boston University, then at UMass Chan Medical School, where he held his first professorship. In 2010, he returned to Germany and founded the Institute for Innate Immunity at the University Hospital Bonn. Last year he moved back to Berlin to be Scientific Director of the German Rheumatism Research Centre Berlin. Prof Latz' research interests concern how the innate immune system maintains health and under what circumstances it can promote disease. In particular, he investigates the molecular mechanisms that lead to activation or inhibition of the immune system and how these influence the inflammatory reactions in various diseases, such as rheumatic diseases, arteriosclerosis or Alzheimer's disease.

Prof. Latz is spokesperson of the Collaborative Research Centre "Metaflammation and Cellular Programming" (SFB 1454) and was previously co-spokesperson of the Cluster of Excellence "ImmunoSensation²", both at the University of Bonn. He has also co-founded several biotech companies which translate his discoveries into novel therapeutics and preventive approaches. Prof. Dr. Latz was elected as a member of the German National Academy of Sciences (Leopoldina) in 2016 and has received several awards, including the Gottfried Wilhelm Leibniz Prize in 2018.

Dagmar Wachten **PL7**

Uni Bonn — GERMANY
https://www.iiibonn.de/dagmar-wachten-lab/dagmar-wachten-lab-science

Dagmar Wachten is a Professor and Head of the Institute of Innate Immunity at the University of Bonn — Germany

Her research aims to unravel how tissue ecosystems are maintained by cellular communication. She is especially interested in how cells interact through cilia-related signaling pathways in the context of the innate immune system. Her laboratory has developed spatially-resolved optogenetic tools and biosensors to manipulate and monitor cell signaling in sub-cellular compartments. Using these tools, her laboratory has made seminar discoveries on the role of signaling pathways, especially G-protein coupled receptor and cAMP, in tissue development, homeostasis and disease.

Emre Yaksi PL8

NTNU Kavli — NORWAY
https://www.ntnu.edu/employees/emre.yaksi

Emre Yaksi is a Professor at the Norwegian University of Science and Technology (NTNU), Trondheim, Norway, an adjunct Professor at Koc University, Istanbul, Turkey, and an EMBO member — Norway.

Prof. Yaksi has a long track record in systems neuroscience, from using two-photon calcium imaging data to analyse activity patterns of large neuronal populations to electrophysiological recordings of single neurons in zebrafish and Drosophila.

His laboratory at the Kavli Institute for Systems Neuroscience at NTNU studies how sensory information interacts with animals' internal states using zebrafish as model system. To achieve this, he focuses on the habenula, a brain region associated with predicting potential outcomes. His laboratory revealed that habenular neurons respond to sensory cues and integrate information with the ongoing activity of the brain. Moreover, his team identified that distinct functional modules in habenula are born in discrete developmental time windows and are driven by the activation of different the cortico-limbic forebrain regions. Beyond fundamental neuroscience questions, the Yaksi laboratory also implements systems neuroscience and bioinformatics approaches to investigate the role of astroglia-neuron interactions in brain physiology and pathophysiology.

Jan Terje Andersen IS1

University of Oslo and Oslo University Hospital of Oslo — NORWAY
https://www.ous-research.no/andersen/

His research group is studying the cellular processes and molecular interplay underlying the functions of the two most abundant proteins in blood, albumin and IgG. Such knowledge offers opportunities for development of novel concepts that will secure improved half-life and biodistribution of IgG and albumin based therapeutics. The laboratory has an eye on translational research, is highly innovative and is the research group at the University of Oslo and Oslo University Hospital with most registered innovations at Inven2. The laboratory is collaborating extensively with biotech and pharmaceutical companies.

The head of the laboratory, Jan Terje Andersen, has obtained the Fridtjof Nansen Prize for Early Career Achievements, Oslo University Hospital Early Career Award and is a member of The Young Academy of Norway.

Marit Otterlei **IS2**

NTNU — Norway
https://www.ntnu.edu/employees/marit.otterlei

Based on the scientific discovery of the novel PCNA interaction motif, APIM, Otterlei founded the NTNU spin-off company APIM Therapeutics in 2009, and has since then been in charge of the development of a peptide drug containing the APIM sequence for use in cancer therapy as a part time CSO in APIM Therapeutics. Clinical phase I was finalized in 2021, and the drug, ATX-101, is well tolerated and show cancer stabilizing activity. Two Phase Ib/II studies are ongoing.

The research group's current focus is to further explore peptides targeting the bacterial DNA sliding clamp for anti-bacterial activities.

Select a clinical indication for further development

Explore the beta-clamp's role outside DNA replication, i.e. elucidate the involvement in regulation of cellular signaling and metabolism.

Explore the interaction between the APIM-peptide and its target.

Tonje Steigedal **IS3**

Lybe Scientific – Norway
https://lybescientific.com/

Tonje Steigedal is the CEO and co-founder of Lybe Scientific based in Trondheim, Norway. Lybe Scientific is a university startup developing high quality nanoparticle-based solutions for life science, diagnostic and aquaculture purposes with a special focus on products within nucleic acid extraction and sample preparation. The company serve customers within hospitals, aquaculture and fish health monitoring laboratories as well as academic and research institutions.

Steigedal holds a MSc in Biotechnology and a PhD in Medical Technology and has more than 10 years experience in business development work.

Minisymposia Abstracts

M01

Decoding transcriptional regulation of cell wall integrity in Arabidopsis

T. Tichá (1), Z. Bartosova (1), L. Bacete (1), S. Zwartkruis (1), T. Hamann (1).
(1) Norwegian University of Science and Technology, Department of Biology, Trondheim, NORWAY.

The plant cell wall is an essential protective layer surrounding plant cells and plays a key role during growth, development, and interaction with the surrounding environment. Biotic and abiotic stresses affect cell wall structure and composition, impair the functional integrity of the wall, and lead to drastic changes in plant performance and biomass production. The Cell Wall Integrity (CWI) maintenance mechanism monitors the functional integrity of the wall and maintains it by initiating adaptive changes in cellular and cell wall metabolism. This mechanism involves several receptor-like kinases and ion channels in the plasma membrane, which perceive stimuli arising from CWI impairment and modulate downstream signaling cascades, leading to changes in cytoskeleton reorganization, phytohormone production (e.g., ABA, JA, SA), gene expression, and cell wall composition and structure. THESEUS1 is one of these kinases and forms an essential component of the mechanism responsible for detecting mechanical stimuli arising. Importantly, our knowledge regarding the mechanisms regulating CWI monitoring and maintenance on the transcriptional level is very limited. To address this knowledge gap, we have performed a transcriptomic analysis of Col-0, the1-1 (knock-out), and the1-4 (gain-of-function) seedlings exposed to osmotic stress (sorbitol) and a cellulose biosynthesis inhibitor (isoxaben) impairing CWI. The results implicate 44 differentially expressed transcription factors in THE1-mediated CWI maintenance. Results from hypersensitivity assays using Knockout alleles for the candidates suggested that 19 candidates affect responses to sorbitol and isoxaben. Gene ontology analysis implicates several candidates in phytohormone production. We have investigated their involvement in phytohormone production using MS/MS spectrometry and are currently performing gene expression analyses to investigate their involvement in regulating cell wall-related gene expression.

M02

A Na^+/H^+ exchanger with potential

Valeriia Kalienkova (1,2), Martin F. Peter (1,3), Jan Rheinberger (3), Cristina Paulino (1,3).
(1) University of Groningen, Groningen, Netherlands. (2) University of Bergen, Norway. (3) University of Heidelberg, Heidelberg, Germany.

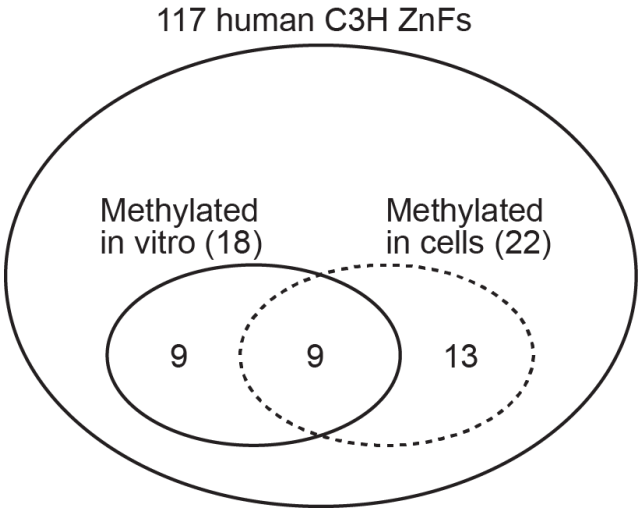
The newly characterized sperm-specific Na^+/H^+ exchanger (sNHE) SLC9C1 stands out by its unique tripartite domain composition. It unites a canonical NHE transport domain (TD) with regulatory domains usually found in ion channels, namely a voltage-sensing domain (VSD) and a cyclic-nucleotide binding domain (CNBD). These domains endow the protein with a unique activation mechanism - the transport activity occurs only upon membrane hyperpolarization, with V1/2 modulated by cAMP. SLC9C1 is a mechanistic chimera and the first reported secondary-active transporter activated exclusively by membrane voltage, akin to CNBD ion channels. Our structures of the sea urchin homolog SpSLC9C1 in absence and presence of ligands reveal the overall domain arrangement and new structural coupling elements, which mediate the interactions between the three functional units (TD, VSD and CNBD). Further, cAMP, and not cGMP, induces significant mobility in the cytoplasmic domain. The structures allow us to propose a gating model, where at rest the TD is locked in the inward-facing conformation by the interactions with the cytoplasmic domain. Movements in the voltage sensor upon membrane hyperpolarization presumably displace the newly characterized coupling helices, and indirectly cause the release of the TD from its locked state. We further propose that modulation by cAMP occurs via disruption of the inter-protomer interactions within the cytoplasmic domain, which facilitates the downward S4 movement at resting membrane potential.

M03

CARNMT1-meditated histidine methylation of C3H zinc fingers – identifying novel substrates and exploring sequence requirements

Jędrzej M. Małecki (1), Sara Weirich (2), Manuel Ramirez (1), Lisa Schroer (1), Lars Hagen (3), Jakin Al-Egly (1), Carmen Herrera (1), Erna Davydova (1), Jan H. Anonsen (1), Albert Jeltsch (2) and Pål Ø. Falnes (1).
(1) Department of Biosciences, Faculty of Mathematics and Natural Sciences, University of Oslo, 0316 Oslo, Norway. (2) Institute of Biochemistry and Technical Biochemistry, University of Stuttgart, Allmandring 31, 70569 Stuttgart, Germany. (3) 3Department of Clinical and Molecular Medicine, Faculty of Medicine and Health, Norwegian University of Science and Technology, 7491, Trondheim, Norway.

During the last years, it has become clear that protein histidine methylation is widespread and functionally important, and CARNMT1 was recently reported as a novel protein histidine methyltransferase (HMT). We here describe our independent uncovering of CARNMT1 as a protein HMT, and our extensive efforts on defining its substrate specificity and methylation targets. We found that recombinant CARNMT1 methylated several proteins in extracts from CARNMT1 KO cells, and, using protein mass spectrometry, we identified several fully methylated CARNMT1 targets, all of which were C3H zinc finger (C3H-ZnF) proteins. These included the previously identified U2AF1, ZC3H15 and ZC3H15, but also the novel substrates RBM22, PPP1R10, PRR3 and RNF113A. Using peptide arrays, we investigated CARNMT1-mediated methylation of a comprehensive set of 117 human C3H-ZnFs. Somewhat surprisingly, we found that only 18 of them were efficiently methylated by CARNMT1, and several of these are also methylated in vivo. This indicates a good correlation between in vitro and in vivo methylation, and that only a small subset of human C3H-ZnFs are actually CARNMT1 targets. To investigate the specificity of CARNMT1, we systematically substituted the His-proximal residues in four different substrate peptides. This generated four rather different substitution profiles, which were still quite restrictive for each peptide, indicating that the sequence-based prediction of CARNMT1 substrates may be challenging. We also identified several of the homologous methylation events in C. elegans and showed that they could be introduced by nematode CARNMT in vitro. Our study indicates that CARNMT1 is an evolutionary conserved HMT with a complex mode of substrate recognition.

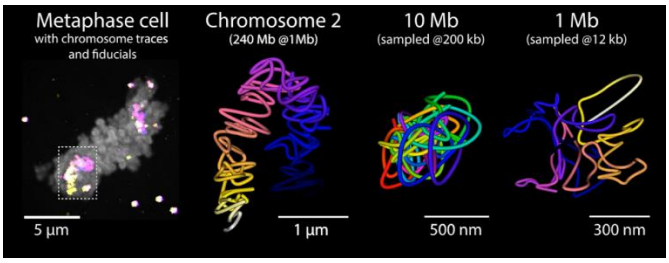


M04

Nanoscale 3D DNA tracing reveals the mechanism of self-organization of mitotic chromosomes

Kai Sandvold Beckwith (1,2), Andreas Brunner (2), Natalia Rosalia Morero (2), Ralf Jungmann (3) and Jan Ellenberg (2,4).
(1) Dept. Biomedical Laboratory Science, Norwegian University of Science and Technology, Trondheim, Norway. (2) Cell Biology and Biophysics, European Molecular Biology Laboratory, Heidelberg, Germany. (3) Max Planck Institute of Biochemistry, Martinsried, Germany. (4) Karolinska Institut, Stockholm University, Stockholm, Sweden.

How genomic DNA is folded during cell division to form the characteristic rod-shaped mitotic chromosomes essential for faithful genome inheritance is a long-standing open question in biology. We used nanoscale DNA-tracing in single dividing cells to directly visualize how the 3D fold of genomic DNA changes during mitosis, at scales from single loops to entire chromosomes. Combined with data-driven modeling and molecular perturbations, we can show that very large and strongly overlapping loops formed by Condensins are the fundamental structuring principle of mitotic chromosomes. These loops compact chromosomes locally and globally to the limit set by chromatin self-repulsion. The characteristic length, density and increasingly overlapping structure of mitotic loops we observe in 3D fully explain how the rod-shaped mitotic chromosome structure emerges by self-organization during cell division.



M05

Omics-based profiling of a microbial community able to metabolize an oxidized polyethylene-like wax

Ronja M. Sandholm (1), Ravindra R. Chowreddy (2), Vincent G.H. Eijsink (1), Gustav Vaaje-Kolstad (1) and Sabina Leanti La Rosa (1).
(1) Faculty of Chemistry, Biotechnology and Food Science, NMBU - Norwegian University of Life Sciences, Ås, Norway. (2) Norner Research AS, Porsgrunn, Norway.

Synthetic polymers, such as plastics, are used in many applications due to their ease of synthesis and durable properties. The durability and resistance of these polymers render them recalcitrant to biodegradation, leading to significant pollution challenges on a global scale. We aim to identify plastic-degrading organisms and their enzymes to tackle the plastic challenge and develop biotechnological recycling technologies. To obtain potential plastic-degrading microorganisms, soil was sampled from a plastic-contaminated landfill in the Innlandet county of Norway. Putative degraders were enriched using polyethylene-like wax (PELW) as the sole carbon source. Long-read Oxford Nanopore sequencing and the Aviary pipeline allowed to recover 47 Metagenome Assembled Genomes (MAGs). Taxonomy was assigned using the GTDB-tk software. Meta-RNA was sequenced using Illumina technology, and reads were pseudoaligned against the metagenomic dataset using Kallisto. In the PELW-degrading community, Acinetobacter guillouiae was the MAG with the highest relative abundance (57,8%). In addition, *A. guillouiae* was the most active MAG in the community, with the highest number of transcripts when grown on PELW. Transcriptional analysis revealed that genes involved in alkane degradation were upregulated, suggesting that PELW components are being converted to fatty acids. Ongoing efforts include proteomic analyses of the isolated *A. guillouiae* to further elucidate the enzymes involved in the degradation of PELW., This work will eventually shed light on the mechanisms behind the metabolization, and will lead to the identification of enzymes that could be utilized in the enzymatic recycling of PELW-like plastics.

M06

Identification of enzymes involved in degradation of a novel exopolysaccharide from *Lactiplantibacillus pentosus*

Victor Daisuke Kietzmann (1), Ahmad Tsjokajev (1), Pascal Michael Mrozek (1), Gordon Jacob Boehlich (1), Bjørge Westereng (1), Gustav Vaaje-Kolstad (1).
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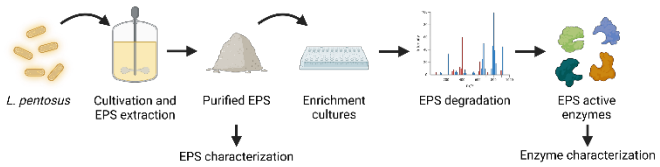
Bacterial exopolysaccharides (EPS) play an increasingly important role in the food and health industry. Among the most intensely studied orders of bacteria in this context are lactic acid bacteria (LAB), or *Lactobacillales*. A plethora of research has been published in recent years on the various health benefits of many different EPS produced by LAB. However, while the structures and properties of many of these EPS have been analyzed extensively, relatively little is known about how these complex polysaccharides are degraded. To contribute to closing this gap in knowledge, a novel EPS from *Lactiplantibacillus pentosus* was investigated. In brief, the EPS was purified from *L. pentosus* cultures, and its structure elucidated using nuclear magnetic resonance spectroscopy, size exclusion chromatography and monosaccharide composition analysis. The EPS was then utilized as a sole carbon source in enrichment cultures to obtain bacterial communities capable of its degradation and metabolization. After confirming EPS degradation, two relevant strains from the *Sphingobacterium* and *Luteolibacter* genus were isolated, and their full genomes sequenced. Both genomes showed a plethora of carbohydrate active enzymes (CAZymes) possibly involved in EPS degradation. In the next step of the project, differential transcriptomic analysis will be used to identify the cellular and secreted CAZymes involved in EPS catabolism. This will shed more light on the fate of EPS in bacterial communities and identify key enzymes for depolymerization of the novel *L. pentosus* EPS.



