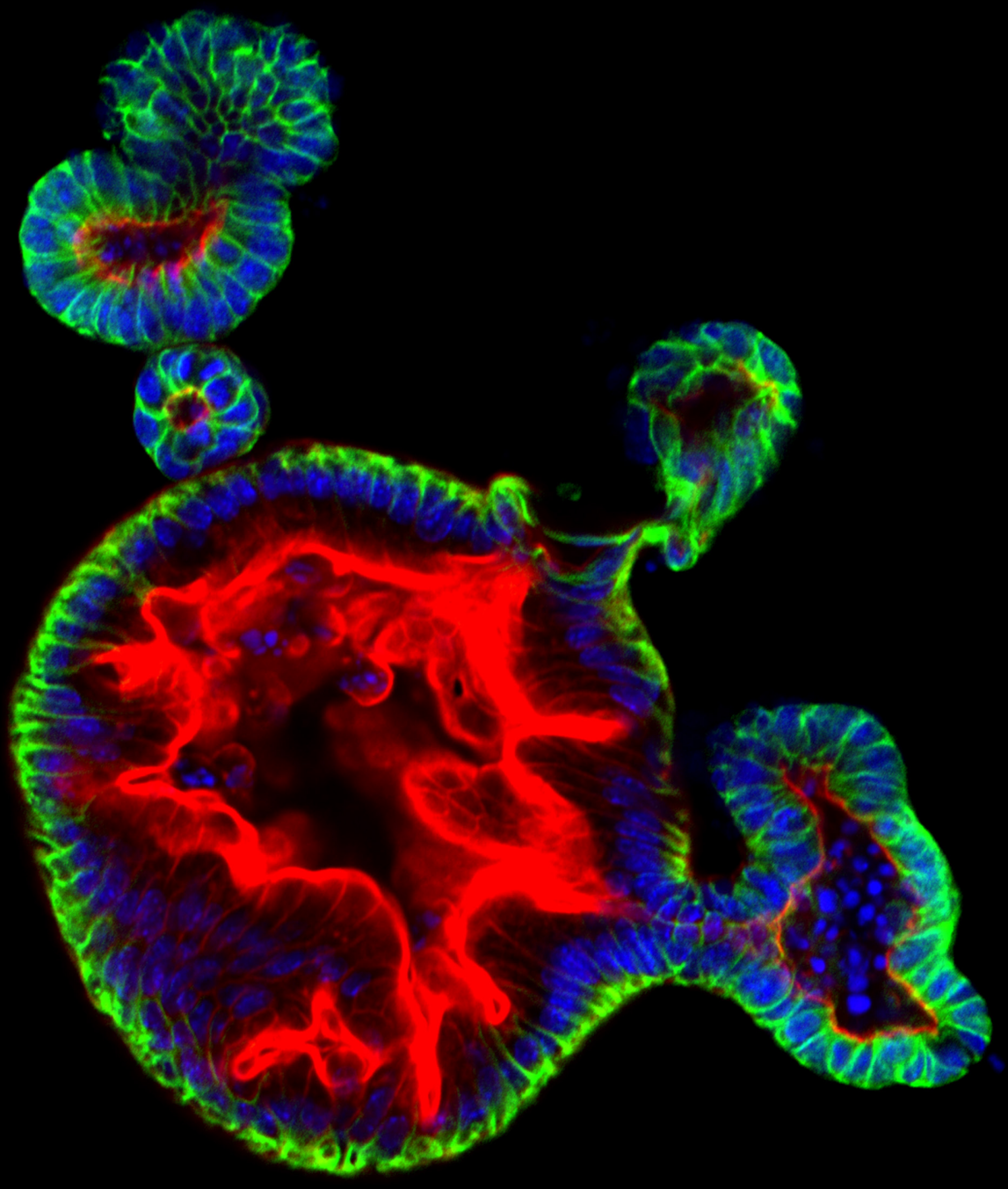
Norwegian Biochemical Society
55th Contact Meeting
Røros, Norway
24 - 27 January 2019



N:B:S

Norsk Biokjemisk Selskap

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Front cover image by Mara Martin Alonso, Centre of Molecular Inflammation Research (CEMIR), NTNU.

Small intestine organoid from mouse growing on matrigel, stained for E-cadherin (green), F-actin (red) and nuclei (blue). These organoids mimic the organisation and cellular population of the intestinal epithelium showing a crypt-like structure. The image was captured on a Zeiss confocal microscope at the Cellular and Molecular Imaging Core Facility (CMIC), Norwegian University of Science and Technology (NTNU).

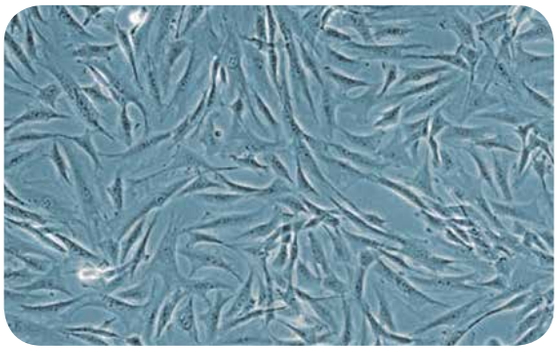
Come and speak to Johanna and Uniza from Nordic BioSite about

IHC Services
ELISA Kits
Antibodies
Sequencing
PCR
Nucleic Acid Isolation
Proteins
Sample Storage

Nordic BioSite
- in Life Science Research

Contents

PromoCell



PromoCell delivers human primary cells, stem cells and blood cells, as well as products for cancer cell culture, all of consistently excellent quality.

Our products are applied in several research fields including Cancer and Aging, Inflammatory and Infectious Diseases, Cardiovascular and Respiratory Diseases, Diabetes and Obesity, Immunology and Neuroscience.

You can source more information on our extensive range of cell culture and cell biology products by visiting our website: **www.promocell.com**

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Welcome to Røros and the 55th NBS Contact Meeting

Dear fellow researcher!

We would like to welcome you to the 55th Annual Contact Meeting of the Norwegian Biochemical Society (NBS), Røros! This year's meeting is organized by Norwegian University of Science and Technology. The meeting hosts more than 250 delegates from universities in Norway as well as several university colleges, biotech companies and grant agencies. We are very happy to welcome world-leading experts in developmental biology, immune system, signaling, immunotherapy, physiology, epigenetics, epitranscriptomics and autophagy. 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, institutes, schools and universities, a place to introduce new undergraduate 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 Norwegian scientists at the minisymposia and the poster sessions. We suggest that you look through this book and use it to plan which minisymposia and posters that 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. We have carried this practice further and hope for the traditional vigour in the bar, on the dancing 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:

Astrid Skjesol	Bjørnar Sporsheim
Ingrid Bakke	Sjannie L Nilsson
Kjartan W Egeberg	Lars Hagen
Lene M Grøvdal	Magnar Bjørås
Magnus Steigedal	Marit Otterlei
Tore Brembu	Trude H Flo
Trygve Brautaset	Vidar Beisvåg
Menno Witter	

Practical information

The venue

Surrounded by mountains in the UNESCO-protected town of Røros, Røros Hotell 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. The Røros Museum is a 10-minute walk away, and Røros Central Station is just over 1 km from the hotel.

Meeting Schedule

The meeting starts at 14:45 Thursday (24th of January). Registration is possible from 10:30 and onwards. The meeting ends after the banquet Saturday evening (26th of January).

Check-in and check-out

Check-in from 15:00 Thursday 24th. Check-out before 11:00 Sunday 27th. Late check out might be requested for NOK 100,-/hour.

Meals

Breakfast is served at the hotel Mondays - Saturdays 07:00 – 10:00, Sundays 08:00 – 10:30. All meals, except 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 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/auditorium 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.

Wireless Internet

Wireless Internet is available throughout the hotel and conference rooms.

Secretariat/Technical room

The secretariat is located at the reception of the conference area. The secretariat will be staffed during prior to plenary and minisymposium sessions and during the exhibition/poster sessions. You can download your presentations for plenary sessions and minisymposia here. Otherwise you have to be at the conference room at least 15 minutes before your session starts to download your presentation.

Website

The meeting website is available at: https://www.biokjemisk.no/contact-meeting-2019/

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". We kindly ask all plenary session speakers to deliver files with the presentations, preferably on a memory stick, to the organizers at least 15 minutes before the session in "Falkbergetsalen". If you want to use your own PC/Mac contact the Secretariat/Technical room in advance to make sure we can do the appropriate arrangements.

Minisymposia

Minisymposia will be held in parallel at 3-4 different locations at the conference area (Falkbergetsalen, Christianus, Sextus, and Kinoen) Thursday, Friday and Saturday. On Saturday "Plenumssalen" at the hotel will also be used. 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. If not you should be at the session room at least 15 minutes before the session starts downloading your presentation.

If you want to use your own PC/Mac contact the Secretariat/Technical room in advance to make sure we can do the appropriate arrangements.

Poster sessions

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

Thursday	*18:30-19:30 odd numbers (P1, P3…)*
Friday	*18:00-19:00 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 wine or soft drink, per person at poster sessions. The poster awards will be announced during the Banquet on Saturday.

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. On Friday night, there will be a live band, "**Jävlar På Kärlek**", 21:15-23:00 followed by a DJ. On Thursday and Saturday, the DJ will run the party.

Outdoor activities

In the program for Saturday it is reserved some time for outdoor activities and relaxation.

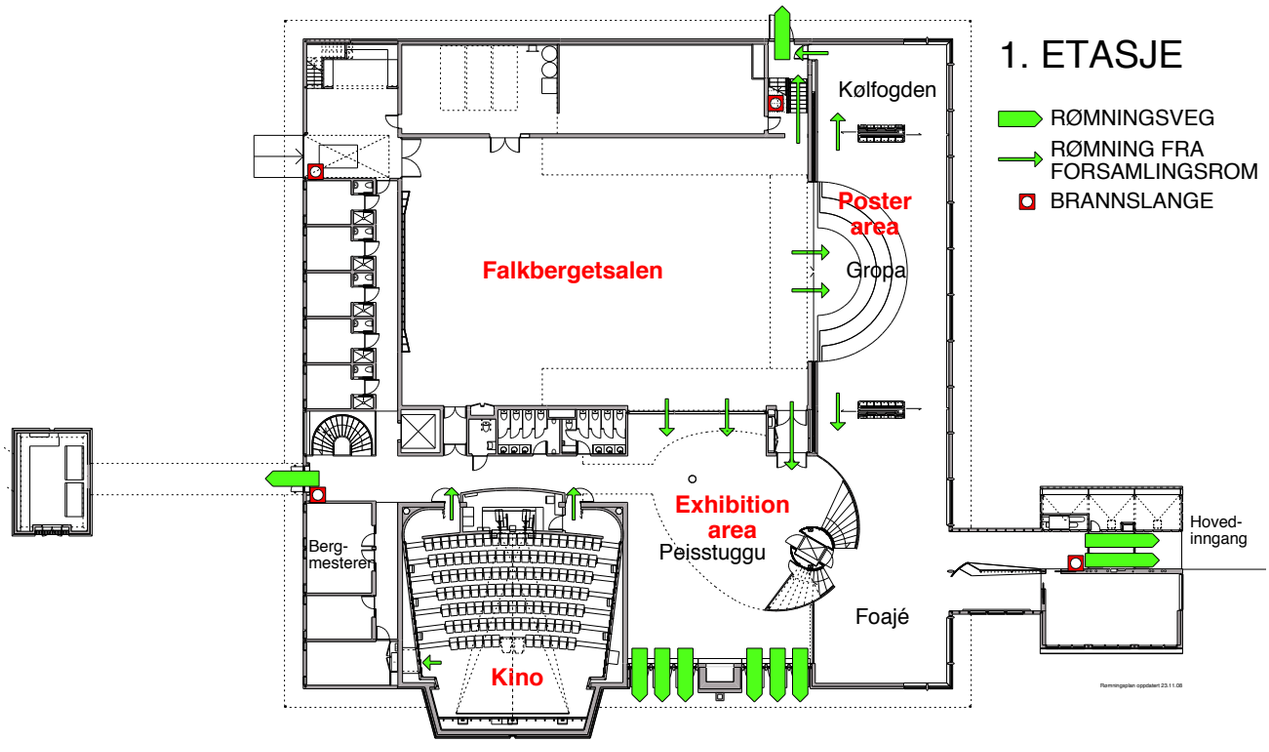
Guided tour in Olavs`s Mine (Olavsgruva) with underground concert
Guided tour through the mines Nyberget and Olavsgruva, 50 m underground and 500 m into the mountain, ending in Bergmannshallen where NTNU student/musician Even Brodwall will give a concert, playing with the amazing acoustics in the mines! https://rorosmuseet.no/olavsgruva
Time: Saturday 26th, 10:00 at the Hotel reception for departure by bus. Return for lunch at 12:00.
Price: Kr 150 per person.
Deadline for registration: Thursday 24th 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!

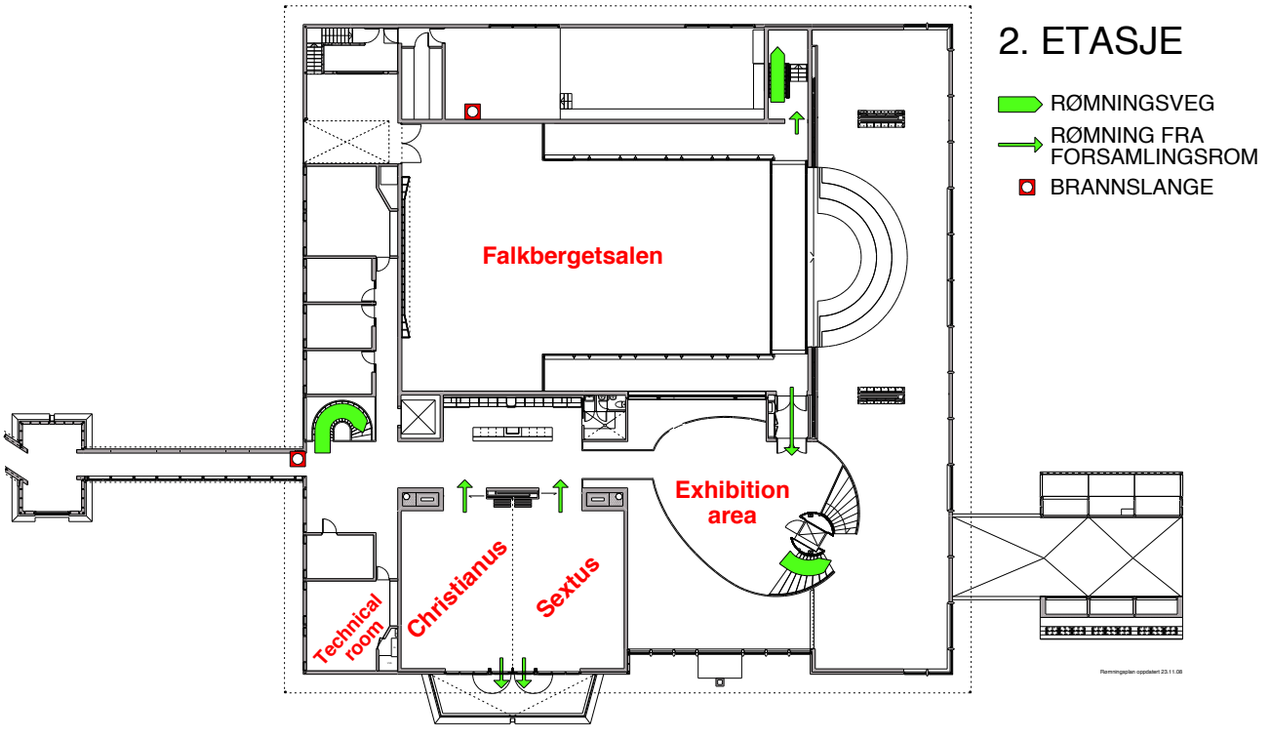
Updated information on other social activities will be presented daily on the information board at Røros Hotel.

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.

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

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


1. ETASJE
RØMNINGSVEG
RØMNING FRA FORSAMLINGSROM
BRANNSLANGE
Kølfogden
Poster area
Falkbergetsalen
Gropa
Exhibition area
Peisstuggu
Berg-mesteren
Foajé
Kino
Hoved-inngang


2. ETASJE
RØMNINGSVEG
RØMNING FRA FORSAMLINGSROM
BRANNSLANGE
Falkbergetsalen
Exhibition area
Technical room
Christianus
Sextus

Organizing committee

The meeting is organized by NBS members from the Norwegian University of Science and Technology (NTNU)

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Notice of the NBS general assembly

Innkalling til generalforsamling for Norsk Biokjemisk Selskap

Tid: lørdag 26. januar 2019 kl. 18:00

Sted: Røros Hotel, Røros

Dagsorden:

1. Godkjenning av innkalling og dagsorden.
2. Styrets beretning.
3. Kommandoen og møteklubba overføres fra president Aurora Martinez til president elect Klara Stensvåg.
4. Valg av generalsekretær elect.

   Basert på valgkomiteens nominasjon er styrets kandidat Magnus Steigedal, NTNU
5. Nye regler for utdeling av reisestipend?

   De siste åtte årene har NBS vært rundhåndet med å dele ut reisestipend, i og med at alle stipendiater og masterstudenter som har søkt, har fått støtte (inntil kr. 10 000 for Europa, ellers inntil kr. 15 000). De siste par årene har utdelingen vært begrenset til én gang pr. master/phd-periode. Hensikten med en liberal utdelingspolitikk var å redusere størrelsen på NBS fond.

   Fondet er nå nede i rundt kr 1 200 000, og generalsekretæren mener at det er på tide å redusere utbetalingen av reisestipender ytterligere, for om mulig å bevare fondet på den nåværende størrelsen. Dette kan oppnås på flere måter:

   - En grundigere vurdering av søknadene og tildeling av stipend til de beste.
   - Kreve at søkerne må ha vært NBS-medlem i minst ett år før søknaden.
   - Begrense stipendene til kun å være tilgjengelige for masterstudenter.

   Det er ønskelig med en diskusjon når det gjelder behovet for å redusere utdelingen av stipender og eventuelt en avstemning mellom alternativene ovenfor og andre forslag som måtte komme.
6. Halv pris for nye medlemmer som melder seg inn i høstsemesteret?

   Foreslått av Marte Innselset Flydal

   "Men - jeg synes at det med at årsavgiften for medlemskap i NBS gjelder for et kalenderår og ikke for et år fra sist betaling gjør at det har en bismak å verve medlemmer på høsten da det faktisk går fra veldig billig til en ganske dyr medlemsavgift (hvor billig det er å være medlem er nemlig et godt argument for å melde seg inn!)"

   Forslaget tas opp til avstemning.
7. Fellesmøter med andre organisasjoner og krav om NBS-medlemskap for deltakelse på Biokjemisk Kontaktmøte.

   Årets Kontaktmøte fungerer også som årsmøte for Norsk Fysiologisk Forening. NFF-deltakere har, grunnet et klart krav i NBS' statutter om at alle deltakere på Biokjemisk Kontaktmøte må være NBS-medlemmer, vært nødt til å melde seg inn i

NBS for å kunne delta. Sånn bør det vel ikke være, og styret foreslår derfor en endring av paragraf 1 i Statutter for Biokjemisk Kontaktmøte som følger:

Nåværende paragraf 1:

Generelle retningslinjer
Formålet med Biokjemisk Kontaktmøte er å fremme biokjemien i Norge ved å være et forum som er både faglige og sosialt skapende. Kontaktmøtet skal ivareta NBS medlemmers faglige interesse ved å invitere et utvalg foredragsholdere som representerer forskningsfronten innen sitt fagfelt, og samtidig er kjente for å være dyktige forelesere.
Innbetalt medlemskontingent til NBS er et absolutt krav for registrering og deltagelse på møtet.
Dersom flere melder seg på til Biokjemisk Kontaktmøte enn det er plass til, skal prioritet gis etter ansiennitet som medlem av NBS, og at møteavgift er betalt før fristens utgang.

Forslag til ny paragraf 1 (endringer er uthevet)

Generelle retningslinjer
Formålet med Biokjemisk Kontaktmøte er å fremme biokjemien i Norge ved å være et forum som er både faglige og sosialt skapende. Kontaktmøtet skal ivareta NBS medlemmers faglige interesse ved å invitere et utvalg foredragsholdere som representerer forskningsfronten innen sitt fagfelt, og samtidig er kjente for å være dyktige forelesere.
Innbetalt medlemskontingent til NBS er et absolutt krav for registrering og deltagelse på møtet. **Dette gjelder ikke dersom Kontaktmøtet er arrangert som et fellesmøte med en annen organisasjon. Det vil da være tilstrekkelig med medlemskap i denne organisasjonen.**
Dersom flere melder seg på til Biokjemisk Kontaktmøte enn det er plass til, skal prioritet gis etter ansiennitet som medlem av NBS, og at møteavgift er betalt før fristens utgang.

Orienteringssaker

8. FEBS-delegat Winnie Eskild redegjør for aktiviteten i FEBS-styret.
9. Rapporter fra lokallagene.
10. Kontaktmøtet 2020: Arrangementskomiteen fra Bergen forteller.
11. Arrangør av NBS Kontaktmøte 2021: Det er Tromsø som står for tur!

Eventuelt.

Blindern 22. desember 2018

Tom Kristensen, generalsekretær

Exhibitors and sponsors

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Liv Eggset Falkenberg
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Program overview

Thursday, 24th of January

10.30	**Registration**			
12.30	**Lunch**			
14.45	**Welcome: Magnar Bjørås (Falkberget)**			
15.00	**PL1: Keynote Lecture:** ***How fish colour their skin: A paradigm for development and evolution of adult patterns.*** **Christiane Nüsslein-Volhard**, Max Planck Inst. for Developmental Biology, Germany. Chaired by Trude Flo **(Falkberget)**			
15.45	**PL2:** ***Evolution of Mammalian Diving Capacity Traced by Myoglobin Net Surface Charge.*** **Michael Berenbrink,** Inst. of Integrative Biology, University of Liverpool, UK**.** Chaired by Sjannie L Nillson **(Falkberget)**			
16.30	**Exhibition**			
17.00	**Paralell Minisymposium Session 1**			
	1. Inflammation **(Falkberget)** Chair: Magnus Steigedal	**2. Biotechnology** **(Christianus)** Chair: Tore Brembu	**3. Biochemistry/ Structural Biology** **(Sextus)** Chair: Bjørn Dalhus	**4. Cancer** **(Kinoen)** Chair: Marit Otterlei
17.00	**M1.** ***Lysine-specific demethylase 1A (LSD1) as the master regulator of Paneth cell differentiation.*** Rosalie Zwiggelaar	**M5.** ***Production of acetoin from methanol in genetically engineered Bacillus methanolicus*****.** Eivind Bøe Drejer	**M9.** ***Characterization of the light-harvesting complex in the ALB3b knock out lines of the diatom Phaeodactylum tricornutum.*** Charlotte Volpe	**M13.** ***The APIM-peptide: A novel PCNA-targeting anti-cancer drug.*** Caroline K.Søgaard
17.15	**M2.** ***The TLR4 adaptor TRAM controls the phagocytosis of Gram-negative bacteria by interacting with the Rab11-family interacting protein 2.*** Harald Husebye	**M6.** ***Modelling in the molecular life sciences – Building a responsible modelling community.*** Rune Kleppe	**M10.** ***14F7, an antibody that recognise a tumour-specific ganglioside.*** Hedda Johannesen	**M14.** ***Preclinical efficacy of the MTH1 inhibitor karonudib in B-cell lymphoma.*** Thea Kristin Våtsveen
17.30	**M3.** ***Anti-proliferative and anti-inflammatory effects of inhibiting cytosolic phospholipase A2 in combination with calcipotriol for the treatment of psoriasis.*** Felicity J Ashcroft	**M7.** ***Developing methods for high throughput screening of 3D cell culture*****.** Hanne Haslene-Hox	**M11.** ***An insight into DNA scanning by DNA base repair proteins – a single-molecule approach.*** Ahrash Ahmadi	**M15.** ***Metalloproteinase (Mmp)-17 affects intestinal stem cell regeneration after irradiation in the intestine.*** Sigrid Hoel
17.45	**M4.** ***Invariant chain regulates endosomal fusion and endosome maturation.*** Azzurra Margiotta	**M8.** ***Inhibiting mutagenesis by targeting the DNA sliding clamps.*** Synnøve Brandt Ræder	**M12.** ***Regulation of protein synthesis through methylation of human eukaryotic elongation factor 1 alpha (eEF1A).*** Pål Ø. Falnes	**M16.** ***The role of PARP1 in cAMP-mediated induction of DNA-damage induced autophagy in pediatric acute lymphoblastic leukemia.*** Nina Richartz

18.00	**Exhibition**
18.30	**Poster Session 1 (odd numbered posters are presented)**
19.30	**Break**
20.00	**Dinner**

Friday, 25th of January

07.00	**Breakfast**
09.00	**PL3: The EMBO Keynote Lecture:** ***Imaging Immunity – Using Multiplex 2D and 3D Imaging to Develop a Spatiotemporal Understanding of Host Defense.*** **Ronald N. Germain,** Laboratory of Immune System Biology, NIH, USA. Chaired by Oddmund Bakke **(Falkberget)**
09.45	**PL4:** ***Using Protein Kinase Signaling of DNA Damage and Mitosis for Precision Cancer Medicine: Multi-Omics and Computational Approaches.*** **Michael B. Yaffe,** Center for Precision Cancer Medicine, MIT, USA. Chaired by Marit Otterlei (**Falkberget)**
10.30	**Exhibition**
11.00	**PL5:** ***Outsourcing cancer immunity to healthy donors.*** **Johanna Olweus,** K.G. Jebsen Centre for Cancer Immunotherapy, UiO, Norway. Chaired by Anne-Marit Sponaas **(Falkberget)**
11.45	**PL6: The FEBS National Lecture:** ***DNA Demethylation, Chromatin Plasticity and Cancer.*** **Primo Leo Schär,** Dept. of Biomedizin, Univesity of Basel, Switzerland. Chaired by Magnar Bjørås **(Falkberget)**
12.30	**Lunch**
14.00	**Paralell Minisymposium Session 2**

	5. Microbiology **(Falkberget)** Chair: Ingrid Bakke	**6. Physiology/ Neurobiology** **(Christianus)** Chair: Menno Witter	**7. Biochemistry/ Structural Biology** **(Sextus)** Chair: Trygve Brautaset	**8. Cell Biology/ Molecular Biology** **(Kinoen)** Chair: Lars Hagen
14.00	**M17.** ***The effect of rearing water treatments on the microbiota associated with cod larvae.*** Ragnhild I. Vestrum	**M23.** ***Biophysical and structural studies of a protein complex involved synthesis and vesicular packing of dopamine*****.** Svein Isungset Støve	**M29.** ***Interaction between the actin N-terminal acetyltransferase NAA80 and PFN2.*** Rasmus Ree	**M35.** ***Enhanced Antibody Validation.*** Marko Sankala
14.15	**M18.** ***Using the SpyCatcher-SpyTag technology for topology mapping of outer membrane proteins in Gram-negative bacteria.*** Jack C. Leo	**M24.** ***A germline homozygous mutation in human Oxidation Resistance 1 gene cause developmental delay, epilepsy and cerebellar atrophy.*** Xiaolin Lin	**M30.** ***Elucidating the role of co-chaperone DNAJC12 in neurometabolic disease.*** Marte I. Flydal	**M36.** ***Serum generates large scale contraction waves at epithelial edges.*** Stig Ove Bøe
14.30	**M19.** ***Global assessment of Mycobacterium avium subspecies hominissuis genetic requirement for growth and virulence*****.** Niruja Sivakumar	**M25.** ***Micro- and mesoscale dynamics of engineered neural networks in response to Parkinson´s related pathology*****.** Ioanna Sandvig	**M31.** ***Crystal structure of the second isoform of human phosphoglucomutase-1 (PGM1) and its substrate and product complexes.*** Paul Hoff Backe	**M37.** ***Cultured meat-a feeding strategy based on cell biology*****.** Sissel Beate Rønning

	5. Microbiology (Falkberget) Chair: Ingrid Bakke	6. Physiology/ Neurobiology (Christianus) Chair: Menno Witter	7. Biochemistry/ Structural Biology (Sextus) Chair: Trygve Brautaset	8. Cell Biology/ Molecular Biology (Kinoen) Chair: Lars Hagen
14.45	**M20.** ***Bacterial adhesion to living and non-living surfaces.*** Dirk Linke	**M26.** ***Coding mechanisms and neural plasticity in the olfactory system: Lessons we can learn from a miniature insect brain.*** Elena Ian	**M32.** ***FAM173B is a mitochondrial methyltransferase that targets mitochondrial ATP synthase to optimize its function.*** Jędrzej Małecki	**M38.** ***cPLA2α – a major fibrosis regulator and potent therapeutic target in chronic kidney disease*** Linn-Karina Selvik
15.00	**M21.** ***Deciphering the carbon distribution in metabolic pathways during antibiotic production by Streptomyces superhost strains using 13C-isotope-labeling experiments.*** Kanhaiya Kumar	**M27.** ***Spike characterization of olfactory local interneurons and projection neurons.*** Jonas Hansen Kymre	**M33.** ***CompACT: the complex N-terminal maturation processing of β-actin.*** Adrian Drazic	**M39.** ***Actin N-terminal acetylation impacts Golgi structural integrity.*** Tobias B. Beigl
15.15	**M22.** ***Insights into the role of modularity in lytic polysaccharide monooxygenase (LPMO) functionality.*** Zarah Forsberg	**M28.** ***Structure and function of individual projection neurons and centrifugal neurons in the male moth brain.*** Christoffer Berge	**M34.** ***NAD highlights new metabolic interplays between mitochondria and peroxisomes*** Magali VanLinden	**M40.** ***IAP antagonists shift human osteoclastogenesis to cell death.*** Ingrid Nyhus Moen
15.30	**Exhibition**			
16.00	**Paralell Minisymposium Session 3**			

	9. Cancer/ Immunology (Falkberget) Chair: Sjannie L Nilsson	10. Bioinformatics/ Genomics (Christianus) Chair: Vidar Beisvåg	11. Genome dynamics (Sextus) Chair: Hilde Nilsen
16.00	**M41.** ***There is a battle between the immune system and cancer. The Nobel Prize in Physiology or Medicine 2018*** Inger Sandli	**M45.** ***NorSeq: The Norwegian Consortium for Sequencing and Personalized Medicine.*** Robert Lyle	**M51.** ***Transcription-associated AAG-initiated base excision repair regulates gene expression.*** Barbara van Loon
16.15		**M46.** ***ELIXIR.NO - The national infrastructure for bioinformatics.*** Morten Rye	**M52.** ***Direct PCNA interactions via APIM are important for the RAD5 homologues' role in regulating DNA damage tolerance.*** Mareike Seelinger
16.30		**M47.** ***Online platform for biological network analysis in ELIXIR.*** André Voigt	**M53.** ***Mitophagy inhibits proteinopathies and cognitive deficits in experimental models of Alzheimer's disease.*** Evandro F. Fang

	10. Cancer/ Immunology **(Falkberget)** Chair: Sjannie L Nilsson	**9. Bioinformatics/ Genomics** **(Christianus)** Chair: Vidar Beisvåg	**11. Genome dynamics** **(Sextus)** Chair: Hilde Nilsen
16.45	**M42.** ***Cd74, invariant chain, a master regulator of the antigen loading compartment, the immunoendosome?*** Oddmund Bakke	**M48.** ***Genome-scale metabolic modeling: Metabolic engineering to increase production of nylon precursors in Pseudomonas.*** Christian Schulz	**M54.** ***Centromeres License the Mitotic Condensation of Yeast Chromosome Arms.*** Pierre Chymkowitch
17.00	**M43.** ***Uracil-DNA Glycosylase UNG1 Isoform Variant Supports Class Switch Recombination and Repairs Nuclear Genomic Uracil.*** Antonio Sarno	**M49. High-throughput screening identifies synergistic drug combinations in colorectal cancer cell lines.** Evelina Folkesson	**M55.** ***Synthetic lethality between DNA repair factors Xlf and Paxx is rescued by inactivation of Trp53.*** Sergio Castañeda Zegarra
17.15	**M44.** ***A role for immunoglobulins in the osteolytic bone disease of multiple myeloma.*** Marita Westhrin	**M50.** ***The Epigenetic landscape of two phenotypic extreme skeletal muscles - Soleus and EDL.*** Mads Bengtsen	**M56.** ***Genetic interaction between non-homologous end joining factors in mice and human.*** Mengtan Xing
17.30	**Exhibition**		
18.00	**Poster Session 2 (even numbered posters are presented)**		
19.00	**Break**		
20.00	**Dinner**		

Saturday, 26th of January

07.00	**Breakfast**
09.00	**Outdoor activities**
12.00	**Lunch**
13.30	**PL7:** ***Epitranscriptomic regulation in the mammalian nervous system.*** **Hongjun Song,** Dept. of Neuroscience, Perelman School of Medicine at the University of Pennsylvania, USA. Chaired by Magnar Bjørås **(Falkberget)**
14.15	**PL8:** ***Lysosomes as targets for cancer therapy.*** **Marja Jäättelä,** Inst. of Integrative Biology, University of Liverpool, UK**.** Chaired by Lene M Grøvdal (**Falkberget)**
15.00	**Exhibition**
15.30	**Innovation Session (Falkberget)** Chaired by Trygve Brautaset
15.30	**IS1:** ***How can you make the most impact out of your research results?*** **Tonje Steigedal,** NTNU TTO.
15.45	**IS2:** ***Can they, can I.*** **Inger Sandli,** Dept. of Biosciences, UiO.
16.00	**IS3:** ***The APIM-story; from discovery of a motif to medical application.*** **Marit Otterlei,** Dept of Clinical and Molecular Medicine, NTNU.
16.15	**IS4:** ***Designing small RNA-mediated gene.*** **Pål Sætrom,** Dept of Clinical and Molecular Medicine, NTNU.
16.30	**Exhibition**
17.00	**Paralell Minisymposium Session 4**

	12. Biotechnology/ Bioinformatics **(Christianus)** Chair: Marit Otterlei	**13. Epigenome/ epitranscriptome** **(Sextus)** Chair: Pål Falnes	**14. Cell Biology/ Molecular Biology** **("Plenumssal Hotell")** Chair: Lene M Grøvdal
17.00	**M57.** ***Use of OGG1 inhibitors to alleviate inflammation and treat cancer.*** Torkild Visnes	**M61.** ***Unraveling the functional role of Lsd1 in murine intestinal development.*** Emilie Kvaløy	**M65.** ***A structurally unresolved loop improves the affinity of an essential human NAD biosynthetic enzyme for its substrate*****.** Dorothee Houry
17.15	**M58.** ***The genes controlling citrate and spermine secretion in the prostate*****.** Morten Rye	**M62.** ***Dynamic epitranscriptomic marks; critical regulators of meiosis and the developing brain*****.** Arne Klungland	**M66.** ***Molecular mechanisms of ESCRT recruitment to damaged endolysosomal membranes*****.** Maja Radulovic
17.30	**M59. SynPromU - a new enabling technique for gene expression.** Lisa Tietze	**M63.** ***SMUG1 - a classical DNA glycosylase and an RNA processing enzyme*****.** Hilde Nilsen	**M67.** ***Critical Nodes of Viral Modulation Revealed Through an Integrated Network Analysis of Host-Virus Interaction Landscape.*** Korbinian Bösl
17.45	**M60.** ***Isolation and characterization of potential immune modulating proteins from Methylococcus capsulatus (Bath).*** Kristin Hovden Aaen	**M64.** ***Non-canonical roles of DNA glycosylases removing oxidative DNA base lesions in brain.*** Magnar Bjørås	**M68.** ***Esterases, "hubs" in biology.*** Lars Jordhøy Lindstad

18.00	**NBS General Assembly (Christianus)**	**NFF General Assembly (Sextus)**
19.00	**Break**	
19.30	**Reception**	
20.00	**Banquet (Falkberget)**	

Plenary speakers

Christiane Nüsslein- Volhard **PL1**

Professor
Max Planck Inst. for Developmental Biology, Germany

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How fish colour their skin: A paradigm for development and evolution of adult patterns

Colour patterns are prominent features of most animals; they are highly variable and evolve rapidly leading to large diversities between species even within a single genus. As targets for natural as well as sexual selection, they are of high evolutionary significance. The zebrafish (*Danio rerio*) displays a conspicuous pattern of alternating blue and golden stripes on the body and on the anal- and tailfins. Pigment cells in zebrafish – melanophores, iridophores and xanthophores – originate from neural crest-derived stem cells associated with the dorsal root ganglia of the peripheral nervous system. Clonal analysis indicates that these progenitors remain multipotent and plastic beyond embryogenesis well into metamorphosis, when the adult colour pattern develops. Pigment cells share a lineage with neuronal cells of the peripheral nervous system; progenitors spread along the spinal nerves. The proliferation of pigment cells is regulated by competitive interactions among cells of the same type. An even spacing involves collective migration and contact inhibition of locomotion of the three cell types distributed in superimposed monolayers in the skin. This mode of colouring the skin is probably common to fish, whereas different patterns emerge by species specific cell interactions among the different pigment cell types. These interactions are mediated by channels involved in direct cell contact between the pigment cells, as well as unknown cues provided by the tissue environment.

