
ESSEN
BioSCIENCE


QIAGEN


BioNordika
bergman


GATC
BIOTECH


biotechne


elixir
NORWAY


Inter Instrument AS
Totalleverandør innen mikroskopi og bildeanalyse


matriks
KJEMISK TEKNOLOGI
Agilent Technologies


puls
et selskap i handicare


Nordic
BioSite


MERCK MILLIPORE


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VWR
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NORBIS


NERLIENS MESZANSKY


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Alere


OLYMPUS
Your Vision, Our Future


emp
BIOTECH

Contents

Cover photo by Ingar Leiros

Organizing Committee

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Committee Leader

Ole Kristian Greiner Tollersrud
Programme, Logistics and Economy

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Chief Exhibitor/Provider Contact

Tony Christopeit
Exhibitor/Provider Contact

Inger Lin Uttakleiv Ræder
Editor of Book of Abstracts

Stian Olsen
Abstracts and Posters

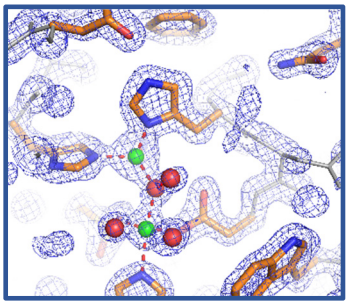
Kirsten Krause
Plenary and Mini-sessions

Ronny Helland
Web Site Editor

Dear all NBS friends and colleagues

It is a great pleasure for everybody in the organizing committee to welcome you all to the 52nd Norwegian Biochemical Society (NBS) Contact Meeting, held in Tromsø, 21st -24th of January 2016.

This meeting is downtown Tromsø at the new "The Edge Hotel" where we aim for a compact NBS meeting with a high-quality scientific program. The basis for the meeting is inspired by the previous NBS Contact Meetings with plenary speakers in a wide range of topics, mini sessions, poster sessions and the presence of many exhibitors. Further, this year we have the pleasure to welcome the biotechnology companies Lytix Biopharma AS and ArcticZymes AS. They are both doing successful business with offspring from UiT- The Arctic University of Norway.



On Saturday night, we all have the pleasure to participate at the banquette with entertainment from a live band and excellent food. All of this will happen during the Arctic winter and under the beautiful Aurora Borealis, the Northern Lights.

On behalf of the organizing committee, I warmly wish you all an inspiring NBS meting

Hanna-Kirsti S. Leiros

Leader of the organizing committee

Practical information

Conference Hotel

Clarion Hotel The Edge
Phone: +47 77 66 84 00
Kaigata 6, 9008 Tromsø

Meeting Agency

VIA Egencia Norge AS, Meetings & Incentives, avd. Tromsø
E-mail: meet.tromso@viaegencia.com
Phone: +47 77 64 80 09

Secretariat

The secretariat is located in the entrance hall of the conference hotel and will be staffed whole Thursday and during all breaks on Friday.

Talks

Speakers are asked to deliver their presentation file to the secretariat in good time before the time of their respective talk. Speakers for Thursday presentations will be asked to do this during registration. Please inform if you want to use Mac or PC for running your presentation. Plenary lectures will take place in Margarinfabrikken 1/2. Minisessions will be held in 2-3 parallel sessions in Margarinfabrikken 1, Margarinfabrikken 2 and Prostneset 1/2. All speakers are kindly asked to stick to their assigned times. Minisession talks should be limited to 12 minutes to allow for a few questions.

Posters

Posters will be displayed in two sessions in Margarinfabrikken:
Thursday 18:15-19:15: odd numbers (P1, P3, P5, …)
Friday 17:30-18:30: even numbers (P2, P4, P6, …)

Presenting authors of odd number posters are asked to mount their poster as early as possible before the session on Thursday and take it down before 16:00 on Friday. Even number posters should be put up after 16:00 on Friday and should be taken down before 16:00 on Saturday. The presenting authors are expected to be available for questions during the respective poster session.
The winner of the best poster award will be announced during the Banquet on Saturday. Eppendorf is sponsor of the 1st prize.

Exhibition

The exhibition will be open in Margarinfabrikken 3, the foyer outside Margarinfabrikken and the entrance hall during the periods indicated in the program. We encourage all participants to visit the exhibition. In your conference bag, you will find a sheet of paper with all the exhibitor logos. A price will be given to the participant who visits the most stands (a visit is indicated by a stamp mark over the logo from the respective exhibitor). If several participants visit all exhibitor stands, the lucky winner will be drawn. The winner will be announced during the Banquet on Saturday.

Taxi

You can order a Taxi at the Hotel desk or directly to:
Tromsø Taxi (+47) 03011
Din Taxi (+47) 02045

Bus

City buses run within the city of Tromsø from around 06.00 (6am) Monday to Friday, from around 07.00 (7am) Saturday and around 08.00 (8am) on Sunday until midnight. There are one to four departures every hour with the highest frequency during peak hours (morning and afternoon) Monday to Friday. Tickets may be purchased on board the buses and are payable in cash only (NOK, and Euro notes).

- Single tickets bought onboard the bus cost NOK 50 for adults and NOK 25 for seniors (over 67).
- A day ticket (valid for 24 hours) purchased onboard the bus costs NOK 90 for adults/ seniors.

Pre-purchased tickets are cheaper and a single ticket costs NOK 35 for adults. In the city centre these can be bought at:

Troms fylkestrafikk customer service centre (Roald Amundsens plass 1)
WITO-kiosk (Storgata 68)
Narvesen Stortorget (Main Square Tromsø city centre)

More info can be found at http://www.visittromso.no/en/City%20Buses

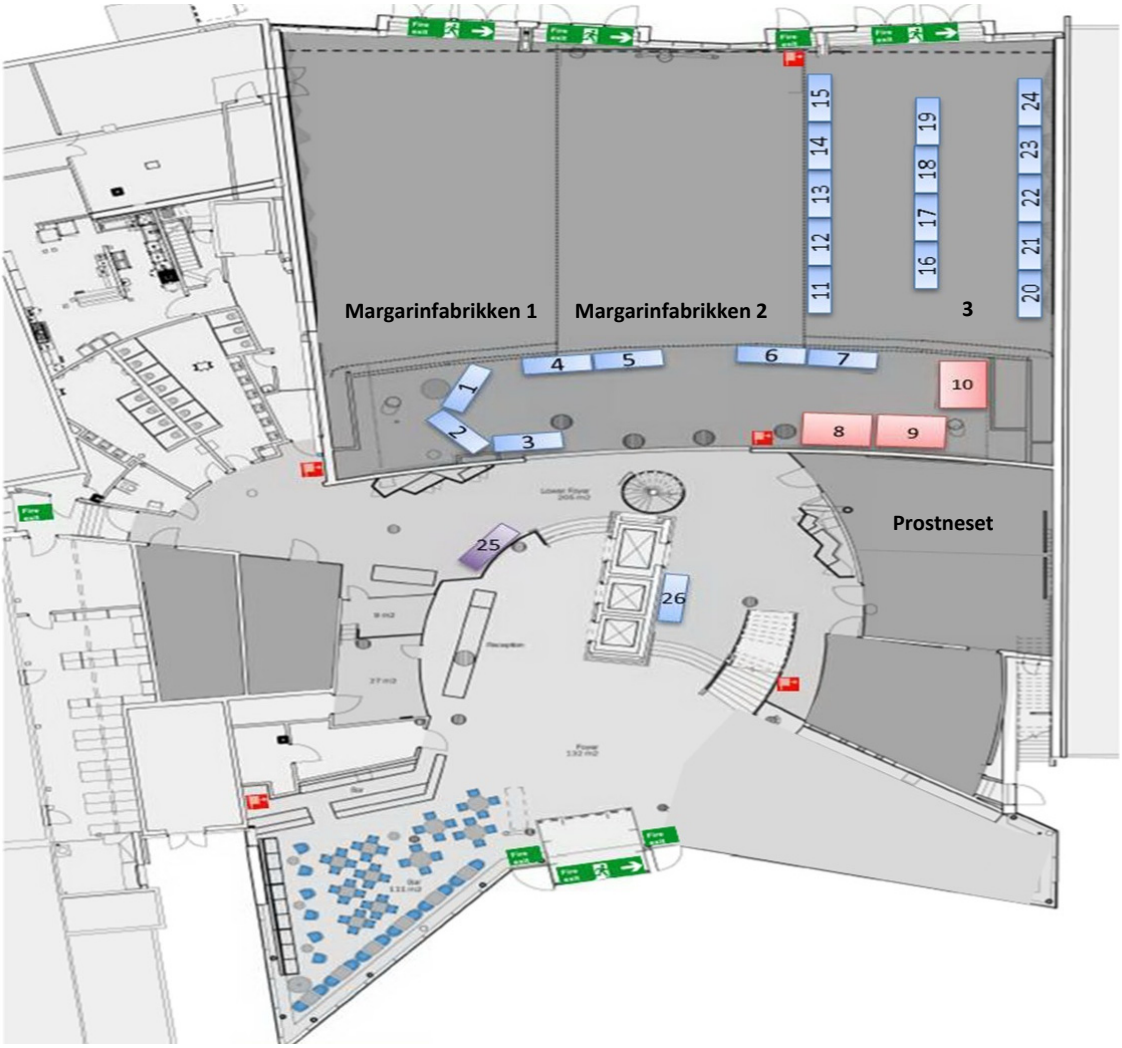
Tourist Information Office

Visit Tromsø-Region
Kirkegata 2, Tromsø
Postal address: Post box 311, 9253 Tromsø
Phone: +47 77 61 00 00
E-mail: info@visittromso.no