M07

The role of lytic polysaccharide monooxygenases as virulence factors

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(1) Division of Host-Microbe Systems & Therapeutics, Department of Pediatrics, University of California San Diego, La Jolla, CA 92093, USA. (2) Faculty of Chemistry, Biotechnology and Food Science, NMBU - Norwegian University of Life Sciences, Ås, 1433 Norway.

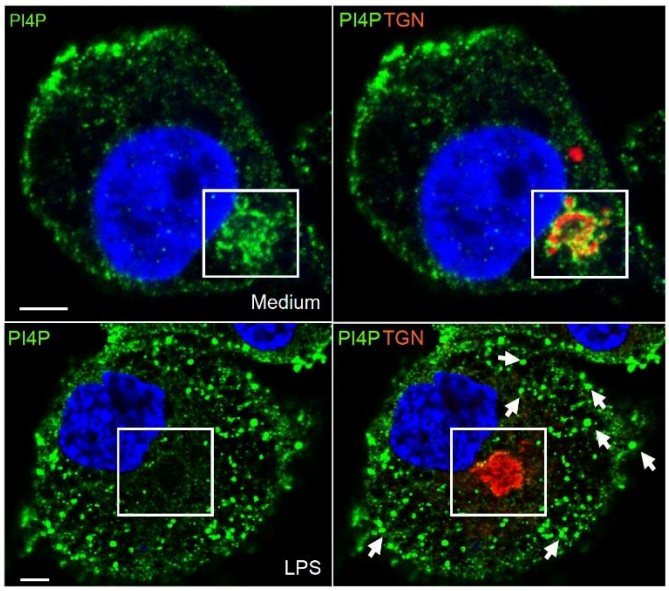
Lytic polysaccharide monooxygenases (LPMOs) are most known for their ability to depolymerize crystalline polysaccharides by oxidation, but some organisms also use these enzymes in virulence. One of these organisms is the opportunistic pathogen *Pseudomonas aeruginosa*. We have shown that the LPMO of this bacterium, called CbpD, is important for the ability to establish systemic and respiratory infections (1). Immunization of mice by CbpD resulted in protective immunity against *P. aeruginosa pneumonia*, indicating that LPMOs from pathogens may be effective vaccine antigens (2). In my presentation I will discuss LPMOs in pathogens in general, but with a focus on the function of CbpD from *P. aeruginosa*. References: 1.Askarian F. et al. The lytic polysaccharide monooxygenase CbpD promotes *Pseudomonas aeruginosa* virulence in systemic infection. Nat Commun. 2021 23;12(1):1230. 2. Askarian F. et al. Immunization with lytic polysaccharide monooxygenase CbpD induces protective immunity against *Pseudomonas aeruginosa pneumonia*. Proc Natl Acad Sci USA. 2023 25;120(30).

M09

Rab11-FIP2 controls NLRP3 inflammasome activation through Rab11b

Caroline Gravastrand (1), Mariia Yurchenko (1), Stine Kristensen (1), Astrid Skjesol (1), Carmen Chen (1), Zunaira Iqbal (1), Karoline Ruud Dahlen (1), Unni Nonstad (1), Liv Ryan (1), Terje Espevik (1), Harald Husebye (1).
1) Centre of Molecular Inflammation Research, Department of Clinical Molecular Medicine, Norwegian University of Science and Technology, Trondheim, Norway.

The trans-Golgi network (TGN) is the docking site for retrograde cargo from the endolysosomal system. The LRR- pyrin domain-containing protein 3 (NLRP3) has been shown to translocate to the TGN following LPS priming, and onto early endosomes following NLRP3 inflammasome activation in nigericin treated primed cells. The GTPases Rab11a and Rab11b and their effector Rab11 Family Interacting Protein 2 (Rab11-FIP2), are regulators of endocytic trafficking at early endosomes that also control retrograde transport to the TGN. Rab11-FIP2 is known to bind phosphatidylinositol (PI) species including phosphatidylinositol 4-phosphate (PI4P) that is enriched in the TGN of resting cells and accumulates on early endosomes following NLRP3 inflammasome activation. Using confocal microscopy and immunoblotting we found that Rab11-FIP2 regulated Lipopolysaccharide (LPS) stimulated Inhibitor of nuclear factor kappa-B kinase subunit beta (IKKb) activation that is known to guide the translocation of NLRP3 to the TGN in human macrophages. The formation of peripheral PI4P containing endosomes and the formation of ASC-specks during NLRP3 inflammasome activation were also a Rab11-FIP2 regulated processes. Furthermore, both Rab11-FIP2 and Rab11b GTPase depletion markedly reduced Caspase-1 mediated cleavage of pro-Interleukin-1b (pro-IL-1β) giving mature IL-1b and the Gasdermin D (GSDMD) p31 pore form. Cleavage of GSDMD results in pyroptotic cell death. Also, Rab11-FIP2 was found to form a complex with NLRP3 and Rab11, but not ASC. We identified the KMKK motif (in human NLRP3 that has recently been reported to bind PI4P to also bind Rab11-FIP2. Taken together our results demonstrate that FIP2 controls NLRP3 inflammasome activation through its binding partner Rab11b, but not Rab11a.



M10

Function of DNA glycosylase coordination in neurodevelopment

Merdane E. Aksu (1), Kayla Grooms (1), Nicholas E. Zachariadis (1), Matthew A. Schaich (2), Rabina Dumaru (1), Arnar Flatberg (1), Kristin Rian (1), Cathrine B. Vågbø (1), Pål Sætrom (1), Keith Caldecott (3), Ben van Houten (2), Barbara van Loon (1).
(1) Department of Clinical and Molecular Medicine, Norwegian University of Science and Technology, Trondheim, Norway. (2) UPMC Hillman Cancer Center, University of Pittsburgh, Pittsburgh, PA, USA. (3) Genome Damage and Stability Centre, School of Life Sciences, Science Park Road, University of Sussex, Falmer, Brighton, UK.

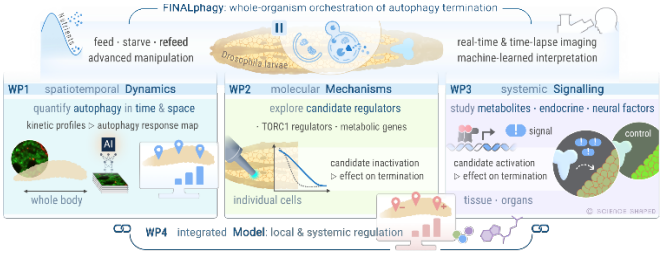
Alkyladenine DNA Glycosylase (AAG) is one of eleven DNA glycosylases that recognizes base damage and initiates Base Excision Repair (BER). In addition to its role in BER, AAG was proposed to impact expression of neurodevelopmental genes and act as reader of epigenetic DNA modifications. Further, very recently we showed that loss of AAG alters brain functions in mice. Despite this the functional roles of AAG in neurodevelopment remain unknown. Here, by using stem cells and induced neurons, we show that lack of AAG alters both DNA damage and global epigenetic DNA modification levels, in particularly of 5-formylcytosine (5fC). Since thymine DNA glycosylase (TDG) is one of the essential BER enzymes acting on 5fC and participating in active demethylation, we next tested functional relation between the two glycosylases. Interestingly, single-molecule and biochemical studies revealed substrate competition between the two enzymes, and AAG-mediated inhibition of 5fC removal by TDG. On functional level 5fC regulation by AAG and TDG is likely essential for unperturbed neuronal differentiation. Since loss of AAG, accompanied by increased 5fC levels, results in perturbed neurodevelopmental transcriptional programs and altered neuronal maturation, evident from single cell and total RNA-seq, as well as immunofluorescene analysis. Taken together, our work for the first time provides insights into functional cooperation between the two DNA glycosylases in regulation of epigenetic DNA modifications of relevance for neuronal differentiation.

M11

Exploring autophagy termination in *Drosophila*

Helene Knævelsrud (1,2,3)
(1) Institute for Basic Medical Sciences, Faculty of Medicine, University of Oslo. (2) Centre for Cancer Reprogramming, Faculty of Medicine, University of Oslo. (3) Institute for Cancer Research, Oslo University Hospital.

When an organism experiences physiological stresses, such as nutrient starvation, it activates several mechanisms to promote its survival, including autophagy. Although autophagy is an intensively studied process that plays a major role both in normal development and in a wide variety of diseases, it remains largely unknown how cells and organisms shut off autophagy in response to returning nutrient availability or as an adaptation to prolonged stress. Therefore, my team is focused on understanding the mechanisms and regulation of this process. We study termination of autophagy *in vivo* in fruit flies and have identified conditions where autophagy is not properly terminated. We identified that in the absence of components of the ATP synthase, autophagy is permanently on. One of the ATP synthase subunits called Stunted (Sun) has a role in mitochondria metabolism, inter-organ communication, and insulin signaling. However, the molecular interplay between Sun and the autophagy pathway is currently unexplored. To fully characterize this link in vivo, we used the Drosophila larval fat body and evaluated autophagy levels. Interestingly, fat body with downregulation of sun shows an increased number of autophagosomes upon refeeding compared to the normal decrease in fat body from control animals. Notably, the nutrient dependent reactivation of mTOR is also impaired in the fat body with decreased sun levels, hinting at a novel role of Sun in autophagy termination. Altogether, these findings offer new insights into the molecular regulation of autophagy termination, potentially providing useful targets for the treatment of cancer and neurodegeneration.



M12

Unravelling the role of nuclear membrane complex ESCRT-III in DNA damage after ionizing radiation

Marie-Catherine Drigeard Desgarnier (1,2), Kasia Gajewska (1,2), Sebastian W. Schultz (1,2), Xian Hu (1,2,3), Anne Grethe Myrann (1,2) Simona Migliano (1,2), Harald Stenmark (1,2,4), Marina Vietri (1,2).
(1) Centre for Cancer Cell Reprogramming, Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway. (2) Department of Molecular Cell Biology, Institute for Cancer Research, Oslo University Hospital, Oslo, Norway. (3) Department of Biosciences, University of Oslo, Oslo. (4) Institute of Basic Medical Sciences, Department of Molecular Medicine, Faculty of Medicine, University of Oslo.

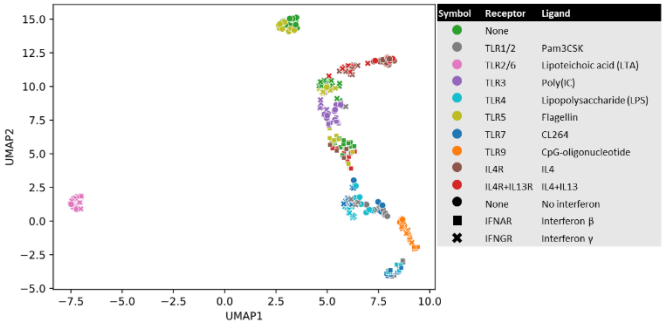
The endosomal sorting complex required for transport (ESCRT-III) is essential for critical cellular functions, including remodeling and repairing cytoplasmic and nuclear envelope (NE) membranes. Among its subunits, CHMP4B is a key component of the ESCRT-III machinery. Interestingly, we observed that CHMP4B forms nuclear puncta, significantly increasing following treatment with various DNA-damaging agents. These puncta are not associated with canonical NE rupture but instead appear at sites of DNA damage. Our data indicate that CHMP4B colocalizes with 53BP1, a protein involved in non-homologous end joining (NHEJ), while excluding BRCA1 and Rad51, which are linked to homologous recombination (HR). Moreover, 53BP1 knockdown leads to a complete loss of CHMP4B nuclear puncta. While direct interactions between 53BP1 and NE proteins are not well-established, 53BP1's role in double-strand break (DSB) end-resection and its proximity to the nuclear periphery suggest a collaborative function with NE proteins in DNA repair. Notably, the increased mobility of DSBs toward the nuclear periphery has been documented, though the mechanisms remain unclear. We hypothesize that unresolved DSBs migrate to the nuclear envelope to modulate the end-resection process. The CHMP4B-53BP1 interaction is particularly intriguing, suggesting the nuclear envelope may act as a hub for DNA damage signaling and repair.DSB mobility is essential for efficient repair, and CHMP4B likely plays a role in this process. Uncovering how CHMP proteins and their interactions with the nuclear envelope contribute to the spatial organization and dynamics of the DNA damage response could pave the way for novel approaches in cancer therapy.

M13

Morphological profiling of mammalian macrophages

Simon Loevenich(1), Sofia Hernandez-Valenzuela(2), Ane Marit Waagbø (1), Marius Eidsaa (1), Kristine Sletta (1,3), Hanne Haslene-Hox (1), Inger Øynebråten(4), Alexandre Courtay (4), and Jordi Carreras-Puigvert(2) and Torkild Visnes (1).
(1) Department of Biotechnology and Nanomedicine, SINTEF Industry, Norway. (2) Department of Pharmaceutical Biosciences, Uppsala University, Sweden. (3) Department of Clinical Science, University of Bergen, Norway. (4) , Department of Pathology, Oslo University Hospital, Norway.

In image-based morphological profiling, we use multi-channel fluorescence microscopy to capture detailed images of stained cells and use advanced image analysis to extract thousands of features from each cell, creating precise and reproducible single-cell profiles. These profiles allow us to classify cell types and study cellular changes with remarkable accuracy. Here, we explore if morphological profiling can be used to score distinct macrophage phenotypes induced by differentiation, polarization, and drug effects. Macrophages are innate immune system cells that regulate host responses in response to signals from the microenvironment, broadly driving both pro-inflammatory and anti-inflammatory responses, depending on context. Macrophages are central to many diseases, and controlling their behavior is a key to many therapeutic strategies. We perform morphological profiling of in vitro polarized human and mouse macrophages, showing that treatment with toll-like receptors (TLR) agonists and/or interferons yield morphologically distinct phenotypes, providing a highly resolved view of pro- and anti-inflammatory macrophages. We further investigate the morphological changes associated with these phenotypes, and further demonstrate how macrophages respond to therapeutically important drugs. Because morphological profiling is a high-throughput, cost-efficient, and highly scalable method, we believe it can complement traditional methods like ELISA or quantitative RT-PCR in studying macrophage phenotypes driven by differentiation, polarization, or drug exposure. Figure: Two-dimensional UMAP representation of mouse macrophage phenotypes. Mouse macrophages were treated with the indicated TLR agonists and/or interferons, imaged, and analyzed. UMAP was used to visualize patterns in >4,000 morphological features, where each symbol represents the median phenotype from one well.



M14

The roles of the choroid plexus: from cerebrospinal fluid secretion to regulation of brain physiology and animal behavior

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The choroid plexus (ChP) is a specialized tissue located within the brain ventricles. The ChP secretes cerebrospinal fluid (CSF) by transporting ions and water into the brain ventricles from adjacent blood vessels. The ChP also plays roles in brain homeostasis by serving as a CSF-blood barrier and immune interface. To date, how the ChP maintains the brain ventricle system and influences brain physiology remain elusive. To gain novel insights into the physiological roles of the ChP, we use zebrafish as a model system. We first revealed that the zebrafish ChP is highly conserved with the mammalian ChPs upon histological and transcriptomic analyses. Next, using novel genetic lines, we characterized the spatio-temporal dynamics of ChP-secreted proteins in the CSF. Finally, by ablating specifically the ChP epithelial cells, we discovered a reduction of the brain ventricular sizes without alterations of the CSF-blood barrier. Taken together, our findings demonstrate that the evolutionarily conserved ChP contributes majorly to CSF production and to the homeostasis of the brain ventricles. Building on these results, we are currently investigating how ChP and CSF regulate brain physiology by measuring neuronal activity and behaviors in animals with altered ChP.

M15

The evolutionary origins of vesicle fusion in synapses - insights from our closest relatives

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Neuronal synapses have a specialized type of regulated secretion - a tightly controlled process involving a cascade of protein interactions before neurotransmitters in vesicles are released. Although the core mechanisms of regulated secretion are highly conserved, the evolutionary origins of this process remain poorly understood. Key proteins involved in this process, such as Unc13, are present even in the unicellular ancestors of animals! Therefore, we here investigate the function of Unc13 in choanoflagellates, the closest single-celled relatives of animals. Unc13 is a pivotal regulator of synaptic transmission, orchestrating processes like vesicle recruitment and SNARE-mediated fusion at neuronal pre-synapses.In this study, we identify and characterize the Unc13 protein homolog in Salpingoeca rosetta (S. rosetta) and find that SrUnc13-1 has a highly polarized localization, especially at the apical part of the cell. Using CRISPR/Cas9, we generated an SrUnc13-1 knockout line in S. rosetta. The knockout line SrUnc13-1- possesses more vesicles, which accumulate at the apical part of the cell, as quantified using electron microscopy. Notably, 20% of SrUnc13-1- cells exhibited a vesicle-filled round structure at the cell apex instead of the flagellum, suggesting defects in ciliogenesis. Additionally, SrUnc13-1- cells displayed multinucleation and detached cytoplasmic bridges, indicating possible cytokinesis defects.These findings suggest that the ancestral role of Unc13 may have been the polarized recruitment and fusion of secretory vesicles. In choanoflagellates, this function is crucial for maintaining vesicle-fusion-mediated membrane integrity necessary for ciliogenesis and cytokinesis.