The colour patterns in closely related *Danio* species are amazingly different; their variation offers a great opportunity to investigate the genetic and developmental basis of colour pattern evolution in vertebrates. Exciting technical developments of the recent years, especially next-generation sequencing technologies and the novel possibilities of genome editing with the CRISPR/Cas9 system, allow to easily expand from model organisms into other species and directly test the function of genes by targeted knock outs and allele replacements. Thus, models and hypotheses about pigment pattern formation derived from zebrafish can now be tested in other *Danio* species. These studies will lay the foundation to understand not only the genetic basis of colour pattern variation between *Danio* species, but also the evolution of colour patterns in other vertebrates.

References:

Irion, U., Singh, A. P. and Nüsslein-Volhard, C. (2016): The developmental genetics of vertebrate colour pattern formation: Lessons from Zebrafish. Current Topics Developmental Biology, http://dx.doi.org/10.1016/bs.ctdb.

Nüsslein-Volhard, C. and Singh, A. P. 2017, Bioessays 39: 3, March 2017

Michael Berenbrink

PL2

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Evolution of Mammalian Diving Capacity Traced by Myoglobin Net Surface Charge

Scott Mirceta (Liverpool University, United Kingdom), Anthony V. Signore (University of Manitoba, Winnipeg, Canada), Jennifer M. Burns (University of Alaska, Anchorage, United States), Andrew R. Cossins (Liverpool University, United Kingdom), Kevin L. Campbell (University of Manitoba, Winnipeg, Canada)

Extended breath-hold endurance enables the exploitation of the aquatic niche by numerous mammalian lineages and is accomplished by elevated body oxygen stores and adaptations that promote their economical use. Little, however, is known regarding the molecular and evolutionary underpinnings of the high muscle myoglobin concentration phenotype of divers. We use ancestral sequence reconstruction to trace the evolution of this oxygen-storing protein across a 130-species mammalian phylogeny and reveal an adaptive molecular signature of elevated myoglobin net surface charge in diving species that is mechanistically linked with maximal myoglobin concentration. This discovery provides insights into the tempo and routes to enhanced dive capacity evolution within the ancestors of each major mammalian aquatic lineage, providing a new perspective on the evolution of this iconic respiratory pigment. Our results also support earlier suggestions of recent amphibious ancestries of echidnas, moles, hyraxes and elephants.

Reference: Mirceta et al. Science 340 (2013), 1234192.
DOI: 10.1126/science.1234192

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Ronald N. Germain **PL3**

Professor
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The EMBO Keynote lecture

Imaging Immunity – Using Multiplex 2D and 3D Imaging to Develop a Spatiotemporal Understanding of Host Defense

Background: Immune responses involve cell-cell interactions within lymphoid tissues, trafficking of activated cells to sites of effector function, and the migration of effector cells within peripheral tissues including tumors. To gain insight into the relationships among cell movement, organ architecture, immune function, and the local tissue environment, we have used intravital multiphoton microscopy and novel multiplex immunohistochemical methods we have developed called Histo-cytometry and Ce3D.

Observations: Innate immune responses have been analyzed and the role of cell death as a primary organizing factor in neutrophil swarming, secondary tissue damage, and the recruitment of monocytes that can develop into immunosuppressive (wound healing) macrophages has been studied. An unsuspected role of fixed macrophage-dependent 'Cloaking' that protect tissues from inflammatory reactions to cell injury under normal conditions has been characterized. The role of cell localization in both innate and adaptive immunity has also been addressed using Histo-cytometry in combination with a new clarification method called Ce3D. These techniques allow the use of 8-12 different antibodies not only to surface markers but to phospho-proteins and cytokines in each cycle of imaging. Together with methods for rapid iteration of staining and analysis, these methods permit imaging of >30 target proteins in a single tissue slice or 3D biopsy sample in a quantitative manner. Recent advances include combining RNA FISH with antibody-based staining to take advantage of RNA-seq data. These multiplex imaging technologies facilitate analysis of the phenotype, number, location, signaling state, and function of immune cells and stromal elements in infected, inflamed, or tumor sites.

Conclusion: This talk will illustrate the power of in situ imaging for the acquisition of a more accurate picture of the molecular, cellular, spatial, and temporal aspects of cell function and signaling events in host immune responses and cancer.

This work was supported in part by the Intramural Research Program of the NIH, NIAID.

EMBO
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Michael B. Yaffe **PL4**

Professor
Center for Precision Cancer Medicine, MIT, USA

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Using Protein Kinase Signaling of DNA Damage and Mitosis for Precision Cancer Medicine: Multi-Omics and Computational Approaches

Jesse C. Patterson, Brian A. Joughin, Andrea E. Prota, Michel O. Steinmetz, Konstantin Krismer, Shohreh Varmeh, Molly A. Bird, Anna Gattinger, Daniel A. Anderson, Andreas Heinzel, Mun-Kyung Hwang, Yi Wen Kong, Ian G. Cannell and Michael B. Yaffe

Targeting specific signaling pathways, either alone or in combination with cytotoxic chemotherapy, may provide enhanced therapeutic efficacy for the treatment of many types of cancer. To explore this, we have focused our efforts on molecularly targeting protein kinases involved in cell stress, the DNA damage response, and mitotic cell division in combination with genotoxic drugs and anti-microtubule agents. We have devised a combined experimental and computational approach, called Visage, to explore drug synergy, and have used this method to identify a novel cancer-specific synergy between inhibitors of the mitotic kinase Plk1, and anti-microtubule agents.

RNA-binding proteins constitute a large class of protein kinase substrates involved in the DNA damage and cell stress response, and that targeting specific RNA-BPs can markedly enhance the anti-tumor response to genotoxic drugs. RNA-BPs generally consist of small modular domains flanked by regions of protein disorder. Phosphorylation within these disordered regions results in enhanced interaction of RNA-BPs with their client RNAs. We have now devised a new computational platform, Transite, that identifies putative RNA-BPs involved in cancer sensitivity and resistance to DNA damaging agents, and identified two RNA-BP targets whose inhibition enhances tumor cell killing by platinum agents. Combining Transite data with Scansite predictions of potential protein kinase-regulated phosphorylation sites on RNA-BPs provides additional avenues of approach for therapeutic re-wiring of protein signaling networks to enhance tumor cell sensitivity to anti-cancer agents and minimize resistance to drug treatment.

Johanna Olweus **PL5**

Professor
K.G. Jebsen Centre for Cancer Immunotherapy, UiO, Norway

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Outsourcing cancer immunity to healthy donors

Recent advances in cancer immunotherapy have greatly improved life expectancy for patients with widespread (metastatic) cancer. Two of the most successful strategies are inhibition of negative immune regulation by checkpoint inhibition, and transfer of T cells gene-modified to express artificial immune receptors called chimeric antigen receptors (CARs). Allison and Honjo were awarded the Nobel Prize in physiology or medicine in 2018 for the therapeutic concept of checkpoint inhibition, and Adoptive Cell Therapy was named Clinical Cancer Advance of 2018 by the American Society of Clinical Oncology due to the impressive effectiveness of CAR19 T cell therapy in treatment of B cell malignancies. In checkpoint inhibition, the effector mechanism is the endogenous T-cell receptor (TCR) repertoire of the patient, recognizing peptides encoded by mutations (neoantigens) presented on major histocompatibility complex (MHC) molecules on the surface of tumor cells. However, the TCR repertoire of the patient is in most cases insufficient at mediating cures. CAR19 T cells, on the other hand, recognize tissue-specific self-antigens on the target cell surface, such as CD19, specific for B cells. It has however, proven difficult to identify tissue-specific cell surface antigens that can be safely targeted in other cancers. As a consequence, existing immunotherapies rarely cure metastatic cancer and are available only for subgroups of patients, calling for alternative options. In my talk, I will discuss the possibility that TCRs identified from healthy donors can be used for genetic modification of T cells in adoptive cell therapy to target a wide range of cancers. We have demonstrated that healthy donor T cells provide a rich source of TCRs reactive to neoantigens, responding to five-fold more mutations than the patient`s own tumor-infiltrating T cells. Moreover, we have demonstrated that healthy donor T cells can recognize a wide range of peptides derived from normally expressed tissue-restricted self-antigens when presented on mismatched HLA. Recognition of such self-peptides in complex with foreign HLA is the basis for graft rejection, and we hypothesize that this immune response can be used to "reject" cancer. As TCRs can recognize peptides independently of cellular localization, the number of potential self-antigens that can be targeted by TCRs is vastly increased relative to CARs.

Primo Leo Schär

PL6

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The FEBS National Lecture:
DNA Demethylation, Chromatin Plasticity and Cancer

During embryonic development and in carcinogenesis, dynamic DNA methylation/demethylation is required to alter gene expression states, facilitating the establishment and/or change of cell-identity. In this context, 5-methylcytosine (5mC)- directed DNA hydroxylases, known as TET proteins, co-operate with the DNA glycosylase TDG and DNA methyltransferases to sustain locus- specific DNA methylation/demethylation activity; TET proteins oxidize 5mC and TDG excises the oxidized 5mCs to initiate a DNA repair process that leads to their replacement by unmodified cytosine. The process is highly active in DNA of differentiating cells but the biological role of this apparently futile cycle of DNA base modification, oxidation and excision is poorly understood.

We tested the hypothesis that 5mC oxidation associated DNA repair is an epigenetic process, targeting DNA strand-breaks to specific genomic regions to induce locus- specific transitions of chromatin states. Profiling DNA demethylation activity and impact in differentiating mESCs, we show that TDG drives chromatin dynamics differentiating cells. TDG proficient cells show higher differentiation-induced gains of active histone marks H3K4me2, a higher mobility of nucleosomes and more significant changes in chromatin accessibility. This TDG-driven chromatin plasticity is functional in the activation of developmental, i.e. lineage-specific, genes. These results establish a role for DNA repair-mediated DNA demethylation in generating chromatin plasticity in stem cells, thereby facilitating site-directed transitions in epigenetic states required for cell lineage commitment.

DNA repair-mediated dynamics in DNA methylation is also implicated in cancer cell plasticity. Aberrant patterning of DNA methylation is a feature of most, if not all, cancers and contributes to carcinogenesis by stably deregulating both oncogenes and tumor suppressor genes but also by shaping the phenotype of cancer cells. Many cancers acquire a CpG island methylator phenotype (CIMP), characterized by the simultaneous hypermethylation of multiple gene promoters. We dissected colon cancer (CC) subtype-specific methylation profiles with the aim to understand underlying mechanisms and functions of methylation change. This identified two groups of hypermethylated CpGs; (i) CpGs showing hypermethylation in all CCs in an age and lifestyle dependent manner; and (ii) CpGs showing hypermethylation in CIMP-CCs under the genetic control of $BRAF^{V600E}$. We show in cell- and mouse models that $BRAF^{V600E}$ downregulates TET1 and TET2, thereby causing CIMP. We will discuss an (epi)genetic progression model for CIMP-CC, whereby epigenetic dysregulation establishes functional changes achieved by genetic mutation in the classical non-CIMP pathway of colon carcinogenesis.

Hongjun Song PL7

Professor
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Epitranscriptomic regulation in the mammalian nervous system

N6-methyladenosine (m^6A), installed by the Mettl3/Mettl14 methyltransferase complex, is the most prevalent internal mRNA modification. We used both in vivo mouse model and in vitro human iPSC-derived 2D and 3D brain organoid models to examine functional roles of m^6A signaling in the nervous system. We found that m^6A depletion by Mettl14 knockout in embryonic mouse brains prolongs the cell cycle of radial glia cells and extends cortical neurogenesis into postnatal stages. m^6A depletion by Mettl3 knockdown also leads to a prolonged cell cycle and maintenance of radial glia cells in mice. m^6A sequencing of embryonic mouse cortex shows enrichment of mRNAs related to transcription factors, neurogenesis, the cell cycle, and neuronal differentiation, and m^6A tagging promotes their decay. Further analysis uncovers previously unappreciated transcriptional pre-patterning in cortical neural stem cells. Similarly, m^6A signaling regulates human cortical neurogenesis in 2D and 3D forebrain organoids via regulation of cell cycle progression. Comparison of m^6A-mRNA landscapes between mouse and human cortical neurogenesis reveals enrichment of human-specific m^6A tagging of transcripts related to brain-disorder risk genes. In the mature nervous system, m^6A-seq shows a dynamic but distinct landscape of m^6A-tagged transcriptomes and m^6A tagging promotes stimulation induced protein translation. We found that axonal injury leads to dynamic changes of m^6A dynamics in dorsal root ganglion neurons and m^6A signaling is required for injury-induced protein translation of regeneration-associated genes and functional axonal regeneration. Our studies suggest developmental stage- and cell type-specific epitranscriptomic modification of transcriptomes and functions in the mammalian nervous systems.

Marja Jäättelä **PL8**

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Lysosomes as targets for cancer therapy

Rapidly dividing and invasive cancer cells are strongly dependent on effective lysosomal function. Accordingly, transformation and cancer progression are characterized by dramatic changes in lysosomal volume, composition and cellular distribution. Depending on one's point of view, the cancer-associated changes in the lysosomal compartment can be regarded as friends or foes. Most of them are clearly transforming as they promote invasive growth, angiogenesis and drug resistance. The same changes can, however, strongly sensitize cells to cell death induced by lysosomal membrane permeabilization. Here, I will compile our current knowledge on cancer-associated changes in lysosomal composition and discuss the consequences of these alterations to cancer progression and the possibilities they open for cancer therapy.

Tonje Steigedal

IS1

PhD, Project Manager at NTNU Technology Transfer

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How can you make the most impact out of your research results?

The universities are the main providers of new knowledge, most commonly materialized in papers, posters and oral presentations to the scientific community. It is however, equally important to try to transfer the knowledge and research results into new products and services in the marketplace. This will facilitate a greater impact of your research results!

All universities have Technology Transfer Offices (TTO) that are there to help you transfer your research results from the lab bench or clinic and to the society. The TTOs are there to evaluate and develop your ideas, secure Intellectual Property (IP), network and find potential industry partners, attract funding, verify technology, support and facilitate clinical trials and animal experiments, support contract management and legal arrangements, help with business development and commercialization, set up license agreements and create new spin-off companies. The TTO is there to help you make the most impact of your research. Does this sound interesting? Contact your local TTO representative!

Inger Sandlie

IS2

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Can they, can I

My research has focused on antibodies. Antibodies protect against infections and are important therapeutics. The most abundant proteins in blood vessels are antibodies, but also albumin. Albumin and antibodies have completely different shapes and completely different functions. Albumin is a transporter. It has pockets for cargo that is carried around in the blood and tissues.

In 1993, my research group was busy studying how antibodies work, how they function and in particular how their shape determines function, when we accidentally stumbled over a variant that was supereffficient in killing bacteria or any target cell of choice. We patented the variant, and then did nothing. Later, I met an American. He had started and was running a company that produced and sold designer-antibodies, and was really mad at me. It turned out that our publications and patent had made problems for him, as they were prior art. It was a painful lesson. It showed me that research from my group could have commercial potential, and I realized that we should have been more ambitious. I thought: Can he, can I. Can they, can we! We continued the research. Took on new projects, asked new questions involving antibody design, and also design of other molecules that are important in the immune response. We worked with old and new collaborators. We published and applied for funding, hired PhD students and postdocs. Our research ability improved as we established new methods and got access to expensive advanced equipment and instruments. Together we formed the Center for Immune Regulation. Whenever we saw the opportunity, we patented our designer molecules. Some of the PhD students were extremely creative, while others were not, but then had other, equally important skills. Many became co-inventors on the patents that we filed. Two in particular, established their own companies based on their own research and their own ideas: Agnete Fredriksen who is chief research officer at Vaccibodies and Geir Åge Løset, who is CEO at Nextera. They loved their projects, which is what a lot of the PhD students do. They have a drive to succeed, and they want to set their mark, make visible footprints. And the new students think: Can they, can I.

In my talk, I will show more examples. I will show how Jan Terje Andersen got interested in the fact that both antibodies and albumin have long serum half-life, because they bind a receptor that is sitting in the wall of blood vessels. Inspired by antibody design, we then set out to make super-albumin: Albumin that would bind more strongly to the receptor than the normal kind and have even longer serum half-life. Such albumin could then be fused to any drug, so that not only albumin, but also the drug could gain long serum half-life. We paired up with a company that produces and purifies albumin in a huge facility in Nottingham. It is owned by Danish Novozymes. 13 The company is busy fusing other drugs to our new albumin variants, and the goal is monthly injections. We strongly believe that this will benefit many.

Marit Otterlei IS3

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The APIM-story; from discovery of a motif to medical application

PCNA is an essential protein that potentially interacts with more than 500 proteins containing either of the two PCNA interacting motif, the PIP-box and APIM. When discovering APIM, we realized that the majority of the APIM-containing proteins are involved in cellular stress responses, including both DNA damage and other cellular stress responses, while several of the PIP-box containing proteins are essential for DNA metabolism. This raised the idea that APIM-containing peptides targeting PCNA could have the capacity to impair the cellular stress defence system which could potentially be exploited in cancer therapy. We engineered cell penetrating APIM-containing peptides that were well tolerated in absence of cellular stress, but altered cellular signalling and reduced DNA repair/DNA damage tolerance mechanism in stressed/treated cells, thereby increasing the efficacy of multiple anti-cancer treatments. These encouraging results were the basis for establishing the NTNU spinoff company APIM Therapeutics, which aim to develop APIM-peptides for use in cancer therapy. APIM Therapeutics is currently performing a Phase I (dose escalation) study in patients with advanced solid tumors.

Pål Sætrom

IS4

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Designing small RNA-mediated gene regulation

MicroRNAs (miRNAs) are approximately 22 nucleotide short RNAs with critical roles in human development and disease. In complex with Argonaute proteins, miRNAs recognize target messenger RNAs (mRNAs) via base-pairing and down-regulate targeted mRNA and protein levels. This post-transcriptional down-regulation happens in the cytoplasm and constitutes miRNAs' main regulatory effect. But in the nucleus, the miRNA:Argonaute complex can further interact with chromatin-modifying enzymes, thereby also affecting transcriptional regulation.

Whereas miRNAs are endogenous gene regulators, Argonaute proteins fail to discriminate miRNAs from exogenous short RNAs – as long as such short RNAs resemble miRNAs. Exogenous short RNAs designed to enter the miRNA pathway, such as short interfering RNAs (siRNAs), can therefore be used for targeted gene regulation.

Here, I will outline our efforts into developing methods for designing short RNAs for targeted gene regulation, before focusing on one example RNA designed to up-regulate the transcription factor CEBPA. This short activating RNA is now undergoing a phase 1 clinical trial for liver cancer. I will close by pointing to some of my lessons learned regarding more and less successful efforts in innovation.

Minisymposia abstracts

M1

Lysine-specific demethylase 1A (LSD1) as the master regulator of Paneth cell differentiation

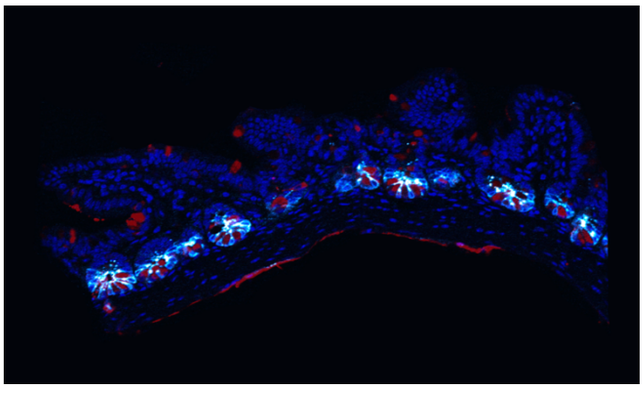
R. Zwiggelaar (1), H. Lindholm (1), M. Alonso (1), J. Ostrop (1), M. Fosslie (2), J.A. Dahl (2), M. Rye (3), F. Drabløs (3), M. Oudhoff (1)

(1) Centre of Molecular Inflammation Research, Department of Clinical and Molecular Medicine, NTNU, Trondheim, Norway. (2) Department of Cancer Research and Molecular Medicine, Faculty of Medicine, NTNU - Norwegian University of Science and Technology, Trondheim, Norway. (3) Department of Microbiology, Division of diagnostics and intervention, Institute of Clinical Medicine, Oslo University Hospital, Rikshospitalet, Oslo, Norway

The gut lining consisting of specialized intestinal epithelial cells (IECs) is in charge of protection from pathogens and absorption of nutrients. Paneth cells reside in the bottom of the crypt where they secrete antimicrobial peptides and supply niche signals to intestinal stem cells (ISCs). LSD1 is an epigenetic enzyme that removes specific methyl groups on lysine residues 4 and 9 of histone 3 tails (i.e. H3K4, H3K9) and has been shown to induce cell differentiation in different organs. However, the precise role of LSD1 during IEC differentiation is unknown. Here we show that LSD1 is in charge of Paneth cell differentiation.

We generated a mouse strain that lacks *Lsd1* only in IECs (*Lsd1*$^{\Delta IEC}$) by crossing *Villin*-Cre mice with *Lsd1*$^{f/f}$ mice. *Lsd1*$^{\Delta IEC}$ mice lack Paneth cells throughout the small intestine. Paneth cells supply niche signals such asWnt3 and EGF to ISCs and are required for organoid survival. Regardless of Paneth cell absence, ISC populations were increased in *Lsd1*$^{\Delta IEC}$ small intestine and organoids treated with LSD1 inhibitor. GSEA of transcriptome data shows an enrichment towards a fetal gene signature in *Lsd1*$^{\Delta IEC}$ crypts. Methylation status of H3K4 reveals that LSD1 may act on the promoter/enhancer of a variety of genes known to be involved in development and IEC differentiation.

Our results demonstrate that LSD1 is in control of Paneth cell differentiation through repression of subsets of genes in ISCs. Inhibition of LSD1 may be beneficial for patients with inflammatory bowel disease suffering from Paneth cell metaplasia, a pre-neoplastic condition of colon cancer. Finally, we are able to grow organoids devoid of Paneth cells which is in contrast to the current dogma that they depend on Paneth cells for supplying niche signals.



M2

The TLR4 adaptor TRAM controls the phagocytosis of Gram-negative bacteria by interacting with the Rab11-family interacting protein 2

Astrid Skjesol (1), Mariia Yurchenko (1), Lene Melsæther Grøvdal (1), Korbinian Bösl (1), Federica Agliano (1,2), Francesco Patane (1,2), Giuseppe Teti (2), Hera Kim (1), Caroline Gravastrand (1), Kaja Elisabeth Nilsen (1), K. Kandasamy (1), Bjørnar Sporsheim (1), Douglas T. Golenbock (3), Harald Stenmark (1,4), Mary McCaffrey (5), Terje Espevik (1), Harald Husebye (1).

(1) Centre of Molecular Inflammation Research, Norwegian University of Science and Technology, Trondheim, Norway. (2) Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy. (3) Program in Innate Immunity, Division of Infectious Diseases and Immunology, Department of Medicine, University of Massachusetts Medical School, Worcester, USA. (4) Centre for Cancer Cell Reprogramming, Faculty of Medicine, University of Oslo, Norway. (5) Molecular Cell Biology Laboratory, Biochemistry Department, Biosciences Institute, University College Cork, Cork, Ireland

Phagocytosis is a complex process that eliminates microbes and is performed by specialised cells such as macrophages. Toll-like receptor 4 (TLR4) is expressed on the surface of macrophages and recognizes LPS on Gram-negative bacteria. Moreover, TLR4 has been suggested to play a role in the phagocytosis of Gram-negative bacteria, but the mechanisms remain unclear. Here we have used primary human macrophages and engineered THP-1 monocytes to show that the TLR4 sorting adapter, TRAM, is instrumental for phagocytosis of *Escherichia coli*. We find that TRAM forms a complex with the Rab11 family interacting protein 2 (FIP2) that is recruited to the phagocytic cup. This promotes activation of the actin-regulatory GTPases Rac1 and Cdc42. Our results show that FIP2 guided TRAM recruitment orchestrates actin remodelling and IRF3 activation, two events that are both required for phagocytosis of Gram-negative bacteria.

M3

Anti-proliferative and anti-inflammatory effects of inhibiting cytosolic phospholipase A2 in combination with calcipotriol for the treatment of psoriasis.

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Psoriasis is a chronic inflammatory skin condition affecting 2-3% of the population. Long-term treatment options include topical administration of the vitamin D analogue calcipotriol. Localised skin irritation, recently linked to stimulation of prostaglandin (PG) E2 production, is a common adverse effect and while combining calcipotriol with corticosteroids is beneficial, this can limit its long-term use. We have previously reported the safe and effective use of a topical cytosolic phospholipase A2 (cPLA2) inhibitor, AVX001, for the treatment of psoriasis (Omland et al. 2017). Here we study the mechanisms involved and investigate its therapeutic potential in combination with calcipotriol. Using HaCaT keratinocytes, we show that cPLA2 is a mediator of epidermal growth factor signaling and that inhibition with AVX001 suppresses growth and cell cycle progression. When combining sub-effective doses of AVX001 with calcipotriol we observed a strong synergistic inhibition of HaCaT viability and show that decreased proliferation via a block in G1-S cell cycle progression is the most likely mechanism of action. Consistent with its pro-irritant effects, calcipotriol increased PGE2 production in both unstimulated and lipopolysaccharide (LPS) stimulated human peripheral blood mononuclear cells. Pre-treatment with AVX001 dose-dependently inhibited LPS-induced PGE2 production and abolished the pro-inflammatory effects of calcipotriol in both the unstimulated and LPS-stimulated populations. Together these data suggest an important role for cPLA2 in keratinocyte proliferation and support the use of AVX001 in combination with calcipotriol for the topical treatment of psoriasis.

M4

Invariant chain regulates endosomal fusion and endosome maturation.

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The major histocompatibility complex class II associated invariant chain (Ii) has an essential role in antigen presentation by regulating major histocompatibility complex class II (MHCII) trafficking to endosomal compartments and preventing peptides from binding the MHCII groove in the endoplasmic reticulum. Ii affects endocytic transport by delaying endosomal maturation, it has fusogenic properties and increases endosomal size. The delayed endosomal maturation and slower degradation could affect antigen processing and loading. However, it is not clear how Ii regulates these processes. In fact, we observed that the general SNARE inhibitor NEM affects the size of Ii-positive enlarged endosomes. Four SNARE proteins form a complex and mediate fusion of vesicles. We performed a siRNA screen against all human SNAREs and analyzed the effect of the silencing on the size of Ii-positive endosomes. Interestingly, depletion of some candidates showed a decreased endosomal size compared to control cells. We observed that these molecules interact with Ii and this reinforce our hypothesis from the NEM experiments and may thereby regulate endosomal maturation. Further work to clarify the role of these candidates in relation to Ii is currently on going. Our data support the hypothesis that a SNARE complex is involved in Ii-mediated endosomal fusion and thereby this may also be an important part of the mechanisms that modulates endosomal maturation and thereby enables optimal antigen loading.

M5

Production of acetoin from methanol in genetically engineered Bacillus methanolicus.

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Platform chemicals are a class of compounds which serve as the starting point for most industrially synthesized organic compounds. Many of the platform chemicals we rely on today are produced by refining of natural gas and oil, and there is a need for the development of a sustainable and scalable source of new platform chemicals to supply industrial processes in the future.

One of the most promising biologically produced platform chemicals is acetoin, a four carbon ketone compound. Acetoin was identified as one of the 30 platform chemicals to prioritize for development by the United States Department of Energy in a 2004 report, highlighting its potential as feedstock for chemical industry. Methanol is a propitious feedstock for biotechnological industry due to its relatively low price, abundance, purity, and the fact that it is a non-food raw material.

Here we show for the first time proof of concept for production of acetoin from methanol in genetically engineered *Bacillus methanolicus* cells. This was achieved by overexpressing the *alsSD* operon from related *Bacillus* species, coding for α-acetolactate synthase and α-acetolactate decarboxylase, respectively.

M6

Modelling in the molecular life sciences – Building a responsible modelling community

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The Centre for Digital Life Norway (DLN; www.digitallifenorway.org) aims to develop a transdisciplinary approach to biotechnology in a growing community of research projects. These projects bring together life scientists and scientists from other disciplinary fields such as mathematics, physics, computer science, and engineering, to solve societal challenges using bio-based and responsible technologies. A central activity in DLN projects is modelling, in the sense of representing an organism or certain processes within, using computers. The modelling activity in the centre spans a wide range of such formal modelling approaches; from statistical and machine learning to dynamic- and agent-based modelling. Furthermore, the systems of interest span a wide dimensional scale – from whole organisms and populations to single chemical reactions. This opens up for a community with a wide perspective on possible modelling approaches and their possible applications. DLN has data and model management as one focus area – making research data and models Findable, Accessible, Interoperable and Reusable (FAIR). Equally important, we want to solidify a responsible approach to the modelling practices in the centre, by integrating Responsible Research and Innovation (RRI) with the more core methodological activities. Thus, making modelling practices; inclusive, reflexive, anticipatory and responsive, to how models can be used to infer predictions and understanding about the biological systems investigated, and the societal perspective of their use. Examples of activities and approaches related to the above mentioned will be presented.

M7

Developing methods for high throughput screening of 3D cell culture

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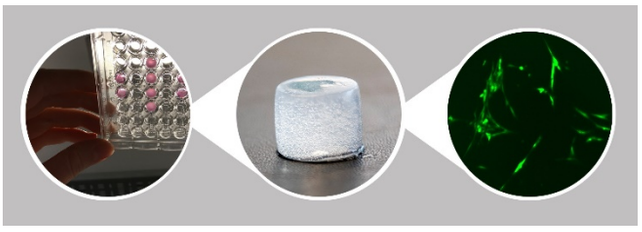
Cultivation of cells in a 3D environment is aimed toward building more robust and physiologically relevant in vitro laboratory models, and bridge the gap to in vivo experiments. In the field of tissue engineering it is vital to understand the interplay between cells and their physical and chemical environment. As this interplay changes in response to cell choice, scaffold design and other culture conditions, it is necessary to screen a large number of experimental conditions using a high-throughput platform. Screening generates a large data output from various analytical approaches, which must be interpreted using bioinformatics and in silico models to gain a greater understanding of the behaviour of cells and further optimize their cultivation into three-dimensional tissues.

Alginate, a linear polysaccharide from seaweed, is used both in food and in biomedical applications. The low toxicity and immunogenicity together with the ability to form hydrogels at physiological conditions makes them attractive scaffolds in tissue engineering. We have tailored alginate gel kinetics, mechanical properties and gel dissolution to be relevant for soft tissue engineering, and optimized the geling protocols for 96-wellplate format and robotic handling. In addition, to enable screening in this format, it is necessary to transfer and optimize quantitative methods for viability developed for 2D cell culture into 3D cell culture in alginate scaffolds.



M8

Inhibiting mutagenesis by targeting the DNA sliding clamps

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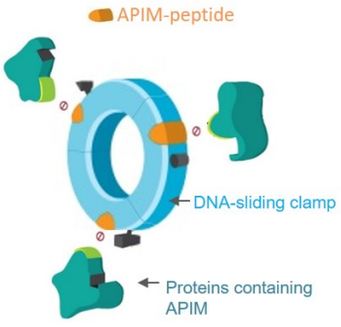
All organisms are dependent on a stable genome. If DNA lesions are left unrepaired prior to DNA replication, the replication machinery is stalled at the damage site, and this may lead to replications collapse, double strand breaks and genome instability. To avoid this, cells have evolved DNA damage tolerance systems, such as DNA translesion DNA synthesis (TLS). In TLS specialized DNA polymerases are able to bypass the DNA lesions on cost of fidelity, as these polymerases are "sloppier" than replicative polymerases due to a larger catalytic sites and lack of proofreading activities. Increased mutagenesis can increase the survival, but also the development of resistance against drugs such as chemotherapeutics in eukaryotes and antibiotics in prokaryotes.

The prokaryotic and the eukaryotic DNA sliding clamps, called β-clamp and PCNA respectively, are essential strongly structurally conserved proteins that encircles the DNA and tethers both the replicative polymerases and the TLS polymerases to the DNA. Blocking the binding sites for the TLS polymerases on the DNA sliding clamps are therefore a promising drug target strategy for both prokaryotic and eukaryotic cells, as this may sensitize cells for both antibiotics and chemotherapeutics.

Proteins that interact with PCNA contains one of the interacting motifs PIP-box and APIM, or both. In prokaryotes, the equivalent motif is called clamp binding motif (CBM). Here we show that peptides containing the APIM sequence are able to block the PCNA-interaction of TLS polymerase POL ζ and reduce UV-induced mutation frequency in human cells. Furthermore, the APIM-peptide also interacts with the β-clamp, and in addition to having antibacterial effect in several bacterial strains, a strong reduction in both mutation frequency and the ability to develop resistance against antibiotics is detected.

In conclusion, targeting DNA sliding clamps, and thereby TLS, with APIM-peptides have a promising therapeutic potential both for inhibiting resistance against chemotherapeutic agents in human cells and antibiotics in bacteria.



M9

Characterization of the light-harvesting complex in the ALB3b knock out lines of the diatom Phaeodacthylum tricornutum

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Diatoms are a major group of eukaryotic phytoplankton belonging to the phylum Heterokont that evolved through a secondary endosymbiosis. Diatom plastids differ significantly from the ones in green algae and higher plants due to their peculiar inheritance and evolution. Diatoms are characterized by a peripheral fucoxanthin (Fx)-chlorophyll (Chl) a/c antenna complex (FCP) and their high ecological success has often been attributed to the ability of the FCPs to absorb in the blue-green region of the light spectrum. This is mainly due to the peculiar bathochromatic shift that occurs when the carotenoid Fx binds to FCPs extending the absorption proprieties. For this reason three spectral state of Fx exist - blue, red and green. FCP proteins are mainly integrated in the thylakoid membrane by the Albino3b integrase. ALB3b K.O. mutants in the diatom Phaeodactylum tricornutum show a reduced antenna and different absorption proprieties compared to the WT resulting in a green coloration of the cells. In order to investigate the composition of FCPs in the mutant lines sucrose gradient centrifugation was carried out and the resulting bands were collected and analyzed. The results show that the remaining FCPs in the mutant are still intact and present in a higher oligomeric state compared to the WT. Moreover, unusual pigment ratios in the mutant`s FCPs and the presence of extra bands on SDS-Page gel might indicate a functional replacement of the missing FCPs. MS analysis of the purified FCPs will indicate which protein is significantly reduced in the mutant lines and might shred some light on the existence of a special FCP pool that might preferentially bind to a more long wavelength absorbing Fx (red) and be responsible for the spectral proprieties of diatoms.