Comfort Hotel Xpress Tromsø
Scandic Grand Tromsø
Thon Hotel Polar
ATM
Bus-tickets
WI-TO
40
Kulturhuset
Storgata
ATM
24 26
Bus-tickets
NARVESEN
28 37
Strandtorget
Nerstranda Shopping
ATM
Strandgata
Kirkegata
Tromsø Domkirke
Bankgata
Fredrik Langes gate
Clarion Collection Hotel Aurora
Clarion Collection Hotel With
26 28
42
Quality Hotel Saga
ATM
Husfliden
33 42
Sjøgata
ATM
20 21 32 34
Clarion Hotel The Edge
Kaigata
Bus info Tickets
Roald Amundsens plass
Amalie Hotell
Radisson Blu Hotel Tromsø
Express boats
2 to Finnsnes / Harstad
3 to Skjervøy
4 to Lysnes (Senja)
Prostneset
Nordnorsk Kunstmuseum
Scandic Ishavshotel
Regional buses
to Alta, Narvik, Bodø
District buses
Samuel Arnesens gate
Tourist information
I like TROMSØ!
www.visittromso.no

Exhibition area

Margarinfabrikken 3, Margarinfabrikken foyer and the entrance hall



1. BioStruct (forskerskole)
2. Tekna
3. Puls AS
4. You Do Bio/emp Biotech GmbH
5. Bio-Techne
6. VWR International AS
7. Nordic BioSite AS
8. Sarstedt AS
9. Sarstedt AS
10. GATC Biotech
11. Matriks-Agilent Technologies
12. Eppendorf Norge
13. Inter Instrument AS
14. Essen Bioscience
15. Saween&Werner AB
16. Merck Millipore
17. Sigma Aldrich
18. BioNordikaBergman AS
19. Elixir (forskerskole)
20. LI-COR
21. Nerliens Meszansky AS
22. Norbis (forskerskole)
23. Alere AS
24. Mettler Toledo
25. Qiagen
26. Olympus Norge AS

Organisation	Stand	Website/E-mail	Phone
Alere AS	23	www.alere.no kundeservice.no@alere.com	(+47) 24 05 68 00
BioNordikaBergman AS	18	www.bionordikabergman.no info@bioberg.no	(+47) 23 03 58 00
BioStruct	1	http://biostruct.uit.no biostruct@uit.no	
Bio-Techne	5	www.bio-techne.com kate.wilmore@bio-techne.com	(+44) (0) 1235 529449
Elixir	19	www.elixir-europe.org nils-peder.willassen@uit.no	(+47) 776 44651
emp Biotech GmbH	4	www.empbiotech.com ahurst@empbiotech.com	+46 (0)40 456 711
Eppendorf	12	www.eppendorf.com Milter.M@eppendorf.dk	(+45) 43 24 00 05
Essen BioScience	14	www.essenbioscience.com debi.chakraborty@essenbio.com	+44 (0)7710158031
GATC Biotech	10	www.gatc-biotech.com a.gigova@gatc-biotech.com	(+49) 7531 8160 4117
Inter Instrument	13	www.interinst.no anja@interinst.no	(+47) 67 10 79 60
Kilab as		www.kilab.no jon@kilab.no	(+47) 63 94 21 20
LI-COR Biosciences UK Ltd	20	www.licor.com/bio benjamin.smiszek@licor.com	(+45) 20 54 86 54
Matriks – Agilent Technologies	11	www.genomics.agilent.com Erik@matriks.no	(+47) 92 42 22 07
Merck Millipore	16	www.merckmillipore.com kari.amlie@merckgroup.com	(+47) 810 62 645
Mettler Toledo	24	no.mt.com SteinErik.Rognan@mt.com	(+47) 22 30 44 90
Norbis	22	www.norbis.no contact-norbis@uib.no	
Nerliens Meszansky AS	21	www.nerliens.no lise.rodsten@nmas.no	(+47) 22 66 65 00
Nordic Biosite	7	www.nordicbiosite.com jenny.wiklund@nordicbiosite.com	(+46) (0) 8 5444 3341
Olympus Norge AS	26	www.olympus.no bente.standnes@olympus.no	(+47) 982 05 600
Puls AS	3	www.puls-norge.no ole.j.lavik@puls-norge.no	(+47) 23 32 30 00
Qiagen	25	www.qiagen.com customercare-no@qiagen.com	(+47) 47 36 54 54
Saveen&Werner AS	15	www.swab.no urban@swab.se	(+46) 40 674 76 61
Sigma-Aldrich Norway AS	17	www.sigmaaldrich.com/norway hildegunn.nordeide@sial.com	(+47) 23 17 60 40
Sarstedt Norge	8/9	www.sarstedt.com/en info.no@sarstedt.com	(+47) 64 85 68 20
Tekna (Biotek)	2	www.tekna.no tone.juel@tekna.no	(+47) 22 94 76 25
The Research Council of Norway		www.forskningsradet.no post@forskningsradet.no	(+47) 22 03 70 00
vwr International AS	6	www.vwr.com/ no.vwr.com anne-gry.jakobsen@no.vwr.com	02290
You Do Bio	4	www.youdobio.com peter.roberts@youdobio.com	(+45) 25 57 38 76

A collaboration between
5 Universities granted by:

The Research Council of Norway

BioStruct

The Norwegian PhD network in Structural Biology

BioStruct courses 2016:

KJM9310 BIOSTRUCT - Biomolecular Structure and Function (10 STP)	**UiO: 25. Jan - 11. Feb 2016**
KJE 8701 BIOSTRUCT - Biophysical aspects of protein folding and stability (5 STP)	**UiT: 7. - 18. March 2016**
MBV9270 BIOSTRUCT - Advanced Glycobiology (10 STP)	**UiO: 11. - 22. April 2016**
MOL 950 - BIOSTRUCT - protein expression and purification (5 STP)	**UiB: 25. May - 3. June 2016**
MBV 9220 BIOSTRUCT - Protein Crystal Spectroscopy (5 STP)	**UiO: August 2016**
The BioStruct Annual Conference at Jægtvolden, Inderøya	**25. - 28. August 2016**
KJE 8703 BIOSTRUCT - Crystallisation of biological macromolecules (3 STP)	**UiT: September 2016**
KJE 8704 BIOSTRUCT - Structure guided drug discovery and design (5 STP)	**UiT: October 2016**

The PhD network welcomes all PhD-students and their research groups within molecular/structural biology. We offer training in both experimental and theoretical methods for obtaining structural information of biological molecules. All activities are open for everybody (BioStruct PhD students have priority). Free travel and accomodation for all BioStruct students attending the courses/activities as well as grants for national and international research visits (up to 6 mnd).

Contact us:
E-mail: biostruct@uit.no
Home: http://site.uit.no/biostruct
Facebook: facebook.com/BioStructPhDschool

Norsk Biokjemisk Selskap

Innkalling til ekstraordinær generalforsamling for Norsk Biokjemisk Selskap

Tid: lørdag 23. januar 2016 kl. 15:00

Sted: Clarion Hotel The Edge, Tromsø

Dagsorden:

1. Godkjenning av innkalling og dagsorden.
2. Styrets beretning.
3. Den nye presidenten overtar
   Aurora Martinez overtar som president for NBS etter Arne Klungland.
4. Hvordan skal vi gjøre det økonomisk lettere for master- og phd-studenter å delta på Kontaktmøtet?
   Prisen for deltakelse på Kontaktmøtet øker stadig, og det blir vanskeligere for yngre forskere å prioritere møtet. Dette spørsmålet ble diskutert på julemøtet til NBS-Bergen, som mente at én mulig løsning er at NBS deler ut noen få reisestipender for master- og phd-studenter for deltakelse på møtet.
   Forslag til vedtak: Generalsekretæren tar hensyn til Generalforsamlingens diskusjon av dette og formidler et forslag videre til neste års arrangør.
5. Forum for undervisning
   Det er for tiden stor interesse for utvikling av bedre undervisningsmetoder innen biovitenskapene. Mange har spennende ideer og noen har erfaring. Opprettelse av et forum for undervisning vil kunne tjene som et innovativt senter hvor ideer og erfaring kan deles og videreutvikles. Ved å legge et slikt forum til NBS kontaktmøtene kan vi gi deltakere fra hele landet mulighet til å ta del i denne kompetanseutvikling. Winnie Eskild vil påta seg å organisere de første samlingene men vil arbeide for å rekruttere aktive deltakere fra hele landet som fremover kan overta ledelsen.
   Forslag til vedtak: Det opprettes et forum for undervisning som tildeles 2-3 timer ved hvert NBS kontaktmøte. I første omgang som prøveprosjekt for et eller to år.
6. Arrangør av NBS Kontaktmøte 2018: Det er Oslo som står for tur!

Eventuelt.