M16

Tankyrase inhibition demonstrates anti-fibrotic effects in vitro, ex vivo, and in vivo in preclinical pulmonary fibrosis models

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Idiopathic pulmonary fibrosis (IPF) is a progressive, chronic, and fatal lung disease with limited treatment options. While TGFβ signaling has been implicated, other pathways, particularly WNT/β-catenin and YAP signaling, contribute to IPF. Clinical data suggests that drugs affecting the TGFβ signaling pathway do not deliver robust or sustained efficacy and alternative strategies are needed. The post-translational modifying enzymes tankyrase 1 and 2 (TNKS1/2) are central regulators of WNT/β-catenin and YAP signaling pathways, making them potential therapeutic biotargets for IPF. Here we show that the specific small-molecule tankyrase inhibitor OM-153, while stabilizing the TNKS1/2 target proteins AXIN and AMOT, decreases WNT/β-catenin and/or YAP signaling activities and counteracts pro-fibrotic extracellular matrix synthesis and deposition in key preclinical models. *In vitro*, tankyrase inhibition reduces fibrogenesis induced by a pro-fibrotic cytokine cocktail in primary normal human lung fibroblasts, and matrix turnover in a human fibroblast "Scar-in-a-Jar" assay. Importantly, OM-153 enhanced the efficacy of Nintedanib in in vitro assays. *Ex vivo*, OM-153 treatment shows anti-fibrotic efficacy in precision-cut lung slices (PCLS) from IPF lungs and healthy lungs stimulated with the pro-fibrotic cytokine cocktail. *In vivo*, treatment with OM-153 reduces collagen deposition and improves fibrosis and injury scores, as observed by pathological inspection, in a mouse bleomycin-induced lung fibrosis model. Our studies uncover a potential therapeutic strategy for IPF based on tankyrase inhibition and the results provide a framework for further evaluation.

M17

Toll-like receptor agonists and interferons synergize to render human macrophages cytotoxic to cancer cells

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The ability of human macrophages to kill cancer cells and thereby participate in the antitumor immune response is controversial and remains poorly understood. To clarify this, we established a time-lapse microscopy-based assay to visualize and quantify the killing of cancer cells by human macrophages. Macrophages were differentiated in vitro from monocytes isolated from the blood of healthy donors. To activate the macrophages, we used various stimuli such as interferons (type I and II), a panel of toll-like receptor (TLR) agonists, and combinations of those. Activated macrophages and non-activated control macrophages were co-cultured with human breast, melanoma, and colon cancer cell lines expressing fluorescent proteins. The killing of cancer cells by activated macrophages was monitored over time and quantified by image analysis algorithms. A fluorescent caspase 3/7 probe was used to visualize apoptosis induction in cancer cells. We found that human macrophages can inhibit the growth and kill cancer cells. The anti-cancer activity of macrophages was only seen in activated macrophages and was dependent on the mode of activation. Interferons and some TLR agonists, when used as single agents, induced partial antitumor activity. In contrast, combinations of selected TLR agonists with interferons synergized to induce potent tumoricidal activity in macrophages. Imaging by holotomography revealed that killed cancer cells showed typical morphological features of apoptosis. Thus, two-signal (TLR agonist plus interferon) activated human macrophages can efficiently kill cancer cells of various origin. These results suggest a new strategy for cancer immunotherapy based on optimized activation of tumor-associated macrophages.

M18

A multi-omic approach to genetic variants in breast cancer: Insights from the Norwegian Breast Cancer Study

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Breast cancer (BC) is the most frequently diagnosed cancer globally. Genetic susceptibility accounts for five to ten percent of breast cancer cases, making it one of the most significant risk factors for the disease. Most genetic predisposition is believed to result from the combined effects of single nucleotide polymorphisms (SNPs). Individually, these SNPs increase risk by less than 1.5-fold but collectively contribute significantly to breast cancer susceptibility. Genome-wide association studies have identified susceptibility loci that cumulatively explain approximately 18.3% of the familial relative risk of BC, with a overrepresentation in non-coding regions.

This project aims to investigate BC genetic variants and their intricate connections to somatic gene regulation, shedding light on their roles in breast cancer. We aim to predict causal germline variants located in genetic regions known to harbour a higher proportion of variants with regulatory impacts in association to BC. Specifically, we will integrate multi-omic QTL layers to assess interactions in relation to BC variant causality.

The Norwegian breast cancer study (NBCS) dataset is based on 2,980 individuals and comprises of germline genotypes and somatic data, characterized of several finely curated omic layers. These somatic molecular layers include DNA methylation, gene expression, copy number alterations (CNA), micro RNA (miRNA) and long non-coding RNA (lncRNA). Cis- and trans-acting QTLs have been predicted using germline genotypes analysed with the different molecular layers from tumour.

Using the QTL mapper TensorQTL, we have replicated well-known BC cis-QTLs, and identified novel ones. We have identified 180 trans-acting QTLs (FDR <0.05) overlapping all five molecular layers. These preliminary results suggest that germline variants predict BC specific gene regulation in tumors. Such predictors may be essential for identifying treatment targets and the assessment of BC susceptibility.

M19

Blocking S100A9-signaling is detrimental to the initiation of anti-tumor immunity

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S100A9, a multifunctional protein mainly expressed by neutrophils and monocytes, poses an immunological paradox. In virus infections or sterile inflammation, it functions as an alarmin attracting innate immune cells, as well as mediating proinflammatory effects through TLR4 signaling. However, in cancer, S100A9 levels have been shown to associate with poor prognosis and lack of response to immunotherapy. Its expression by myeloid cells has been related to an immune suppressive phenotype, the so-called myeloid derived suppressor cells (MDSCs). Targeting S100A9 in cancer has therefore been proposed as a potential way to relieve myeloid-mediated immune suppression. Surprisingly, we found that blocking the extracellular TLR4 signaling from S100A9 using the inhibitor Paquinimod, resulted in increased tumor growth and a detrimental effect on anti-PD-L1 efficacy in the CT26 tumor model. This effect was caused by a reduction in the tumor immune infiltration to about half of untreated controls, and the reduction was made up of a 5-fold decrease in Ly6Chigh monocytic cells. The suppressive Ly6G+ myeloid cells compartment was not reduced by Paquinimod treatment, suggesting alternative mechanisms by which S100A9 contributes to myeloid-mediated suppression. Intratumoral injection of recombinant S100A9 early after mice inoculation with CT26 cells had an anti-tumor effect. These findings indicate an important yet understudied role of S100A9 as an alarmin and immune stimulatory signal in cancer settings, and highlight the potential to exploit such signals to promote beneficial antitumorresponses.

M20

Spatial metabolic profiling of bone marrow niches in multiple myeloma patients using imaging mass cytometry

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Multiple myeloma (MM) is the second most common hematological malignancy characterized by aberrant proliferation of monoclonal plasma cells in the bone marrow. Myeloma bone disease is present in approximately 80% of patients upon time of diagnosis, but it is still largely unknown why some patients never experience bone lesions. The spatial positioning of cells and structures within the bone marrow tumor microenvironment (TME) may influence cellular fitness and function by variable access to nutrients depending on location. Gaining a deeper understanding of the metabolic landscape within the MM bone marrow may give valuable insight into cellular TME interactions which may be important for disease development. Here, we obtained biopsies taken at time of diagnosis from patients with bone disease (n=55) and from patients without bone disease (n=10). Sections from each patient were processed and stained with an antibody panel targeting immune- and metabolic markers, before analyzed using imaging mass cytometry. We find that the bone marrow tissue can be structured into cellular neighborhoods defined by cell lineage and functional markers. Tumor plasma cells are located in unique cellular neighborhoods and differ by distinct growth characteristics and metabolic activity. In line with this, we find a highly vascularized focal plasma cell niche predominantly expressing markers related to OXPHOS. Interestingly, plasma cells from the focal niche are located closer to the bone in patients with bone disease when compared with patients without bone disease. Moreover, when comparing patient groups within the focal niche, we find that plasma cells from patients with bone disease exhibit higher expression of OXPHOS-related markers and a lower expression of glycolysis-related markers compared to plasma cells from patients without bone disease. In summary, spatial profiling of MM patients reveal distinct metabolic activity within the TME that may impact disease progression.

M21

Achieving Spatial Transcriptomic Data from Colonic Mucosal Compartments using FFPE Tissue and Laser Capture Microdissection

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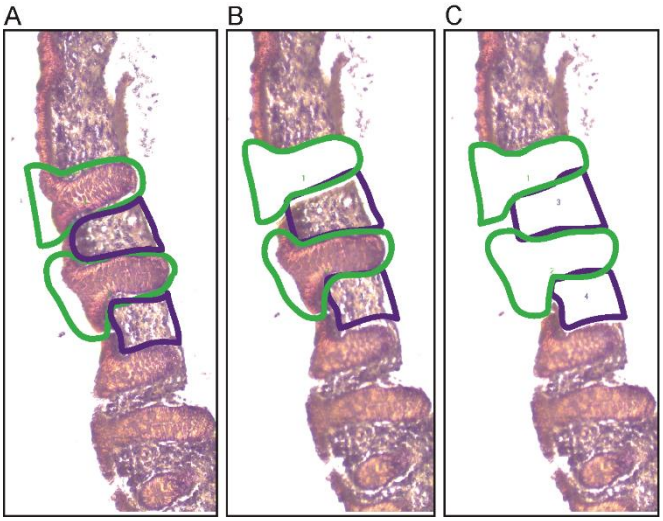
Inflammatory bowel disease (IBD) is a chronic condition marked by heterogeneous gastrointestinal inflammation. The colonic mucosa has a complex architecture with distinct functional compartments, where epithelial dysfunction precedes or results from immune dysregulation. Therefore, precise analysis of mucosal compartments is essential for understanding the cellular and molecular mechanisms driving disease pathogenesis. Laser capture microdissection (LCM) allows for targeted isolation of specific tissue regions for downstream RNS-sequencing, making it a valuable tool for spatial transcriptomics. LCM is compatible with both frozen and formalin-fixed paraffin-embedded (FFPE) tissues. While frozen sections provide superior RNA quality, they require specialized storage. FFPE tissues are valuable archive material and maintain excellent morphology, but hold challenges in RNA extraction due to fragmentation. Here, we present an optimized LCM protocol for FFPE colonic tissues. Our optimizations included adjustments to tissue preparation to achieve better visualization and shorter duration. Additionally, we provide a comprehensive overview of the best performing workflow and specific LCM software settings to collect sufficient tissue for RNA extraction and sequencing. Despite small amounts and compromised RNA quality from FFPE samples, analyses demonstrated clear separation of epithelial and lamina propria compartments (PC1 58.4%) and also inflamed and uninflamed tissue (PC2 7.8%), all with tissue-distinct and IBD relevant biological processes. To further validate the results and correlate in vivo and in vitro gene expression during colonic inflammation, we compared the epithelial data with transcriptomic data from stimulated epithelial organoids derived from exactly the same patients. These findings underscore the potential of using LCM-based spatial transcriptomics and FFPE-derived RNA for next-generation sequencing in studying IBD.



M22

CDK12/CDK13 inhibition disrupt transcriptional elongation and replication fork progression critical for glioblastoma survival

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Glioblastoma is the most prevalent and aggressive malignant tumor of the central nervous system. These highly heterogeneous tumors are marked by significant genomic instability and rely on a neurodevelopmental transcription factors-driven transcriptional program facilitated by RNA polymerase II (RNAPII). RNAPII dependent transcriptional cycle requires phosphorylation of key residues of its C-terminal domain (CTD) by transcriptional cyclin-dependent kinases (tCDK), including CDK12 and CDK13. Here, we show that glioblastoma stem cells (GSC) are exceptionally sensitive to pharmacological inhibition or genetic ablation of the tCDKs, which markedly reduces the proliferation of GSCs and patient-derived organoids. Furthermore, CDK12/CDK13 inhibition reduces GSC migration and invasive potential, as well as tumor growth in a xenograft mouse model. Mechanistically, CDK12/CDK13 inhibition leads to a specific and rapid, genome-wide loss of serine-2 phosphorylation of the RNAPII CTD in GSCs, thereby effectively abolishing the transcriptional elongation. In addition to abrogating the GSC transcriptional program, blocking CDK12/CDK13-mediated transcriptional elongation unexpectedly disrupts DNA replication without causing DNA damage. This novel approach based on targeting transcription to inhibit glioblastoma proliferation has the potential to be synergistic with replication-based chemotherapy strategies currently in clinical use, warranting further investigation into CDK12/CDK13 as therapeutic targets.

M23

Smashing the Limits of Single Cell Transcriptomics - Introducing Evercode

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Single-cell RNA sequencing (scRNA-seq) has seen exponential growth in the number of cells profiled per project, with increasing scope including biological replicates, time-course studies, and deep profiling of specific cell types. While conventional approaches face scalability constraints, combinatorial barcoding technology has enabled faster scaling. This method offers improved sensitivity, mappable reads, lower input requirements, and large increases in sample multiplexing and cell processing as well as being species agnostic. With the Parse Biosciences technology, we demonstrate the ability to process hundreds of samples and scale beyond 1 million cells in a single experiment, with compatibility for automation using standard liquid handling instruments. This approach democratizes large-scale scRNA-seq, setting a new standard and paving the way for transformative advances in single-cell applications.

M25

Miniaturization of T cell cultivation and utilization for process development

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The use of T-lymphocytes in adoptive cell therapy shows great promise for treatment of cancer, and an increasing number of cell therapies is being developed. The rapid increase in novel immunotherapies necessitate alternative approaches in process development, to increase capacity and provide opportunities for flexible production of a large variety of products. Good therapeutic cell manufacturing needs to encompass rapid production of the right type of cells, with optimal activity. Both T-cell quality and cellular subsets can have large impacts on therapeutic efficacy.
With in vitro cell expansion, resulting T-cell populations are heterogeneous with many subsets. Less differentiated populations of T-cells lead to a more persistent anti-tumor response. In particular, the memory stem-like T-cells (TSCM) have higher renewal properties and the ability to reconstitute the entire heterogeneity of memory T-cell subsets. However, we currently lack a complete understanding of how cultivation parameters impact the resulting T-cell populations, and current cultivation approaches provide for limited throughput and side-by-side comparisons of such conditions.
Here, we asked whether miniaturized high-throughput systems could be adapted to achieve screening of T-cell cultivation processes. Furthermore, we asked how process parameters traditionally measured manually (e.g. cell culture density) could be replaced by high-throughput-compatible analyses and automatic read-outs.
T-cell cultivation was optimized in microtiter plates, and the set-up was used to compare the impact of signalling molecules and other additions on T-cell proliferation and early memory markers. Robotic methods for cell processing and image-based high-throughput methods were developed for quantification of cell culture density, viability and specific T-cell markers. The established platform is generic and readily translatable for screening of a large number of process parameters and media components.

M26

Cell Encapsulation in Sulfated Alginate Beads for Therapeutic Applications in Type 1 Diabetes and Acute Liver Failure

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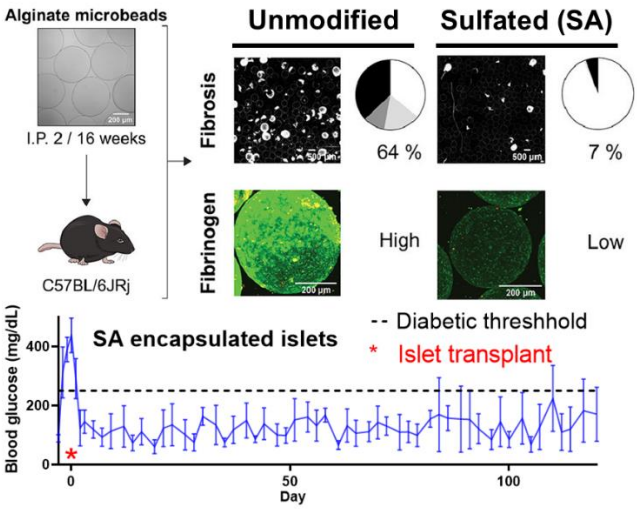
Introduction: Cell encapsulation is a promising approach for treating conditions such as type 1 diabetes (T1D) and acute liver failure (ALF). Alginate-based hydrogel beads are well-suited for encapsulation; however, their therapeutic efficacy is often hampered by the foreign body response and pericapsular fibrotic overgrowth (PFO). PFO compromises the viability and function of encapsulated cells. We demonstrate that chemically sulfated alginate (SA) mitigates PFO in mice and supports the sustained function of encapsulated islets (for T1D) in vivo and human pluripotent stem cell-derived hepatocytes (hPSC-Heps, for ALF) in vitro. Methods: Hydrogel beads (500–1000 µm) were produced from 1.8% (w/v) blends of high-guluronate (HiG) alginate and SA. Rat islets or hPSC-Heps were encapsulated, and both cell-containing and empty beads were implanted in mice. Diabetic mice received encapsulated islets, and glycemic control, oral glucose tolerance, C-peptide levels, and islet viability were assessed over 120 days. hPSC-Hep function was evaluated in vitro via ureagenesis and albumin secretion. Results: In mice, beads with SA showed a >9-fold reduction in PFO compared to unmodified HiG beads. SA beads containing hPSC-Heps exhibited minimal PFO, while HiG beads showed severe PFO. SA beads supported hPSC-Hep function in vitro. In diabetic mice, SA-encapsulated islets achieved long-term glycaemic correction, glucose responsiveness, high viability, and measurable C-peptide levels over 120 days. Conclusion: Sulfated alginate shows promise for therapeutic applications in cell encapsulation for T1D and ALF by mitigating fibrotic responses and enabling encapsulated cell function. Further validation in non-human primates would support progression toward clinical trials.