M10

14F7, an antibody that recognise a tumour-specific ganglioside

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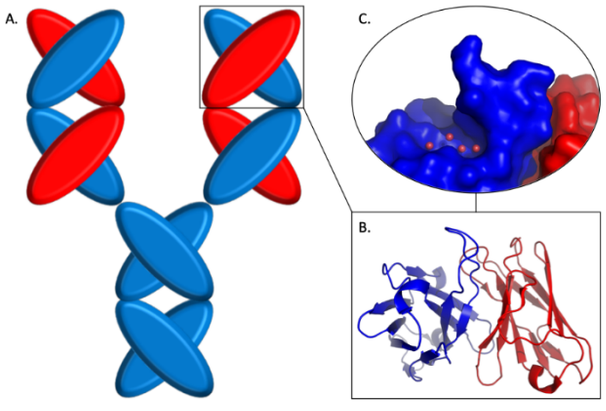
When a healthy cell mutates into a cancerous cell, it exhibits uncontrolled proliferation and the gene expression pattern in the cell is altered. These changes can be exploited by cancer immunotherapy for diagnostics and therapeutic purposes. One such tumour-specific antigen is the N-glycolyl GM3 ganglioside that is highly similar to the most common ganglioside N-acetyl GM3, differing only by having a terminal hydroxyl group instead of a hydrogen. It is located on the cell surface of several different tumours, but does not exist in healthy human cells (Malykh, Schauer, & Shaw, 2001). The ganglioside is recognised by a monoclonal IgG antibody named 14F7 that was developed at the Centre for Molecular Immunology in Havana, Cuba. To be able to exploit the favourable properties of 14F7 it would be helpful to know precisely how the N-glycolyl GM3 ganglioside and the 14F7 antibody interact at the molecular level. To this end, we have generated recombinant 14F7 in the single chain Fv (scFv) format, expressed the protein using an established periplasmic expression system (Gunnarsen et al., 2010), and crystallised it alone (Figure 1b), and together with the trisaccharide part of the N-glycolyl GM3 ganglioside. The resulting structure illustrates that the ganglioside binds in a groove created by the heavy chain CDR H3-loop, and there are water molecules in the active site that might be important for 14F7´s unique specificity (Figure 1c).

Figure 1: Structure of the 14F7 scFv. In this figure, red represent the heavy chains and blue the light chains of the antibody. A. Schematic representation of mAb with a square highlighting the variable part used for generating the scFv. B. Cartoon representation of the 14F7 scFv structure (Bjerregaard-Andersen et al., 2018). C. Close-up view of the 14F7 heavy chain groove created by CDRH3 and CDRH1, with four water molecules in the area where we expect ligand binding (surface representation).



M11

An insight into DNA scanning by DNA base repair proteins – a single-molecule approach

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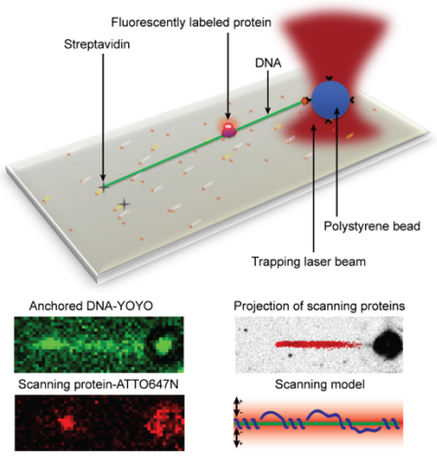
Accumulation of DNA damage in cells may cause genomic instability, leading to cancer, aging and a diverse set of pathological conditions. In order to maintain genomic stability, DNA damage is corrected by several classes of DNA repair proteins. Despite decades of intensive research and great progresses in identifying the structures and biochemical functions of DNA repair proteins, a detailed understanding of the molecular mechanisms by which they search for and recognize errors in DNA remains elusive. Here, we present a single-molecule characterization of the scanning mechanisms by several DNA repair proteins including EndoV, hOGG1, AlkD and AlkF. In our single-molecule assay an elongated 12-kbp fragment of λ-DNA is exposed to fluorescently labelled proteins and their interactions are recorded as trajectories of movement of proteins along the DNA, with images taken at rates up to 130 Hz. We find that during DNA scanning, EndoV switches between three different scanning modes which can be generally classified as *helical sliding*, *hopping* and *base interrogation*, each with a distinct range of activation energy barriers. By comparing the scanning properties of wild-type EndoV and a wedge-deficient mutant EndoV, we show that the highly conserved wedge motif in the structure of this protein plays a central role in switching DNA scanning into base interrogation mode. In addition, we show that DNA scanning by AlkD resembles a single-mode random walk in contrast to the multi-mode scanning utilized by the other DNA repair proteins in this study. This result resonates well with the lack of base flipping in AlkD.



M12

Regulation of protein synthesis through methylation of human eukaryotic elongation factor 1 alpha (eEF1A)

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Lysine methylation has been intensively studied in the case of histones, but is also frequently found on many non-histone proteins. One prominent example is eukaryotic elongation factor 1 alpha (eEF1A), which plays an essential role in the process of protein synthesis, but also exerts several non-canonical functions such as regulation of the actin cytoskeleton and the promotion of viral replication. The functional significance of the extensive lysine methylations on eEF1A, as well as the identity of the responsible lysine methyltransferases (KMTs), have until recently remained largely elusive. However, we have discovered several novel KMTs that target specific lysines in eEF1A, e.g. human eEF1A-KMT3 (METTL21B) and eEF1A-KMT4 (ECE2) which target Lys-165 and Lys-36, respectively, as well as the bifunctional eEF1A-KNMT (METTL13), which methylates both Lys-55 and the N-terminus of eEF1A. Our studies and characterizations of human eEF1A-specific methyl-transferases indicate that methylation of eEF1A can be dynamic and inducible, and modulates mRNA translation in a codon-specific fashion. Here, an overview of our recent progress on eEF1A methylation will be given, and its possible functional and regulatory significance will be discussed.

M13

The APIM-peptide: A novel PCNA-targeting anti-cancer drug

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Proliferating cell nuclear antigen (PCNA) is a scaffold protein involved in multiple cellular processes including DNA replication, DNA repair, translesion synthesis, cellular signaling and apoptosis. PCNA orchestras these events through dynamic interactions with multiple proteins. The AlkB homologue 2 PCNA-interacting motif (APIM) can mediate protein-binding to PCNA, and is present in more than 300 proteins of which the majority are involved in stress-related pathways. A novel cell penetrating APIM-containing peptide targets PCNA and impairs these PCNA-APIM-protein interactions, thus compromising the pathways in which these interactions are essential. In several pre-clinical cancer models, we demonstrate that addition of the APIM-peptide has the ability to enhance the efficacy of various anti-cancer drugs with different mode of actions, with minimal impact on healthy cells. The APIM-peptide targets multiple canonical and non-canonical functions of PCNA simultaneously to compromise the cancer cells ability to recover from the stress induced by combinatory anti-cancer drugs. Altogether our results collectively support a potential for the APIM-peptide in clinical translation to improve therapy of multiple cancer types.

M14

Preclinical efficacy of the MTH1 inhibitor karonudib in B-cell lymphoma

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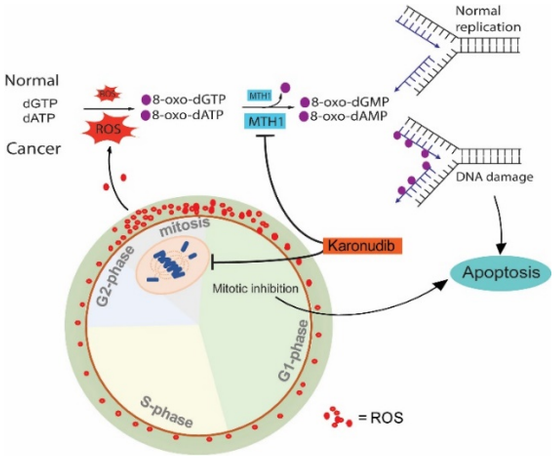
Some B-cell lymphomas are still considered incurable with standard of care, calling for new therapeutic targets. A novel approach is to manipulate the nucleotide metabolism, and karonudib (TH1579), recently developed to inhibit MTH1 (MutT homologue 1/NUDT1), is a potential new drug for lymphoma treatment. MTH1 belongs to the Nudix phosphohydrolase superfamily which converts oxidized nucleotide triphosphates to the corresponding monophosphate. Cancer cells, and particular lymphomas, have a high level of MTH1 compared to normal cells. Inhibiting MTH1 will increase the oxidized nucleotides pool which will be incorporated in the DNA and ultimately lead to induction of apoptosis. Karonudib reduced viability in a wide range of B-cell lymphoma cell lines at doses tolerated by activated normal B cells. Induction of apoptosis was seen by active caspase 3 and TUNEL staining already after 12 h treatment independent of TP53 mutational status. Furthermore, a strong arrest in prometaphase due to failure in spindle assembly was detected in cells exposed to karonudib, suggesting a dual inhibitory mechanism. Karonudib was well tolerated *in vivo* and inhibited tumor growth and led to prolonged median survival of 18 vs 38 days for control and karonudib treated mice respectively in a patient-derived xenograft model. These preclinical data demonstrate the efficacy of karonudib against different B-cell lymphoma subtypes, suggesting a potential broad therapeutic use in treatment of B-cell lymphoma.



M15

Metalloproteinase (Mmp)-17 affects intestinal stem cell regeneration after irradiation in the intestine

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The intestinal epithelium is the most rapidly self-renewing tissue in the adult mammalian body. This rapid turnover is driven by cycling intestinal stem cells (ISCs) that reside at the bottom of crypts. ISC maintenance relies on a specific niche, which is provided by epithelial and nearby mesenchymal cells that secrete these niche factors.

Smooth muscle cells (SMCs) are an abundant cell type in the intestine. SMCs form the muscular wall that surrounds the epithelium. The matrix metalloproteinase (Mmp)-17 belongs to a major enzyme group that cleaves extracellular matrix proteins and other ligands. Unpublished work from our lab has shown that mice lacking Mmp-17 (KO) have impaired epithelial regeneration in the colon after inflammation-induced injury compared to wild type (WT) littermates. In addition, the expression of Mmp-17 was shown to be specifically expressed by SMCs in the intestine. However, the precise role of Mmp-17, and what substrates it cleaves, in intestinal regeneration is still unclear.

We used whole-body irradiation to induce a loss of ISC and other proliferating intestinal epithelial cells without causing severe inflammation. We found that the intestines in KO mice were significantly more damaged 3 and 6 days after irradiation compared to WT mice. In addition, small intestines of KO mice had shorter crypts and longer villi 3 days after irradiation. Further research is still needed to confirm the specific role of Mmp17 in intestinal regeneration.

M16

The role of PARP1 in cAMP-mediated induction of DNA-damage induced autophagy in pediatric acute lymphoblastic leukemia

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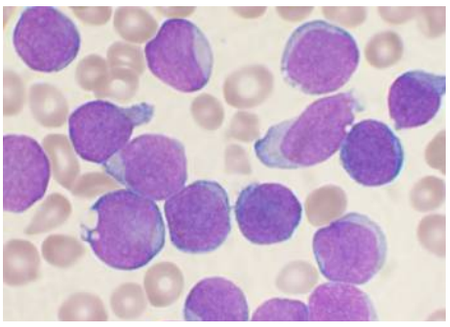
B cell precursor acute lymphoblastic leukemia (hereafter named ALL) is one of the most common forms of pediatric cancers. Despite a general good prognosis, due to improved multimodal DNA damage-based chemotherapy, ALL is still the most common cause of cancer-related deaths in children. Furthermore, pediatric ALL survivors often suffer from severe long-term side effects of the harsh chemotherapy treatments. It is therefore a steady search for new strategies to improve the treatment of this disease.

Previous research from our group has shown that activation of the cAMP signaling pathway inhibits DNA damage-induced killing of ALL-derived cell lines and primary patient-derived cells, and that enhanced autophagy is involved. ALL cells are exposed to cAMP elevating factors in the bone marrow, and we previously proposed that cAMP signaling could be a possible target for improved treatment of ALL. Here we elucidate this possibility by exploring the mechanisms involved in cAMP-induced autophagy.

Poly [ADP-ribose] polymerase 1 (PARP1) is involved in repair of single-stranded DNA lesions. Here we show that PARP1 is involved in the cAMP-mediated induction of autophagy both in an *in vitro* model of ALL and in a human xenograft model of ALL cells in NOD-*scid*IL2Rgamma^{null} (NSG) mice. Treatment of the leukemic cells with PARP1-inhibitors Olaparib or PJ34, reduced both the cAMP-mediated induction of autophagy and the inhibition of DNA damage-induced cell death. Furthermore, we revealed that the cAMP-induced autophagy involved polyADP-ribosylation (PARylation) of proteins in the leukemic cells, which in turn resulted in activation of the autophagy inducer AMPK. Our findings may provide a new treatment strategy for ALL patients by combining PARP1 inhibitors with conventional DNA damaging treatment.



M17

The effect of rearing water treatments on the microbiota associated with cod larvae.

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(1) Department of Biotechnology and Food Science, NTNU

Our aim was to assess how different rearing water treatments influence the microbiota in the rearing water and further how this influences the microbiota associated with reared cod larvae (*Gadus morhua* and the microbiota associated with the feed given to the cod larvae. In this experiment, cod larvae were reared with three different water treatment systems: a recirculating aquaculture system (RAS), a flow-through system (FTS) and a microbial maturation system (MMS). Water microbiota and microbiota associated with feed and cod larvae, was examined using Illumina sequencing of 16S rRNA amplicons.

Analyses show that both water and larval associated microbiota were similar in the MMS and the FTS, while the microbiota in the RAS was significantly different from both other systems. After day 30, all three systems received the same intake water, and on day 46 there were no differences in larval microbiota between the three systems. These results clearly indicate that the water treatment does indeed influence the microbiota of the rearing water, which then influences the larval associated microbiota.

The water and larval microbiota, however, differed significantly from each other in all rearing systems at all sampling points, and bacterial species present in high abundances in the cod larvae, were hardly present in the water and feed at all. The correlation between the water, larval and feed microbiota will be analyzed further, and more details will be presented at the meeting.

M18

Using the SpyCatcher-SpyTag technology for topology mapping of outer membrane proteins in Gram-negative bacteria

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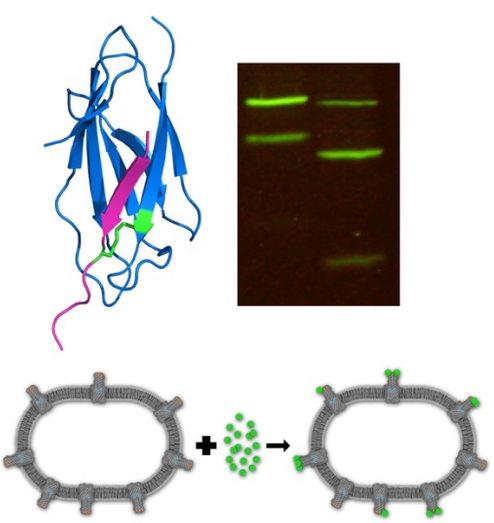
(1) - Bacterial Cell Surface Group, Section for Evolution and Genetics, Department of Biosciences, University of Oslo, Norway

The SpyCatcher-SpyTag system was developed seven years ago by the Howarth laboratory in Oxford. This is based on a modified domain from a *Streptococcus pyogenes* surface protein (SpyCatcher), which recognises a specific 13-amino-acid peptide (SpyTag). Upon recognition, the two form a covalent isopeptide bond between the side chains of a lysine in SpyCatcher and an aspartate in SpyTag. The SpyTag system is versatile as the tag is a short, unfolded peptide that can be genetically fused to exposed positions in target proteins; similarly, SpyCatcher can be fused to reporter proteins such as GFP, and to epitope or purification tags. This technology has been used, among other applications, to create covalently stabilised multi-protein complexes, for modular vaccine production, and labelling proteins e.g. for microscopy. We have used if for determining outer membrane protein localisation and topology in bacteria, especially for investigating the secretion of autotransported virulence factors of Gram-negative bacteria. As an example, we have mapped the topology of a putative secretion mutant of the *Yersinia* adhesin YadA, a trimeric collagen-binding autotransporter from the enteric pathogen *Yersinia enterocolitica*. By introducing a proline residue into a flexible region of the so-called linker we created a partly stalled secretion variant of YadA. Using the SpyCatcher-SpyTag system, we could demonstrate less efficient surface exposure of this mutant and a different labelling pattern compared with the wildtype, showing that the proline substitution results in a significant secretion defect and giving insight into the autotransport process of YadA.



M19

Global assessment of Mycobacterium avium subspecies hominissuis genetic requirement for growth and virulence

Marte S. Dragset (1,2,3¶), Thomas R. Ioerger (4¶), Maja Loevenich (1), Markus Haug (1), Anne Marstad (1), Niruja Sivakumar (1), Pere Joan Cardona (2), Geir Klinkenberg (5), Eric J. Rubin (3), Magnus Steigedal (1,3), Trude H. Flo (1)

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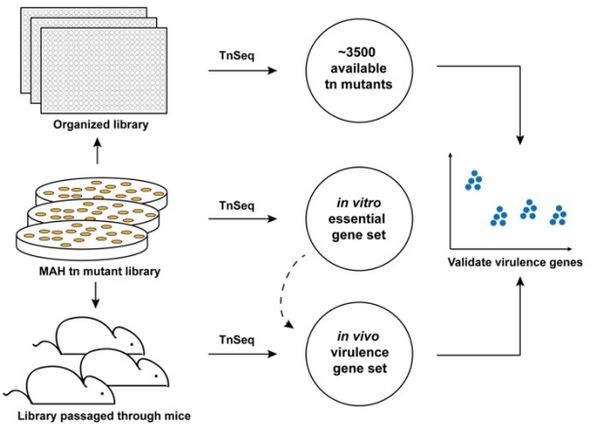

Nontuberculous mycobacterial infections are mainly caused by the opportunistic and enviromental pathogen *Mycobacterium avium* subsp. *hominissuis* (MAH) and they are currently receiving hightened attention due to increased incidence combined with difficult treatment. Insights into the disease-causing mechanisms of this species have been hampered by difficulties in genetic manipulation of the bacteria. In our study we were able to identify and sequence a highly transformable, virulent MAH clinical isolate susceptible to high-density transposon mutagenesis, facilitating global gene disruption and subsequent investigation of MAH gene function. By transposon insertion sequencing (TnSeq) of this strain, we defined the MAH genome-wide genetic requirement for virulence and *in vitro* growth, and generated an organized plated library of ~3500 transposon mutants for valdidation and hypothesis-driven research. Surprisingly, we found that the vast majority of genes required for MAH growth and virulence (96% and 97%, respectively) have orthologs in the tuberculosis-causing pathogen *M. tuberculosis* (*Mtb*). Some of the virulence genes in our screen are well-established virulence genes identified in *Mtb* mouse model TnSeq experiments including *uvrABC* (the UvrABC endonuclease complex) and *secA2* (alternative ATPase of Sec secretion pathway). However, we also found growth and virulence genes specific to MAC species. Finally, we validated novel mycobacterial virulence factors that might serve as future drug targets for MAH-specific treatment, or translate to broader treatment of related mycobacterial diseases; one encoding a probable MFS transporter and another a hypothetical protein located in immediate vicinity of six other identified virulence genes. In summary, we provide new, fundamental insights into the underlying genetic requirement of MAH for growth and host infection.

M20

Bacterial adhesion to living and non-living surfaces

Dirk Linke (1)
(1) University of Oslo, Department of Biosciences

Trimeric Autotransporter Adhesins (TAAs) are key virulence factors in various Gram-negative pathogenic species, including *Yersinia, Bartonella, Neisseria,* and others. Their main function is to adhere to host cells, enabling persistence, tissue invasion and inflammatory processes. Some of the TAAs in addition can bind and inactivate components of the complement system, rendering the bacterial cell partially invisible to the immune system. In recent work, we have studied details of the adhesive process using different systems, from ELISA-like assays and x-ray crystallography to electron microscopy. To complement this structural work, we have developed assays suitable for high-throughput screening of inhibitors of adhesion. These assays can potentially be adapted to other adhesins and adhesin classes, using live bacterial cells. In a first round of screening with a library of 28.000 compounds, we have found 17 promising candidate hits for future projects. We hope to develop anti-adhesive substances that can be used to treat different diseases, and that are suitable for coating implants and other medical devices where bacterial adhesion is problematic. We will also use them to study binding sites and binding modes in our *in vitro* and *in vivo* experimental systems.

M21

Deciphering the carbon distribution in metabolic pathways during antibiotic production by Streptomyces superhost strains using 13C-isotope-labeling experiments

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One task of the Centre for Digital Life Norway project INBioPharm is to develop optimized *Streptomyces* superhost strains for heterologous production of new bioactive compounds by using Systems and Synthetic Biology approaches. One important experimental input to this task is the deciphering the participation of important metabolic pathways for antibiotic production and generation of high-resolution quantitative metabolite profiles of the *Streptomyces* host production strains.

Fermentation medium coupled with either L-glutamate or phosphate limitation triggered antibiotics production. Contrary to phosphate limitation, nitrogen (L-glutamate) limitation triggered the stringent stress response as observed by a sharp decline in the CO_2 production and biomass concentration. Phosphate limitation downregulated the sugar and nucleotide phosphate metabolites pools, whereas nitrogen limitation was found to reduce the TCA cycle metabolites pool. The consumption of L-glutamate in broth reflected in the depletion of intracellular L-glutamate and the corresponding decrease in intracellular glutamine and α-Ketoglutarate, an entry point of L-glutamate into metabolic pathway. The intracellular succinic acid pool of *Streptomyces coelicolor* A3(2) M145 was found decreasing in exponential phase and its trend was reverse in production phase. The decrease in intracellular succinic acid was resulted in an increase in its excreted concentration and vice-versa. 13C-isotope-labeling experiments showed the degree of participation of carbon from L-glutamate and glucose in antibiotic and its precursor compound. This also revealed the contribution of different metabolic pathways during antibiotics production.

M22

Insights into the role of modularity in lytic polysaccharide monooxygenase (LPMO) functionality

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Lytic polysaccharide monooxygenases (LPMOs) catalyze the oxidative cleavage of glycosidic bonds using a single copper atom as redox co-factor. The reactivity of LPMO-Cu(I) with a dioxygen co-substrate (O_2 or H_2O_2) in futile reactions (i.e. reactions lacking a carbohydrate substrate) results in oxidative damage of the LPMO active site and surrounding residues, and thus in enzyme inactivation. We have recently shown that weakening of substrate binding properties, resulting from point mutation(s) on the LPMO substrate-binding surface or truncation of carbohydrate-binding modules (CBMs) leads to an increase in off-pathway inactivation events and oxidative damage. About 20% of the bacterial LPMO enzymes are modular and most of these contain one or two additional CBMs connected by inter-domain linkers. A few LPMOs are also linked to other catalytic modules, in particular glycoside hydrolases (GHs). We have studied several modular bacterial LPMOs, including a naturally existing bi-catalytic LPMO-GH enzyme, and its truncated variants, with respect to activity, operational stability, substrate binding, and synergistic effects. Our results provide insights into the unique role of modularity in LPMO-driven conversion of polysaccharides, which primarily relates to preventing off-pathway reactions, and reveal the interplay between LPMO and GH domains that are part of the same enzyme.

M23

Biophysical and structural studies of a protein complex involved synthesis and vesicular packing of dopamine

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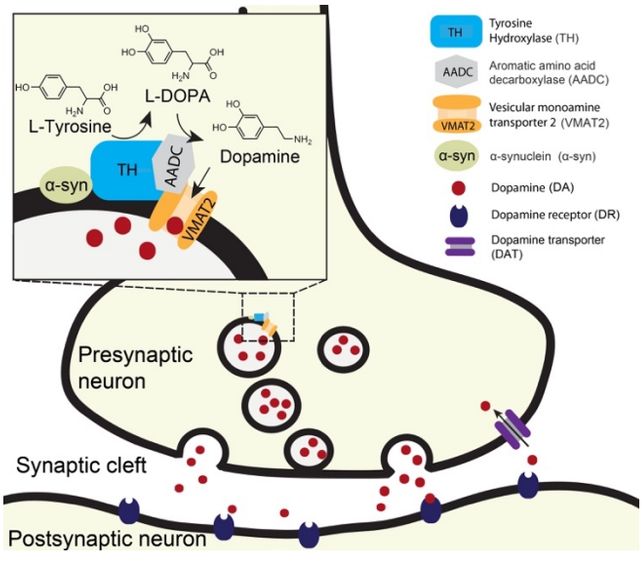
The synthesis of catecholamine neurotransmitters such as dopamine is a highly regulated process, notably at the level of the rate-limiting enzyme, tyrosine hydroxylase (TH), in the biosynthetic pathway. Recent results have pointed to the neuronal vesicular monoamine transporter (VMAT2) as an essential regulator of dopamine homeostasis by packaging cytosolic dopamine into vesicular compartments for subsequent release on neurotransmission, and as an interaction partner and direct regulator of TH function. Low dopamine levels and death of dopaminergic neurons are hallmarks of Parkinson's disease, and dysfunction of both TH, α-synuclein and VMAT2 is implicated in several human neuropsychiatric and neurodegenerative disorders.

We have found that protein complex formation between VMAT2, TH, and possibly α-synuclein are crucial for vesicular transport of TH to the synapsis in dopaminergic neurons. Our results point to phosphorylation of TH Ser31 as an important regulator for the TH association with VMAT2, α-synuclein and synaptic vesicles, but the exact mechanisms behind these interactions are not known. In order to achieve a better understanding of how these proteins interact, and how dopamine synthesis and vesicular packing is regulated we are expressing and purifying TH/α-syn/VMAT2 proteins and protein complexes for biophysical and structural studies.



M24

A germline homozygous mutation in human Oxidation Resistance 1 gene cause developmental delay, epilepsy and cerebellar atrophy

Xiaolin Lin1,2*, Wei Wang9*, Mingyi Yang1,2* , Nadirah Damseh7*, Agata Antonina Rita Impellizzeri6,8, Richard Siller5,6, , Maher Shahrour7, Barak Yaacov7, Motee Al-Ashhab7, Bassam Abu-Libdeh7, Simon Edvardson7, Lars Eide2, Gareth J Sullivan3,5,6#, Orly Elpeleg7#, Magnar Bjørås1,2,5,9#

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The Oxidation Resistance 1 gene (*OXR1*) is essential for protection against oxidative stress. Here we identified three patients with a homozygous mutation in *OXR1* that leads to depletion of OXR1 protein. Clinical features are characterized by developmental delay and marked cerebellar atrophy with onset in early childhood. Patient derived lymphoblasts showed impaired cell proliferation, increased apoptosis, and abnormally high sensitivity to oxidative stress with elevated oxidative DNA damage. The patient iPSC-derived neuroepithelial cells and brain organoids display defects in neural aggregate formation, neurite outgrowth and neuronal differentiation. Further analysis reveals that OXR1 regulates the transcriptional networks required for maintaining physiological level of ROS, promoting neurogenesis and neuronal development. These findings provide the first description of human OXR1 deficiency associated diseases, indicating an essential role for OXR1 in neuronal protection and brain development in human.

M25

Micro- and mesoscale dynamics of engineered neural networks in response to Parkinson´s related pathology

Vibeke Devold Valderhaug (1), Ola Huse Ramstad (1), Rosanne van de Wijdeven (1), Axel Sandvig (1)(2) and Ioanna Sandvig(1)

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It is well-documented that any major disturbance to normal neural network function, for example as a result of trauma, or neurodegenerative disease, such as Parkinson´s disease (PD), will result in severe, permanent functional deficits, but also trigger adaptive and maladaptive network responses which are demonstrated as changes in network structure and function[1]. Such alterations may represent various underlying forms of neuroplasticity, which involve both homeostatic and Hebbian mechanisms, and which can be described as "function-structure" relationships. Such relationships are highly complex and, as a result, poorly understood. However, elucidation of how different forms of plasticity may manifest as adaptive or maladaptive neural network responses and, thereby, how they may promote or hinder functional restoration after a perturbation is of fundamental importance for our ability to achieve functional repair in the damaged CNS.

Exciting perspectives in the study of complex neural network dynamics in healthy and perturbed conditions have emerged with the recent developments within the field of morphogenetic neuroengineering[2,3,4]. Interestingly, the engineered neurons display intrinsic properties such as self-organization, emergence and self-organized criticality and form complex functional networks *in vitro*. This effectively means that the derived neural networks faithfully recapitulate fundamental aspects of neural network behaviour, thus enabling the study of complex network dynamics in reductionist *in vitro* paradigms.

We apply morphogenetic neuroengineering in combination with advanced, state-of-the-art *in vitro* multielectrode arrays (MEAs) to study evolving neural network dynamics in healthy and perturbed conditions. Additionally, by combining MEA technology with microfluidic devices, which allow the structuring of multi-nodal neural networks with definable afferent and efferent connectivity, we create experimental paradigms that capture fundamental features and dynamics of the function-structure relationships observed in different interconnected brain regions[5].

Here we present latest results from our research illustrating the application of the above principles to model PD-related pathology *in vitro,* focusing on monitoring network responses at the micro- and mesoscale, including dynamic structure-function relationships in network connectomes.

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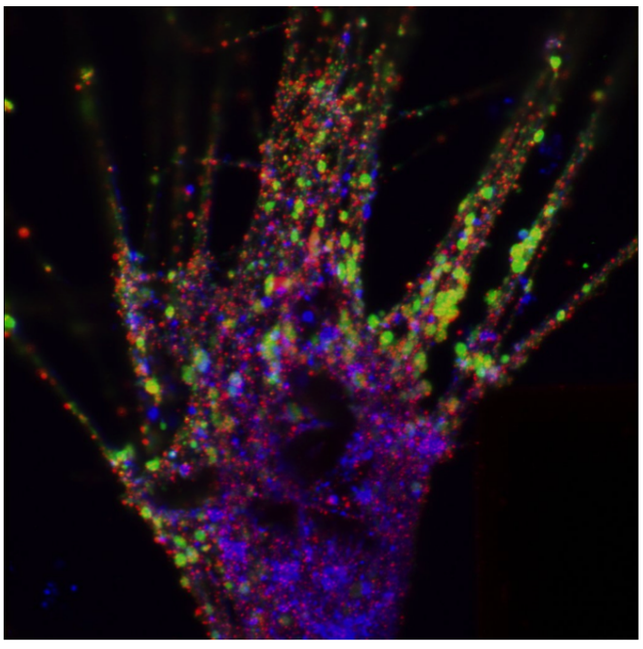


M26

Coding mechanisms and neural plasticity in the olfactory system: Lessons we can learn from a miniature insect brain

Elena Ian (1), C. Giovanni Galizia (2), and Bente G. Berg (1)
(1) Chemosensory lab, Norwegian University of Science and Technology, NTNU, Norway. (2) Universität Konstanz Fachbereich Biologie, Konstanz, Germany

The evidence of phylogenetically highly conserved principles of the olfactory system allows exploration of its basic mechanisms in different animal models including insect species.

Here, we study the primary olfactory center of the moth brain, the antennal lobe (AL), which is the analogue to the vertebrate olfactory bulb. In the olfactory system, only one processing layer separates olfactory sensory neurons (OSNs) from higher integrative areas involved in learning and memory formation (the piriform cortex in vertebrates and the mushroom bodies in insects). A focus of the present study is to elucidate coding principles in the AL underlying transformation of olfactory stimulus representation between the OSNs and the mushroom bodies. Application of the calcium imaging technique allowed us to measure odor-evoked responses from the AL projection neurons, which are analogue to mitral cells in vertebrates. Within the male AL, we demonstrated interaction between the two different sub-systems tuned to plant odorants and female-produced pheromones, respectively. We found that repetitive paired stimulation with a plant odor and the pheromone led to a suppression effect in both sub-systems. The fact that the suppression persisted also after pairing, indicates the existence of a Hebbian-like plasticity in the primary olfactory center, established by temporal pairing of the two odor categories. Ongoing calcium imaging measurements includes stimulation with single plant odorants and their mixtures. This experimental approach offers the opportunity to uncover neural processes underlying more complex mixture interactions within the AL.

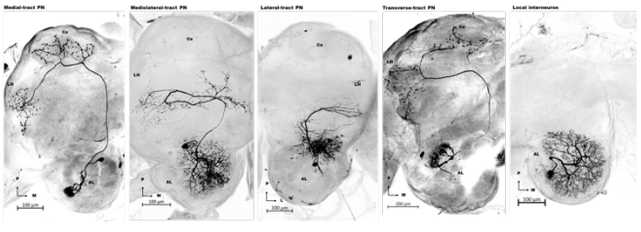
M27

Spike characterization of olfactory local interneurons and projection neurons

Kymre, J.H. (1), Berge, C.N. (1), Chu, X. (1), Pfuhl, G. (1, 2), Solstad, T. (3), & Berg, B.G. (1)

(1) Department of Psychology, Norwegian University of Science and Technology, (2) Department of Psychology, University of Tromsø, (3) Department of Teacher Education, Norwegian University of Science and Technology

The primary olfactory center of the insect brain, the antennal lobe (AL), consists of glomeruli formed by synapses between sensory neurons and two types of central neurons: modulatory local interneurons (LNs), and output projection neurons (PNs). Several subtypes of PNs project via parallel tracts, including the medial, mediolateral, lateral, and transverse tract. The *in vivo* intracellular recording and staining technique is often used to study LNs and PNs, but there is currently no reliable way to estimate neuron category prior to staining. Differences in physiological characteristics among these categories could perhaps be used to estimate neuron identity during recording, allowing for selective sampling. We aim to investigate whether the anatomically distinct types of AL neurons, including LNs and all PN subtypes, have differences in their spontaneous spiking patterns. By intracellularly recording and staining in the AL of the moth *Helicoverpa armigera*, we gathered physiological and anatomical data on 41 LNs and 88 PNs. Significant differences between the neuron categories in interspike-interval based parameters were demonstrated, including differences between PNs from parallel tracts, and between LNs and PNs allocated to distinct tracts. The transverse and mediolateral tract PNs did not differ significantly from any category. Future analyses will reexamine these issues after data-collection is completed, and machine-learning categorization will be applied to raw data.



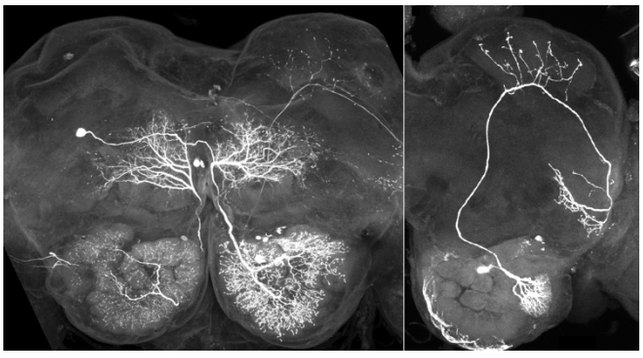
M28

Structure and function of individual projection neurons and centrifugal neurons in the male moth brain

Berge, C. N. (1), Kymre, J. H. (1), Chu, X. (1), Berg, B. G. (1)

(1) Department of Psychology, Norwegian University of Science and Technology

In the insect brain, different types of neurons provide input and output to the primary olfactory center, the antennal lobe (AL). The principal output neurons, projection neurons (PNs), convey odor information from the AL to higher brain areas by passing in one of several parallel antennal-lobe tracts (ALTs). Contrary, centrifugal neurons (CNs) integrate information from higher brain areas and provide input to, and modulate, the processing in the AL. Yet, our understanding of the functional role of the different parallel tracts and CNs in olfactory processing remains incomplete. Here, we have investigated PNs and CNs in the noctuid moth *Helicoverpa armigera*, by using *in vivo* intracellular recording and staining to characterize their physiological responses to odors and morphological features. Most PNs were confined to the medial (m), mediolateral (ml), and lateral (l) ALT, but we also found neurons passing along two additional ALTs. The results demonstrated that PNs in the m-ALT were narrowly tuned, indicating a function related to encoding odor identity, whereas ml-ALT and l-ALT PNs were more broadly tuned, thus suggesting a less specific role in odor processing. Furthermore, we described three types of CNs, two of which were novel. Both of the novel CN types responded to olfactory stimuli, and together with their morphological features, this indicates that they may mediate odor-evoked feedback to the AL. Overall, these findings expands our understanding of PNs and CNs.



M29

Interaction between the actin N-terminal acetyltransferase NAA80 and PFN2

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(1) Department of Biomedicine, Faculty of Medicine, University of Bergen, (2) Department of Bioscience, Faculty of Mathematics and Natural Sciences, University of Bergen, (3) Department of Surgery, Haukeland University Hospital

N-terminal acetylation occurs on approximately 80 % of human proteins and regulates diverse functions, including subcellular localization, protein half-life, complex formation, and folding. N-terminal acetylation is catalyzed by N-terminal acetyltransferases (NATs). Deficiency of these enzymes is associated with cancer, developmental disorder and decreased viability in model organisms. Actin is one of the most abundant proteins in muscle and non-muscle cells, and has long been known to be N-terminally acetylated. It was recently discovered that actin is a substrate of the NAT NAA80. *NAA80*-KO cells have increased motility, altered cytoskeletal morphology and lengthened filopodia compared to control cells, suggesting that N-terminal acetylation of actin has an important role in cytoskeletal function.