Blindern 16. desember 2016

Tom Kristensen, generalsekretær

The Arctic NBS Contact Meeting in Tromsø, 21.-24.1.2016

	Thursday 21.01.2016	Friday 22.01.2016	Saturday 23.01.2016	
07:00		Breakfast	Breakfast	07:00
09:00		Plenary 3: Ilme Schlichting	Plenary 5: Terje Espevik	09:00
09:15				09:15
09:30				09:30
09:45		Plenary 4: Helena Danielson	Plenary 6: Tim Urich	09:45
10:00	Registration			10:00
10:15				10:15
10:30		Exhibition / Coffee	Coffee	10:30
10:45				10:45
11:00		Exhibitor talks Minisymposia 4-6 MS 04-06	Biochenology 1 Øystein Rekdal	11:00
11:15				11:15
11:30			Biochenology 2 Olav Lanes	11:30
11:45				11:45
12:00	Lunch		Lunch	12:00
12:15				12:15
12:30				12:30
12:45		Lunch		12:45
13:00				13:00
13:15				13:15
13:30				13:30
13:45	Welcome		Minisymposia 10-12 MS10-12	13:45
14:00	Plenary 1: Harald Stenmark	Research council of Norway		14:00
14:15				14:15
14:30				14:30
14:45	Plenary 2: Philippe Pierre			14:45
15:00		Exhibition / Coffee	NBS General Assembly	15:00
15:15				15:15
15:30	Exhibition / Coffee			15:30
15:45		Exhibitor talks Minisymposia 7-9 MS07-09		15:45
16:00				16:00
16:15	Exhibitor talks Minisymposia 1-3 MS01-03			16:15
16:30				16:30
16:45		Exhibition / Coffee		16:45
17:00				17:00
17:15				17:15
17:30	Exhibition / Coffee			17:30
17:45		Poster sesion 2		17:45
18:00				18:00
18:15	Poster sesion 1			18:15
18:30				18:30
18:45				18:45
19:00		Dinner		19:00
19:15				19:15
19:30			Reception	19:30
19:45	Get-Together			19:45
20:00	Dinner		Banquet dinner	20:00

Minisessions

Date 21/1	**Margarinfabrikken 1** **MS01:** Structural Bio I **Chair:** Inger Lin U. Ræder		**Margarinfabrikken 2** **MS02:** Cell Biol I **Chair:** Tore Skotland		**Prostneset** **MS03:** Biotech I/ Genetics **Chair:** Ole K. Greiner-Tollersrud
Time	**Speaker**	**Time**	**Speaker**	**Time**	**Speaker**
16:15	Christina Øie	**16:15**	Kirsten Sandvig	**16:15**	Ole K. Greiner-Tollersrud
16:30	Øyvind Halskau	**16:30**	Anja-Rose Strohmaier	**16:30**	Concetta De Santi
16:45	Ulli Rothweiler	**16:45**	Tore Skotland	**16:45**	Marianne Slang Jensen
17:00	Helen V. Thorbjørnsrud	**17:00**	Lorena Arranz	**17:00**	Marko Sankala
17:15	Susann Skagseth		Lorena Arranz	**17:15**	Valentyn Oksenych

Date 22/1	**Margarinfabrikken 1** **MS04:** Structural Bio II **Chair:** Marcin Pierechod		**Margarinfabrikken 2** **MS05:** Cell Biol II **Chair:** Stian Olsen		**Prostneset** **MS06:** Comput Bio I **Chair:** Finn Drabløs
Time	**Speaker**	**Time**	**Speaker**	**Time**	**Speaker**
11:15	Ruth Brenk	**11:15**	Philippe Pierre	**11:15**	Mathias Bockwoldt
11:30	Bjarte Lund		Philippe Pierre	**11:30**	Osman Gani
11:45	Hans Petter Hersleth	**11:45**	Peter McCourt	**11:45**	Finn Drabløs
12:00	Marie Lofstad	**12:00**	Owen Hughes	**12:00**	Christine Stansberg
12:15	Marcin Pierechod		-	**12:15**	Kjetil Klepper

Date 22/1	**Margarinfabrikken 1** **MS07:** Proteomics **Chair:** Gustav Vaaje-Kolstad		**Margarinfabrikken 2** **MS08:** Mol Med **Chair:** Bjørn Altermark		**Prostneset** **MS09:** Cell Biol III **Chair:** Peik Haugen
Time	**Speaker**	**Time**	**Speaker**	**Time**	**Speaker**
15:45	Ole K. Greiner-Tollersrud	**15:45**	Tony Christopeit	**15:45**	Kine Marita K. Sand
16:00	Jedrzej Malecki	**16:00**	Jimita Toraskar	**16:00**	Jakob Mejlvang
16:15	Adrian Naas	**16:15**	Ulrike Neckmann	**16:15**	Anna Eriksson
16:30	Gustav Vaaje-Kolstad	**16:30**	Hanna Noordzij	**16:30**	Hallvard Olsvik

Date 23/1	**Margarinfabrikken 1** **MS10:** Biotech II **Chair:** Adele Williamson		**Margarinfabrikken 2** **MS11:** Cell Biol IV **Chair:** Espen Åberg		**Prostneset** **MS12:** Comput Bio II **Chair:** Nils-Peder Willassen
Time	**Speaker**	**Time**	**Speaker**	**Time**	**Speaker**
13:45	Klara Stensvåg	**13:45**	Bård Smedsrød	**13:45**	Nils-Peder Willassen
14:00	Jennifer Loose	**14:00**	Helene Knævelsrud	**14:00**	Trygve Brautaset
14:15	Adele Williamson	**14:15**	Dimitar Iliev	**14:15**	Edvard Pedersen
14:30	Morten Sørlie		Dimitar Iliev	**14:30**	Boris Simovski

Orals at a glance

Plenary Lectures

Plenary Lecture 1 – Harald Stenmark **Thursday 14:00 – 14:45**

Chair – Terje Johansen

Plenary Lecture 2 – Philippe Pierre **Thursday 14:45 – 15:30**

Chair – Inigo Martinez-Zubiaurre

Plenary Lecture 3 – Ilme Schlichting **Friday 09:00 – 09:45**

Chair – Hanna-Kirsti Schrøder Leiros

Plenary Lecture 4 – Helena Danielson **Friday 09:45 – 10:30**

Chair – Tony Christopeit

Plenary Lecture 5 – Terje Espevik **Saturday 09:00 – 09:45**

Chair – Ole Kristian Greiner-Tollersrud

Plenary Lecture 6 – Tim Urich **Saturday 09:45 – 10:30**

Chair – Kirsten Krause

Research Council of Norway **Friday 14:00 – 15:00**

Chair – Hanna-Kirsti S. Leiros

Biotechnology 1 – Øystein Rekdal **Saturday 11:00 – 11:30**

Chair – Ronny Helland

Biotechnology 2 – Olav Lanes **Saturday 11:30 – 12:00**

Chair – Ronny Helland

Minisession 1 – Structural Biology and Biophysics I **Thursday 16:15 – 17:30**

Chair – Inger Lin U. Ræder

MS01.1 **Multimodal super-resolution optical microscopy visualizes the close connection between membrane and the cytoskeleton in liver sinusoidal endothelial cell fenestrations**

Viola Mönkemöller, Cristina Øie, Wolfgang Hübner, Thomas Huser, Peter McCourt

MS01.2 **Relevance of the protein, fatty acid and lipid component in early stages of liproteine-induced cell death**

Øyvind Halskau

MS01.3 **The structure of a dual-specificity tyrosine phosphorylation-regulated kinase 1A-PKC412 complex reveals disulfide-bridge formation with the anomalous catalytic loop HRD(HCD) cysteine**

Marina Alexeeva, Espen Åberg, Richard A. Engh, Ulli Rothweiler

MS01.4 **Crystal structure of a highly active chorismate mutase variant**

Helen V. Thorbjørnsrud, Jurate Kamarauskaite, Daniel Burschowsky, Peter Kast, Ute Krengel

MS01.5 **The impact of residues 119 and 228 in the Tripoli metallo-β-lactamase TMB-1 involved in resistance to β-lactam antibiotics**

Susann Skagseth, Ørjan Samuelsen, Hanna-Kirsti S. Leiros

Minisession 2 – Cell biology, Neurology and Signaling I **Thursday 16:15 – 17:30**

Chair – Tore Skotland

MS02.1 **Lipid-induced modulation of endocytosis and intracellular transport of protein toxins**

Ieva Ailte Hjelseth, Anne Berit Dyve Lingelem, Simona Kavaliauskiene, Audun Kvalvaag, Jonas Bergan, Tore Skotland, Kirsten Sandvig

MS02.2 **ibidi – cells in focus: In vivo like, physiological conditions for cell based assays during live cell imaging**

Tina Freisinger, Anja-Rose Strohmaier

MS02.3 **Handshaking between PS 18:0/18:1 and long chain sphingolipids in cellular membranes cells**

Tore Skotland

MS02.4 **A Role for the Stem Cell Niche in Myeloid Leukaemias?**
Lorena Arranz

Minisession 3 – Biotechnology and Biocatalysis I/Genetics and Epigenetics Thursday 16:15 – 17:30

Chair – Ole Kristian Greiner Tollersrud

MS03.1 **Critically positioned N-glycans prevent efficient mannose-6-phosphorylation of lysosomal proteins, giving new clues on how to bioengineer therapeutic proteins with increased uptake via the mannose-6-phosphate receptor**

Pirkko Heikinheimo, Gaute Hansen, Hilde M.F. Riise-Stensland, Christophe Flahaut, Jan Ole Olsen, Gry Evjen, Jean-Claude Michalski, Ole K. Greiner-Tollersrud

MS03.2 **Microbial communities and moving bed technology as tools for conversion of marine biomass**

Concetta De Santi, Ragnhild D. Whitaker, Elin Moe, Fredrik Almqvist, Nils-Peder Willassen, Peik Haugen

MS03.3 **Discovery and characterization of thermostable cellulases for degrading lignocellulosic biomass**
Marianne Slang Jensen, Lasse Fredriksen, Alasdair MacKenzie, Phil Pope, Piotr Chylenski, Aniko Varnai, Gustav Vaaje-Kolstad, Vincent G.H. Eijsink

MS03.4 **Advanced CRISPR Genome Editing: Specific Sequence Changes and Whole genome screens**

Marko Sankala

MS03.5 **Inactivation of Ku70 or p53 rescues perinatal lethality of XLF/DNA-PKcs double deficient mice**

Valentyn Oksenych, Magnar Bjoras, Frederick Alt

Minisession 4 – Structural Biology and Biophysics II **Friday 11:15 – 12:30**

Chair - Marcin Pierechod

MS04.1 **Structure-based design of riboswitch ligands**

Thomas Wehler, Ruth Brenk

MS04.2 **Structure-guided drug design for the antibiotic resistance enzyme OXA-48**

Bjarte Aarmo Lund, Sundus Ahkter, Yngve Guttormsen, Tony Christopeit, Annette Bayer, Hanna-Kirsti S. Leiros

MS04.3 **Probing enzyme activation networks - structural and functional studies of flavoproteins in *Bacillus cereus***