M27

Functional Analysis of LPA2 and LPA3 Reveals Their Essential Role in Photosynthetic performance in Diatoms

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The Low Photosystem II Accumulation 2 (LPA2) and 3 (LPA3) proteins are essential for the assembly and stabilization of photosystem II (PSII), facilitating the incorporation of CP43, a core antenna protein of PSII in plants and green algae. However, the role of LPA2 and LPA3 in organisms with chloroplasts derived from secondary endosymbiosis, leading to plastids with additional membranes, is still unknown. To investigate the role of LPA2 and LPA3 in secondary endosymbionts, we generated lpa2 and lpa3 knockout mutants of the diatom *Phaeodactylum tricornutum* using CRISPR/Cas9 technology. The mutants display an impaired photophysiological performance with reduced photosynthetic efficiency, photosynthetic capacity, and maximum light utilization coefficient compared to the wild type. Additionally, 77 K fluorescence measurements revealed that the PSII/PSI ratio of the mutants was approximately 1.5 times higher than that of wild type under both low light (LL) and high light (HL) conditions, indicating that the absence of LPA2 and LPA3 leads to increased preferential excitation energy transfer to PSII over PSI. These findings suggest that both LPA2 and LPA3 play a role in assembly of photosystems in diatoms. Ongoing proteomics analyses will provide further insights into the specific functions of LPA2 and LPA3 in diatoms.

M28

Can CRISPR-Cas9 mediated knockout of susceptibility genes in lettuce reduce the need for chemical pesticides against white mold in Norway?

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Pests and diseases destroy 20-40% of the world's plant-based food production and for some crops the losses are even higher. The primary strategy to mitigate these losses has been the application of chemical pesticides and the development of resistant plant varieties through conventional breeding techniques. However, despite the implementation of these measures, crop losses continue to remain persistently high. This is due to the fact that many pests have developed resistance to pesticides and adapted to the defense system of the resistant plant varieties. White mold (Sclerotinia sclerotiorum) is a fungal pathogen that may cause large yield losses for field grown lettuce. To develop white mold tolerant lettuce, we used CRISPR-Cas9 to knock out putative susceptibility genes that are induced by the pathogen in the early infection process. These susceptibility genes are induced by the pathogen to promote and succeed with the infection of the host. CRISPR-Cas9 mediated editing of one of the S. sclerotiorum responsive S-genes caused out-of-frame mutations that knocked out the gene function and reduced the necrotic lesions caused by the pathogen with more than 50 %, suggesting that it is a functional S-gene. Except from the intended mutation, we observed no off-target effects or foreign DNA in the genome of the edited lettuce plants. Such disease tolerant lettuce plants could potentially reduce yield losses and the need for chemical pesticides in Norwegian agriculture. However, gene edited plants although not containing any foreign DNA, are regulated as GMO's in Norway and has to go through a long and expensive regulatory process which makes it highly uncertain that such plants will enter the market.

M29

A trimeric coiled-coil motif binds bacterial lipopolysaccharides with picomolar affinity - and can be used in LPS detection and removal applications

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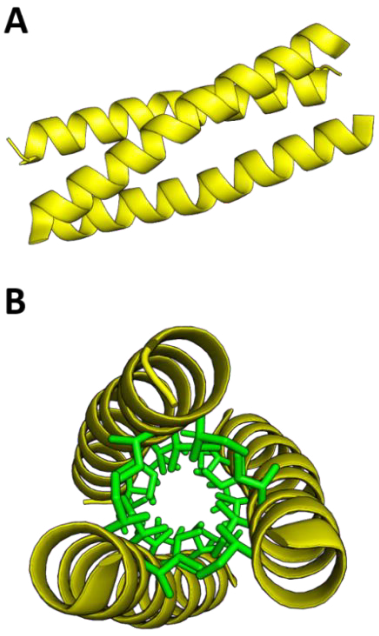
Modified coiled-coils sequences can be used in biotechnology, vaccine development, and biochemical research to induce protein oligomerization. A prominent model for the versatility of coiled-coil sequences is a 30-residue peptide originally derived from a yeast transcription factor, GCN4. In our lab, we have used these peptides extensively in recombinant protein work, especially regarding bacterial virulence factors such as non-fimbrial adhesins.
Unexpectedly, the trimerizing variant of this peptide, GCN4-pII, binds bacterial lipopolysaccharides (LPS) from different bacterial species with picomolar affinity. LPS molecules are highly immunogenic, toxic glycolipids that comprise the outer leaflet of the outer membrane of Gram-negative bacteria. They are the most prominent class of bacterial endotoxins - toxic cellular components of bacteria - and the terms LPS and endotoxins are often used synonymously.
Using scattering techniques and electron microscopy, we show how GCN4-pII breaks down LPS micelles in solution. In an ELISA-like assay, we find that LPS can in principle be detected in minimal concentrations, competitive to the industry gold standard for LPS detection, the LAL assay. Our findings thus suggest that the GCN4-pII peptide and derivatives thereof could be used for novel LPS detection and removal solutions with high relevance to the production and quality control of biopharmaceuticals and other biomedical products, where even minuscule amounts of residual LPS can be lethal. I will present possible biotechnological applications of our patented peptide, including possible emergency room treatments of sepsis patients whose symptoms are based on an LPS-induced cytokine storm.
Citations:
Hatlem et al., Front. Cell. Infect. Microbiol. 13, 2023
Uses, methods and products relating to oligomeric lipopolysaccharide binding proteins. D Hatlem, D Linke, SB Barbirz, US Pat
Figure:
Top view to GCN4-pII trimer bundle.



M30

RGD-alginate microbeads as scaffolds for structuring human pulmonary fibroblasts

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An in vitro lung alveoli model with pulmonary fibroblasts can be useful for investigating small-cell lung cancer. Alginate, a polysaccharide derived from seaweed, can form microbeads by dripping into a divalent ion solution. Here, we investigated the ability of RGD-grafted alginate microbeads to support the adhesion of primary human pulmonary fibroblasts (HPFa). We studied the effect of two adhesion peptides; linear RGD (linRGD) and cyclic RGD (cycRGD).
High MW alginate (68 % G, 237 kDa) (UPLVG, NovaMatrix, Norway) was oxidized to 8% before grafting with GRGDSP or RGD-(D-Phe)-K peptide (Caslo, Denmark) with reductive amination [1]. Alginate (1,8 % (w/V)) was used to form beads with an electrostatic droplet generator and a gelling solution of 50 mM CaCl2 and 1 mM BaCl2. HPFa were seeded on microbeads with 1.3 mM RGD. After three days of culturing the cells were stained for nuclei (DAPI) and actin filaments (phalloidin) before visualized with CLSM.
HPFa adhered to the cycRGD-alginate microbeads and spread on the bead surfaces, exhibiting a stretched morphology after three days of culturing. In contrast, HPFa did not adhere to the linRGD-alginate microbeads and clustered together. However, when seeding HPFa on flat linRGD-alginate gels, the cells showed increased spreading with higher gel stiffness, indicating that HPFa responds to linRGD as an adhesion ligand. To achieve successful adhesion and spreading on linRGD-alginate beads, additional Mn^{2+} ions in cell culture media were required alongside the linRGD adhesion ligand. Under these conditions, HPFa adhered to the beads and exhibited a stretched morphology after three days of culturing.
Hence, both cycRGD- and linRGD-alginate microbeads are promising materials for structuring HPFa. For HPFa on linRGD-alginate gels, increased spreading on linRGD-alginate gels was shown with increased gel stiffness, and Mn^{2+} in culture media was required for adhesion to beads.
1M. Dalheim et al (2016) Biomaterials, 80:146-56.

M31

Preparation of defined gellan oligosaccharides by a combined chemical and enzymatic depolymerization

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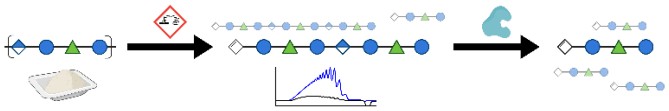
Complex polysaccharides from various sources have seen an increased usage as food additives, but their influence on gut health and biological fate is often not understood well to date. The same viscosity enhancing properties that are central to their application in the food industry complicate the analysis of the full-length polymer in the lab, which could be circumvented by the generation of oligosaccharides. The bacterial exopolysaccharide gellan gum is frequently employed in various food products, especially in Norway as a replacement for Carrageenan, but its role in modulating gut microbiota is still not well characterized. With its low solubility and the property to form hydrogels after heating, it is a suitable model for the generation of oligomers for diagnostic use. Gellan contains a repeating tetramer consisting of glucose, glucuronic acid, glucose and rhamnose. An optimized process of depolymerization was developed, beginning with a treatment with a strong base that invokes a β-elimination at the glucuronic acids, cleaving the polymer into multiples of the repeating tetramer. These soluble oligosaccharides were further degraded by a gellan lyase of the PL33 family, yielding the repeating unit tetrasaccharide. After purification by size exclusion chromatography, the tetrasaccharide was successfully employed to assay downstream degrading enzymes like unsaturated glucuronyl hydrolases. Furthermore, the currently ongoing approach entails labelling the defined oligosaccharide with fluorescent markers. Such glycoconjugates will provide a powerful tool for tracking its uptake in microbial communities. Ultimately, we aim to use both native and modified gellan oligosaccharides to dissect the enzymatic depolymerization of gellan and to obtain insight into the fate of gellan in complex microbial communities like the gut microbiota.



M32

Enzymatic production of long-chain aliphatic diacids as monomers for future plastics

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Polyethylene, the most widely produced plastic globally, accounts for approximately one-quarter of the total plastic production. While its exceptional physical properties make polyethylene indispensable, its non-hydrolyzable structure hampers biodegradation and currently renders enzymatic depolymerization and recycling impossible. This necessitates the development of novel materials with physical properties comparable to polyethylene while including functional groups that allow for hydrolytic cleavage and, thus, (bio)chemical depolymerization and biodegradation. A promising type of such polymers is the so-called aliphatic polyesters, which are synthesized through poly-condensation of linear long-chain diacids and short diols, such as ethylene glycol. Unfortunately, the required diacid monomers tend to be prohibitively costly. Here, we describe our current work towards producing long-chain aliphatic diacids through the terminal oxidation of saturated fatty acids using unspecific peroxygenases (UPOs). We evaluated the ability of 19 UPOs to produce fatty diacids, revealing considerable variation in product profiles and yields between the enzymes. One UPO was identified as the most promising candidate for further protein engineering to achieve gram-scale production of hexadecanedioic acid.

M33

Exploring NINJ1 in Mtb-induced cell death using genetically modified induced pluripotent stem cell (iPSC)-derived macrophages

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Regulated cell death (RCD) and inflammation are intrinsically linked and play key roles in defense against pulmonary infections, including Mycobacterium tuberculosis (Mtb), but with an accompanying risk of causing harmful inflammatory reactions. There is a need for models that can recapitulate the core features of the cell types found in the pulmonary tract. In recent years, induced pluripotent stem cells (iPSC) and iPSC-derived cells have been widely used in disease modeling, development studies and drug screening. The use of iPSCs-derived cells provides the stability of an immortalized cell line, overcomes issues with donor-to-donor variability and are more applicable for CRISPR-Cas9-mediated gene editing. Using iPSCs we have established a protocol for generation of macrophages (iMACs) and have established protocols for KO and KI of genes in iPSCs using CRISPR-Cas9. We have currently knocked out 3 different genes involved in cell death pathways – GSDMD, GSDME and NINJ1 in which we have focused on NINJ1 and its role in plasma membrane rupture (PMR) and cell lysis. Using genetically modified iMACs we have studied the role of NINJ1 in Mtb-induced cell death. RCD pathways have been shown to be induced in Mtb-infected macrophages, including ferroptosis, pyroptosis and necroptosis, but the role of NINJ1 in PMR during Mtb infection is still unknown. The release of LDH was significantly reduced in Mtb-infected NINJ1 KO iMACs compared to WT iMACs, to levels similar of Mtb-infected WT iMACs pre-treated with glycine. Furthermore, by using ligands for specific RCD pathways we found that LDH release was reduced in NINJ1 KO iMACs where pyroptosis and post-apoptotic lysis was induced. Using Mtb and ligands inducing specific RCD pathways we have found that Mtb can induce NINJ1-dependent PMR independently of the RCD pathways.

M34

Dissecting the regulation, structural dynamics, and physiological role of human Ninj1 activity during Mtb-induced cell death on a molecular scale

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Mycobacterium tuberculosis (Mtb) causes tuberculosis a leading infectious killer worldwide. Mtb primarily infects macrophages, leading to the death of some of these cells via distinct regulated cell death (RCD) mechanisms. While apoptosis facilitates Mtb elimination, necrotic cell deaths, like pyroptosis, necroptosis, and ferroptosis may enhance bacterial replication and spread. Mtb effectors, including the type VII secretion system ESX-1 and the cell wall lipid PDIM, induce host membrane damage, inducing necrotic cell death. Recently, it was shown that the plasma membrane (PM) protein Ninjurin-1 (Ninj1) facilitates final cell lysis in several cell death settings. Ninj1 oligomerization appears to occur after initial PM integrity disruption, yet the precise mechanisms governing Ninj1 activation and its role in Mtb-induced cell lysis remain unclear. Notably, we discovered that Ninj1 plays a crucial role during Mtb-induced cell lysis: Inhibition of all Mtb-induced RCD pathways independently or simultaneously does not prevent Mtb-induced cell lysis while depletion of Ninj1 mitigates Mtb-induced necrosis. To investigate how Ninj1 oligomerization influences cell fate and the inflammatory response, we will identify PM chemical and physical changes during RCD that correlate with Ninj1 oligomerization to elucidate its activation mechanism. Next, we will analyze Ninj1 dynamics and the functional impact of its macromolecular structures using DNA-PAINT super-resolution microscopy and long-term single-molecule tracking. Finally, we will determine whether Mtb activates Ninj1 via effector-induced PM damage and quantify the impact of this activation on the inflammatory response.

M35

Understanding the association between viral etiology, immune dysregulations, clinical and environmental factors in development of chronic lung disease in children in Nepal: Children's Lung Study in Dhulikhel, Nepal

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Tuberculosis (TB) remains a significant global health challenge. It is caused by *Mycobacterium tuberculosis* (Mtb), which infects 10 million people and claims 1.5 million lives annually, making it the world's leading infectious killer. Macrophages are the first cells infected by Mtb upon inhalation into the human lung and serve as a crucial niche for the bacterium throughout the infection.However, macrophages do not function in isolation; the alveolar microenvironment is believed to influence infection outcomes, underscoring the need for more complex infection models. We have recently established a tractable alveolus-mimetic co-culture model using induced pluripotent stem cell (iPSC)-derived macrophages and alveolar type 2 epithelial cells (AEC2) to study Mtb infection. This model bridges the gap between single-cell cultures, extensively used to characterize cellular responses to Mtb, and animal models, which allow for more comprehensive disease investigations.The cells are cultivated in an air-liquid interface, mimicking the physiological conditions of the lung alveoli. We have validated and characterized both cell types and the overall model using RNA sequencing and microscopy. This co-culture model enables the study of epithelial-immune cell crosstalk, hypothesized to be a critical factor in early Mtb infection. Additionally, we will provide a detailed characterization of Mtb infection within this model. Beyond TB, we aim to use this model to gain deeper insights into the lung alveolar microenvironment and to facilitate research on both sterile and infectious lung diseases.