Using label free quantitative mass spectrometry, we have discovered a novel interaction partner of NAA80, the actin-binding protein profilin-2 (PFN2). We find that the activity of NAA80 towards actin N-terminal peptides is enhanced by the presence of PFN2, but not by PFN1, the major cellular profilin isoform. Our results suggest a model in which PFN2 enhances the rate of N-terminal acetylation of actin.

M30

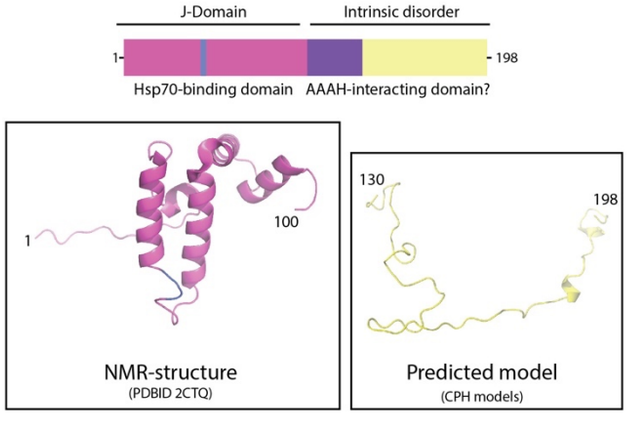
Elucidating the role of co-chaperone DNAJC12 in neurometabolic disease

Marte I. Flydal (1),Kunwar Jung-KC (1), Christer F. Didriksen (1), Mary D. Tai (1), Ming Ying (1), Tanja Scherer (2), Beat Thöny (2), Nenad Blau (3), Aurora Martinez (1)

(1) Department of Biomedicine, University of Bergen, Norway, (2) Division of Metabolism, University Children's Hospital Zürich, Zürich, Switzerland, (3) Dietmar-Hopp-Metabolic Center, University Children's Hospital, Heidelberg, Germany

Dysfunction in any of the tetrahydrobiopterin-dependent aromatic amino acid hydroxylases (AAAHs) can lead to devastating disease as they catalyze rate-limiting reactions in degradation of L-phenylalanine and synthesis of neurotransmitters. However, hyperphenylalaninemia (HPA) and other neurometabolic symptoms caused by deficiencies of the AAAHs were recently found in patients with normal *AAAH* genes, but with mutations in *DNAJC12*. DNAJ-proteins are co-chaperones of the HSP70-molecular chaperone system that assists in proper folding and maintenance of intracellular stability of their clients, and mutational analyses revealed the AAAHs as the specific clients of DNAJC12. The characterization of the DNAJC12/AAAH complexes should provide novel understanding on the stability of the AAAHs in health and disease and provide novel targets for treatment of the associated neurometabolic diseases.

The Enu1/1 mouse model (homozygous for the V106A-*Pah* variant) has provided insights on specific interactions of DNAJC12 with misfolded phenylalanine hydroxylase (PAH). Our results support a role of DNAJC12 not only in folding but also in the degradation of misfolded PAH by the ubiquitin-dependent proteasome/ autophagy systems. We are attempting the expression and purification of the recombinant human DNAJC12 to study its interactions with the AAAHs at the structural and functional level and understand their interplay with other members of the complex quality control system for proper folding. Preliminary results show that the 24-kDa DNAJC12 protein is dimeric with a tendency to also form soluble aggregates, possibly associated with the predicted intrinsic disorder in the C-terminal domain.



M31

Crystal structure of the second isoform of human phosphoglucomutase-1 (PGM1) and its substrate and product complexes

Paul Hoff Backe (1,2), Jon K. Lærdahl (2), Lene Svendsen Kittelsen (1,2), Bjørn Dalhus (1,2), Lars Mørkrid (1), Magnar Bjørås (2,3)

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Human phosphoglucomutase 1 (PGM1) is an evolutionary conserved enzyme that belongs to the ubiquitous and ancient α-D-phosphohexomutase superfamily, a large family with members in all three domains of life. PGM1 catalyzes the bi-directional interconversion between glucose-1-phosphate (Glu-1-P) and glucose-6-phosphate (Glu-6-P), a reaction that is important in the cytoplasmic biosynthesis of nucleotide sugars needed for glycan biosynthesis and also essential for normal carbohydrate metabolism. Clinical studies have shown that mutations in the PGM1 gene may cause PGM1 deficiency, an inborn error of metabolism previously classified as a glycogen storage disease, but recently also shown to be a congenital disorder of glycosylation. Here we present three crystal structures of the isoform 2 variant of PGM1, both as an apoenzyme and in complex with substrate and product. The structures show the longer N-terminal of this PGM1 variant, and the ligand complex structures reveal for the first time the structural basis for substrate/product recognition by human PGM1.

M32

FAM173B is a mitochondrial methyltransferase that targets mitochondrial ATP synthase to optimize its function

Jędrzej Małecki (1), Hanneke Willemen (2), Rita Pinto (1), Angela Ho (1), Anders Moen (1), Ingrid Kjønstad (1), Boudewijn Burgering (3), Fried Zwartkruis (3), Niels Eijkelkamp (2) and Pål Falnes (1)

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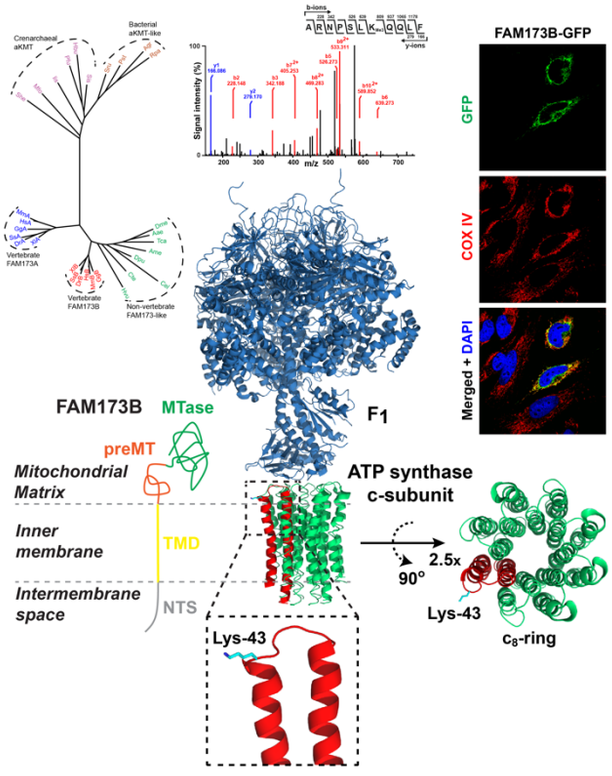
Abstract: Lysine methylation is an important post-translational modification that is also present on mitochondrial proteins. Previously, we identified two lysine (K)-specific methyltransferases (KMTs) responsible for methylation of mitochondrial citrate synthase (CS-KMT), and the beta-subunit of electron transfer flavoprotein (ETFβ-KMT). In this report, we present our most recent findings indicating that mammalian FAM173B is the KMT responsible for trimethylation of Lys-43 in mitochondrial ATP synthase c-subunit (ATPSc), a modification ubiquitously found in all metazoans. ATPSc is part of the oligomycin-binding domain (FO) of the mitochondrial ATP synthase complex (ATPS). In vertebrates, ATPSc forms a ring made of eight c-subunits (c8-ring), which is embedded in the mitochondrial inner membrane, and constitutes the central part of the rotary element of the ATPS complex. This rotary element is propelled by protons that return from the intermembrane space back to the mitochondrial matrix, and induce recurrent conformational changes within the stationary (F1) domain that enable ATP synthesis. Our results demonstrate that cells devoid of active FAM173B also lack methylation of Lys-43 in ATPSc. Lack of methylation causes aberrant assembly of the ATPS complex, and results in decreased ATP-generating ability of the complex, as well as decreased mitochondrial respiration. In summary, our work identifies FAM173B as the long-sought KMT responsible for methylation of ATPSc, a key protein in cellular ATP production, and demonstrates the functional significance of ATPSc methylation.



M33

CompACT: the complex N-terminal maturation processing of β-actin

Adrian Drazic (1), Ulrike Kajan (1), Michael Marie (1), Minglu Dai (1), Evy Timmerman (2), Francis Impens (2), Kris Gevaert (2), Thomas Arnesen (1,3,4)

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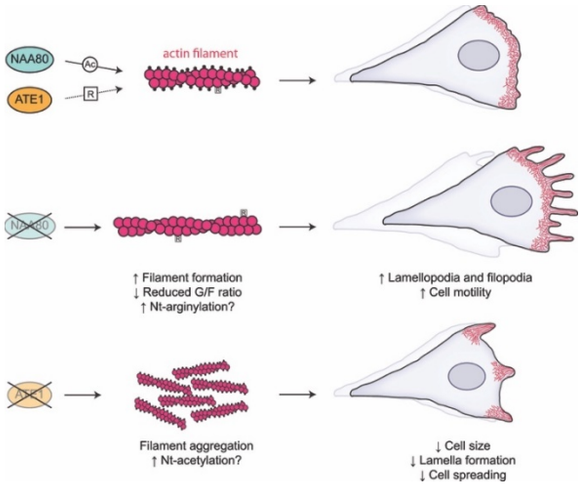
Actin is one of the most abundant proteins in eukaryotic cells and the main component of the microfilament system. There are six isoforms expressed in humans, which play essential roles in numerous cellular activities including muscle contraction, maintenance of cell integrity, and cell motility. The proper structure and function of actin is regulated by posttranslational modifications (PTMs) involving a unique N-terminal (Nt-) maturation process. This includes Nt-acetylation that is catalyzed by the recently discovered NAA80 and present in all actin isoforms, as well as ATE1-mediated Nt-arginylation that is only present in one isoform, ß-actin. Importantly, both PTMs, acetylation and arginylation, are mutually exclusive. We show that actin Nt-acetylation contributes to actin filament formation and controls cell motility, a function known to be affected by Nt-arginylation. Thus far, it is not fully understood how the Nt-maturation of ß-actin is regulated and why only this specific isoform becomes Nt-arginylated. We combine cellular biology and mass spectrometry analysis to determine the abundance and localization of Nt-arginylated ß-actin in various cell systems. Further, we use CRISPR/Cas9-generated NAA80 and ATE1 KO cells in order to potentially shift the balance in favor to one or the other modification. Our studies show specific localization for Nt-arginylated actin at the cell edges. However, Nt-arginylation remains challenging to detect even by state-of-the-art mass spectrometry, and appears to be significantly less abundant than previously described. We have just begun to understand the regulation of the Nt-maturation of actin and future studies are necessary to put all pieces of the puzzle together.



M34

NAD highlights new metabolic interplays between mitochondria and peroxisomes

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Department of Biomedicine, University of Bergen

Nicotinamide Adenine Dinucleotide (NAD) is one of the most important coenzymes serving as a cofactor for many redox and signalling reactions. Its distribution between the different organelles highlights the existence of NAD-dependent reactions in all compartments. The presence of membranes impermeable to NAD results in the physical isolation of these different NAD pools and thus raises questions as to how they are established and maintained and how alterations of any NAD pool will affect NAD-dependent processes inside and outside an organelle. An aim of this project is therefore to provide an in-depth characterization of these pools with regards to content, the effect of selective modulations on cellular processes, and the possible interplay between the pools. We have established tools allowing for the manipulation of NAD levels inside a specific organelle by targeting the catalytic domain of the NAD-consuming enzyme PARP1 to the compartment of interest in engineered cells. Characterization of these cell lines revealed that lowered mitochondrial NAD content impacts cellular processes such as proliferation, response to the inhibition of the NAD biosynthesis salvage pathway and display severe metabolic perturbation. Modulation of the peroxisomal NAD content revealed an interplay between the mitochondrial and peroxisomal NAD pools. Furthermore, we find that compartment-specific consumption of NAD influences the cellular turnover of the coenzyme.Taken together, our data provide new insights into the role and importance of the distinct NAD pools in the context of a compartmentalized cell.

M35.

Enhanced Antibody Validation

Marko Sankala
Merck Life Science

The development of a comprehensive guideline for antibody validation has been a hot topic in the scientific communities worldwide in the last years. To address this topic, we present the results of the Human Protein Atlas and Atlas Antibodies' efforts in enhanced validation of antibodies.

Learn how enhanced validation of antibodies can secure specificity to offer the researcher reliable tools that can be trusted to meet expectations. In this talk, a background to the issue of antibody validation will be given, and the recommendations of the International Group of Antibody Validation (IWGAV) to apply application-based validation presented.

We will explain how enhanced validation was introduced as an extra layer of security to Prestige Antibodies products and the benefit of applying all five methods rather than focusing on only one. We will also explain the principle for each method; Genetic Validation, Orthogonal Validation, Independent Antibody Validation, Recombinant Expression Validation and Migration Capture MS Validation and discuss in which context each method may be used.Marko Sankala

M36

Serum generates large scale contraction waves at epithelial edges

Emma Lång (1), Anna Lång (1), Pernille Blicher (2), Gabriel Wang (3), Arne Klungland (1), Mark Schüttpelz (3), and Stig Ove Bøe (1)
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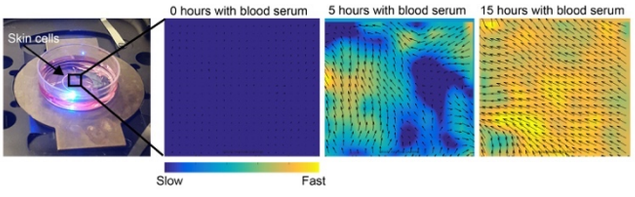
During wounding, epithelial cells in the immediate vicinity of the wound come into contact with blood components through bleeding or inflammation-induced vasodilation. In addition, several types of solid tumors are exposed to blood due to tumor-induced synthesis of leachy blood vessels that infiltrates the tumor. However, little is known about how blood liquid affects the motility of normal and cancerous tissue.

In the present work, we demonstrate that multiple serum-borne components cooperate to produce tissue-scale contractions in quiescent keratinocyte monolayers. These contractions emerge from a combination of myosin-dependent contractile forces and self-propelled collective migration towards a contraction center. After a contraction maximum has been reached the polarity of migrating cells is reversed leading to collective migration in the opposite direction against a cell density gradient. If epithelial edges are present, contraction centers form between 200 and 400 µm from the cell sheet perimeter, which leads to contraction-mediated migration away from the wound site followed by a subsequent directed expansion towards the cell sheet boarder. Such single wave-like motions lead to a net displacement of cell mass towards epithelial edges with minimal tissue density distortions across large length scales. We find that multiple serum components, including EGF, TGFα, thrombin and IL-1 each have the capacity to activate global contractions, while TGF-β-mediated signaling is required for density-induced cell polarity reversal and tissue expansion towards the edge. In addition, a serum-induced supra-cellular actinomyosin network at the apical side of the cell sheet is required for global cell sheet coordination and elasticity. The study demonstrates how large-scale contractions can facilitate the static-to-motile transition of epithelia upon contact with blood liquid.



M37

Cultured meat-a feeding strategy based on cell biology

Sissel Beate Rønning (1), Ragnhild Stenberg Berg (1), Mona Elisabeth Pedersen (1), Eva Veiseth-Kent (1), Dimitrios Tzimorotas (2)
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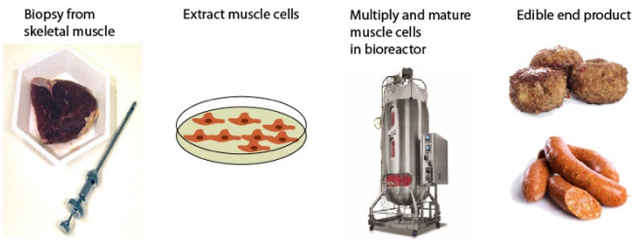
There is an increasing pressure on the world's livestock sector to meet the growing demand for high-value animal protein. A revolutionary new alternative to the traditional way of producing animal protein is cultivation of muscle cells outside the living animal in a bioreactor, thus bypassing animal production. Optimistic estimations suggest that using this modern technology, 10 000 kg cultured meat can be generated from as little as 1 g of beef muscle. The methodology for culturing meat is inspired by techniques used for medical purposes such as tissue reconstruction of damaged muscle tissue and large-scale production of biopharmaceuticals using mammalian cells. Although bioreactors are widely used for large-scale production of biopharmaceuticals using mammalian cells, this technology must be modified before it can be used for edible animal protein production. The basic technology for culturing meat includes the following steps: 1) Sample and harvesting of the muscle stem cells, 2) multiplying the number of cells, and differentiation of the satellite cells into muscle cells and fibers, before 3) assembly into a final meat product (See figure for overview). Previous work demonstrate that it is possible to culture bovine muscle cells in small bioreactors (up to 250 ml). We have up-scaled this culturing to bench bioreactors (up to 500 ml), and we monitored nutrition utilization during the cultivation. Our experiments demonstrated viable cells even after 20 days after seeding.



GrowPro
GrowPro-Sustainable bio-production of animal proteins for human consumption
Funded by the Bionær NFR 2018-2021

M38

cPLA2α – a major fibrosis regulator and potent therapeutic target in chronic kidney disease

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Chronic kidney disease (CKD) is a global public health challenge affecting more than 12 % of western world population. There is an unmet clinical need for identification of new treatment targets and development of novel agents acting on the disease mechanisms. Common causes of CKD are diabetes, hypertension and glomerulonephritis. Tubulointerstitial fibrosis is the result of all kidney diseases leading to chronic renal failure

This study was conducted to determine if inhibition of cPLA2α, either by knock out or selective inhibition with AVX002 (1), reduces renal fibrosis induced by unilateral ureteral obstruction (UUO) and aristolochic acid nephropathy (AAN) in mice. In UUO, kidneys of cpla2α-/- mice exhibited significantly less interstitial collagen deposition than wt mice. In both models performed on wt mice, inhibition of cPLA2α using AVX002, significantly and dose dependently reduced collagen deposition compared with vehicle injected mice. TGF-β1 plays a significant role in progression of fibrosis, inducing expression of fibrotic markers (2). Kidneys from cpla2α-/- mice and AVX002 treated mice had significantly reduced expression of TGF-β1 and the fibrotic markers α-SMA and fibronectin. In AAN, AVX002 dose dependently reduced plasma concentration of eicosanoids relevant for fibrosis.

We present evidence that cPLA2α is a key regulator of renal fibrosis. Loss of active cPLA2α decreases progression of renal fibrosis, and reduces expression of key fibrotic markers. AVX002 also reduces production of pro-inflammatory and pro-fibrotic eicosanoids, demonstrating that AVX002 inhibits cPLA2α activity, and that cPLA2α plays a central role in fibrosis. To conclude, our study shows that cPLA2α is a key therapeutic target in CKD.

1. Huwiler A. et al. Br J Pharmacol. 2012;167(8):1691-701.
2. Meng XM et al. Nat Rev Nephrol. 2016;12(6):325-38.

M39

Actin N-terminal acetylation impacts Golgi structural integrity

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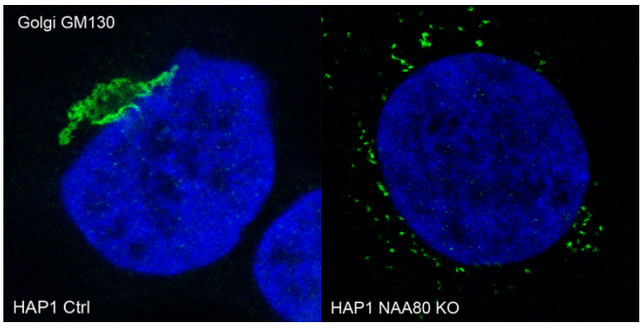
The probably most abundant modification of human proteins is N-terminal acetylation. So far six members of the N-terminal Acetyltransferase (NAT) family, NatA – F, were known to catalyse this reaction, in which an acetyl group of Acetyl-CoA is transferred to the N-terminal α-amino group of a protein. Importantly, various links between this modification and essential cellular processes were found reaching from degradation and folding on the protein level to severe malfunctions like cancer or the inheritable Odgen syndrome. A newly discovered member of the NAT family NatH/NAA80 was found to acetylate one of the most well-known and abundant proteins in human cells: actin. Since actin is involved in a huge variety of cytoskeletal functions like membrane stabilisation, internal transport processes or cell division and motility, there is a vast space of possibilities how N-terminal acetylation of actin can affect cellular functioning. Interestingly, it was already shown that a knockout (KO) of NAA80 in human cells leads to a significantly altered cell phenotype including accelerated motility, an increased ratio of filamentous to globular actin and a higher number of filopodia and lamellipodia. Here, we revealed by immunofluorescence staining with different Golgi markers that NAA80 KO cultures harbour an increased proportion of cells with a fragmented Golgi. Furthermore, this Golgi phenotype could be successfully reduced by re-introducing NAA80, suggesting a crucial role of actin N-terminal acetylation on Golgi integrity. By using state-of-the-art methods like cell shape and motility-restricting micropattern chips and high-speed confocal live-cell imaging the underlying mechanism of this effect are further investigated.



M40

IAP antagonists shift human osteoclastogenesis to cell death

Moen IN. (1), Westrin M. (1), Klaharn M. (1), Lien E. (1,2), Bjørkøy G. (1,3), Standal T. (1), Starheim KK. (1,4).

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Bone remodeling involves the removal of mineralized bone and formation of bone matrix mediated by osteoclasts and osteoblasts, respectively. To maintain skeletal integrity these processes needs to be tightly regulated, and an imbalance in bone homeostasis is connected to several pathological conditions. One outcome of dysregulated bone remodeling is increased bone degradation, which is a component of several diseases such as rheumatoid arthritis (RA), Paget's disease of the bone, osteoporosis, and myeloma bone disease. The RIPK1 protein kinase triggers a kinase cascade to regulate macrophage cytokine production and death. The cellular inhibitor of apoptosis proteins 1 and 2 (cIAP1 and 2) are essential to drive RIPK1-dependent pro-inflammatory signaling. We tested whether human osteoclastogenesis could be blocked by the IAP-inhibitors Birinapant and LCL-161, which both are in phase II clinical trials. Birinapant and LCL-161 led to a reduction in the number and viability of human osteoclasts. Both inhibitors induced cell death in an autocrine TNF-dependent manner. Surprisingly, while apoptosis is considered the dominant form of RIPK1-dependent cell death, IAP-inhibitors triggered both apoptosis and necroptosis in osteoclasts. In conclusion, we show that proinflammatory driven osteoclast up-regulation can be reduced by switching osteoclastogenesis to RIPK1-dependent cell death.

M41

There is a battle between the immune system and cancer. The Nobel Prize in Physiology or Medicine 2018

Inger Sandlie
Dept. of Biosciences, UiO

For the immune system to win, the tumor must display its dangerous mutations on MHC molecules, and specificT cells must be present, they must recognize MHC with mutant peptides on the surface of tumorr cells and be activated.

The Nobel prize winners found that after activation, brakes develop on the T cells, and the immune system is inhibited. If the brakes are blocked however, the immune system will go on killing or increase its killing of cancer cells and thereby prolong life or possibly cure the patient. Furthermore, some tumor cells express surface molecules that make them able to initiate T cell apoptosis. If these molecules are blocked, the T cells will go on killing with very good result for some patients.

James P Allison and Tasuku Honjo shared the Nobel prize in Medicine and Physiology 2018 for their discovery of cancer therapy by inhibition of negative immune regulation, so called checkpoint therapy. The Nobel prize web site says:

"The Laureates have shown how different strategies for inhibiting the brakes on the immune system can be used in the treatment of cancer. Their discoveries are a landmark in our fight against cancer."

Allison and Honjo have also inspired efforts to combine different strategies to release the brakes on the immune system. A large number of checkpoint therapy trials are currently underway against most types of cancer, and new checkpoint proteins are tested as targets.

Several Norwegian biotechnology companies develop anticancer vaccines that aim to increase the number of anticancer T cells and activate them. Some use them in combination with the new checkpoint therapy.

M42

Cd74, invariant chain, a master regulator of the antigen loading compartment, the immunoendosome?

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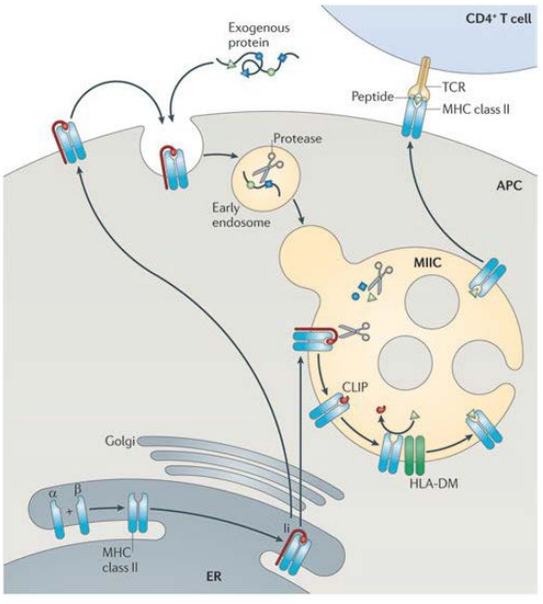
Invariant chain (CD74) is a multifunctional molecule expressed in antigen presenting cells; mostly in concert with MHC II but also decoupled, for instance in mature dendritic cells (DCs). In addition, CD74, which is internalized from the plasma membrane is a membrane receptor for MIF, macrophage migration inhibitory factor.

Invariant chain, with its two leucine based endosomal sorting signals that binds AP1 and AP2 adaptors was first found to be an essential partner for the proper trafficking of MHC II and therefore efficient antigen loading in the endosomal pathway and antigen presentation. A portion of CD74, CLIP, occupies the antigen binding groove of MHCII before it is replaced by a more specific antigen. The trimeric CD74 delays furthermore endosomal maturation participating in forming the peptide loading compartment. This property depends on a complete molecule and can be eliminated by a single point mutation of the cytosolic tail. The trimeric molecule has endosomal fusion properties independent on Rab5, PI3 kinase and EEA1 and I will discuss its role in endosomal maturation and how this property can be exploited to study maturation, endosomal fusion and fission. Invariant chain is found to alterate the expression of a large numer of genes and interacts with molecules involved in intracellular membrane traffic and is therefore a prime candidate for being a key molecule in the formation of the immunoendosome, the multivesicular endosomal loading compartment in antigen presenting cells. Furthermore, CD74 interacts with MHCI and can be used as a vector for simultaneously increasing both MHCI and MHCII mediated immune responses towards specific antigens and is ready to be tested in clinical therapeutic DC based cancer immunotherapy.



MHCII antigen presentation From Neefjes, J et. al., Nature Rev Immunol.,11, 823-36, 2011.
Nature Reviews | Immunology

M43

Uracil-DNA Glycosylase UNG1 Isoform Variant Supports Class Switch Recombination and Repairs Nuclear Genomic Uracil

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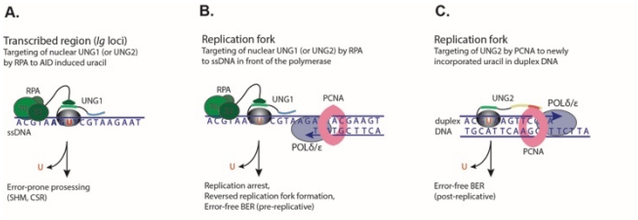
UNG is the major uracil-DNA glycosylase in mammalian cells and is involved in both error-free base excision repair of genomic uracil and mutagenic uracil-processing at the antibody genes. However, the regulation of UNG in these different processes is currently not well understood. The *UNG* gene encodes two isoforms, UNG1 and UNG2, each possessing unique N-termini that can mediate translocation to the mitochondria and the nucleus, respectively. A strict subcellular localization of each isoform has been widely accepted despite a lack of models to study them individually. To determine the roles of each isoform, we generated and characterized several UNG isotype-specific mouse and human cell lines. We found a distinct UNG1 isoform variant that is targeted to the cell nucleus where it supports antibody class switching and repairs genomic uracil. We propose that the nuclear UNG1 variant, which in contrast to UNG2 lacks a PCNA-binding motif, may be specialized to act on single ssDNA through its ability to bind RPA. RPA-coated ssDNA regions include both transcribed antibody genes that are targets for deamination by AID and regions in front of the moving replication forks. Our findings provide new insights into the function of UNG isotypes in adaptive immunity and DNA repair.



Simplified model showing targeting of nuclear UNG1 and UNG2 by RPA and PCNA to different genomic contexts
A. Targeting of nuclear UNG1-HMW (or UNG2) to AID-induced uracil in transcribed ssDNA by the flexible winged helix (WH)-domain of RPA2 (32 kD). The positively charged N-terminus may interact with the negatively charged DNA backbone. UNG1 motifs are indicated with similar colors as in Figure 1A. The AID hotspot is indicated in bold. The action of UNG in this genomic context mediates error-prone processing during SHM and CSR.
B. Targeting of nuclear UNG1-HMW (or UNG2) by RPA to the ssDNA template strand in front of the moving replicative polymerase. The action of UNG1 (or UNG2) in this genomic context will result in replication arrest followed by formation of a reversed replication fork and pre-replicative error-free BER before the replication will then start up again.
C. Targeting of UNG2 by PCNA to newly incorporated uracil in duplex DNA behind the moving replicative polymerases (POLδ and POLε). UNG2 motifs are indicated with similar colors as in Figure 1A. The action of UNG2 in this genomic context will mediate post-replicative error-free BER.

M44

A role for immunoglobulins in the osteolytic bone disease of multiple myeloma

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Most patients with myeloma develop a severe osteolytic bone disease (BD) causing pain and fractures. The myeloma cells secrete immunoglobulins (Igs) and the presence of monoclonal Igs in the patients' sera is the main diagnostic criteria. Igs have not been linked with the bone disease in myeloma.

In this work, we isolated Igs from serum of myeloma patients using protein G. We found that Igs from patients with BD (n=18) promoted osteoclast differentiation, whereas Igs from patients without BD (n=13) did not. The effect was mediated, at least partly, by FcγRII, since inhibiting FcγRII reduced the effect on osteoclastogenesis. When we fractionated the Igs by size-exclusion chromatography we found that the "osteoclast promoting activity" was in the high-molecular weight fractions, suggesting that they are in complexes. Since complex formation can be determined by glycosylation, we compared Ig glycosylation in healthy controls and patients, and examined whether it changes during disease progression. These analyses showed that patient IgG was less galactosylated (p= 0.02) and less sialylated (p=0.04) compared with control IgG. Also, patients with BD (n= 43) had less galactose on IgG compared with patients without BD (p=0.02, n=29). Further, the glycosyltransferases ST6GAL1 and B4GALT11, which adds sialic acid and galactose to the sugar chain, respectively, are less expressed in plasma cells from patients with BD (n=137) compared with those without (n=36, $p<0.002$, $p<0.001$). Importantly, we observed a significant reduction of IgG glycosylation (p= 0.02, n=8) in samples obtained from individual patients before and after the onset of BD.

Taken together, our data support that immunoglobulins may directly promote bone loss in multiple myeloma.

M45

NorSeq: The Norwegian Consortium for Sequencing and Personalized Medicine

Robert Lyle

Department of Medical Genetics, Oslo University Hospital and University of Oslo

The National Consortium for Sequencing and Personalized Medicine (NorSeq; norseq.no) is a consortium with partners at the universities and university hospitals in Oslo, Bergen, Trondheim and Tromsø. The aim of NorSeq is twofold:

1. To provide cost-efficient high throughput DNA sequencing to researchers

2. To facilitate the development and implementation of personalized medicine in Norway.

Currently we have a total of 23 sequencers from Illumina and Pacific Biosciences. In addition, we provide single-cell sequencing technology based on the 10x Genomics Chromium system.

An important part of our activities is to advise researchers on what is the best strategy for their particular project and thereby help researchers choose the sequencing protocol that is optimal for them in their research. We also perform some bioinformatics analysis for users and work to expand our offering in this area. If users need more bioinformatics assistance than we can provide they are referred to Elixir.

NorSeq is funded by a generous grant from The Research Council of Norway (RCN) which has made it possible for us to acquire state-of-the-art sequencing equipment. In addition, NorSeq receives funding to support the daily activities from The Regional Health Authorities and the universities and university hospitals in Oslo, Bergen, Trondheim and Tromsø.

M46

The genes controlling citrate and spermine secretion in the prostate

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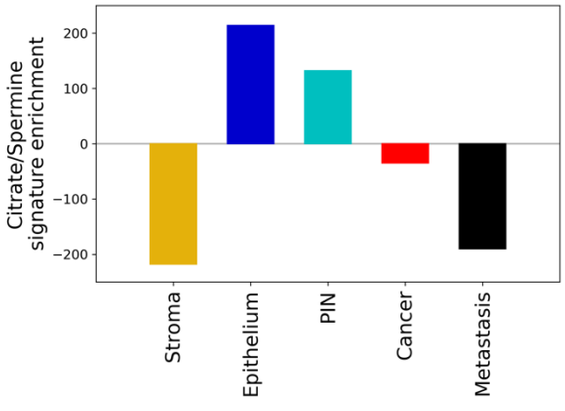
Secretion of metabolites citrate and spermine into prostate lumen is a unique hallmark for prostate epithelial cells, which is lost in prostate cancer. Despite its obvious importance, the molecular mechanisms and genes controlling citrate and spermine secretion in the prostate remains mostly unknown.

In this study we have used simultaneous measurement of citrate/spermine and transcriptomics to correlate metabolite levels to gene expression. We then use bioinformatics and reinforce these gene correlations in 12 prostate cancer cohorts containing 2915 tissue samples to create a gene signature of 150 genes connected with citrate and spermine secretion. We further explore the signature in public data, interrogating over 18 000 samples from various tissues and cell-lines.

The signature show upregulation in prostate epithelial cells, negative correlation to prostate stroma, and is uniquely expressed in the prostate compared to other tissues, validating its accuracy. Several novel zinc-binding proteins are present in the signature, suggesting new mechanisms for controlling zinc homeostasis in citrate/spermine secretion. In prostate cancer, the expression of the signature is gradually lost from low grade (Gleason <= 7) to high grade cancer (Gleason >= 8) and metastatic lesions, and is significantly ($p<0.05$) associated with better patient endpoints in 5 out of 9 cohorts (1847 samples in total), demonstrating clinical relevance. Signature expression is also lost in all common prostate normal and cancer cell-lines, underlining the need for improved model systems to study this essential and unique prostate feature.



M47

Online platform for biological network analysis in ELIXIR

André Voigt (1), Eivind Almaas (1)

(1) Department of Biotechnology, NTNU

Network analysis has been a highly successful approach for investigating biological systems in recent years. While a great variety of tools for network analysis have been developed, the implementation of custom workflows adapted to the users' specific needs often requires the user to have extensive programming and command-line experience. Using the ELIXIR bioinformatics platform, we have developed an online service for network analysis of biological data. In line with the ELIXIR paradigm, the service is composed of individual customizable modules using the extensive and well-tested NetworkX Python library. These modules can be seen as blocks, which can be connected and chained in a graphical programming environment (the output of one or more blocks serving as input to one or more others) in order to suit the user's workflow. The platform includes complete implementations of several common workflows, but users are encouraged to reassemble the modules as suits their purpose. With this service, we hope to provide a platform which makes it possible for biotechnologists less familiar with traditional programming environments to take advantage of complex network analyis.

M48

Genome-scale metabolic modeling: Metabolic engineering to increase production of nylon precursors in Pseudomonas

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Genome-scale metabolic modeling has experienced a sharp increase in popularity during recent years and is a widely used and powerful methodology to assess metabolic phenotypes and capabilities of an organism. Currently, there exist more than 160 well curated metabolic network reconstructions spanning more than 100 species, such as the Bacteria *Bacillus*, *Clostridium*, *Escherichia*, *Pseudomonas*, and *Salmonella*, the Eukaryota *Homo sapiens*, and *Saccharomyces*, and the Archaea *Methanosarcina*, to name just a few.