Ingvild Gudim, Marie Lofstad, Kristoffer Andersson, Marta Hammerstad, Hans-Petter Hersleth

MS04.4 **A comparison of the dimanganese active sites of class Ib ribonucleotide reductase and manganese catalase by CD and MCD spectroscopy**

Marie Lofstad, Lars H. Böttger, Åsmund K. Røhr, Hans-Petter Hersleth, Marta Hammerstad, Edward I. Solomon, Kristoffer Andersson

MS04.5 **The structure of *Salinibacter ruber* Single-Strand Binding protein reveals a novel, octameric architecture of bacterial SSB proteins**

Marcin Pierechod, Ulli Rothweiler, Taiana de Oliveira

Minisession 5 – Cell biology, Neurology and Signaling II **Friday 11:15 – 12:30**

Chair – Stian Olsen

MS05.1 **Protein synthesis arrest and GADD34 are part of the anti-viral cellular tool box**

Philippe Pierre

MS05.2 **Identification of adult hemogenic sinusoidal endothelial cells in adult bone marrow**

Peter A. McCourt, Ana Oteiza, Melonie Storan, Brenda Williams, Chad Heazlewood, Karen K. Sørensen, S Li, Christian Nefzger, Yoshiaki Kubota, Jose Polo, Susie Nilsson

MS05.3 **Amnis Imaging Flow Cytometry: high speed, high content image analysis of cells in flow**

Owen Hughes

Minisession 6 – Computational biology I **Friday 11:15 – 12:30**

Chair – Finn Drabløs

MS06.1 **Phylogenetic analysis of NAD biosynthesis and consumption**

Mathias Bockwoldt, Ines Heiland

MS06.2 **Open source data and utilities for protein target prediction of small molecules**

Osman Gani, Dilip Narayanan, Richard A. Engh

MS06.3 **Identification and analysis of genes in immediate-early response processes**

Shahram Bahrami, Finn Drabløs

MS06.4 **NORBIS – the national research school in bioinformatics, biostatistics and systems biology**

Christine Stansberg

MS06.5 **MotifLab – a regulatory sequence analysis workbench**

Kjetil Klepper, Finn Drabløs

Minisession 7– Proteomics **Friday 15:45 – 16:45**

Chair - Gustav Vaaje-Kolstad

MS07.1 **Development of a new validation method for identification of lysosomal proteins, and its application in therapy**

Ole K. Greiner-Tollersrud

MS07.2 **METTL20 is a Novel Lysine-Specific Methyltransferase that Targets the Beta Subunit of Electron Transfer Flavoprotein (ETFβ) and Modulates Its Activity**

Jedrzej Małecki, Angela Y.Y. Ho, Anders Moen, Helge-André Dahl, Pål Ø. Falnes

MS07.3 **Discovery of a potentially novel cellulolytic mechanism linked to the Bacteroidetes Por secretion system**

Adrian E. Naas, Vincent G.H. Eijsink, Phil B. Pope

MS07.4 **Chitin degradation by *Cellvibrio japonicus***

Tina Rise Tuveng, Zarah Forsberg, Cassandra E. Nelson, Bjørn Dalhus, Sophanit Mekasha, Jennifer S.M. Loose, Åsmund K. Røhr, Magnus Øverlie Arntzen, Jeffrey G. Gardner, Vincent G.H. Eijsink, Gustav Vaaje-Kolstad

Minisession 8 – Molecular Medicine **Friday 15:45 – 16:45**

Chair – Bjørn Altermark

MS08.1 **Discovery of a Novel Covalent Inhibitor of the Metallo-β-lactamase NDM-1**

Tony Christopeit, Trine J.O. Carlsen, Anastasia Albert, Susann Skagseth, Hanna-Kirsti S. Leiros

MS08.2 **The role of Nephronectin in breast cancer progression and metastasis**

Jimita Toraskar, Neeruja Balenthiran, Tonje S. Steigedal

MS08.3 **Significance of NFE2L2 Target Genes for Survival of Breast Cancer Patients: High Expression of NQO1 is Associated with Poor Clinical Outcome**

Ulrike Neckmann, Rosalie Zwiggelaar, Tonje S. Steigedal, Geir Bjørkøy

MS08.4 **How does the neonatal Fc receptor (FcRn) handle the transport of its two ligands, IgG and albumin, in the human placenta?**

Hanna Theodora Noordzij, Line Mathiesen, Kine Marita Knudsen Sand, Tom Eirik Mollness, Espen S. Bækkevold, Greg J. Christianson, Derry C. Roopenian, Lisbeth Knudsen, Inger Sandlie, Jan Terje Andersen

Minisession 9 – Cell biology, Neurology and Signaling III **Friday 15:45 – 16:45**

Chair – Peik Haugen

MS09.1 **The neonatal Fc receptor (FcRn)-mediated recycling of IgG and albumin in endothelial cells**

Kine Marita Knudsen Sand, Algirdas Grevys, Frode Skjeldal, Oddmund Bakke, Inger Sandlie, Jan Terje Andersen

MS09.2 **Identification of a novel lysosomal degradation pathway acutely activated upon nutrient starvation**

Jakob Mejlvang, Kenneth Bowitz Larsen, Hallvard Olsvik Lauritz, Hanne Brenne, Steingrim Svenning, Birendra Kumar Shrestha, Jack-Ansgar Bruun, Terkel Hansen, Terje Johansen

MS09.3 **CLEC16A is localized in Rab4a+ endosomes in Jurkat cells**

Anna Eriksson, Ingvild Leikfoss, Vibeke Sundvold-Gjerstad, Greger Abrahamsen, Ole Landsverk, Hanne Harbo, Anne Spurkland, Tone Berge

MS09.4 **FYCO1 Contains a C-terminally Extended, LC3A/B-preferring LC3-interacting Region (LIR) Motif Required for Efficient Maturation of Autophagosomes during Basal Autophagy.**

Hallvard Olsvik, Trond Lamark, Kenji Takagi, Kenneth Larsen, Gry Evjen, Aud Øvervatn, Tsunehiro Mizushima, Terje Johansen

Minisession 10 – Biotechnology and Biocatalysis II **Saturday 13:45 – 14:45**

Chair – Adele Williamson

MS10.1 **Bioactive peptides from marine sources**

Runar Gjerp Solstad, Hans-Matti Blencke, Ekaterina Mishchenko, Chun Li, Inger Kristine Rødum, Tor Haug, Klara Stensvåg

MS10.2 **Controlled electron supply and site-directed mutagenesis give new insights into the catalytic mechanism of lytic polysaccharide monooxygenases**

Jennifer S.M. Loose, Zarah Forsberg, Roland Ludwig, Vincent G.H. Eijsink, Gustav Vaaje-Kolstad

MS10.3 **Structural and Bioinformatic Studies of the 'Lig E'Group of Bacterial ATP-Dependent DNA Ligases**

Adele Williamson, Tim Kahlke, Erik Hjerde, Hanna-Kirsti S. Leiros

MS10.4 **Towards a molecular-level theory of carbohydrate processivity in glycoside hydrolases**

Morten Sørlie

Minisession 11 – Cell biology, Neurology and Signaling IV Saturday 13:45 – 14:45

Chair – Espen Åberg

MS11.1 **Role of specialized hepatic scavenger cells in control of biodistribution of large molecule drugs and nano formulations**

Bård Smedsrød, Kjetil Elvevold

MS11.2 **Functional understanding of Ral signaling in *Drosophila melanogaster***

Helene Knævelsrud, Marc Therrien

MS11.3 **CpG-induced exosome secretion from Atlantic salmon leukocytes**

Dimitar Iliev, Guro Strandskog, Jorunn Jørgensen, Randi Olsen, Mehrdad Sobhkhez, Jack-Ansgar Bruun

Minisession 12 – Computational biology II **Saturday 13:45 – 14:45**

Chair – Nils-Peder Willassen

MS12.1 **ELIXIR.NO - The national technology platform for bioinformatics**

Nils-Peder Willassen, Lars Ailo Bongo, Finn Drabløs, Eivind Hovig, Dag Inge Våge, Inge Jonassen

MS12.2 **Norwegian Center for Digital Life**

Trygve Brautaset

MS12.3 **Sequence assembly in the cloud, on the grid and in the basement**

Edvard Pedersen, Espen Mikal Robertsen, Inge Alexander Raknes, Nils-Peder Willassen, Lars Ailo Bongo

MS12.4 **GSuite tools: Efficient management and analysis of genomic dataset collections**

Boris Simovski, Daniel Vodák, Sveinung Gundersen, Abdulrahman Azab, Diana Domanska, Ivar Grytten, Lars Holden, Antonio Mora, Knut Rand, Eivind Hovig, Geir K. Sandve