M36

Investigating the effects of JAK-inhibitors on inflammatory responses in intestinal epithelial cells using IBD patient-derived colonoids

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Background and Aim: Janus kinase (JAK)- Signal Transducer and Activation of Transcription (STAT) pathway regulates epithelial and cytokine signaling and dysregulation of JAK-dependent cytokines impacts ulcerative colitis (UC) pathophysiology. JAK inhibitors are effective small molecules which disrupt this pathway. We investigated the effects of five different JAK/TYK2 specific inhibitors (Tofacitinib, Upadacitinib, Filgotinib, Deucravacitinib, and Brepocitinib) on patient-derived intestinal epithelial colonoids
Methods: Using colonoids and HT-29 cells, we assessed the effects of 5 JAK/TYK2 inhibitors on Interferon-beta, gamma and lambda 1 (IFNb, g, l1) induced pSTAT1/3 and pTYK2 levels through western blot. Bulk RNA sequencing was performed on colonoids pretreated with Upadacitinib/deucravacitinib and stimulated with IFNg, IFNl1, TNF and IFNg+TNF. Chemokine release was analyzed using multiplex assay and ELISAs.
Result: Type I, II, III IFNs demonstrated differential JAK-STAT pathway effects, with IFNb/g inducing stronger STAT1/3, and TYK2 phosphorylation compared to IFNl1. All inhibitors modulated STAT1/3 and TYK2, with Upadacitinib showing strongest STAT1/3 inhibition. Deucravacitinib specifically inhibited TYK2, while other JAK inhibitors unexpectedly enhanced the TYK2 activation at the lower doses. Transcriptomics analysis unveiled that IFNg, IFNl1, TNF and IFNg+TNF stimulated colonoids shared a distinct gene regulation pattern, while upadacitinib/deucravacitinib attenuated inflammation-associated response. Both upadacitinib and deucravacitinib inhibited epithelial chemokine release.
Conclusion: Our findings demonstrate distinct mechanisms of JAK/TYK2 inhibitors in colonic epithelial cells. The differential effects on STAT phosphorylation and chemokine inhibition highlight pathway-specific responses. Deucravacitinib and upadacitinib´s unique profile provides insights into their clinical efficacy in UC treatment.

M37

Decoding the intracellular complement system in human macrophages

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In recent years, a cell-autonomous and intracellularly active complement system has been identified as an important regulator of basic metabolic pathways underlying the function of immune cells. We have previously demonstrated that intracellular C5a signalling via a mitochondrial C5a receptor contributes to inflammasome activation upon sensing of danger signals in monocytes and macrophages. However, an intracellular role of complement component C3 in this cell type has not yet been established. To investigate the role of intracellular C3 in human macrophages, we have used CRISPR-Cas9 gene edited THP-1 cells lacking C3 and the C3a receptor (C3aR). Following stimulation with LPS, the C3 KO cells, but not the C3aR KO cells, showed a marked decrease in the release of several NF-kB-regulated pro-inflammatory cytokines, including TNF-a, IL-8, and IL-1b, compared to the wild-type cells. This effect was observed both on the mRNA and protein level, indicating that C3 may play a C3aR-independent role in the NF-kB signalling pathway. Supporting this hypothesis, preliminary data showed that phosphorylation of the IKKa/b complex, an activation step required for nuclear translocation of NF-kB, was strongly reduced in the C3 KO cells, but not in the C3aR KO cells. To further understand the mechanisms underlying these observations, we studied the activation of C3 in human monocyte-derived macrophages (MDMs). Using confocal microscopy and immunostaining with an antibody detecting a neo-epitope appearing on C3 split products following cleavage, we showed that intracellular C3 cleavage occurs in human MDMs, both in unstimulated cells and following inflammasome activation via LPS and nigericin stimulation. However, whether it is full-length C3 or one of its split products that regulates cytokine release in macrophages, remains to be determined. Overall, our data demonstrate that intracellular C3 plays an important role in mediating inflammatory responses in human macrophages.

M38

STING-ing CD4+ T cells to Death: The Role of the Innate Immune Receptor STING in Human CD4+ T

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The cyclic GMP-AMP synthase (cGAS)/Stimulator of Interferon Genes (STING) pathway plays a pivotal role in innate immune defense by detecting cytosolic viral DNA and triggering type I interferon (IFN) production. While extensively studied in myeloid cells, its role in T cells is less understood, despite evidence of high STING expression in T cells. Notably, STING signaling has been implicated in apoptotic CD4+ T cell death, but the underlying mechanisms remain unclear. Since STING-targeting therapies are being clinically explored, understanding its effects on T cells is crucial.

This study investigates the functional impact of STING signaling in primary human CD4+ T cells. We find that STING protein is expressed at higher levels in memory CD4+ T cells compared to naïve cells. Upon T cell receptor activation, STING expression is markedly upregulated within 24-72 hours. This upregulation is exclusively restricted to memory T cells and is previously undescribed.

To study functional consequences of STING signaling, CD4+ T cells were exposed to a small-molecule STING agonist. We observe downstream signaling through phospho-TBK1 and phospho-IRF3. High doses of STING agonist subsequently induce cell death, which we characterize as apoptotic based on expression of hallmark apoptotic markers such as caspase-7 and cleaved PARP1. Preliminary data in the project indicates that pharmacological inhibition of STING and TBK1 can reduce STING-induced T cell death.

In summary, our findings reveal that STING is upregulated in activated memory CD4+ T cells and, upon activation, triggers a TBK1-IRF3-dependent apoptotic pathway. These insights may shed light on the memory T cell effector functions and survival in highly inflammatory environments, such as cancer and severe infections, where STING agonists are abundant. In the long term, our results could highlight a therapeutic potential of STING pathway inhibitors in preventing CD4+ T cell death and lymphopenia under these conditions.

M39

Targeting Glutamate Transporters: A Translational Approach to Seizure Therapeutics

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Astroglial cells play a pivotal role in multiple brain processes. These range from maintaining metabolic homeostasis to regulating key aspects of brain development, fostering connectivity and computations within neural circuits. Accumulating evidence indicates that aberrant astroglial functioning contributes to the pathophysiology observed across diverse forms of epilepsy. Previously we demonstrated distinct calcium dynamics in neurons and astroglia transitioning from pre-ictal to ictal activity and upon photic stimulation in hyperexcitable networks. In pre-ictal periods neurons exhibited local synchrony, whereas astroglia were highly active with global synchrony. Generalized seizures, however, were marked by release of astroglial glutamate as well as a drastic increase of astroglial and neuronal activity and synchrony across the brain. Knocking out astroglial glutamate transporters led to recurrent spontaneous seizures, accompanied by massive astroglial glutamate release, overall resembling a neonatal form of epileptic encephalopathy. Currently, we are using a combination of genetic and pharmacological approaches to perturb astroglial calcium and glutamate signalling and glia-neuron interactions to further investigate their role in generation and spread of epileptic seizures. To achieve this, we utilize functional dual channel recording in zebrafish expressing neuronal and astroglial calcium indicators, as well as glutamate sensors in controls and seizure prone animals. Our results demonstrate altered astroglia-neuron interactions with changes in the spatiotemporal dynamics of astroglial calcium signals as brain excitability increases. Our perturbations of astroglial glutamate transporters alter these dynamics and the animals' seizure susceptibility, suggesting astroglia as potential targets in the development of novel therapeutical approaches.

M40

Exploring PCNAs regulatory role in stress

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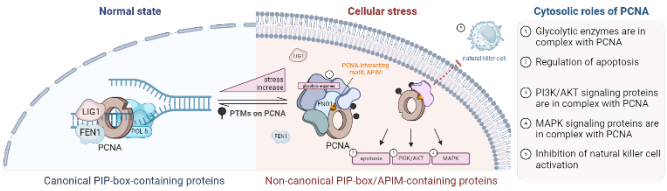
PCNA belongs to the highly conserved family of DNA sliding clamps and is a promising drug target in cancer. PCNA is primarily known for its canonical roles in replication and DNA repair. However, PCNA has been shown to have roles outside of replication, so called non-canonical roles. More than 600 proteins potentially interact with PCNA through two different PCNA interaction motifs: the PIP-box and APIM. Several proteins involved in stress responses contain APIM motifs and the affinity of PCNA for APIM motifs is increased upon stress. ATX-101, contains APIM and was developed in our group, blocks protein-PCNA interactions during stress, but does not inhibit normal replication. ATX-101 was well tolerated in a Phase 1 study. We have shown that the glycolytic enzyme ENO1 interacts with PCNA via an APIM motif. The ENO1-PCNA interaction is disrupted when cells are treated with ATX-101 or when the APIM motif in ENO1 is mutated. This affected the metabolite pools in glycolysis and PPP, including the nucleotide pools. Hsp70, which plays an important role in the formation of the purinosome, a multi-enzyme complex important for de novo purine synthesis, may interact with PCNA via its PIP-box. The significance of the Hsp70-PCNA interaction is under investigation, but our results, together with results implicating PCNA in regulation of both signaling and apoptosis, suggest a central role of PCNA in the regulation of homeostasis during stress. An important response to regulate cellular homeostasis is the integrated stress response. ISR shuts down global translation and initiates translation of specific stress-related proteins. Many translational proteins and two out of the four activation complexes of ISR, contain the APIM motif. We are currently investigating the regulatory role of PCNA in ISR. DNA sliding clamps are gaining interest as novel drug targets and understanding the non-canonical roles, such as roles in translation, may have huge therapeutic implications.



Poster Abstracts

P01

Ixazomib induces prolonged bone formation events in patients with myeloma bone disease: results from a single-center clinical trial

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Multiple myeloma (MM) is a bone marrow cancer often complicated by myeloma bone disease (MBD). In MBD, the bone remodeling homeostasis is severely dysregulated, leading to lytic bone destructions and loss of bone mass. MBD often causes fractures, pain, immobility, and reduced quality of life for patients. Proteasome inhibitors, commonly used cancer-targeting agents in MM therapy, have proven to have an off-target anabolic effect on bone. However, toxicities and side effects limit their long-term applicability as treatment for MBD, especially in patients in remission. Ixazomib is a new generation, orally administered proteasome inhibitor with tolerable side effects, but its long-term effect on MBD in unknown. In a single-center clinical study, we investigated the bone impact of ixazomib given for 24 months in 30 patients with MM in remission. Using a combination of serum bone markers, bone imaging, cell cultures, and histomorphometry, we closely tracked changes in bone metabolism. Our results show a sustained suppression of bone resorption markers in serum coupled with suppression of markers of bone formation. This was corroborated by an overall decrease in bone remodeling activity on NaF-PET/CT scans. Histomorphometry revealed an increase in very large bone structural units after just 3 months, sustained through the trial period, suggesting a net anabolic effect that may be mediated by sustained bone forming events, and associated to inhibition of bone resorption. We found no change in patient derived mesenchymal stromal cells' differentiation potential to bone forming osteoblasts, suggesting remodeling dependent stimulation of bone formation. The results of our trial demonstrate that ixazomib is well tolerated in the remission setting, inducing initial prolongation of bone forming events followed by sustained suppression of bone remodeling, leading to preservation of the newly formed bone and possibly preventing the advancement of MBD.

P02

Lignin degradation under denitrifying conditions by Pseudomonas Veronii

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As a result of fertilizer overload in agricultural farmland, excess fertilizer might leach to nearby water bodies, escalating eutrophication in these environments. One solution to combat this runoff fertilizer is to utilize pits/bioreactors filled with woodchips (lignocellulose) in which microorganisms break down the components in the wood while converting nitrate from the fertilizer to harmless nitrogen gas (denitrification). The underlying biology in this process is only scarcely studied, therefore we have isolated several bacteria from such pits for further study, among these *Pseudomonas Veronii*. The *P. Veronii* isolate had been shown to be a complete denitrifier, i.e., converting NO_3 step-wise to N_2 via NO_2, NO, and N_2O, while growing (slowly) on cellulose prior to the startup of these experiments. Here we tested the isolate for aerobic growth on multiple carbon sources and observed that P. veronii grew rapidly on Beechwood xylan, and slower on mannose, acetate, xylose, CMC, ferrulic- and vanillic -acid.

To check the isolate's ability to grow under denitrifying conditions we set up experiments aimed at monitoring growth (CO_2 production) while measuring gas production (NO, N_2O, N_2) to study the phenotype of the bacterium. Here we tested xylan and lignin because the bacterium had grown rapidly on xylan aerobically, and because whole-genome sequencing of the isolate showed genes potentially involved in lignin conversion. The results showed that growth on xylan was similar and equally rapid to that from growth on glucose. Growth on lignin was much slower; however, still exhibiting full denitrification, indicating that it was able to oxidize lignin although signs of growth was only limited. Samples for proteomics was taken throughout the experiment for later analysis. We expect that these results will provide new insight into anaerobic degradation of lignin in general and shed new light on how *P. Veronii* is involved in natural degradation of wood fibres in Nature.

P03

Towards an in vitro alveoli model: investigating cell adhesion to alginate microbeads in static culture

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Tissue engineering offers a promising approach in the development of an in vitro alveoli lung model, with a potential applications in investigations into small cell lung cancer (SCLC). Improved understanding of the SCLC growth could aid in the development of more effective therapeutic intervention. The in vivo microenvironment of lung tissue is a highly specialized three dimensional (3D) structure, where key aspects have to be mimicked to create a successful in vitro model.
In this project, alginate beads with a diameter of about 200 um were utilized to provide a 3D structure simulating alveoli. The microbeads were suitable for cell cultivation in static cultures. Achieving a functional model requires optimisation of the microenvironment, including conjugation of peptide motifs through reductive amination to facilitate cell adhesion. Further modifications involved cultivating the beads in cell media with varying cation concentrations.
Experiments were performed using primary human pulmonary fibroblasts (HPFa) and pulmonary epithelial cells from a cancer cell line (A549) in monocultures, over three days and seven days. The cells were initially visualized by light microscope and later with confocal laser scanning microscope (CLSM) after fixation and staining. The cells were stained for nuclei (DAPI), actin filaments (phalloidin), and ki-67 antibodies (proliferation).
The peptide with the highest degree of cell adhesion was the cyclic RGD peptide, where the beads exhibited the most extensive cells coverage for both HPFa and A549 independent of media type. Microbeads conjugated with linear RGD significantly enhanced cell adhesion for HPFa cells when cultivated in media with 0.5 mM Mn^{2+}. A549 cells also exhibited increased adhesion under these conditions, though to a lesser extent.
Future experiments include extending the culture duration in static cultures, and cultivating the cells in co-culture systems to enhance the models physiological relevance.

P04

Protein adsorption as a basis for fibroblast adhesion to alginate beads

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Alginate, a linear and unbranched polysaccharide derived from seaweed, can be tailored through enzymatic and chemical modifications to suit biomedical applications. Cell encapsulation in alginate hydrogel microbeads is a promising approach to provide immune isolation in cell therapy without immunosuppression in e.g. type 1 diabetes and acute liver failure. However, the efficacy is hampered by pericapsular fibrotic overgrowth (PFO), resulting in the loss of function in the encapsulated cells. Mitigation of PFO can be achieved by chemical modification to yield alginate with sulfate groups. Proteins adsorbing to the hydrogel surface can initiate PFO leading to the adhesion of macrophages and fibroblasts and the differentiation of fibroblasts into myofibroblasts. In this MSc project, that was recently initiated, we will investigate the adhesion of fibroblasts to alginate hydrogel beads based on different protein adsorbed on the hydrogel surfaces. We use high G alginate, intermediate G alginate and sulfated alginate to form hydrogel microbeads. High G alginate is known to provoke PFO, whereas both intermediate G alginate and sulfated alginate are known to result in minimal PFO. We fluorescently label proteins and study the adsorption of albumin and fibrinogen to the microbead surfaces by confocal laser scanning microscopy (CLSM), both after direct incubation and after exposure to complex mixtures such as serum or plasma, where differences between species may be relevant. We will study potential cell adhesion using normal human dermal fibroblasts (NHDFs) before and after exposure of microbeads to proteins. Additionally, we study the potential differentiation of fibroblasts into myofibroblasts by staining for alpha-smooth muscle actin (SMA) with TGF-beta induced cells as the positive control.

P05

Computational enzyme design

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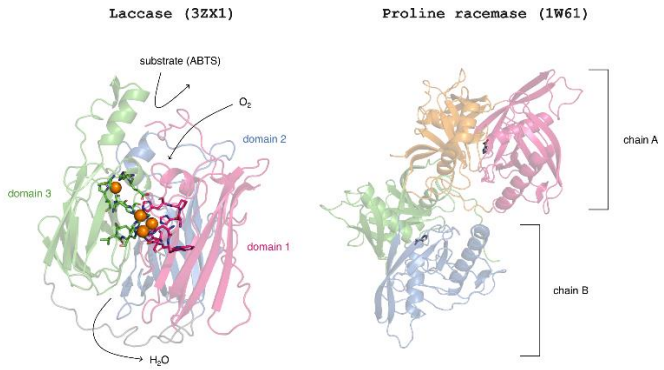
Enzymes are challenging systems to model with computational methods. Because of their size, they are often simulated with molecular dynamics (MD). However, such simulations cannot depict the chemical reactions accelerated by these enzymes because bond breaking and forming are not possible within MD since the method does not use explicit electrons. On the other hand, quantum mechanical (QM) methods, which allow the study of chemical reactions, are too computationally demanding for such huge systems as enzymes. Nevertheless, there are several methods somewhere in between such as EVB (empirical valence bond). We can firstly simulate chemical reaction in solution with QM and then take the results to calibrate EVB, which allows us to simulate the same reaction but in enzyme using only molecular mechanics.By running EVB at several temperatures, we obtain temperature dependence of enzyme activity. Such information is crucial for study and design of cold-adapted enzymes that are the main focus of our group. Currently, I am working on two enzymes – laccase and proline racemase. Laccase is a multicopper oxidase with many applications in industry and a promising biocatalyst in organic synthesis and bioremediation. Proline racemase catalyses isomerisation between L- and D-proline in bacteria and in Trypanosoma cruzi its secretion helps this parasite to avoid the immune system.