While there are several publically available models for some Families or even Genera, in prominent cases as for example *E. coli* or *P. putida* there are multiple models available for the same species, even strains. However, existing models may have been generated with a distinct purpose in mind. Consequently, they could produce low-quality results in other situations. By creating a new genome-scale metabolic model, or a derivation of a published one, it is possible to improve it's low-quality performance and tailor it to a particular focus.

Here, we exemplify this process using *P. taiwanensis* VLB120 with the aim of increasing the production of nylon precursors after inserting a necessary set of heterologous pathways. Together with *E. coli* based examples, we show the advantage of using such models for metabolic engineering in this active project.

M49

High-throughput screening identifies synergistic drug combinations in colorectal cancer cell lines

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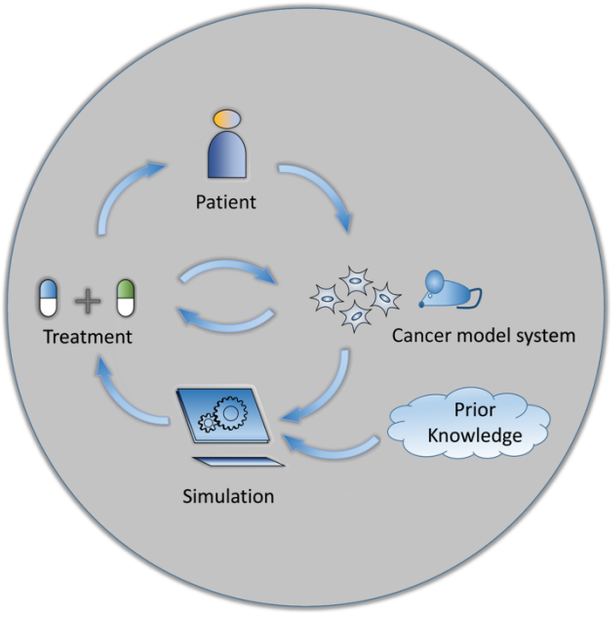
Colorectal cancer (CRC) is one of the most commonly occurring cancer types, and available therapies are frequently facing challenges related to drug resistance. The use of combination therapies has been suggested as a promising strategy to overcome resistance by blocking growth-promoting escape mechanisms. Here, we present data from a high-throughput screening experiment, aimed at identifying drug combinations with synergistic effects in CRC cell lines. By relying on viability as the main phenotypic readout, we screened 21 drug combinations (5 small-molecule inhibitors and 2 chemotherapeutic agents) against three CRC cell lines (HCT116, HT29 and SW620) in 2D and spheroid (3D) cultures. Using this procedure we were able to identify well-documented combinations, such as the combined inhibition of PI3K and MEK, as well as novel synergistic drug combinations. Additionally, some combinations exhibited differences in synergistic effect between 2D and 3D cultures, opening up for a discussion of potential differences in cellular signaling. Based on a newly defined assessment score, taking both potency and synergy into account, we selected a subset of the combinations, which are currently being subjected to further mechanistic studies. The screening data will be used for validating and refining computational models under development within the DrugLogics initiative, an interdisciplinary project aiming at using computational models for prediction of synergy and drug resistance in CRC.



M50

The Epigenetic landscape of two phenotypic extreme skeletal muscles - Soleus and EDL

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By varying the relative composition of different fibre-types within a skeletal muscle, an organism has the ability to fine-tune the muscle function according to physiological demands.

In adult animals, the muscle fibres are in a post-mitotic state. As a consequence, phenotypical remodelling is achieved by regulating the expression of fibre-type specific genes in a process that requires alterations of the epigenetic landscape through different processes such as methylation and acetylation of histones.

The muscle tissue is composed of approximately 40 - 60 % myonuclei, while the remaining are non-muscle cells with a different origin such as stromal and hematopoietic. In order to be able to study the plasticity of the muscle, it is essential to isolate the myonuclei subpopulation from the whole tissue, as a mixed-cell population are prone to increase the number of false-positive results.

In this study, we present a method for isolating myonuclei from whole native tissue.

The resulting pure myonuclear fraction allowed us to explore the epigenetic landscape for the two phenotypic extremes the oxidative Soleus and the glycolytic Extensor Digitorum Longus muscle (EDL).

Using our novel isolation method, we show that that the myonuclei epigenetic environment is significantly different compared to the whole tissue. Genome-wide analysis of the myo-specific epigenetic landscape in the Soleus and EDL muscles show that there are large dynamic differences between the two muscle types and that the two muscles seem to be controlled by two distinct regulatory networks.

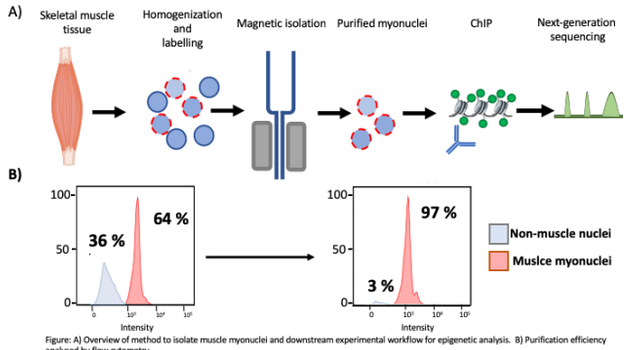

Figure: A) Overview of method to isolate muscle myonuclei and downstream experimental workflow for epigenetic analysis. B) Purification efficiency analysed by flow cytometry.

M51

Transcription-associated AAG-initiated base excision repair regulates gene expression

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Accumulation of DNA damage is considered to promote ageing, as well as accompany development and progression of diseases, such as neurological disordes and cancer. Base excision repair (BER) is the major pathway for the removal of DNA base lesions. The specificity of BER is determined by DNA glycosylases that recognize base lesions and initiate the pathway. Alkyladenine DNA glycosylase (AAG; aka MPG) is the main glycosylase for removal of alkylated DNA bases. Activity of AAG and of other BER enzymes was shown to be strongly impaired in the context of chromatin. It remains however largely unknown how BER efficiently removes base lesions from the chromatin to maintain genome integrity. In this work we demonstrate that majority of AAG localizes at the chromatin and directly associates with the components of transcription machinery. Loss of AAG caused predominantly upregulation of differentially expressed genes, thus suggesting repressive role of AAG in transcription. Analysis of differentially expressed genes resulted in identification of specific gene regions co-occupied by AAG-initiated BER and transcriptional components, which were in direct relation with the distribution of AAG-specific base lesions. Transcription impairments further resulted in perturbed AAG chromatin occupancy and impaired AAG-initiated BER. Taken together our recent results suggest interplay between transcription and BER, important to promote repair of alkylated DNA bases and regulate gene expression.

M52

Direct PCNA interactions via APIM are important for the RAD5 homologues' role in regulating DNA damage tolerance

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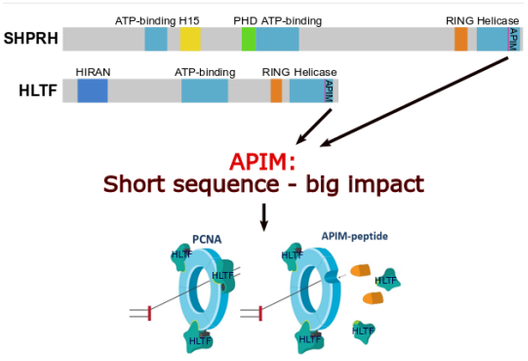

In order to bypass DNA lesions not repaired prior to replication and to prevent replication fork collapse, two branches of DNA damage tolerance (DDT) have evolved; DNA Translesion Synthesis (TLS) and Template Switch (TS). In TLS, special TLS polymerases are able to bypass the DNA lesion in an often error prone manner due to their enlarged catalytic site and lack of proofreading activity. In TS, on the other hand, the nascent strand of the sister chromatid is used as template and this is basically error free. These two branches of DDT (TLS and TS) are believed to be at least partly coordinated by mono- and polyubiquitination of Proliferating Cell Nuclear Antigen (PCNA).

The RAD5 homologues, HLTF and SHRPH, are both ubiquitin ligases involved in both branches of DDT: They are involved in TLS by recruiting TLS polymerases and they are also able to activate TS via polyubiquitination of PCNA. In addition, HLTF and SHPRH have both been suggested to be tumor suppressor genes because loss of function or dysregulation has been linked to cancer. However, well functional DDT pathways under chemotherapy might be a disadvantage, as this will promote cell survival at the cost of mutagenesis. Therefore, DDT pathways are interesting targets in cancer therapy.

Both RAD5 homologues contain an APIM (AlkB homolouge 2 PCNA Interacting Motif) sequence which can potentially bind to PCNA and can therefore possibly be blocked by APIM-containing peptides.

We showed that HLTF and SHPRH have functional APIM sequences and that their binding to PCNA is important for their functions in DDT. Both HLTF and SHPRH colocalized with PCNA in replication foci. In addition, their direct interactions with PCNA affected the mutagenicity of UV-induced lesions as well as the intracellular localization and stability of the two proteins. We impaired the RAD5 proteins´ interaction with PCNA by using both a cell penetrating APIM-containing peptide and APIM-mutant versions of the proteins. This led to export of SHPRH from the nucleus to the cytosol and to a dysregulation of the two branches of DDT, respectively. Thus, the interaction of HLTF's and SHPRH's APIM sequence with PCNA is important for proper regulation of DDT.

M53

Mitophagy inhibits proteinopathies and cognitive deficits in experimental models of Alzheimer's disease

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Accumulation of damaged mitochondria is a hallmark of human aging and age-related neurodegenerative pathologies, including Alzheimer's disease (AD). However, the molecular mechanisms of the impaired mitochondrial homeostasis and their relationship to AD are still elusive. Here we provide evidence that mitophagy, a cellular process mediating selective clearance of dysfunctional mitochondria, is impaired in AD patient hippocampus, in iPSC-derived human neurons and in animal AD models. Mitophagy induction diminishes proteinopathies and prevents cognitive impairment in AD mice by a mechanism involving microglial phagocytosis of extracellular Aβ plaques and suppression of neuroinflammation. Furthermore, mitophagy abolishes AD-related Tau hyperphosphorylation in human neuronal cells and reverses memory impairment in transgenic Tau nematodes. Our findings suggest that impaired removal of defective mitochondria is a pivotal event in AD pathogenesis. Interventions that stimulate mitophagy therefore have therapeutic potential in the prevention and treatment of AD.

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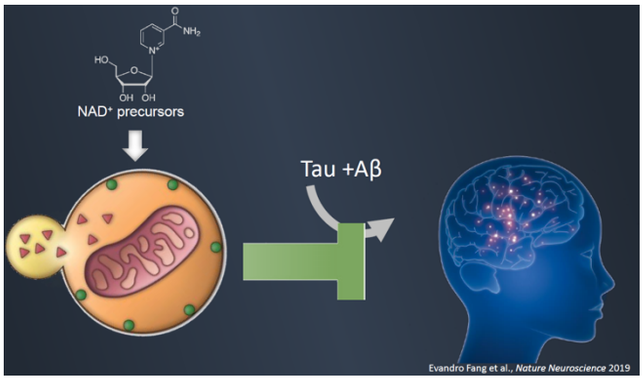
2. Fang, E.F. et al. Mitophagy inhibits amyloid-β and tau pathology and reverses cognitive deficits in models of Alzheimer's disease. Nature Neuroscience (In press).



M54

Centromeres License the Mitotic Condensation of Yeast Chromosome Arms

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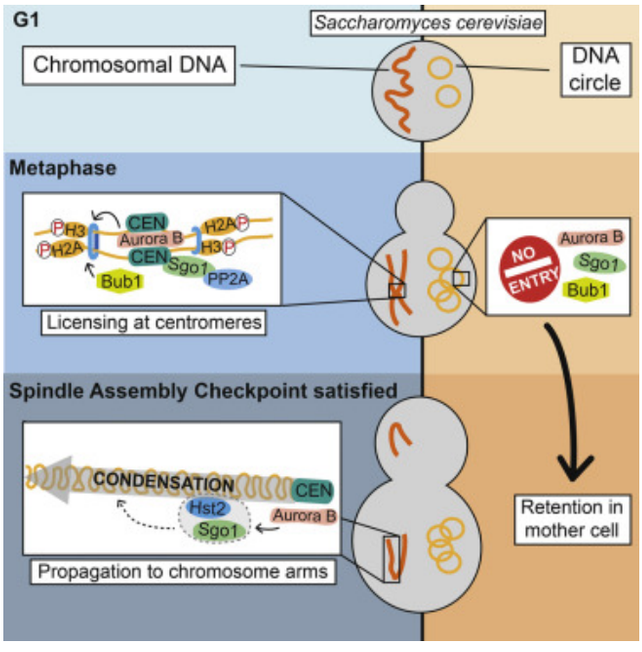
During mitosis, chromatin condensation shapes chromosomes as separate, rigid, and compact sister chromatids to facilitate their segregation. Here, we show that, unlike wild-type yeast chromosomes, non-chromosomal DNA circles and chromosomes lacking a centromere fail to condense during mitosis. The centromere promotes chromosome condensation strictly in *cis* through recruiting the kinases Aurora B and Bub1, which trigger the autonomous condensation of the entire chromosome. Shugoshin and the deacetylase Hst2 facilitated spreading the condensation signal to the chromosome arms. Targeting Aurora B to DNA circles or centromere-ablated chromosomes or releasing Shugoshin from PP2A-dependent inhibition bypassed the centromere requirement for condensation and enhanced the mitotic stability of DNA circles. Our data indicate that yeast cells license the chromosome-autonomous condensation of their chromatin in a centromere-dependent manner, excluding from this process non-centromeric DNA and thereby inhibiting their propagation.



M55

Synthetic lethality between DNA repair factors Xlf and Paxx is rescued by inactivation of Trp53

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Non-homologous end joining (NHEJ) is a DNA repair pathway that senses, processes and ligates DNA double-strand breaks (DSBs) throughout the cell cycle. During NHEJ, core Ku70 and Ku80 subunits bind DSBs as a heterodimer and promote further recruitment of accessory factors (e.g., PAXX, DNA-PKcs, Artemis) and downstream core subunits XRCC4 and DNA ligase 4 (Lig4).

Inactivation of *Ku70* or *Ku80* genes in mice results in immunodeficiency and high levels of genomic instability; deletion of individual *Xlf*, *Paxx* or *Dna-pkcs* genes results in viable mice with no or modest DNA repair defects. PAXX interacts directly with factor Ku70/Ku80, and is redundant with XLF. Isolated PAXX- and XLF-deficiencies in mouse models reveal no overt phenotype, whereas a combined deficiency results in embryonic lethality, which correlates extensive apoptosis in the central nervous system. These findings indicate important overlapping functions between PAXX and XLF. To determine if the embryonic lethality is *Trp53*-dependent, we intercrossed *Xlf-/-Paxx+/-Trp53+/-* mice and demonstrated that triple knockout *Xlf-/-Paxx-/-Trp53-/-* mice are viable, although possess reduced body weight, size of spleens and thymi, and severe lymphocytopenia. In addition, inactivation of *Trp53*rescues embryonic lethality of *Xlf-/-Dna-pkcs-/-* mice. Finally, a combined inactivation of *Paxx* and *Dna-pkcs* results in live-born fertile *Paxx-/- Dna-pkcs-/-* mice indistinguishable from*Dna-pkcs-/-* knockout controls.

M56

Genetic interaction between non-homologous end joining factors in mice and human

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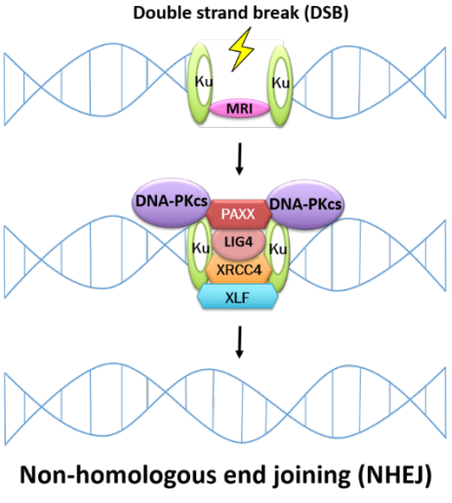
DNA double-strand breaks (DSBs) are highly cytotoxic lesions to the cells. Non-homologous end joining (NHEJ) is the major pathway to repair DSBs in mammals. NHEJ includes a variety of proteins, such as the Ku70/Ku80 heterodimer (Ku) to recognize, DNA-PKcs/Artemis to process, and XRCC4/LIG4 to ligate the DNA ends. XLF and PAXX are accessory NHEJ factors that are structural paralogs of XRCC4. However, the precise role of XLF and PAXX in DNA repair is unknown.

Lack of NHEJ factors, such as Ku, DNA-PKcs, XLF, PAXX, or MRI results in live mice that possess different levels of DNA repair defects, while genetic inactivation of *Xrcc4* or *Lig4* leads to embryonic lethality. Combined inactivation of *Xlf* and *Dna-pkcs*, *Xlf* and *Paxx*, or *Xlf* and *Mri* results in synthetic lethality in mice and increased genomic instability in cells. We found that deletion of *Ku70* or *Trp53* rescues the lethality of $Xlf^{-/-}$ $Dna\text{-}pkcs^{-/-}$, and deletion of *Trp53* rescues the lethality of $Xlf^{-/-}$ $Paxx^{-/-}$ in mice.

In addition, we characterized the genetic interactions between *XLF*, *PAXX*, *XRCC4*, and *DNA-PKcs, ATM* during DSB response in *NHEJ*-deficient human HAP1 cells, and found that XLF functions redundantly with both DNA-PKcs and ATM kinases, while PAXX functions overlap with neither DNA-PKcs nor ATM kinases; XRCC4/LIG4 show complementary functions with ATM but not DNA-PKcs in etoposide-induced DSB-sensitivity assays.



M57

Use of OGG1 inhibitors to alleviate inflammation and treat cancer

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Oxidative damage to macromolecules such as DNA is important in the aetiology of many diseases such as inflammation and cancer. The altered oncogene expression in cancer cells causes genomic instability and lost redox homeostasis, causing a high level of damage to macromolecules such as DNA. Pathways for preventing accumulation of oxidative DNA lesions raise the threshold of how much oxidative stress a replicating cell can handle and are therefore promising targets for cancer therapy [1]. Here, we investigate the effect of inhibiting oxidative DNA repair pathways with our recently developed OGG1 inhibitor TH5487 [2]. We find the compound to be toxic to a range of human cancer cell lines, but well tolerated by non-transformed lines, thus demonstrating cancer phenotype lethality. Treated cells accumulate DNA damage markers and experience severe S-phase problems, leading to growth inhibition and cell death through the accumulation of oxidative DNA damage specifically in mitochondrial DNA. This study validates OGG1 as a potential novel therapeutic cancer target and exemplifies targeting of cancer phenotypic lethality.

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M58

The genes controlling citrate and spermine secretion in the prostate

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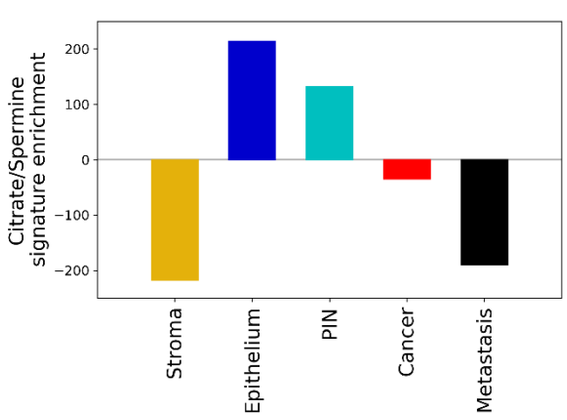
Secretion of metabolites citrate and spermine into prostate lumen is a unique hallmark for prostate epithelial cells, which is lost in prostate cancer. Despite its obvious importance, the molecular mechanisms and genes controlling citrate and spermine secretion in the prostate remains mostly unknown.

In this study we have used simultaneous measurement of citrate/spermine and transcriptomics to correlate metabolite levels to gene expression. We then use bioinformatics and reinforce these gene correlations in 12 prostate cancer cohorts containing 2915 tissue samples to create a gene signature of 150 genes connected with citrate and spermine secretion. We further explore the signature in public data, interrogating over 18 000 samples from various tissues and cell-lines.

The signature show upregulation in prostate epithelial cells, negative correlation to prostate stroma, and is uniquely expressed in the prostate compared to other tissues, validating its accuracy. Several novel zinc-binding proteins are present in the signature, suggesting new mechanisms for controlling zinc homeostasis in citrate/spermine secretion. In prostate cancer, the expression of the signature is gradually lost from low grade (Gleason <= 7) to high grade cancer (Gleason >= 8) and metastatic lesions, and is significantly ($p<0.05$) associated with better patient endpoints in 5 out of 9 cohorts (1847 samples in total), demonstrating clinical relevance. Signature expression is also lost in all common prostate normal and cancer cell-lines, underlining the need for improved model systems to study this essential and unique prostate feature.



M59

SynPromU - a new enabling technique for gene expression

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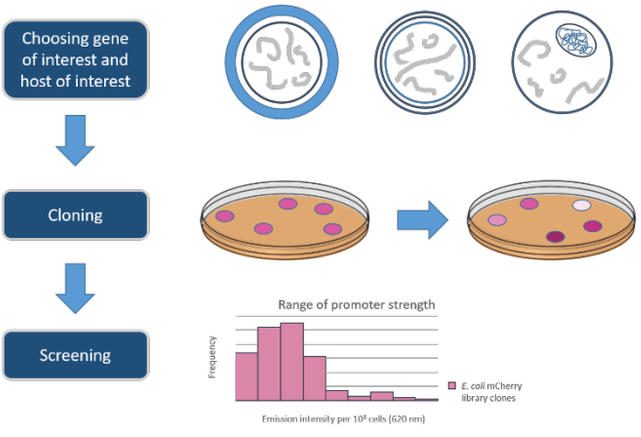
Proteins are utilised in a wide range of applications, from industrial biotechnology to medicine. Due to their wide use, the demand for proteins and their production is steadily increasing in the global market. This increasing demand is challenging for state-of-the-art protein production platforms. The current procedures mostly utilise trial-and-error-based optimisation approaches. Those procedures are costly and time consuming. In addition, there is a limitation in the choice of host organism for the production. The development of a novel protein production platform that allows a free choice of host organism, especially leading to the utilisation of unconventional hosts, is a step towards meeting the global protein production demands. Our universal platform utilises a fast straightforward approach, allowing the design of optimised tailored protein production in the organism of choice. The procedure is based on a selection strategy that replaces the current trial-and-error-based approaches.



M60

Isolation and characterization of potential immune modulating proteins from Methylococcus capsulatus (Bath)

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The non-commensal gram-negative bacteria *Methylococcus capsulatus* (Bath), mainly found in soil and water, has shown to reduce soybean meal-induced enteritis in Atlantic salmon and dextran sulfate sodium (DSS) induced colitis in mice. The immunomodulatory mechanisms behind the anti-inflammatory effects has not been identified. This bacterium encodes several proteins with homology and/or structural similarities to immunoregulatory proteins found in mammals. In this study, we have overexpressed and purified six of these proteins from *M. capsulatus* (Bath), and their putatively immunomodulating effects will be studied in human primary cells and cell lines. Some of the selected proteins showed anti-inflammatory properties when tested in an assay of IL-1β induced IL-8 release in human epithelial colorectal adenocarcinoma Caco-2 cells. To further investigate the selected proteins' effects on inflammation-associated pathways, human embryonic kidney (HEK) cells overexpressing Toll-like receptor 4 (TLR4), in addition to peripheral blood mononuclear cells (PBMC) cells, will be used. In the future, the potential immunomodulatory properties of these proteins may be the exploited to improve livestock gut health and/or treatment in lifestyle-associated inflammatory disorders in humans.

M61

Unraveling the functional role of Lsd1 in murine intestinal development

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After its discovery in 2004, the lysine-specific demethylase 1 (LSD1) has been a subject of extensive research, owing to its widespread expression across several tissue types and implication in various human diseases and cancers. Researchers have attempted to uncover its role in the development, morphology and physiology of organisms, but its function in intestinal development remains unknown.

LSD1, an epigenetic regulator of several genes, act on methyl-groups linked to lysines 4 and 9 on histone 3-tails (i.e. H3K4 and H3K9). LSD1 has been implicated as a key player in embryogenesis and tissue-specific differentiation, since *Lsd1* knock-out mice exhibit lethality at embryonic day 6.5 (E6.5). By breeding *Villin*-Cre mice with *Lsd1*$^{f/f}$ mice, we generated offspring with intestinal epithelium deficient of *Lsd1* (*Lsd1*$^{\Delta IEC}$). Intestinal tissues from adult *Lsd1*$^{\Delta IEC}$ mice, as well as organoids generated from *Lsd1*$^{\Delta IEC}$ mice display abnormal quantities of stem cells and differentiated cell types. We observe a reduction of goblet cells and complete eradication of Paneth cells, whereas the opposite holds true for stem cells and tuft cells. GSEA of WT- and *Lsd1*$^{\Delta IEC}$ transcriptome data shows an enrichment of fetal gene signatures. We are therefore investigating the role of LSD1 during intestinal development. Staining of different intestinal epithelial cell (IEC) types at different timepoints (E16.5-P14) in *Lsd1*$^{\Delta IEC}$ mice will give us an indication of how and when LSD1 affects IEC differentiation during development. Moreover, we will attempt to forcefully differentiate stem cells to Paneth cells in embryonic *Lsd1*$^{\Delta IEC}$ spheroids, to test the hypothesis of IEC lineage specification by LSD1 being an intrinsic feature of stem cells.

M62

Dynamic epitranscriptomic marks; critical regulators of meiosis and the developing brain

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The dynamics of epitranscriptomic marks, her N6-methyladenosine (m6A) and N1-methyladenosine (m1A) in RNA, were identified very recently. Early studies on m6A modifications in mRNA of various model organisms have identified crucial roles of this mark in meiosis and for fertility. The reversible nature of this modification points towards important regulatory roles. While the modification itself seems to act as a canonical Adenosine, specific reader proteins that bind m6A translate m6A containing mRNAs into gene activities by modulating e.g. their stability and translation. Recent studies identified crucial roles for some of these reader proteins, including YTHDF1 and YTHDF2, in brain development and behavior. At present, we design reporter models for in depth analysis of m6A reader proteins in meiosis, with a particular focus on the maternal-to-zygotic-transition (MZT), and early brain development.

We also work on characterizing the more mysterious role of the dynamic RNA mark m1A that also seem to affect fertility and neuronal morphology.

Recent relevant work from our laboratory and our collaborators include:

Tang et al., ALKBH5-dependent m6A demethylation controls splicing and stability of long 3'-UTR mRNAs in male germ cells. PNAS 2018,115:E325-E333.
Li, Zhao et al., Ythdf2-mediated m6A mRNA clearance modulates neural development in mice. Genome Biol 2018,31:69

M63

SMUG1 - a classical DNA glycosylase and an RNA processing enzyme

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Single-strand-selective monofunctional uracil-DNA glycosylase 1 (SMUG1) removes uracil and oxidized pyrimidines, such as 5-hydroxymethyluracil, via the Base Excision Repair (BER) pathway. Recent data from Ung-/-, Smug1-/- and Ung/Smug1-double knockout mice shows that there is a synergistic increase in genomic uracil in the Ung/Smug1-double knockout compared to either single mutant [1]. This suggests that SMUG1 efficiently prevents genomic uracil accumulation, also in the presence of UNG.

In addition to its classical BER function, SMUG1 interacts with Dyskerin 1 (DKC1), a component of the DKC1-H/ACA ribonucleoprotein complex, which is essential for telomerase biogenesis. We showed previously that SMUG1 functions in ribosomal RNA quality control [2], and that Smug1-/- cells and tissues, consequently, accumulate hmU in ribosomal RNA.

Here, we will present data showing that SMUG1 is required for co-transcriptional processing of the telomerase RNA component (hTERC) by regulating the presence of base modifications between the CR4/CR5 region and the H-box. Increased levels of hTERC base modifications are accompanied by reduced DKC1 binding and reduced hTERC stability. Consequently, SMUG1-deprived cells exhibit telomerase deficiency, leading to impaired bone marrow proliferation in SMUG1-knockout mice.

References:

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M64

Non-canonical roles of DNA glycosylases removing oxidative DNA base lesions in brain

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Base excision repair (BER) corrects DNA damage from oxidation. BER is initiated by a DNA glycosylase that recognizes and removes the damaged base. Accumulation of oxidative DNA damage has been proposed as a potential cause of age-related cognitive decline. Adult neurogenesis is crucial for maintenance of hippocampus-dependent functions involved in behavior. We have generated DNA glycosylase deficient mice that display cognitive and behavior abnormalities, or altered recovery after ischemic stroke. We showed a decline in post hypoxic-ischemia neurogenesis of NEIL3 deficient mice when compared to wild type mice. Further, we demonstrated that Neil3-/- mice displayed learning and memory deficits and reduced anxiety-like behavior. It appears that Neil3-dependent repair of oxidative DNA damage in neural stem/progenitor cells is required for maintenance of induced and adult neurogenesis to counteract the age associated deterioration of cognitive performance and regeneration after brain injury. Unexpectedly, NEIL2 deficient mouse show improved learning and reduced anxiety but no change in global accumulation of oxidative lesions in brain relevant for cognitive function (i.e. hippocampus and amygdala). Furthermore, Neil2 deficient mouse was hyper-resistant to post hypoxic-ischemia neuronal cell death. Non-canonical function of DNA glycosylases (e.g. NEIL1, NEIL2, NEIL3, MUTYH and OGG1) removing oxidative damage in brain will be discussed.

M65

A structurally unresolved loop improves the affinity of an essential human NAD biosynthetic enzyme for its substrate

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Nicotinamide adenine dinucleotide (NAD) is an essential redox cofactor, but also participates in diverse NAD-dependent signalling pathways including histones deacylation and DNA repair. In these pathways, NAD is cleaved and nicotinamide (Nam) is released and recycled to regenerate NAD. Nicotinamide phosphoribosyl-transferase (NamPT) catalyzes the first step in NAD regeneration by converting phosphoribosyl pyrophosphate and Nam into nicotinamide mononucleotide, which then condenses with the AMP moiety of ATP to NAD. Most prokaryotes use a more complex pathway for NAD biosynthesis from Nam, and only a few bacterial species harbour a gene encoding NamPT. Despite the presence of conserved residues involved in catalysis, the eukaryotic NamPT displays a by far higher affinity for Nam than the enzyme from prokaryotes. We identified a ten-amino acid loop insertion in the vertebrate enzyme that could not be resolved in any of the structures deposited in the database. Interestingly, this insertion appears to be connected to a beta-sheet that is involved in substrate binding. We wondered whether the loop may have an impact on the catalytic properties of the vertebrate enzyme. Using purified proteins expressed from recombinant DNA, we found that the loop insertion substantially increases the affinity of the human NamPT for its substrate Nam.

M66

Molecular mechanisms of ESCRT recruitment to damaged endolysosomal membranes

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Plasma membrane or endomembrane damage is associated with development of human diseases. Therefore, repair of the damaged cellular membranes is an important mechanism that contributes to our health. The endosomal sorting complex required for transport (ESCRT) machinery is crucial for endosomal sorting of growth factor and chemokine receptors in mammalian cells. ESCRT components have been found to mediate budding of enveloped viruses, abscission of the intercellular bridge that connects two daughter cells during cytokinesis, and sealing of the reformed nuclear envelope during mitotic exit. Common to all these processes is that they involve membrane involution and scission of a cytosol-containing membrane stalk. Thus, the ESCRT machinery has evolved to perform a number of related functions in membrane dynamics, suggesting that the ESCRT machinery could be specialized for sealing small holes in cellular membranes. Here we show that, under various conditions that cause injury to the lysosome membrane, components of the ESCRT-I, -II and -III are recruited. This recruitment occurs before that of Gal3 and the lysophagy machinery. Subunits of the ESCRT-III complex show a particularly prominent recruitment, which depends on the ESCRT-I component TSG101 and the TSG101- and ESCRT-III-binding protein ALIX. Interference with ESCRT recruitment abolishes lysosome repair and causes otherwise reversible lysosome damage to become cell lethal. Vacuoles containing the intracellular pathogen *C. burnetii* show reversible ESCRT recruitment, and interference with this recruitment reduces intravacuolar bacterial replication. We conclude that the cell is equipped with an endogenous mechanism for lysosome repair which protects against lysosomal damage-induced cell death but which also provides a potential advantage for intracellular pathogens.

M67

Critical Nodes of Viral Modulation Revealed Through an Integrated Network Analysis of Host-Virus Interaction Landscape

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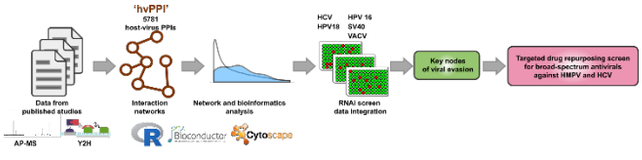
Viruses are one of the major causes of various acute and chronic infectious diseases and thus a major contributor to the global burden of disease. Several studies have shown how viruses, with their limited arsenal of proteins, have evolved to sabotage the host innate immune response by modulating key effector proteins and signaling pathways; by probing the host-virus protein-protein interaction landscape. A collective view of these multiple studies could advance our understanding of viral evasion mechanism and provide new therapeutic avenues for treatment of viral diseases. We performed an integrative meta-analysis to elucidate the host-virus interactome of 17 different viruses. Network and bioinformatics analysis showed how viruses are efficient in achieving maximal effect with a small genome by targeting multifunctional and highly connected host proteins. Viruses target host proteins with a high occurrence of disordered regions. We also identified the core cellular process subnetworks that are targeted by all the viruses and integration with functional RNAi data showed a large proportion of the targets are required for viral replication. We performed an interactome-informed drug repurposing screen and identified novel broad-spectrum antivirals against Hepatitis C virus and Human metapneumovirus. Altogether, this orthogonal datasets could serve as a platform for hypothesis generation and follow-up studies to broaden our understanding of viral evasion landscape.



M68

Esterases, “hubs” in biology.

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Acetylations play a key role in numerous biological regulatory processes. This is also a key element in hemicelluloses (mannan and xylan) that are major constituents in woody biomass like Norway spruce and birch. The high degree of acetylations of hemicelluloses inhibits other enzymes rendering the hemicellulose harder to decompose. Hence, acetylesterases are central in order to utilize this highly complex and abundant source of biomass that can be used in a wide range of products. We look into the microbial degradation of complex mannan and its potential use as a prebiotic to stimulate gut bacteria beneficial to health in humans and farm animals. Some bacteria have genetic toolboxes for processing complex mannans and their growth could thus potentially be selectively promoted by tailored mannan. We have characterized two carbohydrate esterases from a beneficial human gut bacterium that play a central role in the microbial utilization of mannan. The esterases collectively remove acetyl groups that are differently positioned in mannan. One esterase works specific on the 2-*O*-acetyls, which on mannose is in the axial orientation, whereas the other esterase removes 3-*O*- and 6-*O*-acetyls. This fundamental insight on how the esterases work on mannan and other hemicelluloses, can also be used in the industry and biorefineries to exploit the hemicellulose better.

Poster abstracts

P1

Epigenetic alterations associated with EMT within ER positive breast cancers

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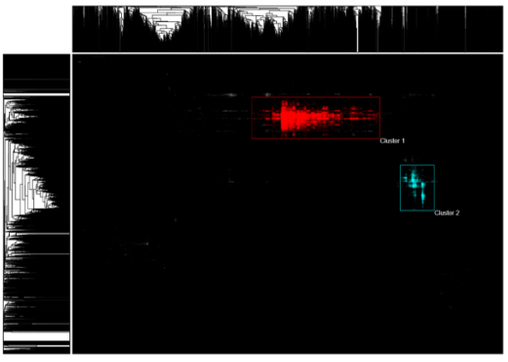
Background: Genome-wide expression methylation quantitative trait loci (emQTL) analysis have previously been shown to identify correlations between the DNA methylation level of CpG sites and gene expression, and to reveal gene regulatory networks involved in breast cancer pathogenesis.