Posters at a glance

P1	**Static and dynamic interactions between the glycine-rich loop of protein kinases and ATP site inhibitors** Kazi Asraful Alam, Ulli Rothweiler, Richard A. Engh
P2	**Production of sialic acids and derivatives by enzyme catalysis** Tor Olav Berg, Bjørn Altermark, Ronny Helland, Ingar Leiros, Inger Lin U. Ræder
P3	**Towards an optimal Tyrosine Hydroxylase** Marte Innselset Flydal, Maite Bezem, Anne Baumann, Lars Skjærven, Petri Kursula, Aurora Martinez
P4	**Structural Insight into the Function of Ribonucleotide Reductase** Marta Hammerstad, Hans-Petter Hersleth, Ane B. Tomter, Åsmund K. Røhr, Kristoffer Andersson
P5	**A structural and functional investigation of Ribonucleotide reductase Class III in *Bacillus cereus*** Hedda Johannesen, Hans-Petter Hersleth, Marta Hammerstad, Kristoffer Andersson
P6	**Nucleotide binding and hydrolysis of heat shock protein HSP70 as probed by biophysical and crystallographic studies of the nucleotide binding domain.** Dilip Narayanan, Tony Christopeit, Alexander Pflug, Richard A. Engh
P7	**Residue profiling of antibiotic resistant OXA-beta-lactamases through mutagenesis, enzyme kinetics and 3D structures** Birgit Berg Nesheim, Trine Josefine O. Carlsen, Bjarte Aarmo Lund, Hanna-Kirsti S. Leiros
P8	**Binding of the lytic polysaccharide monooxygenase CBP21 to chitin – a computational approach** Ingvild Isaksen**,** Åsmund Kjendseth Røhr
P9	**Regulatory interactions between the J- and UBA domains of NBR1 enable a switch between membrane binding and protein aggregation** Steingrim Svenning, Hallvard L. Olsvik, Andreas Brech, Johan Isaksson, Elenaz Naderkhani, Tom Egil Hansen, Sebastian W. Schultz, Trond Lamark, Terje Johansen
P10	**Crystallization of *Arabidopsis thaliana* SnRK2-interacting Calcium Sensor, the kinase inhibitor containing EF-hand motifs** Marcin Pierechod, Krzysztof Tarnowski, Arkadiusz Ciesielski, Maria Klimecka, Johan Isaksson, Jarosław Poznański, Grażyna Dobrowolska, Richard A. Engh
P11	**Structure-function study of LsbB family leaderless bacteriocins.** Kirill V. Ovchinnikov, Per E. Kristiansen, Ingolf F. Nes, Dzung B. Diep
P12	**STED microscopy of ASC speck inflammasome formation in mouse macrophages** Kjartan Wøllo Egeberg, Bjørnar Sporsheim, Terje Espevik
P13	**Moving Tolls - novel interactors of TLR9 trafficking** Lene Grøvdal, Kay Oliver Schink, Karin Pelka, Harald Husebye, Eicke Latz, Harald Stenmark, Terje Espevik

P14	**Delivering Biotherapeuticals: Challenge of unwanted liver uptake** Kjetil Elvevold, Bård Smedsrød
P15	**Secretome of the liver sinusoidal endothelial cell** Jaione Simón-Santamaría, Ruomei Li, Sabin Bhandari, Jack-Ansgar Bruun, Bård Smedsrød, Inigo Martinez, Karen Sørensen
P16	**Gastrin induces autophagy in gastric adenocarcinoma cells directly and via an autocrine loop** Barbara Niederdorfer, Shalini Rao, Liv Thommesen
P17	**Regulation of ErbB2 receptor tyrosine kinases by ERM proteins** Nagham Asp, Audun S. Kvalvaag, Kirsten Sandvig, Sacha Pust
P18	**The multiple sclerosis susceptibility genes *TAGAP* and *IL2RA* are regulated by vitamin D in CD4+ T cells** Tone Berge, Ina Brorson, Ingvild Leikfoss, Steffan Bos, Christian Page, Marte Gustavsen, Anja Bjølgerud, Trygve Holmøy, Elisabeth Celius, Jan Damoiseaux, Joost Smolders, Hanne Harbo, Anne Spurkland
P19	***In vivo* proteolytic activity assayed by subcellular localization switching** Clemens Furnes, Monica Mannelqvist, Shirley Vanessa Sarria, Rein Aasland, Anne-Marie Szilvay
P20	**Identification of a novel lysosomal degradation pathway acutely activated upon nutrient starvation** Jakob Mejlvang, Kenneth Bowitz Larsen, Hallvard Olsvik Lauritz, Hanne Brenne, Steingrim Svenning, Birendra Kumar Shrestha, Jack-Ansgar Bruun, Terkel Hansen, Terje Johansen
P21	**Regulation of macropinocytosis by PI3P-binding proteins** Kay Oliver Schink, Kia Wee Tan, Marte Sneeggen, Domenica Martorana, Coen Campsteijn, Camilla Raiborg, Harald Stenmark
P22	**Catching the tubule – Analyzing the role of the PtdIns3P-binding protein WDFY2 in retrograde endocytic transport** Marte Sneeggen, Kay Oliver Schink, Coen Campsteijn, Harald Stenmark
P23	**Bmp4 and Grem1 in breast cancer tumor-stroma communication** Camilla Wolowczyk, Christiana Appiah, Jennifer Mildenberger, Ulrike Neckmann, Geir Bjørkøy, Toril Holien
P24	**The role of the extracellular matrix protein Nephronectin in breast cancer progression and metastasis** Neeruja Balenthiran, Jimita Toraskar, Tonje S. Steigedal
P25	**Hunting for proteins binding to the RUN and GOLD domains of FYCO1** Betty Martine Furulund, Terje Johansen, Hallvard Olsvik
P26	**The long non-coding RNA NEAT1 is upregulated in epithelial-mesenchymal transition and is abnormally expressed in breast cancer** Erik Knutsen, S. Mohammad Lellahi, Annica Hedberg, Tonje Fiskaa, Kristin Andersen, Gunhild Mælandsmo, James Lorens, Ole Morten Seternes, Steinar Johansen, Elin Mortensen, Maria Perander

P27	**n-3 PUFAs modulate SQSTM1 and dampen pro-inflammatory CXCL10 in human macrophages** Jennifer Mildenberger, Ida Johansson, Eli Kjøbli, Trude Helen Flo, Jan Kristian Damås, Geir Bjørkøy
P28	**DNA polymerases from the Arctic** Netsanet G. Assefa, Yvonne Piotrowski, Ronny Helland, Kirsti M. Johannessen, Nils P. Willassen, Atle N. Larsen
P29	**Cool catalysts for biomass conversion** Bjørn Altermark, Inger Lin U. Ræder, Marie J. Halsør, Seila Pandur, Ulli Rothweiler, Arne O. Smalås
P30	**Enzyme Innovations from the Marine Arctic** Yvonne Piotrowski, Netsanet G. Assefa, Kirsti M. Johannessen, Ronny Helland, Nils P. Willassen, Arne O. Smalås, Trond Ø. Jørgensen, Atle N. Larsen
P31	**Maximizing the value of marine by-products** Ole Christian Hagestad, Ragnhild Withaker, Jan Arne Arnesen, Jaran Rauø, Klara Stensvåg
P32	**Bioactive peptides from marine sources** Runar Gjerp Solstad, Hans-Matti Blencke, Ekaterina Mishchenko, Chun Li, Inger Kristine Rødum, Tor Haug, Klara Stensvåg
P33	**A novel expression system specialized for psychrophilic enzymes** Miriam Grgic, Jenny Johansson Söderberg, Peik Haugen
P34	**Quorum sensing in *Aliivibrio wodanis* 06/09/139: N-acyl homoserine lactone synthesis and transcription profiling** Amudha Maharajan, Hilde Hansen, Erik Hjerde, Nils-Peder Willassen
P35	**Characterization of an evolutionarily conserved lysine-specific eEF2 methyltransferase** Erna Davydova, Angela Y.Y. Ho, Jedrzej Malecki, Anders Moen, Jorrit Enserink , Magnus Jakobsson , Christoph Loenarz, Pål Ø. Falnes
P36	**Regulation of Promoter Activity of the Human Oncovirus Merkel Cell Polyomavirus Variants MCC350 and 16b by Large T-antigen** Ibrahim Abdulsalam, Kashif Rasheed, Baldur Sveinbjørnsson, Ugo Moens
P37	**MotifLab – a regulatory sequence analysis workbench** Kjetil Klepper, Finn Drabløs
P38	**Comprehensive detection and classification of circular RNAs in starlet sea anemone** Ksenia Lavrichenko, David Fredman
P39	**META-pipe – Pipeline annotation, analysis and visualization of metagenomic data** Espen Mikal Robertsen, Edvard Pedersen, Martin Ernstsen, Tim Kalhke, Lars Ailo Bongo, Nils-Peder Willassen
P40	**Practical Applications of Informatics Tools to Identify Drug Targets for Novel Compounds from Bio- and Chemoprospecting** Balmukund S. Thakkar, Osman Gani, Richard A. Engh

P41	**Next generation deep sequencing of rat liver sinusoidal endothelial cell and Kupffer cell transcriptomes suggests functional complementarity** Sabin Bhandari, Ruomei Li, Jaione Simón-Santamaría, Peter McCourt, Steinar Johansen, Bård Smedsrød, Inigo Martinez, Karen Sørensen
P42	**The structure of a dual-specificity tyrosine phosphorylation-regulated kinase 1A-PKC412 complex reveals disulfide-bridge formation with the anomalous catalytic loop HRD (HCD) cysteine** Marina Alexeeva, Espen Åberg, Richard A. Engh, Ulli Rothweiler
P43	**The 5-hydroxymethylcytosine Level Increases During Rat Sertoli Cell Differentiation** Miriam Landfors, Cathrine Broberg Vågbø, Håvard Aanes, Magnus Aronsen, Markus Fusser, John-Arne Dahl, Louis C Doré, Chuan He, Ivar Sjaastad, Peter Fedorcsak, Arne Klungland
P44	**Confocal microscopy studies of human stem cell growth on dental implants** Catherine Heyward, Lisa Printzell, Jørgen Hugo, Janne Reseland

Abstracts

PL1: Harald Stenmark

Harald Stenmark

Department of Molecular Cell Biology, Institute for Cancer Research
The Norwegian Radium Hospital, Norway

Harald Stenmark is the director of the Centre of Excellence, Centre of Cancer Biomedicine, and is most known for his studies of how a cell can develop into a cancer cell. Cellular membranes not only serve as barriers between organelles, cells and the environment – they also play active roles in vital processes such as cell signalling, migration and division. His group focus on membrane dynamics processes that mediate tumor suppression. These include endocytic downregulation of growth factor receptors [1], positioning of organelles involved in cell signalling [2], and sealing of the newly formed nuclear envelope and separation of daughter cells during mitotic exit [3-5]. In his lecture, he will discuss some of the molecular players involved in these processes, especially the endosomal sorting complex required for transport (ESCRT) machinery [1]. He will also highlight examples of how the dysfunctions of these components may promote cancer development.