P06

The role of the cGAS-STING pathway in primary human CD4+ T cells

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The cyclic GMP-AMP synthase (cGAS)-stimulator of interferon genes (STING) pathway is an essential part of innate immunity. The pathway is found in many cell types and detects cytosolic DNA and DNA metabolites. Activation of the cGAS-STING pathway induces type I interferon (IFN) production but functions beyond IFN production have been identified.Most research on the cGAS-STING pathway has been performed in innate immune cells. However, T cells express high levels of STING, and for now little is known about the role of STING in T cells. Interestingly, it was reported that STING activation induced apoptotic cell death in T cells.We have studied the expression and function of STING in primary human CD4+ T cells beyond induction of cell death. We hypothesize that STING activation can shape the effector function of the CD4+ T cells that survive. We confirm expression of STING in primary human CD4+ T cells and are the first to describe a strong upregulation of STING in CD4+ T cells after T cell receptor (TCR) activation. The upregulation is mainly restricted to memory CD4+ T cells. In response to concomitant TCR and STING activation, we observed low levels of gene expression of IFN type I/III and after 48h IFN proteins were found in the supernatant. Effector cytokine production related to T-helper 1, T-helper 17, and T-regulatory CD4+ T cells, was found to increase in a dose-dependent manner after STING activation. Exposure to higher doses of STING agonist treatment decreased the expression of specific activation markers on CD4+ T cells. CD4+ T cells could be rescued from cell death by CRISPR/Cas9-mediated knockout of STING.In summary, STING signaling affects T cell effector functions, phenotype, and cytokine production, but can also induce apoptotic CD4+ T cell death. This might be relevant for CD4+ T cell functions in the highly inflammatory environment of cancer or infection and might explain lymphopenia in severe viral lower respiratory tract infections.

P07

TDG-Mediated DNA Demethylation in Hippocampus-Dependent Memory

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The dynamic regulation of DNA methylation (mC) and hydroxymethylation (hmC) is associated with various hippocampus-dependent memory processes. hmC, an oxidized form of mC, is an essential intermediate in the active DNA demethylation pathway. The oxidized hmC derivatives are eventually removed by the thymine DNA glycosylase (TDG) initiated DNA base excision repair (BER). Constitutive knockout or catalytic inactivation of TDG leads to embryonic lethality in mice, demonstrating an essential role of TDG in the epigenetic regulation of early development. However, we do not know whether TDG impacts the epigenetic plasticity and functional identity of terminally differentiated cells such as neurons. It remains elusive whether TDG-dependent removal of mC derivatives is required for encoding, associating, consolidating, and retrieving distinct memories. In this study, we utilized the Cre-LoxP system, specifically driven by the CamkIIα promoter, to achieve conditional knockout of Tdg in excitatory neurons in mice after birth. CamKIIα -miniTdg-/- mice exhibited marked TDG depletion in hippocampal neurons, initiated from postnatal day 19 (P19) and persisting into adulthood. The specificity of TDG deletion was characterized by immunohistochemistry, RT-qPCR, and Mass Spectrometry-based analysis of oxidized hmC derivatives such as fC and caC. Furthermore, we employed single-nuclei RNA sequencing (snRNA-Seq) with the cutting-edge split-pool combinatorial barcoding technology to profile transcriptomic differences in TDG-depleted hippocampal neurons at two postnatal time points: P19 (immediate after TDG depletion) and P30 (approximately 10 days post-depletion). Meanwhile, we established different behavioral tasks, including the Y-maze, Radial Arm Maze, and Fear Conditioning test, to evaluate the effects of TDG depletion on hippocampus-dependent memory processes. We aim to uncover TDG-dependent epigenetic mechanisms underlying hippocampal function in memory.

P08

Towards an in vitro alveoli model: Using alginate beads as a platform for culturing lung epithelial cells in a continuous flow system

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This project aims to develop a continuously perfused microreactor containing alginate beads and epithelial cells as a human in vitro alveoli model, with a long-term objective of creating a system suitable for lung cancer research. Our previous work has shown epithelial cell adherence to alginate beads chemically grafted with cyclic RGD-peptides. However, these models have not been thoroughly explored under continuous flow conditions. Incorporating continuous flow may offer greater similarity to in vivo environments by enabling consistent transport of nutrients and waste. Moreover, it allows for dynamic interactions, such as gradual changes to the medium and introduction of additional cell types, coupled with regulation of flow rate, thus providing a flexible platform. In this work, we demonstrate the operation of a perfused 3D-cell culture system. Alginate beads (≈200 and 500 μm) were produced, and key operational parameters were investigated, including optimization of packing densities, flow rate monitoring at varying packing levels, and bead displacement within the system chambers. We also showcase the system's functionality using epithelial cells seeded on a double layer of alginate-RGD microbeads (200 μm). Cell adhesion was observed with brightfield microscopy in the perfused system operating for 3 days. Future work will focus on extended culture times, more detailed investigations of cell morphology using confocal laser scanning microscopy, and incorporating additional cell types into the system to better replicate the complexity of the alveoli.

P09

Novel insights in late-Infantile Metachromatic Leukodystrophy through patient specific brain organoids

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Metachromatic leukodystrophy (MLD) is a rare genetic disease with autosomal recessive inheritance. It is caused by the mutations in ARSA gene that encodes arylsulfatase A (ARSA) protein. ARSA is essential for regulation of sulfatide metabolism. The mutations in ARSA gene causes either loss or severe reduction of ARSA protein thereby disrupting sulfatide metabolism. This causes accumulation of sulfatides in neural cells, particularly in oligodendrocytes, leading to dysregulation of myelin sheath, demyelination and consequently neurodegeneration. MLD is classified into 3 forms: adult, juvenile, and late-infantile with the latter being the most common and severe form. The clinical manifestation of MLD is characterized by cognitive impairment, and progressive loss of motor functions that eventually result in premature death. Despite detailed knowledge about the severity of disease, the underlying disease mechanism and insights into the pathological events accompanying MLD development are still incomplete. To unravel the pathomechanisms involved in MLD onset, we have established the patient-induced pluripotent stem cell (iPSC)-based brain organoid model. Briefly, PBMCs were isolated from MLD families i.e., carrier parents (control) and affected children. PBMCs were reprogrammed into iPSCs and further differentiated into mature oligodendrocyte-enriched brain organoids. The subsequent LC-MS/MS analysis of MLD and control organoids demonstrated disease-specific variation in the level of sulfatide species and ARSA activity, thus confirming the suitability of the model. To determine novel cell type specific pathways and mechanisms that characterize MLD, the mature organoids were subjected to scRNA sequencing analysis. The differences in the cellular organization of MLD compared to control has been assessed by immunofluorescence analysis of cell-type specific markers. In summary, we will present latest insights in the processes underlying MLD enabled by brain organoid model.

P10

Investigating the role of DEPDC1 in Asymmetric and Oriented Division of the cardiopharyngeal progenitors of Ciona

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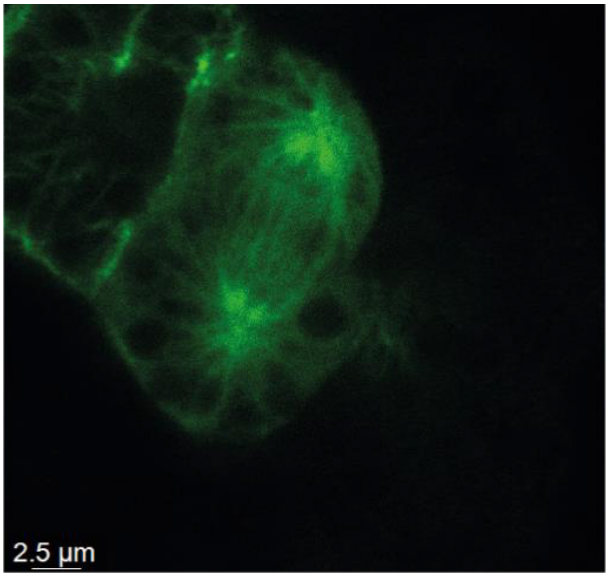
In Ciona, the asymmetric oriented division of cardiopharyngeal progenitors, aka trunk ventral cells, after migration is essential for the first heart vs. pharyngeal muscle fate choice. This study focuses on validating the biomolecular networks that control these divisions, as predicted from a broad CRISPR/Cas9 phenotypic screen, with a specific focus on DEPDC1, a RhoGAP protein. Knockdown experiments via CRISPR/Cas9 reveal that DEPDC1 deficiency leads to a shift from asymmetric and oriented divisions to symmetric and misoriented divisions. Our investigation extends to partners of Depdc1 that integrate polarity cues and mediate spindle positioning, including force distributions. To probe these functional modules, we are developing a suite of molecular tools, which includes optogenetic activators and inhibitors, custom nanobodies and biosensors. Additionally, we are developing tension sensors as a novel tool to directly measure these mechanical forces, enriching the quantitative analysis of spindle dynamics during division. These advancements will not only elucidate the role of DEPDC1 but also refine the genetic engineering toolkit available for Ciona. This research will provide crucial insights into the mechanical and genetic factors influencing asymmetric cell division in Ciona, with broader implications for understanding developmental processes and cellular mechanics.



P11

Predicting microbial traits from genome annotations

Eliah Hudgins (1), Miguel Teixeira (2), Daniel Machado (3).
NTNU (1), Dr. Daniel Machado (2)

The massive throughput of data from next-generation sequencing technologies enables the assembly of complete genomes from isolates, and the recovery of genomic content from uncultivated species, fostering a causal understanding of phenotypic traits, and enlighting that only a minor fraction of microbial diversity can be assessed through cultivation-dependent methodologies.
Despite the advances in sequencing technologies, genotype-phenotype associations remain constrained by the availability of data on the phenotypic counterpart, as the measurement of phenotypic traits under differential conditions, such as oxygen concentration or nutrient availability, lag under additional experimental challenges.
In previous work, specialized databases were integrated into a single resource linking taxonomic data and phenotypic traits to predict gram-staining and oxygen tolerance from genome features annotated with gene ontology terms (GOs) and gene ortholog groups (COGs, KOs).
This work leverages this resource to expand the prediction of phenotypic traits within a machine-learning framework oriented towards biological interpretability.
Such a framework discloses trait-determining features to screen phenotypic landscapes, providing a functional characterization of microbial species independently of their cultivability, enhancing our understanding of microbial diversity, and translating genomic data into actionable biological knowledge.

P12

Understanding the human health impacts of nano- and microplastics

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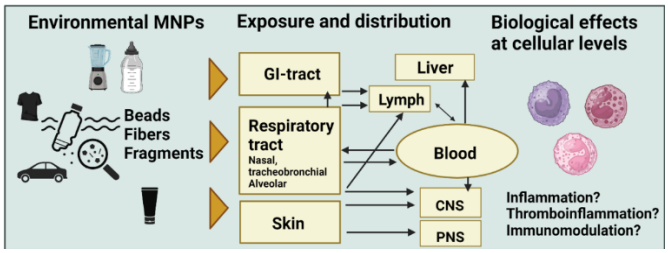
Plastic pollution has become an increasingly global concern, attracting both public and scientific attention. Evidence now demonstrates the pervasive presence of plastics in ecosystems, causing ecological harm and toxic effects. Plastics break down into micro- (1–1000 µm) and nanosized (≤1 µm) particles that accumulate in the environment. Humans are exposed to micro- and nanoplastics (MNPs) in increasing amounts through food and drink consumption, inhalation, and dermal contact. Recently, MNPs have been discovered in human placenta, blood, and heart tissue. The consequences of such exposure to human health are poorly understood. Early studies suggest that exposure to MNPs can induce inflammation, reproductive issues, and oxidative stress in animal models and *in vitro* human cell models.Our core objective is, through an interdisciplinary effort, to explore MNPs' impact on human health with a focus on the immune system. The team has established methods for producing and characterizing exposure-relevant MNPs derived from consumer plastics. Various types of environmentally relevant and pristine plastic particles will be explored in physiologically relevant *ex vivo* blood models depicting thromboinflammatory events of relevance in cardiovascular disease. Preliminary data from the exposure of pristine polystyrene plastic particles point to an increase in thromboinflammatory events, including increased coagulation and complement protein levels, as well as an elevated release of pro-inflammatory cytokines TNFα and IL-8. Plastic particle size and dose have been found to significantly influence the nature of the response.Our project aims to address critical knowledge gaps regarding the impact of MNPs on human health, particularly their effects on inflammation and coagulation.



P13

Regulation of (IFN-γ)-induced protein 10 by complement component C5

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(IFN-γ)-induced protein 10 (IP-10) is a cytokine expressed by a wide rangeof cells, including macrophages, in response to infection. IP-10 activates theCXCR3 receptor on T lymphocytes, macrophages and other immune cells, caus-ing recruitment to infection site and increased pro-inflammatory responses. Theinduction of CXCR3 also increases the secretion of IFN-γ in Th1 CD4+ T cells,which in turn induces higher production of IP-10. The effect is a self-amplifyingpositive feedback loop, highly amplifying IP-10 and its cellular responses.Complement component C5 is an important mediator of innate immunity, and isnormally expressed in immune cells in response to pathogens. Previously, a pa-tient with C5 deficiency was found to produce higher levels of IP-10. Experimentsdone on THP-1 cells have also shown increased levels of IP-10 in response to My-cobacterium tuberculosis infection. In this project, C5 was knocked down usingC5 siRNA in iMACs. These cells were then stimulated with TLR 4 ligand LPS,TLR 2/1 ligand Pam3CSK4, TLR 2/6 ligand FSL-1 and Mycobacterium tubercu-losis. THP-1 C5 knock-out cells were stimulated with LPS, LPS in combinationwith nigericin, and Mycobacterium tuberculosis. The expression and secretion of IP-10 in response to these stimulants were measured using RT-qPCR and ELISA.

P14

Innovative strategies to treat Parkinson's Disease: Addressing Complex I deficiency to alter disease course

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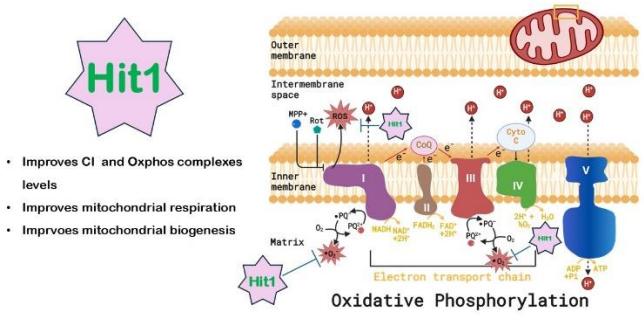
PD is currently the fastest-growing neurological disorder globally [1, 2]. Unfortunately, there are no disease-modifying therapies available that can delay, halt, or reverse the progression of this debilitating condition [1, 3]. Previous research has highlighted mitochondrial dysfunction - specifically, the quantitative and functional deficiencies of mitochondrial respiratory complex I (CI) - as a significant factor in the brains and possibly other tissues of individuals with PD [4,5]. Moreover, a recently reported subtype of idiopathic PD, which accounts for approximately 25% of cases, is characterised by severe and widespread neuronal CI deficiency [6], making it a crucial therapeutic target in PD. Patients with this subtype may particularly benefit from therapies to enhance mitochondrial health and function. Inspired by these findings, we have developed a cell-based screening platform and discovered a small molecule compound, Hit1, that upregulates the quantity of mitochondrial complex I and other key complexes involved in oxidative phosphorylation in SHSY5Y cells. In addition, the Hit1 treatment improves mitochondrial respiration, rescues mitochondrial morphology from rotenone toxicity and increases markers of mitochondrial biogenesis. These results suggest that Hit1 has multiple beneficial effects that could slow the progression of Parkinson's Disease, making it a promising candidate for further therapeutic exploration.

• Bloem et. al., The Lancet, 2021. 397(10291): p.2284-2303
• Ou et. al., Frontiers in Public Health, 2021. 9
• Athauda et. al., Nature Reviews Neurology, 2015. 11(1): p. 25-40
• Fløtnes et. al., Acta Neuropathologica, 2018. 135(3): p. 409-425
• Fløtnes et. al., Frontiers in Cell and Developmental Biology, 2022. 10
• Fløtnes et. al., Nature Communications, 2024. 15(1): p. 3631



P15

Purification and Characterization of Nitric Oxide Dismutases (NODs) and their Role in Anaerobic O_2 Production

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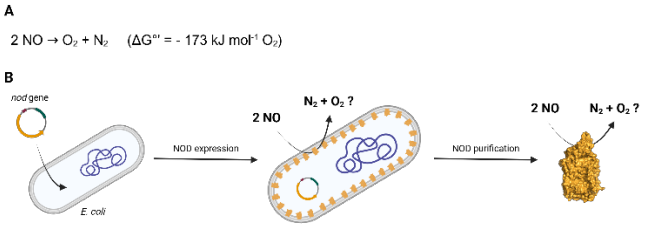
Nitric oxide dismutases (NODs) are integral membrane enzymes postulated to catalyse the dismutation of nitric oxide into molecular nitrogen and oxygen (Fig. 1A).1–3 With almost all the oxygen on earth produced by photosynthesis, this potential oxygenic denitrification is of significant interest, as it would correspond to a previously unknown pathway for oxygen production in the dark.4 In the last decade, many potential nod genes have been reported in different ecosystems and bacterial phyla, and oxygen production by Escherichia Coli transformed with an nod gene was shown.3 However, no NOD was ever purified and characterized. Therefore, we selected and ordered nine different nod genes reported in literature or detected in in-house samples collected from eutrophic lakes and field denitrification beds during previous work. The genes will be expressed in E. coli, followed by enzyme purification and characterization (Fig. 1B). If oxygen production by the NOD can be confirmed, it will be the first molecular evidence for these enzymes' postulated function and confirm earlier proposals for methane-, alkane- and benzene-oxidation in anoxia, as well as open up an avenue of novel uses for the produced O_2. Figure 1.A) Reaction scheme of nitric oxide dismutation. B) Scheme of the project plan.