Aim: We applied the emQTL approach to ER+ breast tumors only to investigate differences within these tumors in respect to DNA methylation and gene expression. The aim was to identify CpG-gene pairs that represented cancer promoting alterations and to understand how DNA methylation and TF activity contributes to ER+ breast cancer pathogenesis.

Result: Genome-wide emQTL analysis in ER positive tumors lead to the identification of 1,197 CpGs in which methylation level was correlated with the expression of 453 genes. The genes were enriched in processes related to EMT, and the CpGs were enriched within enhancer regions and within the binding regions of TFs associated with EMT such as TEAD1, TWIST1, YAP1 and PPARG. The tumors were scored using an EMT score based on their expression of epithelial- and mesenchymal marker genes. The EMT score was significantly correlated with the mean methylation of the CpGs which suggests a link between DNA methylation of these CpGs and tumor phenotype.

Conclusion: Our findings suggest that the EMT-related CpG-gene pairs are associated with gene regulatory networks wired by EMT-related TFs through a relationship between DNA methylation at their binding regions in enhancers and gene expression of their target genes. Our results provide insight into the mechanisms underlying EMT-related breast cancer pathogenesis in ER+ breast tumors.



P2

The generation of transgenic tools targeting specific brain regions via Enhancer-Driven Gene Expression (EDGE)

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Recent years have seen the development of extraordinary molecular tools for neuroscience, from transgenes that allow the control or visualization of neuronal activity to precise and unambiguous neuroanatomical tracing systems. However, the full potential of such tools can only be realized if they are deployed with anatomical specificity that approaches the granularity at which neural circuits operate. This cell-type specificity can only be obtained by molecular genetic methods. Though current methods can specify cell classes with some success, they are limited by the fact that with very few exceptions, native promoters are not specific enough: most genes are expressed in the brain, but in many distinct cell types. This is true regardless of whether one uses homologous recombination (e.g. CRISPR-Cas) or pronuclear injection with minimal promoters. Using precise tissue dissection techniques with ChIP-Seq of histone modifications associated with active enhancers, we have identified enhancers specific to particular brain regions. Combining these region-specific enhancers with a mutated minimal promoter incapable of driving gene expression alone has allowed us to generate lines of transgenic mice which target distinct cell types of particular brain regions. While our first proof-of-principle case targets distinct neurons of the Medial Entorhinal Cortex, we are currently expanding the analysis to additional brain regions. Ultimately, this enhancer-based approach should provide a means to deliver any transgene to any cell type in the brain, greatly enhancing our ability to understand and manipulate the native circuitry of the brain at the level of granularity at which it operates.

P3

Reelin-levels may affect the Accumulation of Intracellular Amyloid-β in the Reelin-Immunoreactive Neuronal Population of Entorhinal Cortex Layer II

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Already by preclinical stages of Alzheimer's disease (AD) the entorhinal cortex (EC) shows volume loss and selective degeneration of EC layer II-neurons is evident even before a memory-based clinical diagnosis of AD is possible. Amongst the characteristics of EC-layer II is the presence of a large population of principal neurons expressing Reelin. Using a rat model for AD (McGill-R-Thy1-APP model; Leon et al., 2010), we previously showed that Reelin-expressing layer II neurons selectively label positive for intracellular Aβ (iAβ), while preliminary results indicate this could also be the case for early-stage AD subjects (Kobro-Flatmoen et al., 2016). Following up on these findings, we are now testing whether increasing or decreasing the levels of Reelin in the Reelin positive EC layer II-neurons will affect the extent to which these neurons accumulate iAβ, and whether this alters the phosphorylation of the protein tau. Towards this end we have generated recombinant adeno-associated viruses carrying either the signaling competent middle fragment of Reelin in order to increase Reelin levels, or micro-RNA targeted to knock-down Reelin messenger RNA in order to decrease Reelin levels. These viruses are separately injected into EC-layer II of one hemisphere of AD animal models, using the APP/PS1 mouse model (Radde et al., 2006), the 3xTg mouse model (Oddo et al., 2003), and the rat model mentioned above, while the contralateral hemisphere is injected with control virus. First results indicate that injecting the micro-RNA carrying virus in EC-layer II indeed reduces the expression of Reelin and that this leads to a concomitant reduction of iAβ.

P4

Intestinal diseases studied by imaging

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The intestinal epithelium functions as one of the most important barriers in our body. It takes up water and nutrients, while at the same time it protects our body from infection and/or inflammation. The intestinal epithelium is characterized by an impressive turnover. It is completely renewed every 3-5 days. This property allows the tissue to rapidly repair upon damage, that for example is induced by pathogens, (food) particles, or chemical insults. The intestinal epithelial cell system has become a commonly used model for stem cell biologists, as the rapid turnover enable a relative ease to study how intestinal stem cells give rise to progenitors and differentiated epithelial cell lineages. 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. The research was performed includes the use of a range of microscopic techniques, like tiled confocal imaging of IF-stained intestinal tissues, 3D rendering of IF stained organoids and semi-automated quantifications of organoids cultures using ImageJ. Imaging and image analysis were performed at the Cellular and Molecular Imaging Core facility, CMIC.

P5

Single-cell Dynamics of Pyroptosis in Mycobacteria Tuberculosis (Mtb) infected human macrophages

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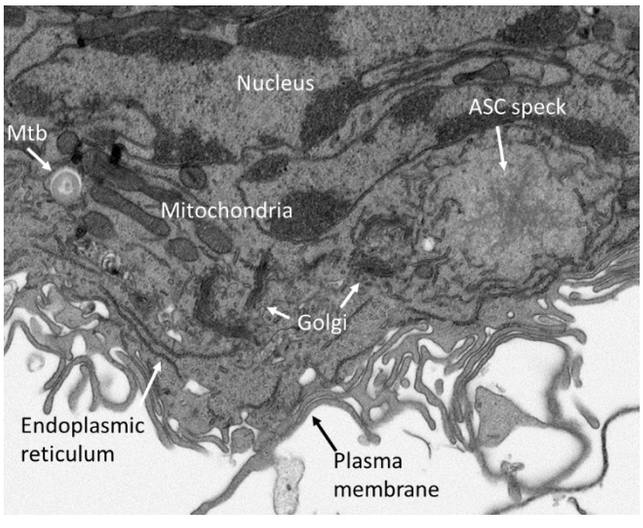
Virulent Mtb infections can cause necrotic cell death. Pyroptosis is a programmed, inflammatory and necrotic form of cell death that can follow activation of inflammasomes, cytosolic sensors of infection. The mechanisms and significance of pyroptosis during Mtb infections are unclear and the heterogeneity of Mtb infected cell cultures complicates studies. We applied live fluorescent imaging of single cells to reveal the order of events, combined with 3D electron microscopy (EM) to reveal ultrastructural changes over 24h of Mtb infection in human macrophages. We found that virulent Mtb can trigger phagosome rupture in infected THP-1 macrophages followed by canonical NLRP3 inflammasome activation, pyroptosis and release of IL-1b. Pyroptosis was the main form of necrosis at early timepoints and proportional to the bacterial burden. The exact mechanisms of NLRP3 activation are not known, but mitochondrial damage has been proposed. However, we found depolarisation of the mitochondria after inflammasome formation, implying that mitochondria are not involved in Mtb inflammasome activation. We used patterned coverslips, allowing relocation of single cells when moving to EM. EM revealed inflammasome complexes as fibrillar bundles in pyroptotic macrophages and the rupture of phagosomes was confirmed. Our ongoing studies continue to provide temporal and ultrastructural insight into the string of events leading up to inflammasome activation and pyroptosis in Mtb infected single cells.



P6

Fluorescent coupling of carbohydrates – A way to visualise microbial selectivity

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In microbial communities, understanding both the mechanisms and transport systems by which carbohydrates are internalised, and their intracellular breakdown and utilisation by host enzymes is an area that still demands much exploration. Coupling fluorescent labels such as 2-AA (anthranilic acid) or 2-AB (2-aminobenzamide) to mono- and oligosaccharides provides a way to track and follow carbohydrates as they are taken up and used by microbes. These labels are small, reducing end specific and enhance the sensitivity of the substrates allowing for detection and monitoring at very low concentrations.

In this study, we have labelled acetylated galacto-glucomannan from steam exploded Norway spruce and acetyl glucuronoxylan from birch. A range of "simplified" (depolymerised and/or deacetylated) substrates were also generated by enzymatic treatments and subsequently labelled. Labelling was confirmed using a combination of analytical technique including MALDI-TOF MS, HPAEC-PAD and HILIC-FLD-MS. Small scale, plate-based growth experiments were performed using the labelled substrates to screen for a number of different microbial targets, which are known to grow on either mannan or xylan based substrates. Both supernatant and cell contents were then analysed using a combination of the aforementioned analytical techniques. Next steps will involve the use of flow cytometry to gain a visual representation of the internalised substrates.

P7

High-throughput method for lipidomic analysis and semi-quantification of lipid classes

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Lipid analysis has gained growing interest in recent decades as lipids serve multiple functions across species, such us energy storage, protection, cell division and signaling and other important biological roles. Currently, direct infusion mass spectrometry (MS) and liquid chromatography – mass spectrometry (LC/MS) are two main analytical strategies used in lipidomics. However, each of these methods faces its own challenges.

Supercritical fluid chromatography (SFC), especially with columns packed with sub-2 µm particles as ultra-high performance SFC (UHPSFC), is an emerging technique with a great potential for fast and comprehensive lipid profiling. Supercritical fluids have lower viscosities than regular liquids, thereby permitting higher throughput analysis than LC. We have established a 6 min long method for lipid characterization and lipid class semi-quantification based on UHPSFC/MS^E technique.

The poster will discuss the development of our lipidome workflow and results from a comprehensive analysis of 192 salmon tissue samples (liver, muscle and gut) from a feeding trial with two different test conditions (feed and salinity). A statistical data analysis of the obtained data unambiguously showed the differentiation among the individual groups and identified lipids with the highest impact on the group clustering. The data are part of a comprehensive study on how the diet affects polyunsaturated fatty acids profile in salmons.

Moreover, we have applied our method for lipid profiling and semi-quantification of lipid classes in marine heterokonts thraustochytrids. Triacylglycerols with polyunsaturated fatty acids were found as prevalent lipids in thraustochytrids.

P8

Large panel sequencing reveals heterogenous mutation pattern in tumor tissue and circulating tumor DNA

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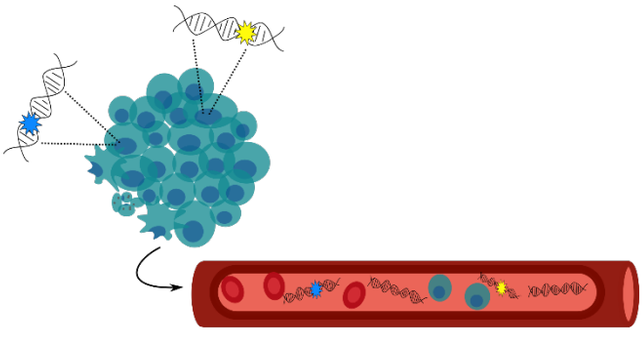
In cancer patients, DNA from tumor cells is released into the circulation (then called circulating tumor DNA, ctDNA) where it mixes into a background of circulating cell-free DNA predominantly from hematopoietic cells. ctDNA contains tumor-specific mutations that can be detected by high-throughput sequencing. Since it is difficult to acquire tumor tissue from some lung cancer patients due to location of tumor and risk for complications, sampling and analyzing ctDNA become an especially attractive approach for this cancer type. Not all somatic mutations detected in circulating cell-free DNA are in ctDNA. Somatic mutations also occur at very low frequency during differentiation of hematopoietic cells and may falsely be interpreted as ctDNA mutations. To distinguish between these mutations can be challenging. Most studies on ctDNA in lung cancer have been performed on patients with stage III and IV cancer. ctDNA level in blood is relatively high in these patients and tumor mutations can be distinguished from other variants based on the relative high allele frequency. The level of ctDNA is far lower in patients with early stage cancer and few studies have performed paired sequencing of both tumor DNA and ctDNA in this patient group. It is still unclear whether ctDNA analyses can replace tumor tissue. In this project, DNA from tumor, plasma and white blood cells from 31 stage I-III lung cancer patients was sequenced with a 275-gene panel. In 50 % of the patients, at least one tumor-specific mutation was detected. We show that a large number of unknown variants are detected in ctDNA. We conclude that it is not possible to use ctDNA without tumor and normal DNA as references and suggest that other applications are more promising.



P9

Enhancing enzymatic saccharification of Norwegian spruce by 2-naphthol impregnation.

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Lignocellulosic biomass is an abundant resource that can be used for renewable production of fuels and chemicals. Lignocellulose is a recalcitrant matrix containing cellulose, hemicellulose and lignin. To be able to access the sugars the recalcitrance needs to be lowered by a pre-treatment.

There are many ways to pre-treat lignocellulosic biomass. Currently, steam explosion is often used. Steam explosion disrupts the lignocellulosic matrix by applying steam followed by a rapid pressure drop. By impregnating or mixing catalysts with the biomass, the efficacy of the treatment can be enhanced greatly. A frequently used catalyst is dilute sulfuric acid. Dilute acid pre-treatment poses downstream problems both economically and environmentally, such as cost of neutralizing the slurry and disposing massive amounts of salts. A way to avoid these problems is to choose a milder catalyst, such as 2-naphthol. 2-naphthol is classified as a carbocation scavenger. When the lignocellulose is disrupted by steam explosion, phenolic groups of de-polymerised lignin are highly reactive and will form condensation reactions leading to enhanced recalcitrance. 2-naphthol is thought to prevent this reaction and thereby makes the cellulose more accessible and results in higher glucose yields.

In this study Norwegian spruce was impregnated with 2-naphthol to see how it affected sugar release after steam explosion of different severities. Treatments are assessed by enzymatic hydrolysis with a commercial cellulase cocktail under different conditions to activate lytic polysaccharide monooxygenases (LPMOs) present in the cocktail.

P10

Screening for modulators of catecholamine neurotransmitter synthesis

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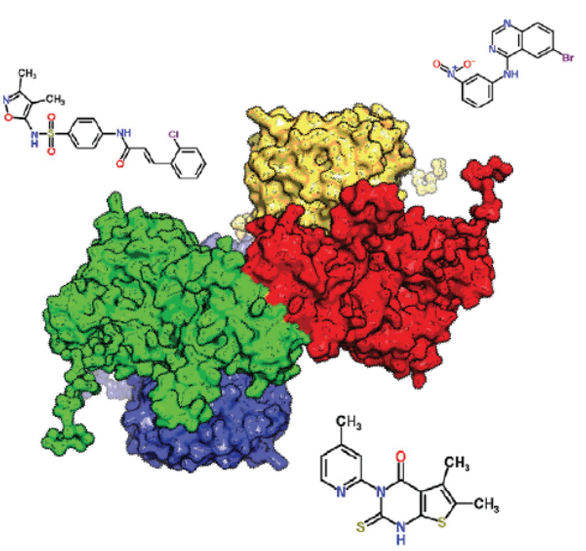
Catecholamine hormones and neurotransmitters are essential for regulation of motor coordination, behaviour, learning and memory. Tyrosine hydroxylase (TH) catalyzes the first and rate-limiting step in the synthesis, generating L-DOPA from L-tyrosine. TH-mutations cause the devastating, rare neurometabolic disorder TH deficiency (THD) with dystonia, and complex encephalopathy with neonatal onset in the most severe cases. Not all patients respond to L-DOPA, the only available medication, that also has several side-effects. Most mutations cause instability and misfolding of TH while maintaining some residual activity. THD thus appear suitable for pharmacological chaperone therapy.

We search for compounds that increase TH stability using a differential scanning fluorimetry-based high-throughput screening1 in a diversity collection with 10 000 cpds, a library of FDA-approved drugs (1280 cpds) and innovative compounds amenable to modification and favorable drug-like and ADME-Tox properties (344 cpds). The initial screening identified several non-selective, inhibitory compounds that preserve TH activity[2-3] and the screening of the Prestwick libraries has led us to 27 novel primary hits, including novel non-inhibitory compounds with high pharmacological chaperone potential. Fourteen hits have been prioritized based on concentration-dependent binding assays and five are being tested in additional binding and functional assays, as well as for stabilization in cells expressing wild-type and mutant TH. Furthermore, they will be tested in a mouse model with the *Th*-p.R203H mutation, equivalent to a recurrent human mutation associated with severe THD, which is non-responsive to L-DOPA and require novel therapies.



P11

Actin N-terminal acetylation by NatH/NAA80 affects cell adhesion and early cell spreading

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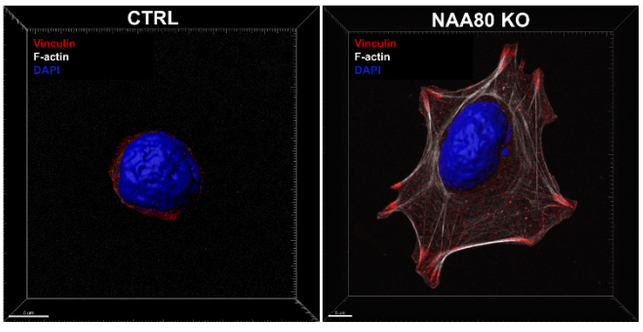
NATs (N-terminal acetyltransferases) constitute a family of enzymes which catalyse the reaction of the transfer of an acetyl group from acetyl-CoA to the N-terminus of around 80 % of the human proteome. NAA80 (N-alpha acetyltransferase 80) or NatH is a NAT and it has recently been discovered that NAA80 is actin's N-terminal acetyltransferase. Actin is the most abundant protein in eukaryotic cells, providing the cells with structure and shape as well as facilitating cell movement and adhesion. It has newly been found that the post-translational N-alpha-terminal acetylation of cytoplasmic beta- and gamma actin provided by NAA80, affects actin function. Elimination of actin acetylation by knockout of NAA80 decreases the ratio of globular to filamentous actin, increases formation of lamellipodia and filopodia and speeds up cell motility. Here, we have investigated how the absence of the N-terminal acetyl group on actin affects cell adhesion and early cell spreading. By using immunofluorescence staining of adhesion markers combined with F-actin stain, we found that HAP1 NAA80 knockout cells display distinct morphological differences compared to the control cells. Specifically, at early timepoints after cell seeding, a more extensive F-actin cytoskeleton was observed in NAA80 KO cells. This was accompanied with a dramatic increase in focal adhesion patches (revealed by vinculin staining) and a 1.5 fold increase in cell spreading area. The dynamicity of early cell attachment and spreading is now being investigated using live cell TIRF and spinning disk microscopy with actin and cell adhesion markers.



P12

DrugLogics: A ensemble model analysis related to drug prediction performance

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(1) NTNU (Norwegian University of Science and Technology), (2) BSC (Barcelona Supercomputing Center)

We have developed a computational pipeline which processes two main inputs: a cancer cell fate decision network and the activity state profile of a particular cell line, derived from gene expression and copy number variations data from the Cancer Cell Line Encyclopedia. Using a logical modeling framework coupled with a genetic algorithm approach, our pipeline trains an ensemble of models to fit to the corresponding steady state activity profile of a specific cancer cell line. Then, based on a given drug panel, a drug response analysis is performed on these trained logical model ensembles and the pairwise drug combination in-silico predictions are compared to the experimentally observed ones.

In this study, we show that even though the ensembles of models are trained to a specific consensus steady state profile and exhibit a match (fitness) of more than 50% to it, they still show a diverse individual stable state pattern landscape which leaves room for uncertainties in our steady state inference and thus allows for a more robust drug response analysis. We also devise strategies to split and compare the cell-specific trained models based on individual performance characteristics (number of true positive predictions) or the prediction of specific drug combination sets. This enables a mechanistic approach to find nodes whose state is decisive for the global behavior of the model, and thus represent potential biomarkers. Lastly, we correlate the models' fitness to a cell-specific activity state profile with prediction performance, and observe that a closer fitness to the steady state suggests more predictive models, corroborating our proof of concept of using an ensemble-based approach for drug combination predictions.

P13

Interaction of Thiosemicarbazones with the Ribonucleotide Reductase R2 subunit Studied by Resonance Raman Spectroscopy

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Ribonucleotide reductases (RNRs) are enzymes that convert RNA building blocks into DNA building blocks, and to be active, existence of a cofactor containing a Fe^{III}_2O center and a tyrosyl radical ($Y^{\cdot}$) in the R2 subunit is mandatory.[1]A strategy for cancer treatment has been to target this molecular system.

Selected Thiosemicarbazones, as free ligands or complexed with two copper(II) ions, have revealed promising inhibiting properties on ribonucleotide reductase R2.[2]We will here demonstrate how resonance Raman spectroscopy (rRaman) utilized with a freeze quench strategy can disclose the kinetics of disappearance of the R2 tyrosyl radical signal. We will in addition present an attempt to explain the rRaman spectra and propose an electrochemical mechanism for the tyrosyl radical quenching.

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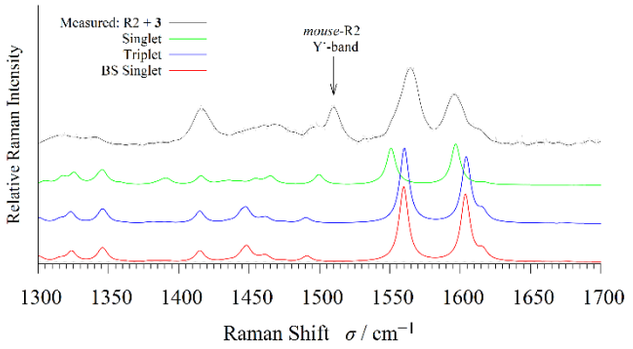

P14

Characterization of a novel π-methylhistidine methyltransferase

Erna Davydova(1), Lisa Schroer(1), Tongri Liu (2), Tadahiro Shimazu(3), Yoichi Shinkai(3), Michael McDonough(2), Christopher Schofield(2), Pål Ø. Falnes(1)

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Methylation is an important post-translational modification that can affect protein activity, interactions, localization, and stability. Methyltransferases (MTases) are the "writers" of this type of modification; the vast majority of MTase enzymes target lysine or arginine residues. However, it is becoming increasingly evident that other residues, like histidines, may also be extensively methylated. Methylation of histidine can occur on either the proximal or the distal nitrogen of its imidazole ring, leading to the formation of either pi (π)- or tau (τ)-methylhistidine, respectively. The presence of methylhistidine residues in human proteins was first reported over 50 years ago[1], however, only one histidine MTase has been identified in animals so far, and it specifically catalyzes τ-methylation of a histidine residue in actin[2,3]. Here, we describe a previously uncharacterized human MTase and present preliminary data suggesting that it is responsible for the formation of π-methylhistidine in a multitude of proteins.

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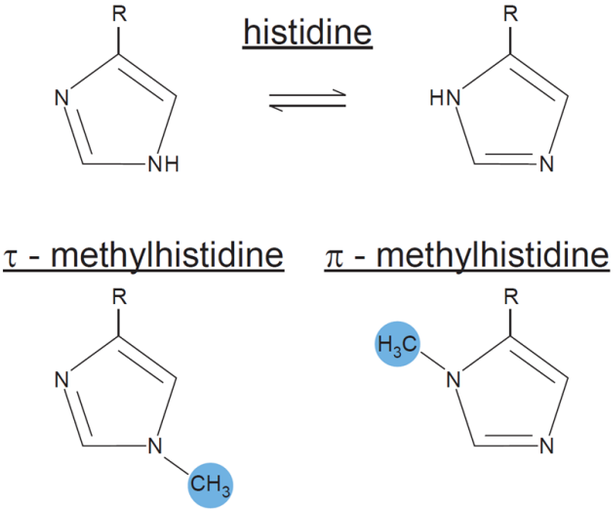

P15

Small variations in nanoparticle structure dictate differential cellular stress responses and mode of cell death

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Nanoparticles show promise in drug delivery, but it is becoming clear that uptake of nanomaterials leads to a variety of cellular stress responses, including redox imbalance, ER stress, and apoptosis. Detailed knowledge of the cellular responses to nanoparticles is imperative to fully exploit their potential as drug carriers. The cellular effects of poly(alkylcyanoacrylate) (PACA) particles are not fully explored. Here we compared the cellular responses to particles composed of cyanoacrylate monomers with varying alkyl chain lengths; butyl (PBCA), ethylbutyl (PEBCA), or octyl (POCA). Surprisingly, these highly similar NPs induced different stress responses and modes of cell death in human cell lines. POCA particles generally induced endoplasmic reticulum stress and apoptosis. In contrast, PBCA and PEBCA particles induced oxidative stress and lipid peroxidation depending on the level of the glutathione precursor cystine and transcription of the cystine transporter SLC7A11. The latter was regulated by the transcription factors ATF4 and Nrf2. PBCA particles strongly activated ATF4 downstream of the eIF2α kinase HRI, whereas PEBCA particles more potently induced Nrf2 antioxidant responses. Intriguingly, PBCA particles activated the cell death mechanism ferroptosis; a promising option for targeting multidrug-resistant cancers. Our findings highlight that even minor differences in NP composition can severely impact the cellular response to NPs and importantly, also highly different induction of protective cellular responses.

P16

Helse Sør-Øst Core Facility for Structural Biology

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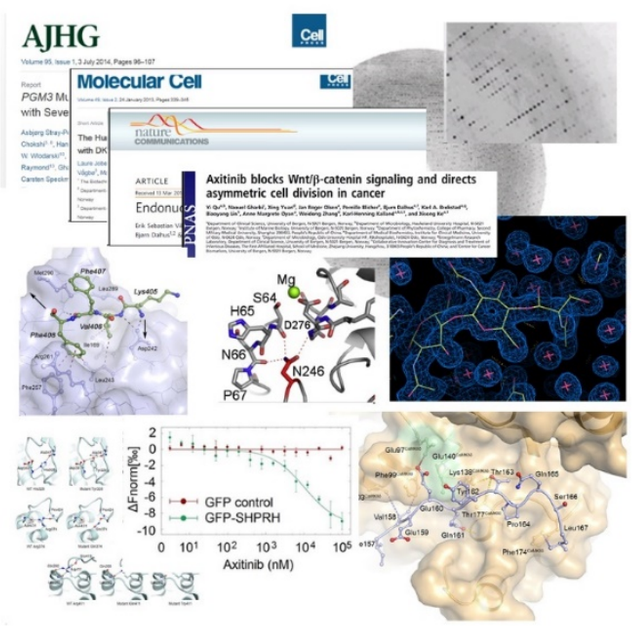
The Core Facility is located at the Oslo University Hospital, Rikshospitalet, and supported by Helse Sør-Øst (HSØ) and University of Oslo. We cover all hospitals and universities in the HSØ region. The facility is also part of NORCRYST – a national consortium for structural biology. Structural biology, including modeling, structure-activity analyses and related bioinformatics, require highly specialized instrumentation and competence. The facility provides experimental and computational service within structural biology to all research groups in the HSØ region in need for such support. We provide access to instruments or carry out experiments for users. Emphasis is on projects related to biomedicine, but we also support general life science or biotechnology projects depending on capacity.

The core facility will provide its users with a range of services within structural biology and supporting methods, including protein expression and purification, crystallization screening, crystal data collection, and structural determination of proteins and protein complexes by X-ray crystallography. In addition, we have all major methods for quantitative protein-interaction studies, including ITC, MST and SPR, and we can study both protein-protein and protein-ligand complexes. We also have a new nanoDSF instrument for investigating protein thermal stability, which can be used to optimize assay conditions, screen for ligand binding, or perform comparative analysis of genetic variants of proteins. We have also light scattering instruments (DLS and MALS) for protein stability/aggregation/complex studies.

The activity is high and we will present the methods and selected projects from users.



P17

Studying substrate specificity by site-directed mutagenesis in a novel bacterial lytic polysaccharide monooxygenase (LPMO

Amanda K. Votvik (1), Anton Stepnov (1), Bastien Bissaro (1), Åsmund K. Røhr (1), Vincent G. H. Eijsink (1) & Zarah Forsberg (1)
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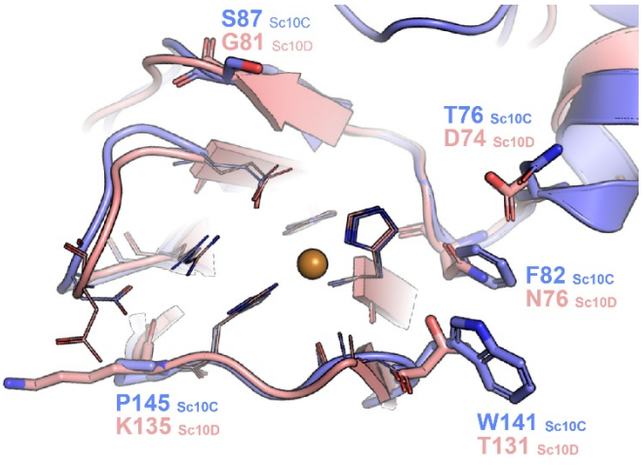
Cellulose and chitin are important biomass resources and abundant industrial by-products, which hold great potential for the future bio-economy. The utilization of these resources is hampered by the higher, crystalline organization of the otherwise simple polysaccharides, making them insoluble and highly resistant to enzymatic degradation. In nature, cellulose- and chitin-degrading organisms secrete a plethora of hydrolytic and redox enzymes, acting in synergy to depolymerize and utilize these polysaccharides for metabolic purposes. These enzymes include copper-dependent lytic polysaccharide monooxygenases (LPMOs) that oxidize crystalline areas of the substrate thus making it more accessible to hydrolytic enzymes. The soil bacterium *Streptomyces coelicolor* possesses seven *lpmo* genes, of which one (called *Sc*LPMO10D) shows an unusual sequence. Compared to previously characterized LPMOs, *Sc*LPMO10D has an extra C-terminal domain and is predicted to be covalently anchored to the cell wall. In addition, conserved residues in the LPMO domain share features with both chitin- and cellulose-oxidizing LPMOs. In this study, we have characterized *Sc*LPMO10D, the first enzyme in this novel LPMO clade, showing that this is a chitin-oxidizing enzyme. Taking advantage of the overall similarity between *Sc*LPMO10D and cellulose-oxidizing LPMOs we have used site-directed mutagenesis to explore how five surface-exposed residues (Fig. 1) contribute to substrate specificity.

Figure 1: Structural superposition of a model of chitin-oxidizing *Sc*LPMO10D (Sc10D) and cellulose-oxidizing *Sc*LPMO10C (Sc10C). Residues that differ between chitin and cellulose-oxidizing LPMOs and that have been targeted by site-directed mutagenesis are labelled and shown as sticks. The catalytic copper ion is shown as an orange sphere.



P18

Biogas production from food waste, the effect of hyperthermophile pre-treatmen

Vilde Holen
NTNU, Lindum AS

This is a presentation of my ongoing master's thesis

Why biogas

Production of biogas from different kinds of biological waste has increased after the EU in 1995 demanded a decrease in landfilling of biologically degradable material [1]. Also, to cope with the ongoing climate crisis, the need of replacing fossil fuels is crucial. Biogas is one of many solutions to the issue because it is a renewable energy source made from substrates such as food waste, sewage sludge and animal manure [2].

Biogas is a mixture of methane and carbon dioxide, and is produced in a process called Anaerobic digestion which is a series of anaerobic microbial reaction steps [3]. In the first step, hydrolysis and acidification, polymers are solubilized into smaller compounds by extracellular enzymes. Fermentation of the hydrolysis products leads to production of smaller substances such as volatile fatty acids (VFA). VFAs are short-chained fatty acids that can diffuse through bacterial cell membranes for further degradation, leading to the second stage, acetogenesis. In acetogenesis, acetogenic bacteria produce acetate (CH_3COOH) and molecular hydrogen (H_2) through oxidation of VFAs. To produce biogas, methanogens in the methanogensis step can utilize either hydrogen and carbon dioxide (CO_2) or acetate. A secondary product, the digestate, is the solid fraction left after completed methanogenesis. The digestate is rich in nutrients, and can be used as a soil fertilizer.

There are many different technical solutions to anaerobic digestion, but in all cases, there is a need of different types of pre-treatment. After a mechanical treatment removing unwanted solid residues, hygenization is necessary to eliminate pathogenic microorganisms.

Hyperthermics AS have developed a patented technology that utilizes hyperthermophilic microorganisms as a new alternative to pre-treatment of biological waste. The first full-scale plant is based and operated by Lindum AS in Drammen, and utilizes a strain of Thermotoga with an optimum temperature at 80 °C [4]. The bacteria is supposed to start degrading the waste and produce CH3COOH, CO2 and H2, which can be used for biogas production in methanogenesis. Therefore, the assumed advantage of applying this technology is to start the fermentation already in the pre-treatment of the waste and to begin the hygenization of the material.

Research on growing Thermotoga maritima (similar to the one used in the thesis) in lab scale has been known and successful for many years [6], but there is a lack of knowledge on industrial full-scale use of the bacteria. In addition, biological waste will have a variating composition, which

could be a challenge when utilizing a pure culture adapted to a specific medium.

Aim

The aim of this thesis is to study the effect of the full-scale hyperthermophillic pre-treatment of biological waste, and compare it to a purely temperature based hygenization. This is based on the hypothesis that the treatment from the Thermotoga species starts the degradation of the waste already in the pre-treatment, and the end products will be useful for methanogenesis.

Materials and Methods

CSTR Experiment

The first experimental part of the thesis was to run a continuous stirred tank reactor (CSTR) experiment. Specifically, Automatic Methane Potential Test System (AMPTS) was used. AMPTS is a system specifically made to run and control real-time methane production in a small scale biogas experiment. Inoculum for the experiment was collected at the full scale biogas plant at Lindum. 12 reactors were run for 23 days as this was the hydraulic retention time (HRT) of the experiment. In this part of the thesis, only food waste was used as the substrate for anaerobic digestion. This experiment was run to study if the methane production differed between differently treated wasted.

Two different treatments were introduced to compare hyperthermophillic pre-treated substrate and substrate pre-treated according to the regulations of the Norwegian food authorities (70°C for at least one hour). In addition, because the hyperthermophile treated material is pH regulated using NaOH, a third treatment was introduced:

Hyperthermophilic pre-treated food waste collected from the full-scale pilot plant

Food waste from buffer tank hygenized at 80 degrees for one hour

Food waste from buffer tank hygenized at 80 degrees for one hour and pH adjusted with NaOH

Both the substrate and the digestate was analysed for total VFA, total alkalinity/buffer capacity (TA), total and soluble chemical oxygen demand (TCOD/SCOD), Ammonium (NH_4-N), total solids (TS) and volatile solids (VS).

Degradation study

To get more information about the degradation happening in the Hyperthermics reactor, the content needed to be studied closer. Again, to compare the hyperthermophillic treatment to temperature-based hygenized waste, sampling was carried out retrieving material from the buffer tank and the main reactor. Material from the buffer tank was hygenized and pH-adjusted in the same way as the CSTR experiment.

Because food waste naturally has a low pH, the regulation to pH 7 demanded a lot of NaOH, which is both expensive and inconvenient. Therefore, in this part of the thesis, the material running through the plant varied between being mainly sludge from VEAS in Slemmestad, sludge from the biogas plant at Lindum and a mixture of Lindum sludge and food waste. The introduction of sludge to the plant is due to its higher pH and buffer capacity, and therefore reduces the need for pH regulation.

Collected material was analysed for VFA, TA, NH_4-N, TCOD, SCOD, TS and VS. In addition, samples were frozen down for further analysis with high performance liquid chromatography (HPLC) and quantitative PCR.

Results

The experiments for the thesis is ongoing, and hopefully results will be presented at the conference.

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P19

Insights into the biosynthesis of amphiphilic siderophores in cyanobacteria

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(1) NTNU - Depeartment of Biotechnology and Food Science

Iron availability is productivity-limiting in many oceanic environments, with phytoplankton requiring large amounts of iron for photosynthesis. To alleviate iron limitation, some marine phytoplankton excrete siderophores, low molecular weight iron chelators that function in iron uptake. In this work, we explore the function of synechobactin, a suite of amphiphilic siderophores produced by *Synechococcus* sp. strain PCC 7002. Using genome mining, we identify the siderophore operon, and hypothesize a biosynthetic pathway based on sequence similarity. By way of nonribosomal peptide synthetases, synechobactin is likely produced from citrate bound with the unusual building block 1,3-diaminopropane. Further, we identify the esterase/lipase SidH as likely responsible for addition of fatty acid tails to the siderophore, and thus responsible for its amphiphilic character. Creating deletion mutants for *SidH* and for siderophore production as a whole, we find that siderophore production is the primary iron acquisition strategy of *Synechococcus 7002* under iron limitation, and that the *SidH*-deletion influences the membrane-association of the siderophore produced. While amphiphilic siderophores are common in marine environments, this is the first time genes responsible for this characteristic has been assigned in cyanobacteria.