[1] Raiborg,C. & Stenmark,H. (2009) The ESCRT machinery in endosomal sorting of ubiquitylated membrane proteins. *Nature* **458,** 445-452.

[2] Raiborg,C., Wenzel,E.M., Pedersen,N.M., Olsvik,H., Schink,K.O., Schultz,S.W., Vietri,M., Nisi,V., Bucci,C., Brech,A., Johansen,T., & Stenmark,H. (2015) Repeated ER-endosome contacts promote endosome translocation and neurite outgrowth. *Nature* **520,** 234-238.

[3] Vietri,M., Schink,K.O., Campsteijn,C., Wegner,C.S., Schultz,S.W., Christ,L., Thoresen,S.B., Brech,A., Raiborg,C., & Stenmark,H. (2015) Spastin and ESCRT-III coordinate mitotic spindle disassembly and nuclear envelope sealing. *Nature* **522,** 231-235.

[4] Thoresen,S.B., Campsteijn,C., Vietri,M., Schink,K.O., Liestol,K., Andersen,J.S., Raiborg,C., & Stenmark,H. (2014) ANCHR mediates Aurora-B-dependent abscission checkpoint control through retention of VPS4. *Nat. Cell Biol.* **16,** 550-560.

[5] Sagona,A.P., Nezis,I.P., Pedersen,N.M., Liestol,K., Poulton,J., Rusten,T.E., Skotheim,R.I., Raiborg,C., & Stenmark,H. (2010) PtdIns(3)P controls cytokinesis through KIF13A-mediated recruitment of FYVE-CENT to the midbody. *Nat. Cell Biol.* **12,** 362-371.

PL2: Philippe Pierre

Philippe Pierre

Centre d'Immunologie de Marseille-Luminy, France

Philippe Pierre is group leader at Centre d'Immunologie de Marseille-Luminy. His main interest is dendritic cell biology and how these cells translate microbial data into immunological instructions.

RUN and FYVE domain containing protein 4 enhances autophagy and lysosome tethering in response to Interleukin-4. Autophagy is a key degradative pathway coordinated by external cues, including starvation, oxidative stress or pathogen detection. Rare are the molecules known to contribute mechanistically to the regulation of autophagy and expressed specifically in particular environmental contexts or in distinct cell types. His presentation will unravel the role of RUN and FYVE domain-containing protein 4 (RUFY4), as a positive molecular regulator of macro-autophagy in primary dendritic cells (DCs). He will show that exposure to interleukin-4 (IL-4) during DCs differentiation enhances autophagy flux through mTORC1 regulation and RUFY4 induction, which in turn actively promote LC3 degradation, Syntaxin 17-positive autophagosomes formation and lysosomes tethering. Enhanced autophagy boosts endogenous antigen presentation by MHC II and allows host control of *Brucella abortus* replication in IL-4-treated DCs and in RUFY4-expressing cells. RUFY4 is therefore the first molecule characterized to date that promotes autophagy and influences endosomes dynamics in a subset of immune cells.

PL3: Ilme Schlichting

Ilme Schlichting

Max Planck Institute for Medical Research, Department of Biomolecular Mechanisms, Heidelberg, Germany

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Ilme Schlichting is a director at the Max Planck Institute for medical Research, Dept. of Biomolecular Mechanisms. Schlichting's research aims at understanding how proteins achieve their unique functional properties. Key insight is obtained from structures of reaction intermediates. Schlichting was the first to successfully combine photolysis of caged compounds and Laue crystallography to study GTP hydrolysis by the Ras protein, to observe ligand binding intermediates in myoglobin, and to resolve the reaction intermediates of a cytochrome P450 at high spatial resolution. Her latest interests include the application of X-ray free-electron lasers (XFELs) for structural biology.

Protein crystallography using synchrotron radiation sources has had tremendous impact on biology, having yielded the structures of thousands of proteins and given detailed insight into their working mechanisms. However, the technique is limited by the requirement for macroscopic crystals, which can be difficult to obtain, as well as by the often severe radiation damage caused in diffraction experiments, in particular when using tiny crystals. To slow radiation damage, data collection is typically performed at cryogenic temperatures.

The femtosecond X-ray pulses provided by X-ray free-electron lasers (FELs) allow the acquisition of high resolution diffraction data from micron-sized macromolecular crystals at room temperature beyond the limitations of radiation damage imposed by conventional X-ray sources. Moreover, the short duration of the pulses enable time-resolved studies at the chemical time-scale of femtoseconds. The novel sources require new approaches for sample preparation, delivery, data collection and analysis. These [1] as well as recent results obtained will be presented.

[1] Schlichting, I. (2015) IUCrJ 2: 246-255. Serial femtosecond crystallography: the first five years.

PL4: Helena Danielson

Helena Danielson

Uppsala University, Sweden

Helena Danielson is Professor of Biochemistry at Uppsala University in Sweden since 2002. She is a specialist in enzyme-based drug discovery and molecular recognition. Her education includes a Master of Science in Chemical Engineering at Lund University in 1982 and, as a Fulbright scholar, a Master of Science in Biochemistry, University of Rochester, Rochester, NY, USA in 1984, and a Ph. D. in Biochemistry at Stockholm University in 1987. As a postdoc at Karolinska Institutet in Stockholm Helena Danielson started a research project on HIV protease as a drug target for AIDS, and has since expanded her research to other enzymes and diseases, more recently also with an interest in membrane receptors, cell signaling and neurological function. Helena Danielson has focused on developing enzymology for drug discovery, and in particular SPR-biosensor based biomolecular interaction analysis for detailed studies of enzyme-inhibitor interactions and other important recognition processes in the life science area. Helena Danielson co-founded Beactica AB in 2006 and was Chief Scientific Officer until 2014.

PL5: Terje Espevik

Terje Espevik

Department of Cancer Research and Molecular Medicine, Centre of Molecular Inflammation Research (SFF-CEMIR), Norwegian University of Science and Technology, Norway

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Terje Espevik is professor in cell biology at NTNU and focuses on the immune system. He is head of a Centre of Excellence, the new Centre of Molecular Inflammation Research (CEMIR). The goal is to increase our understanding of the mechanisms that initiates the inflammation response in our body, and how this response can cause damage. Although the focus is on basic research, a main goal of his research is to develop new methods for better diagnosis and therapy of diseases where inflammation serves a pathological role. These includes bacterial and viral infections, as well as many of the common diseases in society, as cancer, Alzheimer and several autoimmune diseases. Terje Espevik has almost 100 group members, and is one of the most cited authors among Norwegian scientists.

Toll-like receptors (TLRs) initiate inflammatory responses against microbes and some host derived molecules by inducing cytokines like TNF and IL-1β. However, TLRs may also activate intracellular signaling mechanisms resulting in type I interferons (IFNs) that are best known for their anti viral effects. During initial bacterial infections low amounts of type I IFNs seems to be required for cell-mediated immune responses. However, severe bacterial infections may lead to high amounts of type I IFNs that can result in production of immunosuppressive molecules increasing the risk for secondary infections during sepsis. Type I IFNs have also been implicated in mediating deleterious inflammation during infection with different Gram-negative bacteria through the activation of caspase 11, leading to the production of IL-1β and IL-18. TLR-mediated type I IFN responses occur from intracellular compartments like endosomes and phagosomes. Both *Staphylococcus aureus* (SA) and *E. coli* (EC) are potent inducers of IFNβ in human monocytes and macrophages and our aim has been to delineate mechanisms behind this response. In human monocyte-derived macrophages SA induced production of IFNβ through TLR8-dependent sensing of SA RNA in the phagosome, which triggered IRF5 nuclear accumulation. The TLR8-mediated activation of IRF5 was dependent on the kinases TAK1 and IKKβ, which reveals a role of the IRF5-activated IKKβ in immune responses. In contrast to SA, EC requires the small GTPase Rab11a to induce an IFNβ response. Rab11a recruits TLR4 and TRAM to EC phagosomes resulting in IRF3 phosphorylation. A screen among the Rab11 interacting proteins (Rab11FIPs) revealed that depletion of RAB11FIP2 by siRNA reduced the induction of IFNβ in response to EC and LPS. In conclusion, our study demonstrates a new role for TLR8 in the sensing of SA in human primary phagocytes. For EC-induced IFNβ, Rab11a and Rab11FIPs have essential roles in trafficking of TRAM to EC phagosome, which is needed for IRF3 phosphorylation.

PL6: Tim Urich

Tim Urich

Institute for Microbiology, Ernst-Moritz-Arndt University of Greifswald, Germany

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Tim Urich is Professor at the Institute of Microbiology at Ernst-Moritz-Arndt University Greifswald in Germany. He was trained in Microbiology and Biochemistry at Darmstadt University of Technology (Germany), where he worked with Arnulf Kletzin on sulfur-cycling enzymes of hyperthermophilic prokaryotes. He did post-doctoral studies with Christa Schleper at University of Bergen (Norway) developing and applying functional metagenomics techniques to study uncultivated microorganisms in soils. He then was junior group leader at University of Vienna, before recently moving to Greifswald. His research interests widely span several aspects of the biology of microorganisms with a focus on physiologies and interactions of microorganisms directly in their environment. His team applies an interdisciplinary mix of methods centered at functional metagenomics. Current research interests include soil microbiomes and their role in carbon and nitrogen cycling and consequences for greenhouse gas emissions and aspects of human and animal microbiomes in health and disease. He is also interested in the physiology and ecology of methanogenic archaea.

Biotechnology 1: Øystein Rekdal

Øystein Rekdal

CSO, Lytix Biopharma AS, IMB, University of Tromsø

Lytix Biopharma

Through structure-activity relationship studies we have designed a chemically modified oncolytic peptide derived from the host defense peptide lactoferricin, named LTX-315.