P16

CRISPR-mediated editing of lettuce (Lactuca sativa for improved shelf-life and pathogen resistance

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Lettuce is a globally cultivated crop and holds a significant economic importance in the agricultural sector. However, cultivation of lettuce faces multiple challenges, including fungal pathogens such as S. sclerotiorum that can cause 20-70 % yield loss in field grown lettuce. Current plant protection practice involves using chemical pesticides, which can contribute to negative effects on the environment and development of pesticide resistant pathogens. Therefore, it is crucial to develop alternative methods to overcome these challenges and one such upcoming method is to use the genome editing tool CRISPR-Cas9, which allows targeted editing of the genome of many organisms, to develop disease tolerant crop plants. In this work we have used RNA sequencing to identify genes upregulated by *S. sclerotiorum* 24-48 hours after infection when the pathogen causes necrotic lesions in lettuce leaf tissue. We then utilized CRISPR-Cas9 to knock out two genes potentially involved in disease susceptibility and tissue browning. The aim of these knockouts was to increase the resistance towards pathogens and increase shelf life. Using PCR and Sanger sequencing, the CRISPR-mediated mutagenesis was confirmed, showing multiple different out-of-frame mutations causing knockout of the targeted genes. Further, phenotypical effects on resistance towards *S. sclerotiorum* was investigated using a detached leaf assay. This analysis showed that there is a statistically significant reduction of the brown, necrotic lesions surrounding the infection sites of lettuce with the mutated susceptibility gene, compared to the wildtype.

P17

A novel CELMOD targeting MYC and Mcl-1in Multiple myeloma

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MYC is one of the most attractive oncoproteins to target for cancer therapy, yet notoriously difficult to target directly and often thought of as "undruggable". Targeted protein degradation is emerging as a new modality of cancer therapy and is a promising strategy to remedy this notion. Multiple myeloma is a plasma cell malignancy that remains incurable, and despite a growing number of targeted cancer therapies there is still an urgent need for more.   In this study we synthesized a novel compound MP-1 by combining the 10058-F4 derivative #474b to the E3-ligase Cereblon binder Pomalidomide via a linker, intended to target MYC for degradation. We here show that human multiple myeloma and lymphoma cell lines are sensitive to MP-1 treatment shown by reduced cell viability measured by Cell-Titer Glo. On western blot we see that MP-1 induces downregulation of MYC protein level and that this effect is dependent on Cereblon and the proteasome. Through mass spectrometry analysis of multiple myeloma cell line IH-1 treated with MP-1 we found that known Cereblon neosubstrates like IKZF1/3 are downregulated with the same efficacy as Pomalidomide alone. We also discovered that it downregulates the protein level of Mcl-1, another oncoprotein highly important for myeloma cell survival. This was corroborated on western blot in both IH-1 and KJON-1 cell lines, where MP-1 treatment led to degradation of Mcl-1 and qPCR showed that Mcl-1 transcription was not effected.Taken together, we have synthesized a novel compound MP-1 that retains characteristics of its IMID compound, but also leads to degradation of MYC protein and possible new neosubstrates like Mcl-1.

P18

Continuous Imaging to Evaluate Growth and Drug Responses of Patient-Derived Colorectal Tumouroids

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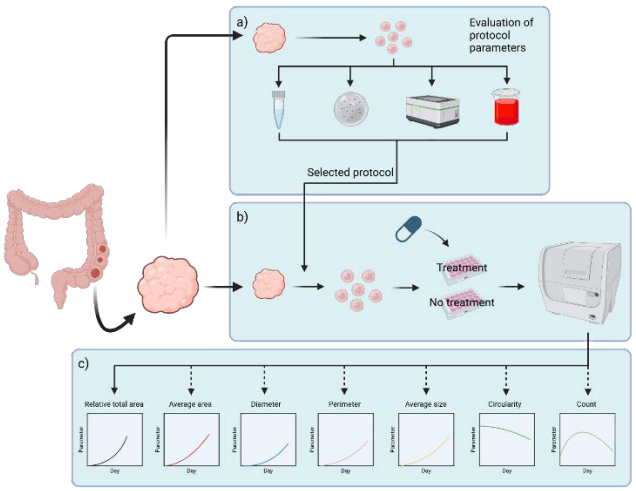
The use of patient-derived tumouroids (PDTs) is expected to have major implications in preclinical drug testing and clinical decision-support. However, data acquisition from these samples in drug screens is often limited by time-consuming procedures, scarce screening material, and destructive, single-parameter endpoint measurements. We seek to increase data collected from PDTs and here present a method for non-destructive, continuous image-based analysis of colorectal tumouroid growth and shape under chemotherapeutic perturbations, conducted within a clinically relevant time-frame. We assessed several readouts automatically derived from continuous imaging data and concluded that tumouroid growth, and the effect of growth-inhibiting drugs, can be robustly monitored by measuring the total tumouroid-covered area in images. We also found that measures of average tumouroid size, diameter, and perimeter provide complementary insights. Our tumouroid analysis method offers a strategy to maximise data extraction from non-destructive imaging techniques while preserving tumouroids for future research, all within a clinically relevant timeframe.



P19

Synthesis of fluorescently labeled gellan gum oligosaccharides for probing microbial uptake

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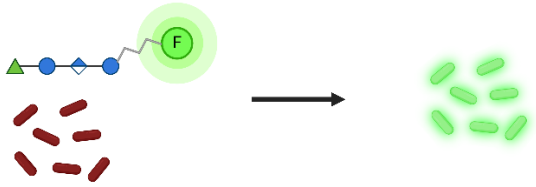
Gellan gum is a linear exopolysaccharide, with a tetrasaccharide repeating unit, produced by the bacterium Sphingomonas elodea and is commercially used as a stabilizing agent in various food products. Despite being used in foods, little is known about its biological degradation and its effect on gut bacterial communities. To identify individual bacterial strains involved in gellan degradation, we devised a method for making fluorescent gellan oligosaccharide glycoconjugates to be used in bacterial uptake assays.For this project, a defined gellan tetrasaccharide was produced using endoenzymes that cleave a specific β-1,4-glycosidic bonds in the gellan chain. The tetrasaccharide was purified using size exclusion chromatography and identified by matrix assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS). Multiple fluorescent labels, which attach selectively to the reducing end, such as carboxyfluorescein and anthranilamide, were synthesized in gram scale for generation of the gellan tetrasaccharide glycoconjugate. The purity and chemical structure of the labels were determined by NMR and MS. Before experimenting with the gellan tetrasaccharide, which was of limited abundance, a variety of the synthesized labels were attached to a model substrate, cellobiose. These model glycoconjugate compounds were utilized for probing a known gellan and cellobiose metabolizing bacterium, Sphingobacterium sp., to develop a robust method and workflow before labelling the gellan tetrasaccharide. The preliminary results showed differential bacterial growth, depending on the label.Ultimately, this method can be used to analyze the bacterial uptake of different polysaccharides providing valuable insight into how individual strains of the complex bacterial communities of the gut microbiota respond to specific substrates.



P20

Single Cell Spatial Genomics at the Nanoscale: Connecting Genomic Structure and Gene Regulation

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The spatial organization of the genome is critical for gene regulation. This is perhaps made most evident in genes regulated by distal enhancers that by some means must be brought into contact with the promoter regions with which they interact. The Cohesin complex structures the genome by creating DNA loops and has been found to be vital for the transcription of certain genes. Furthermore, nuclear positioning, for example by translocations of genes to nuclear speckles has also been demonstrated to enhance transcription. The molecular mechanisms coupling global and local structural alterations to transcription remains poorly understood.We employ highly multiplexed DNA-FISH, combined with RNA-FISH and protein labeling, to visualize genomic structures and link them to transcriptional activity in single cells. By focusing on super-enhancer-regulated genes with known associations to nuclear speckles, we aim to uncover the structural components underlying gene regulation. Our findings will provide mechanistic insights into how genomic architecture governs gene expression.

P21

Novel antibiotic peptides (BTPs) in the fight against antimicrobial resistance

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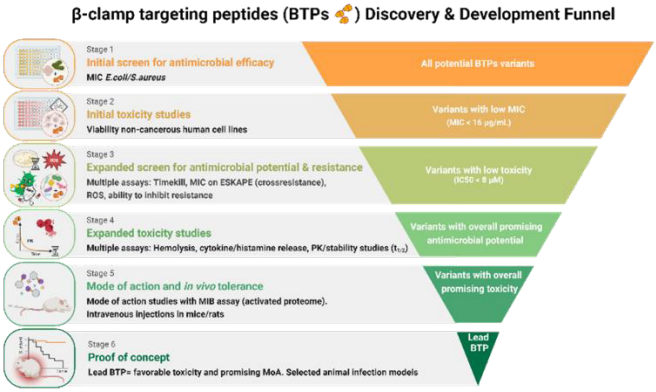
New antibiotics with new targets and models of action are urgently needed to combat antimicrobial resistance (AMR). A promising novel target is the bacterial DNA sliding clamp, the b-clamp, essential for replication. Betatide peptides (BTPs) have a novel target and new mode of action. BTPs demonstrate many promising characteristics for an antibiotic and can be used broadly, in combination or alone, when conventional antibiotics do not work. BTPs inhibit replication, are rapidly bactericidal towards bacteria, including multidrug-resistant ESKAPE species, and enhance the efficacy of other antibiotics. BTPs also inhibit mutagenesis and therefore reduce the ability of resistance development towards themselves but also towards conventional antibiotics. unlike most other synthetic antimicrobial peptides, BTPs exhibit good activity in full blood and in biofilms. BTPs are widely distributed in all organs and tissues and have low toxicity, supporting their potential as antibiotic for systemic use. We aim to develop 2nd generation BTPs that kill multidrug-resistant bacteria and hinder resistance development. these peptides will give new intellectual properties right (IPR) important for further development. We aim to select a lead BTP and demonstrate systemic proof-of-concept within 2025. BTPs are tested in multiple assays to study their antimicrobial efficacy against various bacterial strains and their potential to inhibit resistance development in vitro, as well as their toxicity to mammalian cells in vitro and in vivo. By using our development funnel strategy we have now identified several 2nd generation BTPs with overall improved activity while retaining the same mode of action as 1st generation BTPs, i.e., the same target (b-clamp) and mode of action (inhibit replication and translesion synthesis). BTP given intravenously reduces the colony forming units in blood in a CLP-sepsis model in rats supporting the further development for the use in bacteremia and/or sepsis.



P22

Characterization of novel unspecific peroxygenases with attractive properties for heterologous expression in bacteria

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Fungal unspecific peroxygenases (UPOs) represent attractive biocatalysts due to their activity on a wide range of industrially relevant substrates, including alkanes, primary alcohols and fatty acids. However, heterologous expression of these enzymes commonly results in low yields, especially when using bacterial systems. In this work we present novel UPOs that can be expressed in E. coli with yields up to 20 milligram of pure heme-saturated enzyme per liter of culture medium. The novel UPOs show peroxidase activity towards 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) and peroxygenase activity towards naphthalene and methanol, yielding 1-naphtol and formaldehyde, respectively. They are also able to hydroxylate saturated fatty acids, which is promising, e.g., for production of building blocks for enzymatically recyclable synthetic polyesters. Encouragingly, the enzymes showed activity in the presence of water-miscible organic solvents (e.g., 20 % (v/v) acetone). On the other hand, H_2O_2 tolerance seems to be a limiting factor for these novel UPOs. Tolerance to hydrogen peroxide, along with optimization of additional enzyme properties, could be curtailed by high throughput enzyme design and engineering, which is substantially more streamlined in *E. coli* compared to fungal systems.

P23

Genomics Core Facility, Facilitating Your Genomics Research

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The Genomics Core Facility (GCF) at NTNU offers state-of-the-art resources and services to support researchers in high-throughput genomics. As a part of the National Consortium for Sequencing and Personalized Medicine (NorSeq), GCF contributes to research conducted at NTNU, St. Olav`s hospital/HMN, other academic institutions and regional health authorities in Norway. GCF provides a comprehensive range of services across DNA-, RNA sequencing, and microarray analyses. Established applications include whole-genome sequencing, targeted resequencing (e.g., exome/panels), ChIP-Seq, metagenomics, and RNA sequencing types like total RNA, mRNA, smallRNA, and single-cell RNA sequencing (via 10X Genomics and Parse). The facility also offers advanced spatial RNA sequencing and DNA methylation array analysis, along with human and non-human genotyping services, utilizing Next Generation Sequencing (NGS) and Microarray technology. To enhance data quality and usability, GCF integrates bioinformatics expertise, offering consultation on experimental design, quality control, statistical analyses, data formatting, and visualization. Supported by Illumina instruments, including MiSeq, MiniSeq, NextSeq500, and NovaSeq6000, GCF ensures scalability for projects of any size. The highly qualified staff collaborates closely with researchers, providing tailored support from project planning to publication, fostering impactful discoveries across diverse disciplines.

P24

Structural and functional studies of enzymes involved in thiol-based redox pathways

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Low-molecular weight (LMW) thiols are involved in many processes in all organisms, playing a protective role against reactive species, heavy metals, toxins, and antibiotics, as well as serving as sulfur atom shuttles in phototrophic sulfur oxidizers such as *Chlorobiaceae*. *Actinobacteria*, including *Mycobacterium tuberculosis*, use the LMW thiol mycothiol (MSH) to buffer the intracellular redox environment, whereas Firmicutes, such as the clinically important pathogens *Staphylococcus aureus* and *Bacillus cereus*, use bacillithiol (BSH) as a defense mechanism. The NADPH-dependent FAD-containing oxidoreductase mycothiol disulfide reductase Mtr is known to reduce oxidized mycothiol disulfide (MSSM) to MSH, crucial for maintaining the cellular redox balance. Similarly, the enzyme Bdr functions as a reductase of oxidized bacillithiol disulfide (BSSB). We present the first crystallographic structure of Bdr, and propose a new disulfide reduction mechanism, backed by potentially gated channel, serving as a putative binding site for BSSB, as well as mutational studies underpinning the crucial stabilizing, but not redox-active role of a central cysteine residue. We have also solved the first structure of Mtr, which together with docking calculations provide insight into the putative binding site for MSSM. Lastly, we report enzymatic activity for a novel class of SAM-dependent natural-product methyltransferases (NPMTs), crucial for the biosynthesis of a novel BSH derivative, N-methyl-bacillithiol (N-Me-BSH), a physiologically important LMW thiol found across many bacterial classes. Our studies provide important structural and functional insight to the understanding of specialized NADPH-dependent oxidoreductases, as well as to the field of LMW thiols and cellular defense mechanisms, with potential implications for targeting distinct thiol-based redox systems in bacteria.

P25

Assessment of HRD to identify pathogenic variants in BRCA1/2

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According to the Norwegian cancer register, the cumulative risk for women to develop breast cancer before the age of 80, is approximately 10%. Despite high survival rate in Norway, 650,000 individuals died from the disease in 2022. Women with pathogenic mutations in BRCA1 and BRCA2 have a 70% life-time risk of developing breast cancer, and BRCA1/2 mutations account for about 20% of all hereditary cancers. Pathogenic variants in genes in the homologous recombination pathway impairs a cells' ability to repair double stranded DNA breaks, thereby resulting in homologous recombination deficiency (HRD). HRD, or genomic instability is seen in various cancers and a major factor in tumor development.Newly diagnosed women with breast cancer are offered genetic testing. Identifying pathogenic variants allows for preventive measures. However, genetic testing has limitations including the limited discovery of variants specific to the gene panel. Since pathogenic germline variants in BRCA1/2 can cause HRD in tumors, demonstrating this deficiency offers a supporting approach for identifying pathogenic variants.In this study, we aim to assess whether HRD can be used as a tool to identify pathogenic variants in BRCA1 and BRCA2. Our objective is to analyze breast cancer tissue from women who are strongly suspected of having a pathogenic BRCA variant that has not been identified. Since HRD analysis is conducted by a private laboratory in the United States today, we also want to develop a bioinformatic method for calculating HRD. Objectives: 1: Conduct whole exome sequencing (WES) on breast cancer tumors from the NeoLeteExte trial to establish bioinformatic methods to calculate HRD. 2: Conduct whole genome sequencing (WGS) on breast cancer tumors in women with a suspected pathogenic variant in BRCA1/BRCA2.