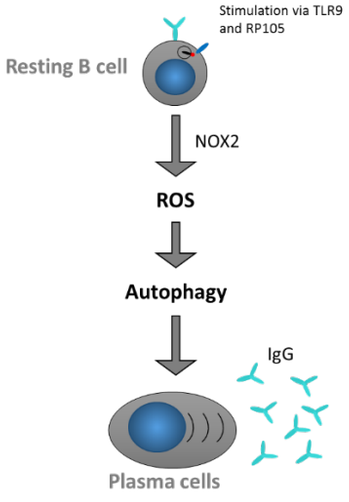
P20

Role of ROS-induced autophagy in IgG versus IgM production; Implications for common variable immune deficiency (CVID)

Karin M. Gilljam (1), Kristine Lillebø Holm (1), Maria Maseng (1), Agnete B. Erkisen (1), Børre Fevang (2), Heidi Kiil Blomhoff (1)
1: University of Oslo, Institute of basic medical sciences, 2: Oslo University hospital,Institute of Internal Medicine

Toll-like receptors (TLRs) are involved in innate polyclonal activation of B cells, and they are important for maintaining long-lasting first line defense against pathogens. We have previously shown that stimulation of B cells via TLR9 and the TLR homolog RP105 results in increased immunoglobulin (Ig) production and autophagic flux. Autophagy is a process important for recycling of damaged proteins and organelles ensuring cell homeostasis. High levels of reactive oxygen species (ROS) may cause oxidative stress, which may be harmful for cells. Nonetheless, ROS may also act as "second messengers" for cells in the immune system. It has been shown that ROS in certain cell types may induce autophagy, however, the role of ROS-induced autophagy and Ig production remains elusive. In order to further reveal the mechanisms involved in autophagy-induced Ig production, we have here explored the interplay between Ig production, autophagy and ROS.

In the present study, we have shown that ROS are rapidly generated upon TLR9/RP105-mediated stimulation of normal B cells, and that this ROS production is required for the initiation of TLR-induced autophagy. Notably, ROS-induced autophagy was shown to be essential for IgG production, but not for IgM production in the cultured B cells. We now explore the interplay between ROS, autophagy and Ig production in B cells from patients with common variable immune deficiency (CVID), as these patients are known to have dysfunctional B cells with reduced TLR responses and IgG secretion. Our preliminary results indicate that CVID-derived B cells undergo normal autophagy upon stimulation via TLR9 and RP105, but that dysfunctional ROS responses may explain the reduced production of IgG in the cells.



P21

Understanding rumen function using (meta) genome-guided metaproteomics

Thea O. Andersen (1) Phillip B. Pope (1)(2) Live H. Hagen (*)(1) Magnus Ø. Arntzen (*)(1)

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The rumen constitutes a specialized ecosystem composed of a dense and complex mixture of anaerobic bacteria, archaea, protozoa, fungi and phages. These microbes interacts closely to break down plant material into nutrients utilized by the animal. The enzymatic machinery encoded in the rumen microbiome is of scientific and industrial interest, leading to extensive efforts to unravel its functional profiles. Despite this, cellulose degradation has so far been attributed to a limited number of cultivated representatives, whereas the bulk of the rumen microbiome remains an under-characterized environment. Nevertheless, advances in culture-independent "meta-omics" approaches continues to increase our understating of microbiomes, and by combining multiple culture-independent meta-omics techniques, we can obtain a detailed real-time and *in situ* molecular portrait of which organisms occupy specific metabolic niches.Here, we are combing biological samples from various animal experiments and large-scale metaproteomics to investigate the active microbial populations controlling rumen digestion. In particular, our proteomic datasets are searched against a cow rumen-specific protein sequence database composed of metagenome-assembled genomes (MAGs) and genomes from cultivated rumen bacteria and fungi. This has demonstrated that saccharolyticactivity is associated to several MAGs from as-yet uncultivable populations, as well as to well-known specialists in cellulosic biomass degradation.

P22

Characterization of Proteins in the Ribonucleotide Reductase Redox Network

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The importance in catalyzing the first reaction in DNA synthesis has rendered the enzyme ribonucleotide reductase (RNR) extensively studied for decades. Still, due to the complexity of this enzyme, especially as a drug target, many questions remain unanswered. To reduce ribonucleotides to deoxyribonucleotides, the manganese-bound bacterial class Ib RNR must be activated via a pathway involving several redox proteins. In our work, we have studied the interaction between proteins involved in this RNR system, including the catalytic subunit (NrdE), the radical-initiating Mn-bound subunit (NrdF), a required superoxide-supplying flavoprotein (NrdI), and several potential ferredoxin/flavodoxin $NADP^+$oxidoreductases (FNRs). In order to map and characterize the modes of interactions in the RNR redox pathway, we have combined biochemical, crystallographic, spectroscopic, kinetic, and bioinformatics analyses. Our studies present important findings on protein-protein interactions [1], electron transfer reactions, and protein structure, kinetics and activity [2,3]. These findings have identified missing pieces of the class Ib RNR redox network, giving new insight into proteins that could be attractive targets for design of novel, selective antibiotics against pathogens that rely on class Ib RNRs.

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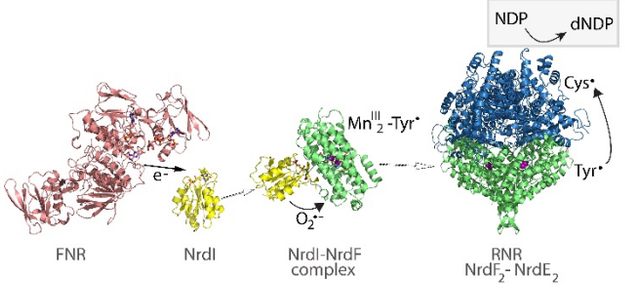

P23

Identification and Characterisation of p62/SQSTM1-Interacting Proteins

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SQSTM1/p62 is a scaffold protein and a selective autophagy receptor for ubiquitinated protein aggregates, damaged mitochondria and intracellular microbes. It helps to link the cargo to autophagosomes for degradation in the lysosome. Proteins in complexes with p62 therefore, could theoretically function either as modulators of autophagy or as substrates

Using immunoprecipitation of epitope-tagged p62 expressed in cells and mass spectrometry, we sought to identify proteins in complexes with p62. Novel proteins were identified, in addition to the known autophagy proteins such as NBR1, TAX1BP1, KEAP and NDP52. The characterisation and role of some of these novel proteins in autophagy will be presented.

P24

Breaking the speed limit – multimode fast scanning of DNA

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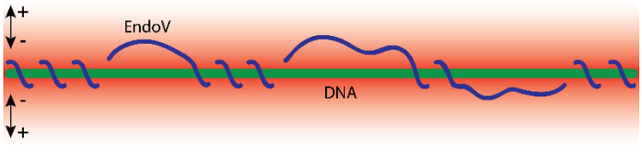
In order to preserve genomic stability, cells rely on various repair pathways for removing DNA damage. The mechanisms how enzymes scan DNA and recognize their target sites are incompletely understood. Using high-localization precision microscopy along with a 133 Hz high sampling rate, we have recorded EndoV, human hOGG1 and bacterial AlkD and AlkF interacting with 12-kbp elongated lambda phage DNA in an optical trap. We observe that EndoV switches between three distinct scanning modes, and that the enzyme in the highly mobile scanning mode may disengage from a strictly 1D helical diffusion and hop along the DNA. We also show that the wedge motif in EndoV affects the DNA scanning.

While nearly all DNA glycosylases bend the DNA and flip the damaged base into a lesion specific pocket upon encounter, the HEAT-repeat like DNA glycosylases, like AlkD, detect and excise bases without base flipping. We observe that AlkD has a monomodal scanning behaviour in contrast to multi-mode scanning for hOGG1, which uses base-flipping. In addition, hOGG1 and AlkD scan DNA with high redundancy and low coverage efficiency, while the endonuclease EndoV has low redundancy and high coverage efficiency.



P25

A model cell line to study intracellular trafficking of TLR9

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Toll-like receptor 9 (TLR9) is an intracellular receptor located to endosomal compartments where it is responsible for recognition of unmethylated CpG DNA derived from virus or bacteria. Activated TLR9 induces signaling pathways leading to production of type I interferons (IFNs) and proinflammatory cytokines like TNF, which initiate an immune response. The distinct groups of cytokines are produced from different endosomal maturation states. Despite the important role of TLR9 in combating pathogens, the receptor has also been found overexpressed in different cancer cells, for instance in breast- and ovarian cancer cells (Berger, Fiegl, Goebel, et al., 2010). The signaling pathway leading to TNF-production is typically associated with cancer promotion while the pathway leading to increased IFN-production is associated with cancer suppression (Pradere, Dapito, Schwabe, 2014). Hence, elucidating the intracellular trafficking of TLR9 could reveal great insight in the conflicting ability of TLR9 to both promote and suppress cancer development.

In this project, an inducible THP1 TLR9 mCherry cell line was established to study trafficking of and signaling from TLR9. Wild type THP1 cells carry monocytic markers, providing a monocyte like morphology. It was found that THP1 TLR9 mCherry cells differentiated with PMA gave a TNF-response but not an IFN-response to CpG-stimulation. However, differentiation with IL-4 and GM-CSF gave a more robust IFN-response. Future experiments will include siRNA targeting trafficking proteins in order to investigate the effect of knock down on TLR9-signaling and -trafficking.

Berger R, Fiegl H, Goebel G, et al. Toll-like receptor 9 expression in breast and ovarian cancer is associated with poorly differentiated tumors. *Cancer science* 2010; 101(4): 1059-66.

Pradere JP, Dapito DH, Schwabe RF. The Yin and Yang of Toll-like receptors in cancer. *Oncogene* 2014; 33(27): 3485-95.

P26

The chitinolytic potential of the fish pathogen Aliivibrio salmonicida

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The Gram negative marine bacterium *Aliivibrio salmonicida* is the causative agent of cold-water vibriosis, a disease with long history in Norwegian aquaculture. The genome of the bacterium contains several genes related to utilization of chitin as a nutrient source. However, this catabolic pathway has been predicted to be incomplete due to disruption of key genes by insertion elements. In an attempt to investigate this hypothesis, we used an approach combining both biochemical and microbiological experiments. Firstly, characterization of the single family 18 chitinase and the two family 10 lytic polysaccharide monooxygenases (LPMOs), demonstrated that all three enzymes were able to depolymerize chitin to soluble chitooligosaccharides. When combining the enzymes, a boost in chitin degradation was observed and the main product formed was chitobiose. Secondly, cultivation experiments showed that the bacterium was able to grow on both soluble (GlcNAc and chitobiose) and insoluble (beta-chitin) substrates as the sole carbon source. Finally, gene deletion studies demonstrated that growth on beta-chitin was dependent on the family 18 chitinase, but not on the LPMOs. In conclusion, our results show that *A. salmonicida* is able to utilize chitin as a nutrient source.

P27

Alkyl adenine glycosylase regulates the expression of neurodevelopmental genes and modulates behavior

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Alkyladenine DNA glycosylase (AAG) recognizes and removes a wide range of DNA damaged bases. The accumulation or inefficient repair of DNA base lesions compromises the genome stability and is associated with several pathologies, as neurological conditions. The malfunction of AAG affects different cellular processes and more recently, it has been suggested that AAG may also influence transcription. Here we demonstrate that loss of AAG in human cell lines alters gene expression, primarily of neurodevelopmental genes. Behavioural studies in wild-type, Aag-deficient and Aag transgenic mice show important role of Aag in modulation of anxiety and spatial memory. By using neural stem/progenitor cells (NPCs) isolated from the brains of neonatal wild-type, Aag-deficient and Aag transgenic mice, we further show that imbalanced Aag expression impairs neural differentiation and the ability to self-renew, while it does not affect NPC proliferation. Taken together our results suggest that besides in canonical DNA repair alkyladenine DNA glycosylase plays important role in regulation of gene expression, thus influencing neurodevelopment.

This project is funded by NFR. Authors would like to thank L.D. Samson for Aag mice.

P28

Unravelling postmortem changes in muscle proteins that may influence eating quality of pork

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The two most important quality parameters for pork are water-holding capacity and meat tenderness. These two traits greatly affect processing properties and eating quality of the meat and will ultimately influence profitability and consumer acceptance and repurchase of pork products. Many factors may influence WHC and tenderness of meat, including rate of postmortem pH decline and ultimate pH, proteolysis and chemical composition of meat, illustrating the complexity of these traits. In an industrial trial, samples from more than 800 pigs were taken, and quality measurements as purge (loss of water during cooler storage) and tenderness were made. Western blot analysis of a selection of 48 pig samples taken at 20 days postmortem showed that meat with a high occurrence of the 30-kDa degradation product of troponin T, a commonly used indicator for postmortem proteolysis in meat, had improved meat quality such as reduced purge and more tender meat. Furthermore, samples taken at 1 and 20 days postmortem were analysed by label-free LC-MSMS to unravel other protein changes or mechanisms that may explain some of the variation seen in meat quality. Raw data from LC-MSMS was analysed by MaxQuant, followed by a partial least square regression (PLSR) analysis. Our results show that systematic variation in several proteins together can be used to explain some of the variation in purge, water loss during cooking and meat tenderness.

P29

Using Styrene/Maleic Acid Lipid particles and Membrane Scaffolding Protein Nanodiscs to solubilize VMAT2 for functional and structural studie

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Vesicle Monoamine Transporter 2 (VMAT2) is an integral membrane protein (IMP) responsible for the uptake of dopamine into synaptic vesicles in neurons. As such it has been implicated as an interesting target for research into various diseases, from psychiatric disorders to Parkinson's disease. Solubilization, purification, and investigation of IMPs have traditionally presented extra challenges compared to cytosolic proteins. Customarily, detergents are used to solubilize the protein and substitute the lipid environment surrounding the protein at physiological conditions in cells. Solubilization of IMPs in detergents complicates all experiments with IMPs, and in many cases the substitution of natural lipids with detergents can alter or destabilize the protein. One of the ways to solve these challenges is to solubilize the protein in nanodiscs (NDs). NDs are nano-size discoidal lipid bilayers bound by lipoproteins such as the membrane scaffolding proteins (MSP) or amphipathic polymers such as the styrene/maleic acid (SMA) co-polymers. Using nanodiscs to solubilize the MPs keeps the membrane protein in its immediate native environment, preserving structure and function.

VMAT2-GFP-His was expressed in SF9 cells and the membrane fraction was prepared. The prep was either incubated with SMA for SMA lipid particles (SMALPs) formation or solubilized with detergent for incorporation in MSPs. Final ND samples were analyzed using dynamic light scattering (DLS), HPLC-analyses with a Bio-SEC column and transmission electron microscopy (EM). NDs of approximately 15 nm were obtained, and incorporation of VMAT2 in the NDs was confirmed using western blot.

P30

Bacteria-mucus interactions in skin using germfree Atlantic salmon yolk-sac fry model

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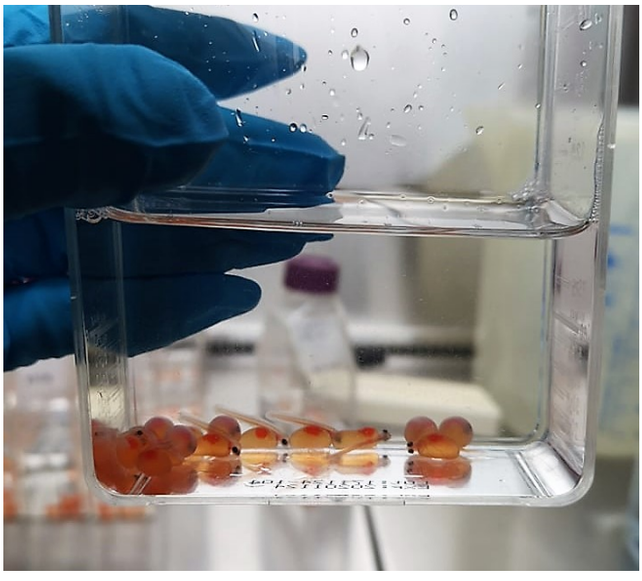
Mucosal tissue, covering the body cavities of animals and the skin of fishes, constitutes a major barrier against microbes and other agents in the external environment. The gut and the resident mucosal microbiota is one of the most studied mucosal surfaces and has shown to contribute to the mucosal barrier through several mechanisms. The fish skin mucus is also colonized by a microbiota, but its function and composition are poorly understood. This makes the skin an interesting structure to investigate, as we know little about the colonization success of bacteria, and which function these play in the "mucosal barrier" of the skin.

The hypothesis of this project is that different bacterial strains have various abilities to colonize the mucosal surfaces of salmon fry. The aim is to characterize growth on a mucin-based and a general cultivation medium for 5 bacterial strains and investigate whether the isolates affect the survival of the fry, and their initial colonization success.

To study this, germfree salmon fry and their surrounding environment were inoculated with single bacterial isolates (mono-associations). After three days of incubation, the number of surviving fry was registered, and colonization success for the bacteria on skin and gut were determined by conducting CFU counts on agar plates. Furthermore, flow cytometry was used to determine bacterial concentrations in the fish water, and qPCR will be used to estimate the bacterial density in fish samples.



P31

The vesicle transport protein protrudin affects Toll-like receptor 4 signalling

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Pattern recognition receptors (PRRs) protect organisms against the invasion of microbes by inducing the innate immune response. Toll like receptors (TLRs) represent one group of these PRRs. One member of the 11 TLRs found in mammals is TLR4. It recognizes lipopolysaccharide (LPS) localized on the surface of gram negative bacteria. Its receptor signalling occurs from the cell surface and phagosomes upon two different pathways. Activation of TLR4 results in the secretion of inflammatory cytokines and type 1 interferons.

Preliminary data showed a link between the TLR4 signalling and the vesicle transport protein protrudin. Protrudin localized in the endoplasmic reticulum (ER) is involved in kinesin 1 dependent vesicle transport. Decreased transcription and secretion of cytokines upon LPS or *E.coli* stimulation of macrophage-like THP1 cells was observed by knocking down protrudin.

The aim of this project is to investigate the impact of the vesicle transport protein protrudin on TLR4 signalling. Signalling was observed to be decreased by protrudin knock down without decreasing mRNA levels of TLR4. But if TLR4 signalling is affected by its intracellular localization regulated by the vesicle transport protein protrudin or if other players regulated by protrudin are involved is unclear. Therefore, further research is necessary to understand if there is a direct link between protrudin and TLR4 signalling.

P32

Antibiotic tolerance vs persistence: How to assay and distinguish the terms

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The scientific community is not agreeing on the definitions of antibiotic tolerance and persistence, and there is confusion on the assays used to characterize these sub-pools of bacteria in a bacterial community. Persistence is linked to metabolic dormancy and thereby increased antibiotic tolerance of a sub-population which are genetically similar to metabolic active and sensitive cells in the population. Persistence is frequently linked to the toxin/antitoxin systems used to modulate metabolic state. Antibiotic tolerance is a more general term associated with acquired increased tolerance to antibiotic stress which is not necessarily driven by genetic modification but rather physiological state dependency. Both types are unlike the antibiotic resistant bacteria, but persisters are believed to contribute to recalcitrant infections, and thereby contribute to the development of resistance. The exact mechanism for persister formation and resuscitation remains to be fully elucidated, and further studies are needed. In our study, we have focused on developing more robust and unambiguous assays of persistence and tolerance, and furthermore, linking growth rate and metabolic state of the population to the frequency of persisters/tolerant bacteria in a population.

P33

Patient-derived immunoglobulins control TLR-induced cytokine response from macrophages

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Multiple myeloma (MM) is a cancer caused by proliferation of malignant plasma cells in the bone marrow. Frequent infections and loss of bone are common complications of the disease. The malignant plasma cells secrete immunoglobulins (Igs), which leads to the presence of high amounts of monoclonal Igs in the circulation. Igs bind to Fc-receptors, present on hematopoietic cells, including macrophages. Toll like receptors (TLRs) recognize conserved microbial structures and activation of TLRs leads to production of pro-inflammatory cytokines. The aim of this study was to investigate how Igs obtained from MM patient with or without bone disease (BD) influence TLR-induced cytokine secretion. We found that THP1 and primary macrophages produced less pro- and anti- inflammatory cytokines when they were stimulated with Igs from MM patient with BD compared with MM patients without BD and healthy controls. These data suggest that in patients with BD Igs may inhibit an efficient innate immune cells response towards infections.

P34

Tapping into the proteome of shipworm symbionts – A novel source of cold-adapted lignocellulases

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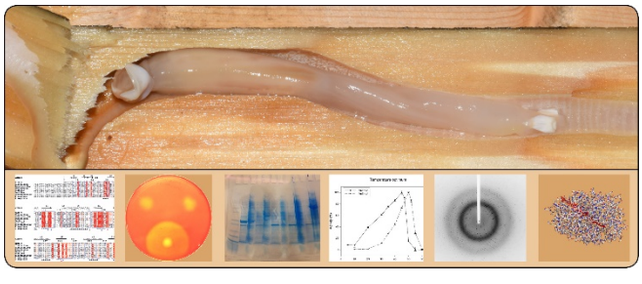
The leftover lignocellulosic biomass from forestry and agricultural activities has the potential to be converted to highly valuable products using enzymes. As of now, the lignocellulases applied in industry are usually thermophilic (T_{opt} 40-60 °C) and have a low pH optimum. The green enzyme technology is still in its infancy, and more enzymes with unique and improved properties are needed to open up for better utilization and product development of the lignocellulose.

Shipworms are marine bivalves that are common in seas worldwide. They are experts at degrading lignocellulose from driftwood, and rasp large tunnels in the wood with their shells before devouring the degraded wood particles. Bacterial symbionts located in the gills aid the shipworms in this process by secreting lignocellulose-degrading enzymes. These bacteria represent an abundant source of industrially relevant enzymes. *Psiloteredo megotara* seems to be the most common shipworm along the Norwegian coast. In northern Norway, the sea is cold all year, meaning that the enzymes from the symbionts need to efficiently degrade lignocellulose at low temperatures. In this project, ten synthetic expression constructs have been carefully designed starting from a *P. megotara* symbiont metagenome. The expression levels and solubility in *Escherichia coli* will be tested. Some of the targets will be expressed intracellularly while others have a PelB signal sequence relocating them to the periplasmic space. The enzymes giving soluble expression will be characterized and their structures solved using X-ray crystallography. Cold-adapted marine enzymes are less studied and under-exploited by the industry. This project will provide enzymes with industrially desirable properties.



P35

Do APOBEC proteins contribute to genomic instability in colitis-associated colorectal cancer?

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The molecular events underlying the progression of inflammatory bowel disease to colorectal cancer (CRC) are not fully elucidated. However, it is clear that the pathogenesis of colitis-associated cancer (CA-CRC) differs from hereditary and sporadic CRCs. We aim to elucidate the molecular events that drive the genomic instability phenotype characteristic of CA-CRCs. Aberrant expression of APOBEC proteins induced by NF-κB in the inflamed colon may contribute to genomic instability by deaminating cytidine leading to C to T transition mutations. Examination of APOBEC expression by qRT-PCR in normal colon tissue, tissue of increasing dysplasia and cancer in a classical CA-CRC patient, showed increased expression of APOBECs in inflammation and high grade dysplasia. Hence, this case report suggests that APOBECs may have contributed to the genomic instability due to expression in inflammation. We will also present detailed immunohistochemical analyses of DNA damage checkpoint activation in the same material.

P36

Human Embryonic Stem Cells as a Model for Paracetamol-induced Epigenetic Deregulation and Neurotoxicity

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Recent epidemiological studies have suggested an association between paracetamol exposure during pregnancy and the risk of neurodevelopmental disorders in children (e.g. ADHD). The molecular mechanisms linking paracetamol and the increased risk of ADHD have not been delineated. Prenatal development is critical for epigenetic patterning, and some medications which are commonly used during pregnancy, such as analgesics, antidepressants and anticonvulsants, have been associated with epigenetic changes. Recent work from our group has shown an association between long-term paracetamol exposure during pregnancy and DNA methylation differences in children with ADHD. To study the mechanisms by which prenatal exposure to medications might affect brain development, we have developed a in vitro protocol for neurotoxicity testing using neural differentiation of human embryonic stem cells (hESCs). We use single-cell RNA sequencing (scRNA-seq) to assess gene expression heterogeneity at hESC and neural rosette stage. Preliminary results show that scRNA-seq provides valuable information about marker genes in each cell type. These markers were used to establish and assess the accuracy of an antibody panel for flow cytometry. This hESC differentiation model will be used to study the effect of paracetamol on DNA methylation and gene expression during neurodevelopment. Further, the model can potentially be used to screen other commonly used pharmaceuticals during pregnancy.

P37

Metabolic modeling for microbial production of bio-concrete

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Production of cement is responsible for roughly 6% of global anthropogenic CO2-emissions, with the looming threat of runaway climate change, alternative construction methods must be considered. In the Digital Life project BioZEment 2.0, bacteria will be used for the dissolution and re-precipitation of limestone to be used as a construction material. Achieving prediction and control in biological systems is a complex and data-hungry task; however, constraint-based modeling has shown an ability to predict the metabolic behavior of microorganisms.

A genome-scale metabolic model (GEM) is constructed from the genomes of the bacteria collected and used in the project, which appear related to the strain Bacillus subtilis. This model can be used for simulations of cellular metabolism under various environmental conditions, using Flux Balance Analysis (FBA) and related methods, allowing changes to media composition or genome to be planned and tested in silico. This will indicate where to focus work in the wetlab.

By coupling the metabolic model to geochemical modeling of the limestone mixture, predictions of both the metabolic activity of the bacteria and its interplay with the environment are expected to improve. This will in turn improve the accuracy of in silico predictions, better supporting lab efforts.

P38

Viral Vector Core Facility at Kavli Institute for Systems Neuroscience/CNC, NTNU

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Recent years have witnessed a tremendous development of molecular tools for visualizing and manipulating cellular mechanisms, including genome editing and gene regulation, allowing research that until recently was considered 'science fiction'. Recombinant viruses are highly efficient delivery vehicles for applying such tools to difficult-to-transfect primary cells and slices, to create stable cell lines, to transduce tissues in vivo for elucidating underlying biological mechanisms and recently for gene therapy applications. A combinatorial approach using viral tools with the vast repertoire of transgenic animals available is a powerful strategy to target specific cells in complex organs such as mammalian brains. Adeno Associated Virus, Moloney Murine Leukemia Virus, Lenti virus and Rabies virus are all common transgene-delivery agents, each having distinct characteristics making them suitable for different research questions. They can be generated in a well-equipped virus lab, however establishing such a dedicated facility in every lab is not feasible, and there are currently no viral core facilities in Norway. Long waiting time for custom made viruses, shipping expenses and transport delays are some of the difficulties experienced when obtaining vectors from facilities abroad. Further, depending on the scientific question one may need novel viral tools with specific features, demanding novel vector designs. We have a well-equipped facility and rare expertise to make all the above-mentioned viruses, which have been used in multiple projects. The Viral Vector Core at Kavli/CNC is a non-profitable facility that offers consultation, design and construction of a wide variety of viral vectors to augment research in Norway.

P39

Nitrifying Capacity and Microbial Community Structure during the Start-up of Freshwater and Brackish water Moving Bed Biofilm Reactor in Recirculating Aquaculture Systems

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Recirculating aquaculture systems (RAS) are used for land-based farming of fish, and involve water recirculation and treatment through mechanical and biological filtration. Recirculation of water is a solution to water shortage, with the additional benefit of increased biosecurity and control of water quality. In 2011, the Norwegian Ministry of Fisheries and Coastal Affairs allowed a production period of Atlantic salmon (*Salmo salar*) up to 1 kg in land-based systems. A longer production time on land may allow complete control of environmental factors (e.g. temperature, pH), as opposed to in sea cages, where the fish is exposed to pathogens and varying environmental conditions. Saline conditions introduce new operational challenges in RAS, especially for the biological nitrification process. The objective of this master thesis is to investigate the development in nitrifying capacity and microbial community composition during the start-up of freshwater and brackish water moving bed biofilm reactors (MBBRs) in RAS. DNA extraction, PCR, and Illumina sequencing of 16S rDNA was performed to map the microbial community. Capacity tests were performed to examine the nitrification capacity of the MBBRs. The preliminary analysis of the nitrification capacity and microbial community will be presented. This study is ongoing and will provide information to optimize start-up and operation of RAS in post-smolt production.

P40

Exosome derived biomarkers for computational drug response predictions in patients with colorectal cancer

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Introduction: Colorectal cancer (CRC) remains one of the world's most prevalent cancers with substantial challenges related to inter-tumour heterogeneity and drug resistance. Extracellular vesicles such as exosomes offer exciting opportunities in the study of key phenotypic biomarkers allowing for treatment follow up. Exosomes mirror the protein and RNA content of the parental cells from which they are derived. With the use of exosomes we aim to obtain cancer biomarkers from metastatic (m)-CRC patient liquid biopsies for drug response predictions using computational modelling developed in our research team[1].

Method: Initial work is being carried out on CRC cell lines derived from primary (HT29, HCT116) or metastatic (SW620) disease. Exosomes were isolated using ultracentrifugation followed by quantification by nanoparticle tracking analysis (NTA), western blot analysis (exosomal markers: TSG101 and ALIX) and transmission electron microscopy (TEM) visualisation. We are currently setting up proteomics (western blot, targeted MS phosphoproteomics) and PCR protocols to evaluate exosomal protein and nucleic acid biomarkers against the cell lines from which they are derived.

Results: We will report on exosomal quality and yield as well as proteomic and nucleic acid biomarker profiles and demonstrate their use in configuring computational models for predicting drug response validated against drug screens available in our research group.

Conclusions: The work reported here serves as a stepping-stone to the establishment of exosomal phenotypic biomarker analysis from cancer patient liquid biopsies for improved treatment follow up.

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P41

Role of Gcn5 and PCAF acetyltransferases during B lymphocyte development

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Double-strand break (DSBs) are constantly generated in our DNA and defects in DSB repair result in various disorders, including immunodeficiency and cancer. During B and T lymphocyte development, DSBs are introduced on purpose to create antibody/antigen receptor diversity during V(D)J recombination and Class Switch Recombination (CSR). DSBs activate the DNA damage response (DDR) pathway leading to recruitment of DDR factors and multiple chromatin modifications at DNA damage sites. In particular, the ATM/H2AX-dependent acetyltransferases Gcn5 and PCAF are involved in many cellular processes through the acetylation of histone H3 at lysine 9 (H3K9ac), but their roles during B lymphocyte development is not well described yet. Here we found that combined B cell specific-inactivation of Gcn5 and Pcaf in mice correlates with severe B lymphocytopenia with a reduction in mature B cell count in spleen and blood, and an increased proportion of pro-B cells in the bone marrow, suggesting a role of Gcn5 and PCAF during the V(D)J recombination. In addition, we showed that Gcn5/Pcaf double deficiency in mice leads to defects in both IgG3 and IgG1 CSR. Using the CRISPR/Cas9 technique, we generated pro-B (vAbl) and mature B (CH12F3) cell lines lacking either Gcn5 or Pcaf, or both Gcn5 and Pcaf to further elucidate the role of these acetyltransferases during the V(D)J recombination and the CSR. We demonstrated that mature B cell lines lacking both Gcn5 and PCAF decrease the CSR to IgA. Currently, we are characterizing the efficiency of V(D)J recombination in double knockout Gcn5/Pcaf and control pro-B cells.

P42

Effect of salmon lice treatment and lice infection on bacterial colonization on Atlantic salmon skin

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Salmon louse (*Lepeophtherius salmonis* Krøyer) causes significant losses in Atlantic salmon aquaculture industry. Lice damage the fish by feeding on their mucus, skin and blood, and the wounds they are causing increase the risk of secondary infections. Most current methods for treatment of salmon lice, are applied after the fish has been infected. There are some preventative measures for example cleaner fish and lice skirts, but none that works on the fish own immune system and responses, like the skin mucus.

In an experiment carried out at NTNU Sealab, the potential preventative effect of an experimental feed called Biofeed Salmon Forte, against salmon lice infection was investigated. A precursor feed, Biofeed Aqua Forte, has previously been found to have a preventative effect on trout against sea lice. Atlantic salmon was fed either the experimental or a control diet (6 tanks for each diet). After 2,5 weeks, the fish was infected by sea lice. The number of lice on the fish was registered and compared between groups after 4 weeks.

In this sub-project, the aim is to investigate how the feed affected the microbial colonization of the salmon skin mucus. The density of bacteria in the skin mucus will be estimated by a qPCR approach. Furthermore, analyses of the diversity of 16S rRNA amplicons will be performed to examine the composition of bacterial communities in the skin mucus. Results will be presented at the conference.

P43

Effect of Host Strain and Microbial Water Quality on the Colonization of Salmon Yolk Sac Fry

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The mucosal surface of the fish gut creates an ideal niche for microbes, and both commensals and pathogens are able to adhere to the surface. The microbial ecosystem in the gut has an important role in nutrition and health, and the colonization by commensals is assumed to act as a barrier against pathogens. The fish larva hatches germ-free, but the gut is rapidly colonized after hatching by bacteria. The microbial community of the fish gut varies between species and depends on factors such as host genetics, diet, habitat, season, and stage of development.

In this project, the aim is to investigate how host strain and microbial water quality influences the colonization of newly hatched salmon fry. From experiments in aquaculture systems, it is known that the fish microbiota is influenced by the microbial composition of the water. Based on this, the hypothesis is that the fry microbiota will differ between the two salmon stains, but exposure to opportunistic bacteria in the water may obscure theses strain-specific differences.

To study this, two strains of Atlantic salmon was hatched under germ-free conditions and was later exposed to either r-selected (slow-growing bacteria, good at competing at limited resources) or K-selected water (rapid-growing, opportunistic bacteria). Samples of the water and gut were collected, and the microbial community of the samples will be characterized by Illumina sequencing of the 16S rDNA amplicons.

P44

Comparison and enxymatic characterization of type vd patatin-like lipases

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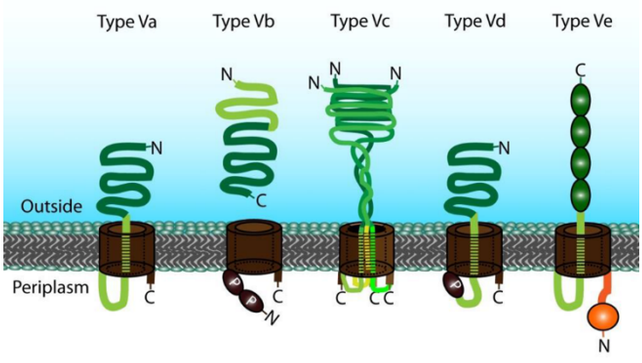
Type V secretion systems (T5dSS) as well as bacterial phospholipases are known virulence factors in many pathogenic bacteria. The patatin-like protein D (PlpD) is a T5dSS which secretes a lipolytic passenger that forms extracellular homodimers. The aim of this work is the enzymatic characterization and comparison of Type Vd secreted phospholipases of the pathogens A. hydrophila , B. pseudomallei , R. solanacearum and P. aeruginosa. A continuous fluorimetric assay was used to confirm lipolytic activity of the target proteins. All studied phospholipases were active over a broad temperature and pH range, displayed phospholipase A1 (PLA1) activity and high-affinity binding to phosphatidylserine. Phospholipases from A.hydrophila and B.pseudomallei also show PLA2 activity and therefore are classified as phospholipase B. Based on size exclusion chromatography and crosslinking, self-associated multimer formation seems to be a conserved feature within the cleaved passengers of T5dSS. Yet, homodimer formation is not essential for enzymatic activity but rather for protein stability. The exact role that T5dSS plays has yet to be determined, but the fact that several of the characteristics tested in this work are conserved across a wide range of pathogens and that there are distinctive correlations between enzymatic activity as well as substrate specificity and intra- and extracellular lifestyle suggests an important role for T5dSS phospholipases for bacterial fitness.