The oncolytic effect of LTX-315 involves perturbation of the plasma membrane and distortion of the mitochondrial membrane with subsequent release of DAMPs (Damage-Associated Molecular Pattern molecules) such as ATP, cytochrome C and HMGB1 (1,2). Multi-domain proteins from the BCL-2 family seem to be partially involved in LTX-315 mediated killing (3). In addition, LTX-315 induces the hallmarks of immunogenic cell death (4).

Preclinical studies have demonstrated that LTX-315 is able to induce complete tumour regression in a number of different types of cancer after intra-tumoural treatment (5,6). Furthermore, LTX-315 induces a systemic tumour specific immune response since both treated and non-treated tumours are eradicated. Tumours did not develop in cured animals when re-challenged with tumour cells.

In preclinical tumour models, combination of LTX-315 and immune checkpoint inhibitors (anti-CTLA4 and anti-PD1) demonstrate synergy . These results, together with LTX-315`s complementary MoA, indicate a strong rationale for combining LTX-315 with immune checkpoint inhibitors in a clinical setting.

Early clinical Phase I data show that LTX-315 is well tolerated and results of efficacy showing clinical response are promising.

References:

1) Forveille *et al*., Cell Cycle (2015)

2) Eike *et al*., Oncotarget (2015)

3) Zhou *et al.,* Oncotarget (2015)

4) Zhou *et al.,* Cell Death & Differentiation (in press)

5) Camilio *et al*., Cancer Immunol Immunother (2014)

6) Camilio *et al*., Oncoimmunology (2014)

Biotechnology 2: Olav Lanes

Olav Lanes

ArcticZymes AS, Sykehusveien 23,

P.O. Box 6462, 9294 Tromsø, Norway

contact@arcticzymes.com

Applications and integration of cold-adapted enzymes into molecular workflows

ArcticZymes is a well-established business located in Tromsø, Norway. ArcticZymes develops, produces and sells enzymes originating from the marine Arctic for use in molecular technologies and diagnostics. Molecular technologies like qPCR and Next-Gen Sequencing (NGS) are sensitive methods used to detect and analyze DNA and RNA from biological and environmental samples. The technologies are adapted for decreasingly amount of starting material and reaction volumes, as exemplified by the emerging field of single-cell analysis to extend the biological understanding and resolution when interrogating tissues or cell populations. Dealing with minute amount of starting material is challenging and sample loss, bias and various kind of contamination is a major concern. This favors enzyme-based solutions in sample preparation compared to ordinary column or bead based approaches. The discovery, development and applications of Arctic marine enzymes will be presented.

Research Council of Norway-

Career development and funding opportunities

Lars Petter Korsnes, Cecilie Anita Mathiesen, Berit Sundby Avset, Per Ivar Høvring

The Research Council of Norway

Research funding in a nutshell.

This brief introduction will give an overview of the sources for funding research in Norway and in the European union. It will cover the funding instruments for the universities and colleges, and the Regional Health Authorities from the Research Council of Norway and the European Union framework programme for Research, Horizon 2020. We will also touch upon the research policies governing the research priorities.

Career opportunities for the young and the "not-so-young" – building and maintaining a competitive CV.

There are many opportunities for those who want to pursue a career doing research. Whether it is at a university, in a hospital or in industry. Whether your dream is to commercialize the perfect drug to cure cancer or to get a Nobel prize – or you just want to have fun doing research on your favourite topic. In this talk we will cover the whole range of grants from how to find a PhD position abroad, to what you need to do to be able to compete for an ERC-grant. Likewise we will mention available grants and programs for applied research, either to solve societal challenges or to transform promising scientific result into new inventions and innovations for commercial developments.

We will discuss the need for international mobility and networking, and how you can get funding for it through the Marie Curie Actions, FRIPRO Mobility grant, overseas research grants in FRIPRO/Research Council projects, and in COST actions. We will also discuss how important it is for young candidates to acquire additional knowledge, in addition to training in research. Finally we will also discuss opportunities for collaboration with industry and commercialization.

Calls and application deadlines for research projects in Horizon 2020 and the Research Council of Norway in 2016 and 2017.

The work programmes for H2020 for the period 2016-2017, was published in October 2015, and they describe the topics that you can get funding for and the deadlines. We will provide a brief overview of the topics that we believe is most relevant for the conference participants, as well as discussing how to read and understand a call text. We will also give an overview of relevant calls from the Research Council in 2016.

Abstracts: Minisessions

MS01.1

Multimodal super-resolution optical microscopy visualizes the close connection between membrane and the cytoskeleton in liver sinusoidal endothelial cell fenestrations

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**Equal contribution*

Liver sinusoidal endothelial cells (LSECs) act as filters between blood and hepatocytes. LSECs are highly fenestrated with transcellular pores having diameters between 50 to 200 nm. The small sizes of these fenestrae have so far prohibited any functional analysis with standard and advanced light microscopy techniques. Only now the advent of super-resolution optical fluorescence microscopy permits the recording of such small cellular structures. Here, we demonstrate the complementary use of two different super-resolution optical microscopy modalities, 3D-structured illumination microscopy (3D-SIM) and single molecule localization microscopy in a common optical platform to obtain new insights into the association between the cytoskeleton and the plasma membrane supporting the formation of fenestrations. We applied 3D-SIM to multi-color stained LSECs to acquire highly resolved overviews of large sample areas. We then further increased the spatial resolution for imaging fenestrations by single molecule localization microscopy applied to select small locations of interest in the same sample on the same microscope setup. The combination of these techniques offers a unique opportunity to significantly improve studies of subcellular ultrastructures such as LSEC fenestrations.

MS01.2

Relevance of the protein, fatty acid and lipid component in early stages of liproteine-induced cell death

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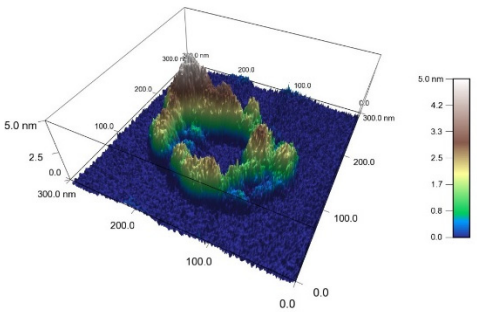
The plasma membrane defines life at the cellular level. Breakdown of its integrity or of the carefully regulated processes taking place at it will usually lead to cell death. Protein-fatty acid complexes (PFAs, liproteins) are cytotoxic complexes which act directly on the membrane in a receptor-independent manner. An example of such a complex is HAMLET (Human α-La Made Lethal to Tumors), which consists of the human milk protein α-Lactalbumin and 20-30 loosely bound oleic acids (OA)[3]. Clinical development of HAMLET met with some successes, e.g. in the treatment of bladder cancer, skin papillomas and colon cancer [4]. Although much attention was initially lavished on the protein component when searching for mechanisms of action, OA has been decisively shown to be the key toxic component. While the protein component of the complex has been traced throughout the cells, little is known about what actually happens to OA. We investigate the membrane, OA and protein components of bovine α-Lactalbumin complexed with OA (BLAOA; a HAMLET-like substance) and how they associate and affect each other. While the main toxic component is the oleic acid/oleat, how this delivered to the cell and whether the polypeptide has a role beyond a simple carrier are open questions. Results on the complex effect on the membrane, the delivery of oleic acid/oleat into the membrane and the behavior of the polypeptide chain will be presented.



From Baumann *et al*. J. Mol. Bio. (2012) 418: **90-102**

1. Chiti F*, et al.* (**2006**), *Annu Rev Biochem* 75:**333-366**.
2. Mossberg AK*, et al.* (**2010**), *PLoS One* 5:**e9384**.
3. Håkansson A*, et al.* (**2000**), *Mol. Microbiol.* 35:**589-600**.
4. Mossberg AK*, et al.* (**2007**), *Int J Cancer* 121:**1352-1359**.

MS01.3

The structure of a dual-specificity tyrosine phosphorylation-regulated kinase 1A-PKC412 complex reveals disulfide-bridge formation with the anomalous catalytic loop HRD(HCD) cysteine

Marina Alexeeva, Espen Åberg, Richard A. Engh and Ulli Rothweiler

Dual-specificity tyrosine phosphorylation-regulated kinase 1A (DYRK1A) is a protein kinase associated with neuronal development and brain physiology. The DYRK kinases are very unusual with respect to the sequence of the catalytic loop, in which the otherwise highly conserved arginine of the HRD motif is replaced by a cysteine. This replacement, along with the proximity of a potential disulfide-bridge partner from the activation segment, implies a potential for redox control of DYRK family activities. Here, the crystal structure of DYRK1A bound to PKC412 is reported, showing the formation of the disulfide bridge and associated conformational changes of the activation loop. The DYRK kinases represent emerging drug targets for several neurological diseases as well as cancer. The observation of distinct activation states may impact strategies for drug targeting. In addition, the characterization of PKC412 binding offers new insights for DYRK inhibitor discovery.

Acta Crystallogr D Biol Crystallogr. 2015

MS01.4

Crystal structure of a highly active chorismate mutase variant

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The shikimate pathway is the biosynthetic pathway for production of the aromatic amino acids. DAHP synthase (DS) catalyzes the first step in the pathway, and the central branch point enzyme, chorismate mutase (CM), catalyzes the conversion of chorismate to prephenate, funneling the pathway towards the synthesis of phenylalanine (Phe) and tyrosine (Tyr) as opposed to tryptophan (Trp).
The chorismate mutase of *Mycobacterium tuberculosis* (MtCM) has only low activity in isolation, but the activity increases by more than a 100-fold upon formation of a complex with DAHP synthase (MtDS).
Directed evolution was utilized in the laboratory of Prof. Peter Kast to improve the naturally sluggish activity of MtCM and discover highly active enzyme variants. Randomized mutations were stringently selected for activity in the absence of MtDS enabling the discovery of a variant with activity that exceeds the activity of the activated MtCM of the MtCM-MtDS complex. The crystal structure of this super-active variant has been solved (1.9 Å) and is in the advanced stages of refinement.
A comparison of the structures of MtCM wild type, the MtCM part of the MtCM-MtDS complex and the structure of the active MtCM variant allows for examination of how specific residues and structural features correlates with increased catalytic activity.