P26

Whole exome sequencing of estrogen receptor positive breast cancer tissue with cross-over neoadjuvant treatment

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Background: Breast cancer (BC) has long been the most common cancer among women in Norway. Since the Cancer Registry began documenting cases in the 1950s, breast cancer diagnoses have since then been doubled to 4,076 in 2023. Over 70% of BC patients exhibit an overexpression of the estrogen receptor (ER). Endocrine therapies for ER+ BC include aromatase inhibitors exemestane and letrozole, which suppress estrogen production by inhibiting aromatase enzyme from converting adrenal androgens into estrogens. Reduced estrogen levels promote tumor shrinkage, facilitating easier surgical removal. The Neoletexe trial explores the lack of cross-resistance between letrozole and exemestane taken at three time points in postmenopausal women with ER-positive breast cancer. Objectives: Identify coding mutations linked to resistance to aromatase inhibitors, with a focus on recurring mutations across multiple time points, that could potentially serve as predictive biomarkers. Methods: Isolation of genomic DNA from tumor tissue samples and quality and quantity assesment. Library preparation involves fragmentation of DNA, hybridization to extract exonic regions and amplification of captured fragments. The final library pool will be sequenced by whole exome sequencing (WES). Data will be analyzed using a pre-established bioinformatic pipeline and results will be interpreted.Research demonstration: This work provides insights into the molecular mechanisms driving tumor progression under aromatase inhibition. This research can facilitate the development of novel personalized treatment strategies, and prevent cross-over neoadjuvant resistance.

P27

Miniaturization of patient- and stem cell derived organoids – increasing throughput and reproducibility

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Traditional cell based in vitro models are hampered by the low translation from laboratory models to clinic – they are not sufficiently complex to replicate physiology nor produce results that predict the outcome in patients or organs after drug or chemical exposure. Recent developments in organoid technology opens for organotypic and more predictive models, however, organoid models are costly and require considerable time and effort to establish. Adding to the matter, high variations in sources of stem cells or tissue, variable procedures for generation of organoids, lack of reproducibility and relevant readouts urges the need for standardisation of organoid models. Using automated systems in organoid differentiation ensures precise timing and accuracy, reducing reliance on individuals and inter-laboratory variations. These methods can be easily adapted for different diseases and tissues by adjusting the settings and materials used. Here, we present approaches for miniaturizing cultures of patient-derived and stem-cell derived organoid models into 96- and 384-well microtiter plate formats and discuss their applications and challenges, using various tissues and cell sources, including colorectal cancer, inflammatory bowel disease, endometriosis and induced pluripotent stem cells. The established models are monitored and responses are measured by bulk and single cell methods, including viability, growth rate and morphology characterized by Cell painting. By using automated systems – organoid models can be miniaturized to increase throughput at reduced time - providing possibilities for increasing analyses and readouts from valuable tissues or stem cells. In safety testing for new drugs, or personalised medicine – this would allow for testing of larger drug libraries, drug combinations, concentration ranges or new formulations. In pathogenesis and organogenesis increased throughput would enable possibilities to study multiple mechanisms and dysfunctions.

P28

The TandemAb concept - Combining structural features of IgG with that of IgA enhances targeted killing of cancer cells

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IgG1-based therapeutics may eliminate cancer cells via Fc-mediated effector mechanisms, such as antibody-dependent cell-mediated cytotoxicity (ADCC) or complement-mediated cytotoxicity (CDC). However, there is a need for more potent formats, tailored for enhanced effector functions mediated by specific immune cells. While IgG1 has been shown to be a poor inducer of ADCC by polymorphonuclear leukocytes (PMNs), dominated by neutrophils, IgA engages FcαRI for efficient ADCC-induction. Despite this, IgA has not yet been explored clinically. One reason for this is its short plasma half-life, which is in contrast to IgG that is rescued from intracellular degradation by the neonatal Fc receptor (FcRn). Here, we present a new antibody concept that combine structural elements of IgA with that of IgG1. We show that this format, named TandemAb, results in favourable plasma half-life combined with efficient engagement of several effector molecules. For instance, IgA2-IgG1 tandem directed against human epidermal growth factor receptor 2 (Her2)-expressing cancer cells demonstrates enhanced capacity to induce ADCC-mediated killing compared to that of IgG1 or IgA2. In addition, enhanced on-target Fc:Fc hexamer formation was shown to potentiates CDC activity of IgA2-IgG1 tandem directed against CD20-expressing tumour cells. Thus, we report on a new antibody format with tailored plasma half-life and effector functions, which should be explored in the context of preclinical tumour model systems.

P29

OGG1 beyond Base Excision Repair

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8-oxoguanine (8oxoG) DNA glycosylase (OGG1) has shown to have a high affinity for C:C base pairs, along with its canonical target 8oxoG:C within double stranded DNA. Based on these findings we investigated OGG1's binding affinity towards the secondary DNA structure termed intercalated motifs (i-motifs). Here, we present a new method to study intercalated motif (i-motif) dynamics in real time using switchSENSE technology. Using this novel method, we were able to confirm OGG1s preference to bind to C:C base pairs as well as its epigenetic derivates over 8oxoG:C. Furthermore, switchSENSE was used to verify and monitor the formation of i-motifs by two independent approaches. After having established conditions for i-motif formation, we show that OGG1 is able to bind various tested i-motifs with a high affinity in the nanomolar range. This affinity persisted when we introduced epigenetic DNA modification within the i-motif forming sequence of one target. In fact, it appears that OGG1's affinity is moderately altered upon the introduction of epigenetic DNA modifications. This postulates a new role for OGG1 in regulation of i-motif dynamics, which could have a genome wide impact on genome regulation by influencing gene expression. The epigenetic DNA modification within the i-motif forming sequence could thereby further fine-tune this regulation.

P30

Structural and functional insights into bacillithiol disulfide reductase – A potential antimicrobial target

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Pathogenic bacteria employ various strategies to counteract oxidative stress imposed by human phagocytes during infections. In many Gram-positive Firmicutes, including clinically important pathogens like *Staphylococcus aureus* and *Bacillus cereus*, a key defense mechanism involves the antioxidant bacillithiol (BSH). The reduced pool of BSH, essential for its activity, is maintained by the NAD(P)H- and FAD-dependent enzyme bacillithiol disulfide reductase (Bdr), which reduces bacillithiol disulfide (BSSB). BSH plays several roles in bacterial survival, including the detoxification of reactive species, toxins, and antibiotics, as well as in biofilm formation and metal homeostasis. Importantly, BSH functions in protein *S-bacillithiolation*, a protective post-translational modification that prevents irreversible oxidative damage to proteins and upregulates redox defense systems during oxidative stress. Despite the importance of Bdr in maintaining BSH functionality, the exact mechanism by which it reduces BSSB remains unresolved. A central question has been whether BSSB reduction involves the conserved cysteine residue Cys14, a hypothesis challenged by structural data showing Cys14 in a position inaccessible to both FAD and BSSB. Here, we show that Cys14 in *B. cereus* does not directly participate in catalysis but instead plays a structural role by stabilizing the active site. Crystallographic structures of Bdr Cys14 mutants (C14A and C14S) reveal impaired stabilization of the FAD and NADPH cofactors. Furthermore, enzymatic assays show that the C14A mutant retains BSSB reductase activity, demonstrating that BSSB reduction proceeds independently of Cys14. These findings offer new insights into the functional role of Cys14 in Bdr and suggest alternative mechanisms for BSSB reduction, with potential implications for targeting BSH-dependent redox systems in pathogenic bacteria.

P31

CDK12/CDK13 Inhibition Disrupts DNA Replication and Cell Cycle in Cancer Cells

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Transcriptional cyclin-dependent kinases (tCDKs), including CDK12/CDK13, play a pivotal role in regulating transcriptional elongation by phosphorylating serine-2 (pSer2) on the C-terminal domain (CTD) of RNA polymerase II (RNAPII). Our group (Pandey) has previously shown that inhibition of CDK12/CDK13 disrupts the phosphorylation of serine 2 and transcriptional elongation in pancreatic cancer cells and glioblastoma, while sparing normal cells. Importantly, we have found that CDK12/CDK13 inhibition also impairs the cell cycle and DNA replication. Using EdU incorporation to mark S-phase cells, we observed a dramatic reduction in the number of replicating cells following 6 hours of treatment with CDK12/CDK13 inhibitors. This project aims to further elucidate the mechanistic effects of CDK12/CDK13 inhibition on DNA replication. We will investigate (A) which specific steps of DNA replication are compromised, (B) how replication timing is altered, and (C) the impact on the replication fork proteome. To address these questions, we will amongst other techniques employ DNA fiber assays, Repli-seq to profile replication timing, and iPOND (isolation of proteins on nascent DNA) with mass spectrometry to analyse changes in replication fork composition. Our findings will provide insights into the molecular mechanisms by which CDK12/CDK13 modulate DNA replication and contribute to transcriptional regulation, with potential opportunities for cancer therapies targeting these kinases.

P32

Transcriptomic and Proteomic Alterations in Colon of People with HIV: Different patterns in Immunological Responders and Non-Responders

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Impaired mucosal barrier function is a key hypothesis for the persistently low CD4+ T cell counts observed in immunological non-responders (INR) among people with HIV. To elucidate the molecular mechanisms underlying incomplete immune recovery in INR, we investigated gene regulation and protein expression in gut tissue samples from INR, immunological responders (IR), and healthy controls (HC). RNA-sequencing was used to analyze the transcriptome, while shotgun proteomic mass spectrometry examined the proteome in biopsies from the sigmoid colon(SC) and terminal ileum (TI). In the colon, 3326 genes were differentially expressed in INR compared to IR, whereas no significant differences were observed in the TI. Gene ontology analysis revealed that these genes in the colon were linked to adaptive immune response, RNA and protein metabolism, regulation, localization, and carcinogenesis. Deconvolution analysis indicated that these transcriptomic changes were not solely due to altered immune cell composition. Proteomic analysis supported these findings, showing greater differential protein expression in the colon than in the TI. Proteins identified in the colon were associated with adaptive immune signaling, tissue repair, cell signaling, and growth. These findings suggest that incomplete immune recovery in INR is linked to specific molecular dysregulations in the sigmoid colon. Targeting the identified pathways and macromolecules may provide a basis for adjuvant therapies to improve outcomes for INR.

P33

UNRAVELING THE IMPACT OF PRPF31-MUTATIONS IN RETINAL DEVELOPMENT USING RETINITIS PIGMENTOSA 11 PATIENT-DERIVED RETINAL ORGANOIDS

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Retinitis pigmentosa type 11 (RP11) is a hereditary retinal disease due to mutations in one copy of the pre-mRNA processing factor 31 (PRPF31) gene. RP11 symptoms usually manifest in early adulthood with impaired night vision, visual field narrowing, and central vision loss in the final stage. The disease is characterized by progressive cell death, primarily in the retinal pigment epithelial layer and, subsequently, the photoreceptor layer. Induced pluripotent stem cell (iPSC)-derived human organoids are powerful models for uncovering disease mechanisms and testing therapies. To study the effects of PRPF31 mutations in retinal development and RP11 disease progression, we are generating retinal organoids (RO) from RP11 patient-derived fibroblasts, reprogramming them into iPSCs and differentiating them into early-stage retinal organoids. Characterization of retinal markers throughout differentiation, from iPSC to mid-late RO, was performed via qPCR (not shown), single-cell RNA sequencing (scRNA-seq), and immunohistochemistry (IHC) and confirmed the presence of all retinal cell types in both patient- and healthy control-derived RO. ScRNA data from D27 organoids revealed significant differences in PRPF31 expression between control and patients in Photoreceptor precursors and multipotent retinal precursors. At the early development stage, the morphology of optic vesicles was not particularly affected. These data indicate that PRPF31 mutations have a minor impact on early retinal development. Subsequent characterization of the more mature RO by proteome, single-cell transcriptome, and IHC analyses of iPSC, early- and late-stage RO is ongoing in our lab and will provide new insight into the pathomechanisms driving visual loss in RP11 patients. Preclinical studies done in our lab with PYC therapeutics drug candidate VP-001 for RP11 show promising results with increased PRPF31 RNA and protein levels and stable or increased viability at low-dose one-time treatment.

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PARP3 modulates microglia functions in hypoxia-ischemia via proinflammatory MAPK pathway

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Perinatal hypoxic-ischemic encephalopathy (HIE) accounts for 25% of developmental pathologies in children. Understanding the events occurring during the acute phase of a stroke is crucial for mitigating the effects. Cell necrosis resulting from HIE triggers phenotypical changes in microglia, including amoeboid morphology, proliferation, and migration toward the damage site. Microglial functionality significantly impacts tissue damage. Oxidative stress from HIE induces DNA damage, activating the DNA Damage Response (DDR). Poly (ADP-Ribose) polymerases (PARPs) are important DDR signaling molecules. PARP-3, a lesser known variant, catalyzes mono (ADP) Ribosylation (MARylation), impacting transcription, RNA processing, cell cycle regulation, and chromatin organization. PARP3 may regulate proinflammatory mediator production in astrocytes, but its role in HIE immune responses is unclear.In this study, we used a Parp3-/- mouse model, an experimental disease model of neonatal HIE, and a Parp3-/- human microglia cell line (CHME3) to explore the role of PARP3 in immune responses to hypoxia-ischemia (HI).

P35

Therapeutic potential of oxygenase MINA in glioblastoma

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Glioblastoma remains the most prevalent and aggressive primary malignant brain tumour in adults, characterised by a poor 5-year survival rate of 5.3%. Existing treatments, such as temozolomide, have minimal effects and severe side effects, which underscores the urgent need for new therapeutic strategies. Our research aims to explore the JmjC-only 2OGoxygenase, MINA, as a promising therapeutic target for glioblastoma. Preliminary data highlights MINA's critical role in glioblastoma proliferation and survival, aligning with its identification as a Myc-target gene associated with poor prognosis in various cancers. Through this study, we aim to elucidate MINA's functional roles, examine the impact of its hydroxylase activity and localisation, and propose it as a novel druggable target. Our research will describe the significance of MINA's cellular localisation and enzymatic activity in gliomagenesis; and the mechanisms by which MINA facilitates glioblastoma proliferation, including transcriptome effects, ribosome biogenesis, global translation rates, and the translatability of the transcriptome. This project seeks to establish pre-clinical proof-ofconcept for targeting MINA, potentially leading to improved therapeutic strategies for glioblastoma treatment.

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The role of IL-32 in T cells in multiple myeloma

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Multiple Myeloma (MM) is the second most common blood cancer and is characterized by abnormal proliferation of malignant plasma cells in the bone marrow. Despite the introduction of several new treatment options over the past decade, MM remains incurable. The immune composition of the bone marrow is altered in myeloma, leading to an immunosuppressive microenvironment in favor of cancer progression. T cells are important for tumor control and MM patients with short survival after diagnosis are characterized by having dysfunctional and exhausted effector T cells and increased frequencies of regulatory T cells (Tregs). IL-32 is a pro-inflammatory cytokine expressed in T cells, but the role of IL-32 in T cells is not clear.
By analyzing single cell RNA data from bone marrow samples from MM patients, we found that IL-32 was expressed in all identified T cell subsets. The expression was higher in Tregs compared with other T cell subsets. Moreover, patients with short survival had higher expression of IL-32 in Tregs at relapse compared with patients with longer survival. To understand the role of IL-32 for T cell function, we depleted IL-32 in primary CD4 T cells, CD8 T cells and Tregs obtained from healthy donors. The effect of depleting IL-32 from the different T cell subsets on T cell survival, differentiation and migration was examined. Our results may shed light on the role of IL-32 for T cell function and a potential role in myeloma disease progression.

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Celular & Molecular Imaging Core facility at NTNU

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The Cellular & Molecular Imaging Core Facility (CMIC) provides a range of imaging services for biological and non-biological samples, both fixed and live cells, from tissue level to subcellular imaging and super resolution. Our services include immunohistochemistry, training in advanced imaging and processing/analysis of images. Here we present three examples of projects conducted at our facility:

Intestinal diseases studied by confocal imaging
The intestinal epithelium functions as one of the most important barriers in our body and is completely renewed every 3-5 days, which allows for rapidly repair upon damage. Importantly, dysregulation of intestinal epithelial (stem) cell biology may lead to a variety of diseases including infection, inflammatory bowel diseases (IBD) and cancer. The study of the intestinal epithelium during homeostasis and disease involves in vivo mouse experiments and in vitro studies of organoids.

STED microscopy of ASC speck inflammasome formation in mouse macrophages
A large number of molecules and structures, including crystals, can activate a signal complex of the innate immune system resulting in formation of NLRP3 inflammasome containing ASC specks and pro-caspase-1. Upon inflammasome activation the vast majority of ASC is aggregated into single dense specks in the cytoplasm. To study the formation of ASC specks, mouse macrophages C57 black/6 (B6) were stable transfected with ASC fused with the fluorescent protein mCherry or mCerulean.

The TLR4 adaptor TRAM controls phagocytosis of Gram-negative bacteria
Macrophages play an essential role in combating infections by phagocytosis and degradation of microbes. The formation of the phagosome is a receptor-mediated and actin-dependent process. In this study we found that silencing of the adaptor protein TRAM strongly reduced phagocytosis of E. coli, but not S. aureus. In conclusion, our data suggest that TRAM has a role in controlling phagocytosis of Gram-negative bacteria and the subsequent IFN-β response in macrophages.

Cellular & Molecular Imaging Core

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