P45

Sensing of HIV-1 by TLR8 activates human T cells and reverses latency

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During HIV-infection, cell-to-cell transmission results in endosomal uptake of the virus by target CD4+ T-cells and potential exposure of the viral ssRNA genome to endolysosomal TLRs. TLRs are instrumental in activating inflammatory responses in innate immune cells, but their function in adaptive immune cells is less well understood. Here we show that synthetic ligands of TLR8 boosted T cell receptor (TCR) signaling, resulting in a higher activation state marked by increased NF-kB and MAPK phosphorylation, inflammatory cytokine production and upregulation of surface activation markers. Adjuvant TLR8 stimulation, but not TLR7 or TLR9, further promoted interleukin (IL)-17 and interferon (IFN)-geffector cytokine production, indicating lineage commitment towards the pro-inflammatory T helper (Th)1 and Th17 axis. Using a cell-to-cell transmission model, we found that endosomal HIV induced cytokine secretion from CD4+ T cells that was significantly reduced by a TLR8 specific inhibitor. TLR8 engagement also enhanced HIV-1 replication in TCR-activated cells and potentiated the reversal of latency in patient-derived CD4+ T cells. Taken together, our results reveal a previously unknown function of TLR8 in human primary CD4+ T cells in shaping immunity and modulating HIV-1 infection. The adjuvant TLR8 activity can contribute to low-grade inflammation in HIV patients and have broad implications for therapeutic targeting and vaccine development.

P46

Can activation of the lactate receptor HCAR1 with lactate injections, influence disease development in an animal models for Alzheimer's disease?

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Alzheimer's disease (AD) accounts for the majority of dementia cases, increasing in prevalence as the population ages. During the development of the disease, there is early loss of tissue and blood capillaries in the hippocampus, together with advancing characteristic features (accumulation of amyloid beta peptides and phosphorylated tau protein, loss of neurons and synapses), and inflammation.

Recent studied have shown that high intensity endurance training is able to delay neuropathology in dementia and increase neurogenesis, angiogenesis and the production of nerve growth factors in both humans and experimental animals. Our group has shown that brain effects of physical exercise depend in part on activation of the lactate receptor, HCAR1. HCAR1 also counteracts tissue-damaging inflammation.

In this project, a group of 77 mice were tested for memory by spontaneous alternation on a Y-maze, before and after subcutaneous injections of lactate or vehicle 5 days a week for 7 weeks. Half of the group were transgenic, mimicking AD (5xFAD), the other half wild-type. The mice were then decapitated and their brains are currently being quantified for gene products that reflect AD development and inflammation, using multiple techniques such as qPCR, immunohistochemistry and mass spectrometry.

If stimulations of HCAR1 counteracts AD pathology, such stimulation may be useful, not as a substitute for, but as an enhancing supplement to physical exercise. This is especially important for people in the risk group – as they are unable to perform physical activity intensive enough to achieve lactate levels that fully activate HCAR1.

P47

The role of diacylglycerol and phosphatidic acid in retrograde transport

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Shiga toxin consists of an A moiety and a B moiety with five subunits each having three binding sites for the glycosphingolipid Gb3. Shiga toxin is endocytosed by both clathrin-dependent and -independent mechanisms, and is transported in a retrograde manner to the Golgi apparatus and the ER before the enzymatically active A1 part is translocated to the cytosol where it inhibits protein synthesis. In fact, by using Shiga toxin we showed for the first time (1992) that a molecule could be transported all the way from the cell surface to the Golgi, the ER and the nuclear envelope. The lipid composition of cells, both lipid classes and certain lipid species, are important for retrograde transport of Shiga toxin. With today's improved mass spectrometry (MS) analysis of lipids, one can increase the understanding of the dynamics of lipids and their role in intracellular transport. We are currently studying how one by changing the balance between different lipids such as phosphatidic acid and diacylglycerol may affect retrograde transport, and we are correlating such findings with the lipid composition (analyzed by MS). The retrograde transport is studied both by microscopy and by using genetically modified toxins which are sulfated in the Golgi apparatus. Moreover, toxicity is used as readout for transport to the cytosol. The characteristics of this transport will be discussed.

P48

South-Eastern Regional Infrastructure for Clinical & Translational Research (SERIT)

Yan Liu, Hilde Loge Nilsen

South-Eastern Regional Infrastructure for Clinical & Translational Research (SERIT), Institute of Clinical Medicine, Department of Clinical Molecular Biology,University of Oslo)

SERIT was established i 2016 and is located at the Department of Clinical Molecular Biology (EpiGen) at the Akershus University Hospital .http://www.med.uio.no/klinmed/english/about/organization/divisions/medicine-laboratory-sciences/clinical-molecular-biology/ .SERIT consists of several laboratory units with a broad range of equipment and a highly competent technical staff that works closely with the scientists. We support translational research by offering instrumentation and expertise in preparation, examination, analysis and interpretation of experimental data within molecular medicine and clinical molecular biology.

P49

Molecular Mechanisms of Hairpin Formation and Passenger Secretion in the Inverse Autotransporter Intimin

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Gram-negative bacteria use different protein secretion systems, ranging from type I through type IX, to invade the host and cause infections. Proteins of the type V secretion system, called autotransporters, can autonomously transport a part of their own polypeptide chain to the bacterial cell surface through an outer membrane-embedded β-barrel domain. The transported part of the protein is called the passenger. Thus, autotransporters can be considered self-contained secretion systems, with several described subclasses.

Intimin, an adhesin of enteropathogenic *Escherichia coli*, is a prototypical member of the Type Ve secretion system or inverse autotransporter pathway. Intimin has been proposed to export its passenger though the β-barrel domain via a hairpin intermediate. During studies on Intimin autotransport, a double HA tag was inserted into the N-terminus of the passenger domain resulting in a stalled secretion mutant caught in the hairpin conformation.

In this project, I have made mutations in three regions of the β-barrel of Intimin to study the molecular details of hairpin formation and passenger secretion. The mutations were made both in wild-type Intimin and the stalled variant to see the effect on passenger domain secretion and hairpin formation, respectively. All mutant proteins were produced, correctly folded and inserted into the outer membrane. Next, using the stalled variant mutants, the formation of the hairpin will be studied by exposure of the HA tag at the cell surface. Using the mutants in the secretion-competent background, I will study the exposure of the C-terminus of Intimin. The results obtained from this study will shed light on the detailed molecular mechanisms of inverse autotransport.

P50

IL-32 is a novel metabolic regulator and growth factor for multiple myeloma cells

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Background /aim

Multiple myeloma is a malignancy of plasma cells. Clinical signs are immunodeficiency, recurrent infections, renal failure, and bone lesions. Recently, we demonstrated that a subset of myeloma patients expresses high levels of interleukin-32 (IL-32) in their plasma cells. These patients experience more bone loss and have a worse prognosis compared with patients that do not express IL-32. Myeloma cells secrete IL-32 in exosomes, and IL-32-containing vesicles promote osteoclast differentiation both in vitro and in vivo. Here, we investigated the role of IL-32 in myeloma cell metabolism, proliferation and survival.

Methods

IL-32 KO cell lines were generated by transfecting three different myeloma cell lines with IL-32-targeting CRISPR/cas9 plasmid. Cell growth and viability of these cells in vitro were assessed by cell counting and annexin/PI flow cytometry, while levels of glycolysis and oxidative phosphorylation were measured by seahorse mito- and glycolysis stress assays. ATP levels were measured by Cell Titer Glo assay. We also examined the effect of silencing IL-32 on tumor growth in a mouse-human scaffold myeloma model.

Results

All three cell lines proliferated less when IL-32 was silenced. H929, INA-6 and JJN-3 cells deficient of IL-32 showed a 31 %, 70% and 69% growth reduction, respectively, compared to WT cells. IL-32-expressing cells had higher levels of glycolysis, oxidative phosphorylation, and ATP compared to IL-32-deficient cells. Importantly, silencing IL-32 in INA-6 myeloma cells completely abolished the ability of these cells to grow in vivo.

Conclusion

IL-32 is a novel, metabolic regulator and autocrine growth factor for myeloma cells and is therefore a potential treatment target.

P51

Glioblastoma cells respond to hypoxia by increased cell growth and altered TCA-cycle progression

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Hypoxia - deprivation of adequate oxygen supply, is a condition frequently occurring in solid tumors, caused by highly proliferating cells exhausting the existing vasculature and increased distances for oxygen diffusion in the expanding tumor. Survival in, and adaption to this hypoxic microenvironment has been linked to tumor progression, metastatic potential and resistance to conventional chemotherapy. As hypoxia does not occur in normal tissue, understanding and targeting the adaptions occurring in hypoxic cells is arising as a new therapeutic strategy. Here, we show that human glioblastoma cells in culture respond rapidly to reduced oxygen tension (1% O2), by increasing growth rate and cell cycle progression within 24 hours. These changes are accompanied by increased glucose consumption and lactate excretion, and accumulation of the hypoxia induced transcription factor subunit HIF1α. Yet, induced hypoxia do not shift the intracellular ratio of ATP to AMP, rendering the glioblastoma cells ability to drive energy-consuming reactions at the same level as at atmospheric oxygen tension, even when growing faster. Rather, the intracellular metabolite pools of late TCA-cycle, in specific fumarate and malate, and the amino acids synthesized from these, aspartate and asparagine, are reduced in hypoxic cells. In contrast, the oncometabolite 2-hydroxyglutarate synthesized from α-ketoglutarate, is accumulating, altogether indicating altered TCA-cycle progression in hypoxic cells.

P52

Role of DNA glycosylases in G4 dynamics

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Base excision repair (BER) corrects DNA damage from oxidation, deamination and alkylation. Such base lesions cause little distortion to the DNA helix structure. BER is initiated by a DNA glycosylase that recognizes and removes the damaged base, leaving an abasic site that is further processed by short-patch repair or long-patch repair that largely uses different proteins to complete BER. At least 11 distinct mammalian DNA glycosylases are known, each recognizing a few related lesions, frequently with some overlap in specificities. Impressively, the damaged bases are rapidly identified in a vast excess of normal bases, without a supply of energy. BER protects against cancer, aging, and neurodegeneration and takes place both in nuclei and mitochondria. However, DNA glycosylases are also used in innate and adaptive immunity, memory and learning. The TDG DNA glycosylase is required to actively remove epigenetic marks in DNA after oxidative modification of 5mC and 5hmC. Furthermore, other DNA glycosylases may also have important roles in epigenetics, thus expanding the repertoire of BER proteins. DNA glycosylases have also been implicated in protecting telomere integrity, and it was recently showed that the NEIL3 DNA glycosylase preferentially removes oxidative lesions from telomere DNA and excise lesions from telomere G-quadruplexes, DNA structures that are normally inhibitory to DNA processing enzymes. Unpublished data from our lab suggest that all NEIL DNA glycosylases (NEIL1, 2 and 3) and NTH1 may have a role in processing G4 structures genome wide, not only in telomere sequences. We are using a panel of DNA glycosylase deficient human cell lines to explore the role of NEIL1, 2, 3 and NTH1 DNA glycosylases in processing of G4 structures and their implications for genome stability, mutagenesis, survival and gene regulation.

P53

Identification of lncRNA expression associated with estrogen receptor status in breast cancer

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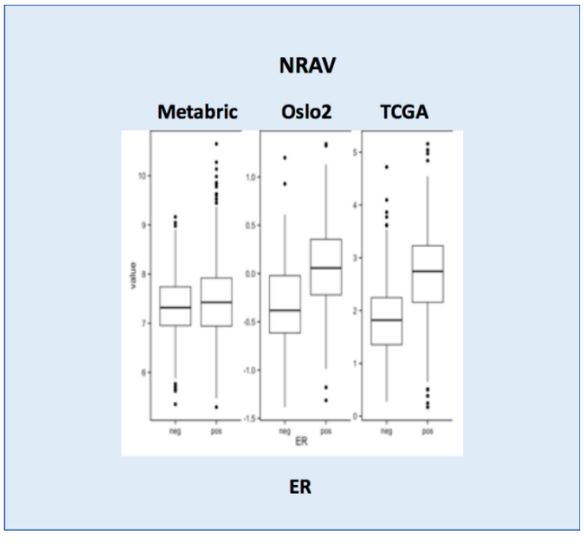
The part of the genome not coding for proteins has moved from being viewed as junk DNA to be investigated as vast, complicated areas that produce diverse non-coding RNAs with different functions. In contrast to protein coding genes, these sequences in the genome lack known domains and motifs. The two most clinically relevant subgroups of breast cancer is estrogen receptor positive and negative (ER+ and ER-) tumors. In this study we want to identify lncRNAs associated with these two subgroups. We re-analysed RNAseq data from The Cancer Genome Atlas Breast Cancer Cohort (TCGA-BRCA) using the Stringtie Ballgown tool suite, and made a catalogue of lncRNAs. Differential expression analysis of 1907 lncRNAs in 1045 breast cancer patients from TCGA identified 1386 significant lncRNAs up- or down-regulated in ER+ and ER- patients. Among the 1386, 743 and 658 lncRNAs were identified and detected in two independent breast cancer cohorts, based on microarray data. When these were tested, 533 and 513 significant lncRNAs were found in the two cohorts, respectively.Among the identified lncRNAs we found DSCAM-AS1, NEAT1 and MALAT1, previously known to be associated with breast cancer. We also identified new candidates, such as NRAV and AC100810, some of which will be further functionally characterized in breast cancer cell lines. To further characterize the candidate lncRNAs, expression data will be integrated with other molecular data levels such as methylation status and immune infiltration.



P54

Impact of non-homologous end joining factors XLF, PAXX, DNA-PKcs and Mri on early stages of mammalian neurodevelopment

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Double-strand breaks (DSBs) are constantly generated in the DNA molecules by endogenous and exogenous agents. If left unrepaired, such lesions lead to cell death through apoptosis and result in various disorders, such as immunodeficiency, neurodegeneration, and cancer. One major DSB repair pathway in mammalian cells is the nonhomologous end-joining (NHEJ) which is active through the entire cell cycle and is especially required for the homeostasis of post-mitotic neurons in the brain. To determine the roles of specific NHEJ factors, genetic inactivation of the corresponding NHEJ genes was established in mice. Previously, we have generated and characterized several mouse models lacking one or two NHEJ proteins, e.g. XLF, PAXX, and DNA-PKcs. In addition, we have recently developed and are characterizing mouse model lacking another NHEJ factor, a modulator of retroviral infection (Mri). Mri-deficient mice were generated through a CRISPR/Cas9 gene editing approach in 2017. sgRNA was designed to target Exon 2 of the *Mri* gene, creating a 14 bp deletion which results in an early stop codon. Here, we isolated brains from the mice lacking one factor, XLF, DNA-PKcs, PAXX, Mri, or two factors, XLF+PAXX, and XLF+DNA-PKcs. We used the brains to establish a neurosphere cell culture as our model system. We determined the impact of accessory NHEJ factors on neurosphere proliferation, self-renewal and differentiation. Our results suggest that XLF, PAXX, DNA-PKcs, and Mri are required for the physiological development of the central nervous system.

P55

Towards the structure of the Yersinia Adhesin A membrane anchor domain in the native membrane

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Yersinia Adhesin A (YadA) is a protein found in the membrane of *Yersinia Enterocolitica*, which is involved in a number of food-borne diseases including enterocolitis, acute enteritis, diarrhea, and mesenteric limphadentisis. YadA plays an important role in the ability of Y. enterocolitica to colonize a host, by aiding in the autotransport of a head domain to the cell surface that can stick to host tissues. A structure of the YadA anchor domain region (YadAM) was solved with the protein in the crystalline form by ssNMR, and we know aim to solve structure in the native membrane, to gain insights on lipid interactions and dynamics. Preliminary results were published in 2015, which included 150 unique assignments. By focusing heavily on both optimization of both the sample preparation and data acquisition we have 600 unique assignments and have set up structure calculations. This project, if successful, will provide the first *in situ* structure of a membrane protein.

P56

Application of supervised machine learning for understanding how input from odor mixtures is processed in the insect primary olfactory center

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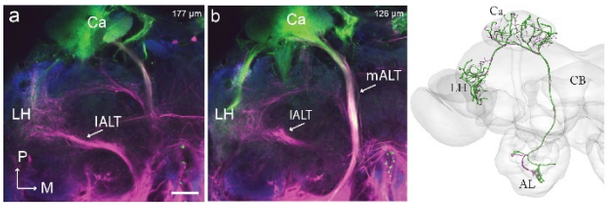
Neural mechanisms underlying information processing of complex odor input is still poorly understood. By utilizing a super-smeller, the noctuid moth *Helicoverpa armigera,* we intend to explore computational principles typifying odor mixture processing in the insect's primary olfactory center, the antennal lobe. Our recent morphological studies of central olfactory pathways in the moth, demonstrated that the connection between the antennal lobe and the mushroom body calyx consists almost exclusively of uniglomerular projection neurons (PNs) confined to the *medial*antennal-lobe tract. This fact enables investigation of one output neuron category specifically. Thus, by applying a calcium indicator into the calyx region, the antennal-lobe dendritic parts of uniglomerular PNs will be labeled via retrograde transport. This, in turn, allows for measuring odor-evoked responses in this prominent population of antennal-lobe PNs.

The previous calcium imaging studies on retrogradely stained uniglomerular PNs demonstrated that this method is highly suitable for collection of big biological data reflecting odor coding within the antennal lobe neural network. Ongoing calcium imaging measurements will provide a data material enabling machine-learning analyses. Based on this data material, algorithms predicting which set of glomeruli will respond to a given odor mixture, and vice versa - which odor stimuli will elicit activity in distinct sets of glomeruli, will be established. An additional intermediate task is to generate a tool for identification of distinct glomeruli across different individuals. By characterizing the glomerular units physiologically and spatially across individuals, a machine-learning approach will be used to create a universal catalog of glomeruli.

There is still a considerable lack of knowledge about the logic behind glomerular response patterns elicited by complex odor stimuli. A research design including the uniglomerular PNs is ideal since this neuron population is specifically involved in odor identification. The constructed models will give insight into the computational processes underlying glomerular interactions. This, in turn, will provide a better understanding of general coding mechanisms characterizing information processing at the level of the primary olfactory center.



P57

The role of SM proteins in Invariant chain-mediated endosome enlargement

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Invariant chain (Ii) is associated with the major histocompatibility complex class II (MHCII) and has an important role in antigen presentation by regulating trafficking of MHCII to the endosomal compartments and preventing antigen peptides from binding MHCII in the ER. Ii is also important for fusion of endosomes as the over-expression of Ii causes a delay in endosomal maturation and an increase in the size of endosomes. The mechanism that is responsible for this effect is not fully understood. Based on experiments in which several fusion related protein families were inhibited, this effect was found to be mediated by SNARE and SM protein families, the former being responsible for fusion of membranes and the latter for tethering of to-be-fused endosomes. A large screening of human SNAREs and SM protein was performed by our lab and resulted in a number of proteins that could potentially be involved in Ii-mediated endosome fusion, as their depletion resulted in a decrease in endosomal size after Ii-induction. This project focuses on promising SNARE and SM proteins, with particular interest in the SM proteins. Our continued experiments further indicated that the candidate proteins and Ii interact, while also showing that the candidates from the screening interact amongst themselves. We use immune-fluorescence microcopy and high resolution live-cell imaging to determine the role of these candidates in regulating Ii-mediated endosome fusion and their potential role in antigen presentation.

Participants

A

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Berge, Christoffer	NTNU	Participant
Bergh, Sofie Kjerstad	NTNU	Participant
Bjørås, Magnar	NTNU/OUS	Organizer
Blankvoort, Stefan	Kavli institute, NTNU	Participant
Blicher, Pernille	Universitetet i Oslo	Participant
Bordin, Diana	NTNU	Participant
Borgen, Sigurd Skålvoll	Nerliens Meszansky	Exhibitor
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Falkenberg, Liv Eggset	NTNU	Participant
Falnes, Pål	Universitetet i Oslo, Institutt for biovitenskap	Participant
Fang, Evandro F.	UiO	Participant
Ferrucci, Francesca	rikshospitalet	Participant
Flo, Trude Helen	NTNU	Organizer
Flydal, Marte	Universitetet i Bergen	Participant
Folkesson, Evelina	NTNU	Participant
Forsberg, Zarah	KBM, NMBU	Participant
Forstrøm, Rune	Rikshospitalet	Participant
Frei, Dominik	Inter Instrument AS	Exhibitor
Fyhn, Marianne	Universitetet i Oslo	Participant

G

Germain, Ronald N.	Laboratory of Immune System Biology, NIH, USA	Invited speaker
Gidon, Alexandre	NTNU	Participant
Gilljam, Karin	University of Oslo	Participant
Gottschamel, Johanna	Nordic Biosite AS	Exhibitor
Granlund, Atle Van Beelen	NTNU	Participant
Grødem, Sverre	University of Oslo	Participant
Grønstad , Christina	Sarstedt AS	Exhibitor
Grøvdal, Lene	NTNU	Organizer

H

Hagen, Lars	NTNU	Organizer
Hammerstad, Marta	University of Oslo, Department of Biosciences	Participant
Hansen, Per Odin	BioNordica AS	Exhibitor
Haslene-Hox, Hanne	SINTEF	Participant
Haug, Markus	NTNU, IKOM/CEMIR	Participant
Haug , Kirsti	VWR	Exhibitor
Heck, Kathleen Anne	NTNU	Participant
Helgesen, Emily	Oslo University Hospital	Participant
Hellesvik, Monica	Institutt for biovitenskap, Universitetet i Bergen	Participant

Hersleth, Hans-Petter	Universitetet i Oslo	Participant
Hesjedal, Maria Bårdsen	NTNU	Participant
Heslop, Bill	Learning Science Ltd	Exhibitor
Hildrestrand, Gunn Annette	Rikshospitalet, Oslo Universitetssykehus	Participant
Hoel, Sigrid	CEMIR, NTNU	Participant
Hoel, Camilla	Ortomedic AS	Exhibitor
Holen, Vilde	NTNU Trondheim	Participant
Holm, Kristine Lillebø	Universitetet i Oslo	Participant
Horn Mathisen, Amalie Johanne	NTNU	Participant
Houry, Dorothee	University of Bergen	Participant
Huse, Camilla	IKOM, NTNU	Participant
Husebye, Harald	NTNU, IKOM	Participant
Hyldbakk, Elisabeth	Avexxin / NTNU	Participant
Høgset, Anders	PCI Biotech AS	Participant
Hårstad , Heidi	Merck Life Science AS	Exhibitor

I

Ian, Elena	NTNU	Participant

J

Jacobsen, Petter B.	DMBA	Participant
Johannesen, Hedda	UiO	Participant
Johannessen, Fredrik Gullaksen	University of Bergen	Participant
Johannessen, Mona Susan	University of Tromsø	Participant
Jäättelä, Marja	University of Copenhagen, Dept of Cellular and Molecular Medicine, Denmark	Invited speaker

K

Kaarbø, Mari	Oslo University Hospital	Participant
Kandanur, Sai Priya Sarma	UNIVERSITY OF OSLO	Participant
Karlsen, Emil	NTNU	Participant
Khan, Uniza	Nordic Biosite AS	Exhibitor
Kim, Haelin	NTNU	Participant
Kleppe, Rune	Senter for Digitalt Liv Norge, UiB	Participant
Klepper, Kjetil	NTNU	Participant
Klungland, Helge	NTNU	Participant
Klungland, Arne	Oslo University Hospital	Participant
Kobro-Flatmoen, Asgeir	NTNU	Participant
Kompatscher, Maria	CEMIR, NTNU	Participant
Kornfeld, Benedikt	NTNU	Participant
Korsnes, Lars Petter	Norges Forskningsråd	Participant
Korvald , Eirin	VWR	Exhibitor
Kovcic, Vlado	CEMIR, NTNU	Participant
Kozlowska, Ada	FYSCELL, IBV, UiO	Participant
Kristensen, Tom	Universitetet i Oslo	Participant
Kroustallaki, Penelope	Akershus University Hospital - University of Oslo	Participant

Kuiper, Jeroen	University of Oslo	Participant
Kumar, Kanhaiya	NTNU	Participant
Kvaløy, Emilie	CEMIR, NTNU	Participant
Kymre, Jonas Hansen	NTNU	Participant

L

Leivers, Shaun	NMBU	Participant
Lensjø, Kristian Kinden	Universitetet i Oslo, Institutt for Biovitenskap	Participant
Leo, Jack	UiO	Participant
Leonenko, Anastasia	BioCat, UiT	Participant
Li, Yanjiao	Oslo University Hospital	Participant
Lien, Hilde Julie	NTNU	Participant
Lien, Guro	OUS Rikshospitalet	Participant
Lin, Xiaolin	UIO	Participant
Lindhardt, Magnus	Merck Life Science AS	Exhibitor
Lindstad, Lars Jordhøy	NMBU	Participant
Linke, Dirk	UiO	Participant
Linke, Manuela		Guest
Liu, Yan	Akershus University Hospital	Participant
Lode, Kristin	NTNU	Participant
Luna, Luisa	Oslo University Hospital, Rikshospitalet	Participant
Lundberg , Harrieth	Tekna/Biotec Missions AS	Exhibitor
Lyle, Robert	Department of Medical Genetics, Oslo University Hospital	Participant

M

Malecki, Jedrzej	IBV, UiO	Participant
Mallasvik, Hanne	NTNU	Participant
Margiotta, Azzurra	University of Oslo	Participant
Marinai, Stefan	Bio-Rad Norway AS	Exhibitor
Markussen , Lisa Merete	Sarstedt AS	Exhibitor
Martinez, Aurora	Department of Biomedicine, University of Bergen	Participant
Maseng, Maria	UiO	Participant
Messemer, Annika	NTNU	Participant
Meås, Hany	CEMIR, NTNU	Participant
Misund, Kristine	NTNU	Participant
Moen, Ingrid Nyhus	NTNU	Participant

N

Nair, Rajeevkumar Raveendran	NTNU, Kavli Institute for Systems Neuroscience, CNC	Participant
Nesse, Gaute J.	Rikshospitalet	Participant
Neurauter, Christine Gran	OUS	Participant
Nielsen, Nicole	Bio-Techne	Exhibitor
Nilsen, Nadra	Inst for Kreftforskning og Molekylærmedisin, NTNU	Participant
Nilsen, Hilde	Universitetet i Oslo/Akershus Universitetssykehus	Participant
Nilsson, Sjannie Lefevre	Uni. Oslo, Dept. Biosciences	Organizer

Nilsson, Gøran E.	Uni. Oslo, Dept. Biosciences	Participant
Nonstad, Unni	NTNU	Participant
Nordeide, Hildegunn	Merck Life Science AS	Exhibitor
Nthiga, Thaddaeus Mutugi	UiT Norges arktiske universitet	Participant
Nüsslein-Volhard, Christiane	Max Planck Inst. For Developmental Biology, Germany	Invited speaker

O

Obermann, Tobias	NTNU	Participant
Oksenych, Valentyn	NTNU	Participant
Olweus, Johanna	K.G. Jebsen Centre for Cancer Immunotherapy, UiO, Norway	Invited speaker
Otterlei, Marit	NTNU	Organizer
Ottestad, Anine Larsen	NTNU	Participant

P

Pandey, Deo	Rikshospitalet, Oslo University Hospital	Participant
Pannone, Marco	Rikshospitalet, Oslo University Hospital, Dept. of Microbiology (UiO)	Participant
Pedersen, Turid Margrethe	Institutt for indremedisinsk forskning, OUS HF / UiO	Participant
Pettersson, Mimmi	Mettler-Toledo International	Exhibitor
Pettersson, Mimmi	Mettler-Toledo International	Exhibitor
Piras, Paola	ADInstruments	Exhibitor
Prydz, Kristian	Institutt for biovitenskap, Universitetet i Oslo	Participant

R

Radulovic, Maja	Oslo University Hospital, Institute for Cancer Research	Participant
Ranum, Helene Wold	Oslo University Hospital	Participant
Ree, Rasmus	Institutt for biomedisin, Universitetet i Bergen	Participant
Richartz, Nina	University of Oslo	Participant
Rindal, Christine	Nerliens Meszansky	Exhibitor
Rodahl, Lina	Forskningsrådet	Participant
Ryan, Liv	CEMIR, NTNU	Participant
Rydmark, Marcella	University of Oslo	Participant
Rye, Morten	NTNU	Participant
Ræder, Synnøve	NTNU	Participant
Røe, Målfrid	BioNordica AS	Exhibitor
Rønning, Sissel	Nofima AS	Participant
Røsand, Øystein	IKOM, NTNU	Participant
Røst, Lisa Marie	IBT, NTNU	Participant

S

Sagen, Ellen Lund	Inst. for indremedisinsk forskning, OUS Rikshospitalet	Participant
Sandlie, Inger	Universitetet i Oslo, Institutt for Biovitenskap	Invited speaker
Sandvig, Kirsten	Institutt for Kreftforsking, Radiumhospitalet, Oslo Univ.sykehus	Participant
Sandvig, Ioanna	NTNU	Participant
Sandvig, Axel	NTNU	Participant
Sankala, Marko	Merck Life Science AS	Exhibitor
Sarno, Antonio	NTNU	Participant

Schroer, Lisa	University of Oslo	Participant
Schulz, Christian	NTNU	Participant
Schär, Primo Leo	Dept of Biomedizin, University of Basel, Switzerland	Invited speaker
Sebastianpillai, Marianna	NTNU	Participant
Seelinger, Mareike	NTNU	Participant
Selvik, Linn-Karina	Avexxin AS / IBI, NTNU	Participant
Sivakumar, Niruja	CEMIR, NTNU	Participant
Sivertsen, Elisabeth	Bio-Rad Norway AS	Exhibitor
Skjesol, Astrid	NTNU	Organizer
Skotland, Tore	Institute for Cancer Research, Oslo University Hospital	Participant
Skuggen, Linda	OUS HF Rikshospitalet	Participant
Skåne, Anna	Norges Miljø- og biovitenskapelige universitet	Participant
Song, Hongjun	Dept of Neuroscience, University of Pennsylvania, USA	Invited speaker
Sponaas, Anne Marit	NTNU	Participant
Sporsheim, Bjørnar	CMIC, NTNU	Organizer
Standal, Therese	NTNU	Participant
Steigedal, Magnus	NTNU	Organizer
Steigedal, Tonje	NTNU Technology Transfer AS	Invited speaker
Steinkjer, Bjørg	NTNU	Participant
Stensvåg, Klara	UiT The Arctic University of Norway	Participant
Strand, Berit Løkensgard	NTNU, Department of Biotechnology and Food Science	Participant
Støve, Svein Isungset	University of Bergen	Participant
Szwed, Marzena	Oslo University Hospital	Participant
Sætra, Ragnhild Sofie Ragnhildstveit	NTNU	Participant
Sætrom, Pål	NTNU	Invited speaker
Søgaard, Caroline	NTNU	Participant
Søndenaa, Herman	Tekna	Exhibitor
Sørlie, Morten	NMBU	Participant

T

Thommesen, Liv	Dept Biomedical Laboratory Science/ NTNU	Participant
Thorfinnsdottir, Lilja	Institutt for bioteknologi og matvitenskap, NTNU	Participant
Tietze, Lisa	NTNU	Participant
Tran, Maria Phuong Anh	Universitetet i Bergen	Participant
Trondsen, Susann	IK, UiT	Participant
Trunk, Thomas	University of Oslo	Participant

U

Ullmann, Sindre	CEMIR, NTNU	Participant

V

Vaaje-Kolstad, Gustav	NMBU	Participant
Van Loon, Barbara	NTNU, Department of Cancer Research and Molecular Medicine	Participant
VanLinden, Magali	University of Bergen	Participant
Vatsveen, Thea Kristin	OUS/UiO Radiumhospitalet	Participant
Veiseth-Kent, Eva	Nofima AS	Participant

Vestrum, Ragnhild Inderberg	NTNU	Participant
Visnes, Torkild	SINTEF	Participant
Voigt, André	NTNU	Participant
Volpe, Charlotte	NTNU	Participant
Votvik, Amanda	Norges Miljø og Biovitenskapelige Universitet	Participant

W

Wang, Wei	NTNU	Participant
Wang, Caroline	NTNU	Participant
Weel-Sneve, Ragnhild	Oslo University Hospital	Participant
Wennerström, Anna	UiO/Campus Ahus	Participant
Westhrin, Marita	NTNU	Participant
Wittek, Kristian	Bergman Diagnostika AS	Exhibitor
Witter, Menno	NTNU	Organizer
Wolowczyk, Camilla	NTNU	Participant

X

Xing, Mengtan	NTNU	Participant

Y

Yaffe, Michael B.	Center for Precision Cancer Medicine, MIT, USA	Invited speaker
Yang, Mingyi	Dep. Microbiology, Oslo University Hospital	Participant
You, Panpan	Akershus universitetssykehus HF	Participant

Z

Zegarra, Sergio Miguel Castaneda	IKOM, NTNU	Participant
Zhao, Xu	Oslo University Hospital, Rikshospitalet	Participant
Zobolas, John	NTNU	Participant
Zoric, Nina	Rikshospitalet	Participant
Zuo, Rujuan	Oslo University Hospital	Participant
Zwiggelaar, Rosalie	NTNU	Participant

Ø

Østensen, Martin	NMBU	Participant
Østhagen , Benthe	VWR	Exhibitor
Østli, Even	Matriks - Agilent Technologies	Exhibitor

Å

Årstøl, Erland	NTNU	Participant

Notes

Thursday January 24th

10.30 Registration

12.30 Lunch

14.45 Welcome (Falkberget)

15.00 PL1: Keynote Lecture: Christiane Nüsslein-Volhard: *"How fish colour their skin: A paradigm for development and evolution of adult patterns"* (Falkberget).

15.45 PL2: Michael Berenbrink: *"Evolution of Mammalian Diving Capacity Traced by Myoglobin Net Surface Charge"* (Falkberget).

16.30 Exhibition

17.00 Paralell Minisymposium Session 1:

1. Inflammation (Falkberget),

2. Biotechnology (Christianus),

3. Biochemistry/ Structural Biology (Sextus),

4. Cancer (Kinoen).

18.00 Exhibition

18.30 Poster Session 1 *(odd numbered posters)*

19.30 Break

20.00 Dinner

Friday January 25th

07.00 Breakfast

09.00 PL3: The EMBO Keynote Lecture: Ronald N. Germain: *" Imaging Immunity – Using Multiplex 2D and 3D Imaging to Develop a Spatiotemporal Understanding of Host Defense"* (Falkberget).

09.45 PL4: Michael B. Yaffe: TBA (Falkberget).

10.30 Exhibition

11.00 PL5: Johanna Olweus: *"Outsourcing cancer immunity to healthy donors"* (Falkberget).

11.45 PL6: The FEBS National Lecturer: Primo Leo Schär: *"DNA Demethylation, Chromatin Plasticity and Cancer"* (Falkberget).

12.30 Lunch

14.00 Paralell Minisymposium Session 2:

5. Microbiology (Falkberget),

6. Physiology/ Neurobiology (Christianus),

7. Biochemistry/ Structural Biology (Sextus),

8. Cell Biology/ Molecular Biology (Kinoen).

15.30 Exhibition

16.00 Paralell Minisymposium Session 3:

9.Cancer/ Immunology (Falkberget),

10. Bioinformatics/ Genomics (Christianus),

11. Genome dynamics (Sextus).

17.30 Exhibition

18.00 Poster Session 2 *(even numbered posters)*

19.00 Break

20.00 Dinner

Saturday January 26th

07.00 Breakfast

09.00 Outdoor activities

12.00 Lunch

13.30 PL7: Hongjun Song: *"Epitranscriptomic regulation in the mammalian nervous system"* (Falkberget).

14.15 Pl8: Marja Jäättelä: *"Lysosomes as targets for cancer therapy"* (Falkberget).

15.00 Exhibition

15.30 Inovation Session (Falkberget)

16.30 Exhibition

17.00 Paralell Minisymposium Session 4:

12. Biotechnology/ Bioinformatics (Christianus),

13. Epigenome/ Epitranscriptome (Sextus),

14. Cell Biology/ Molecular Biology (Plenumssal Hotell).

18.00 NBS General Assembly (Christianus) **and NFF General Assembly** (Sextus).

19.00 Break

19.30 Reception

20.00 Banquet (Falkberget)

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