MS01.5

The impact of residues 119 and 228 in the Tripoli metallo-β-lactamase TMB-1 involved in resistance to β-lactam antibiotics

Susann Skagseth[1], Ørjan Samuelsen[2,3] and Hanna-Kirsti S. Leiros[1]

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Metallo-β-lactamases (MBLs) are enzymes with the ability to hydrolyze β-lactam antibiotics including penicillins, cephalosporins, and carbapenems resulting in bacterial strains resistant to virtually all β-lactams. The worldwide dissemination of these MBLs in Gram-negative bacteria poses an increasing clinical threat. The MBL TMB-1 (Tripoli Metallo-β-lactamase) was initially discovered in a *Achromobacter xylosoxidans* isolate [1]. Subsequently, TMB-2 from *Acinetobacter* spp. was detected differing from TMB-1 with one single mutation (S228P). Residue E119 is close to the active site, and in-between a conserved $H_{116}xHxD_{120}$ motif.

In this study, three site-directed mutations on TMB-1 were made; E119Q/S/A, and TMB-1, mutants and TMB-2 were expressed and purified. Enzyme kinetic studies, thermal stability and crystallization experiments are in progress for all TMB variants.

The mutations are expected to have an impact on the activity of the TMB-1. Mutation at position 228 has shown to affect the catalytic efficiency in GIM-1 MBL [2], while mutation at 119 has only been studied in NDM-1 MBL [3], and an effect is expected when removing one negative charge (E119) adjacent to the catalytic site.

[1] El Salabi et al. 2012. [2] Skagseth et al. 2015. [3] Chiou et al. 2013.

MS02.1

Lipid-induced modulation of endocytosis and intracellular transport of protein toxins

Ieva Ailte Hjelseth[1,2,3], Anne Berit Dyve Lingelem[1,3], Simona Kavaliauskiene[1,2,3], Audun Kvalvaag[1,3], Jonas Bergan[1,3], Tore Skotland[1,3] and Kirsten Sandvig[1,2,3]

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Protein toxins from plants and bacteria, such as ricin and Shiga toxin, are composed of two moieties (A and B), one that binds to cell surface receptors and one that enters the cytosol and inactivates ribosomes, thereby inhibiting protein synthesis. To enter the cytosol, the toxins are endocytosed by clathrin-dependent or -independent mechanisms, transported to the Golgi apparatus and retrogradely to the ER, before the enzymatically active moiety is translocated to the cytosol. All these steps are subject to regulation by lipids. Not only lipid classes, but also lipid species turn out to be essential for regulation of the various steps. When studying the transport steps in cells, it is important to be aware of that also cell density in itself can influence the lipid composition as well as retrograde transport of protein toxins. Recent experiments have revealed that addition of lysophospholipids to cells can modulate toxin binding as well as different endocytic mechanisms. By adding specific lipids one can obtain a strong reduction of clathrin-dependent endocytosis of transferrin and accumulation of transferrin-receptors at the cell surface, under conditions where there is only a minor effect on uptake, intracellular transport and toxicity of ricin, demonstrating a specificity of the inhibition. Both the head-groups of the lysophospholipids as well as their fatty acid chain length and saturation play a role for the inhibition. The explanation for this unexpected regulation is currently under investigation and will be discussed.

MS02.2

ibidi – cells in focus: In vivo like, physiological conditions for cell based assays during live cell imaging

Tina Freisinger and Anja-Rose Strohmaier

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Long-term imaging of living cells has become an increasingly important technique in cell biology. Only during live cell imaging, cellular behavior and dynamics such as migration or cytoskeletal rearrangements can be properly investigated. Therefore, it is crucial to provide in vivo near environmental conditions by controlling the pH and oxygen levels as well as humidity and temperature. Further, sample preparation including the right surface for cell attachment is an important step in live cell imaging.
This seminar will focus on how to integrate cell culture with live cell microscopy and cell based assays such as cell migration and chemotaxis with an emphasis on scientific applications and results from the field.

MS02.3

Handshaking between PS 18:0/18:1 and long chain sphingolipids in cellular membranes

Tore Skotland

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Quantitative lipidomic studies of PC-3 cells and exosomes released from these cells revealed a similar degree of upconcentration from cells to exosomes of the very long-chain sphingolipids, PS 18:0/18:1 and cholesterol. Moreover, the amount of PS 18:0/18:1 expected to be in the inner leaflet of exosomes could theoretically cover approximately 80% of the area of the long chain sphingolipids in the outer leaflet. This, together with the similar upconcentration of the above mentioned lipids from cells to exosomes, made us speculate that these lipids are handshaking in the membrane and sorted together as a membrane domain (BBA 1831 (2013) 1302).

We later performed a similar study with PC-3 cells treated with the ether lipid precursor hexadecylglycerol. As expected, we obtained cells and exosomes with higher amounts of ether lipids, but still obtained a similar ratio of PS 18:0/18:1 to the very long-chain sphingolipids in the exosomes. We have now also analysed exosomes from human urine and once again obtained the same ratio for these lipids. Finally, atomistic molecular dynamics simulations with SM d18:1/24:0 and PS 18:0/18:1 support the idea of handshaking, and show that the presence of cholesterol increases the interdigitation between these two lipid species.

It should be noted that although most reports in the literature state that long chain sphingolipids are found in areas abundant in phospholipids carrying saturated fatty acids, our data indicate that PS 18:0/18:1, which carries an unsaturated fatty acid in the *sn-2* position, is a main player in such structures.

MS02.4

A Role for the Stem Cell Niche in Myeloid Leukaemias?

Lorena Arranz

NCMM Young Associate Investigator, Group Leader Stem Cell Aging and Cancer, UiT – The Arctic University of Norway

Acute myeloid leukaemia (AML) is the most common form of acute leukaemia occurring in adults, and the prognosis for patients remains bleak. Overcoming these problems will require improved understanding of AML. Interestingly, oncogenes frequently mutated in human AML are only able to induce myeloproliferative neoplasms (MPN) in mouse models, indicating that these lesions are insufficient to cause AML. Until recently the focus has been on the search for additional genetic mutations with little consideration of the bone marrow HSC niche. The latter has a significant influence on haemopoiesis under healthy conditions. Further, our recent work uncovered an unprecedented role for the bone marrow HSC niche in MPN pathological conditions (Arranz *et al*. Nature, 2014). We specifically showed the role in disease progression of the neuroglial components and mesenchymal stem cells in the bone marrow JAK2-V617F^{+}. Currently, the primary aims of the recently established research group are to test the potential role of the HSC niche in leukaemic transformation and to study the importance of this to human AML. Our recent research will be presented, followed by a glimpse over the research group and our future directions.

MS03.1

Critically positioned N-glycans prevent efficient mannose-6-phosphorylation of lysosomal proteins, giving new clues on how to bioengineer therapeutic proteins with increased uptake via the mannose-6-phosphate receptor.

Pirkko Heikinheimo[1], Gaute Hansen[2], Hilde M.F. Riise-Stensland[3], Christophe Flahaut[4], Jan Ole Olsen[2], Gry Evjen[2], Jean-Claude Michalski[4] and Ole K. Greiner-Tollersrud[2]

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Mannose-6-phosphorylated glycans are ligands for uptake of therapeutic lysosomal proteins from the circulation via the mannose-6-phosphate receptor (MPR) into many cell types. A low mannose-6-phosphorylation content may prevent a fast uptake via MPR, and constitutes a problem in enzyme replacement therapy. By characterizing the site-specific N-glycan structures in arylsulphatase B and lysosomal alpha-mannosidase (LAMAN), we show that efficient mannose-6-phosphorylation occurs on glycosylation sites within a restricted region of the protein surface, and that glycosylation sites within a subregion prevent mannose-6-phosphorylation of distal sites. The loss of a glycosylation site in this subregion in human LAMAN, resulted in a LAMAN variant with an increased number of mannose-6-phosphorylated sites and more efficient sorting to the lysosomes. We suggest that inhibitory glycans are located close to the interface with the phosphotransferase complex, interfering with the conformation of the complex. By identifying regions of a lysosomal protein which are efficiently mannose-6-phosphorylated, and subregion to which the attached glycans inhibit mannose-6-phosphorylation, the bioengineering of glycosylation variants with increased uptake via MPR will be possible.

MS03.2

Microbial communities and moving bed technology as tools for conversion of marine biomass

Concetta De Santi[1], Ragnhild Dragøy Whitaker[2], Elin Moe[3], Fredrik Almqvist[4], Nils-Peder Willassen[1] and Peik Haugen[1]

[1]*Department of Chemistry, UiT-The Arctic University of Norway;* [2]*Norwegian Institute of Food, Fisheries and Aquaculture Research;* [3]*Instituto de Tecnologia Quimica e Biologica, Portugal;* [4]*Department of Chemistry*, *Umeå University, Sweden*

There is an urgent need to develop new and green technologies for use of rest-raw material from the fish industry. Inspired by the RAS (Recirculating Aquaculture system) technology, this project aims at establishing and optimizing microbial communities on the Moving Bed Technology (MBT) bio-beads to convert cheap biomasses into new products and increase the value of marine rest raw materials.
Optimized microbial communities (i.e., the biocatalyst) will originate from 100 marine bacterial isolates collected from the Arctic region. Each isolate has been screened for specific activities (e.g., cellulase, lipases, proteases), genome sequenced and analyzed for their secondary metabolites production potential using a computer-based approach (e.g., the Anti-smash software).
Based on the microbial genetic and metabolic potential, the bacterial communities will be specifically established as biofilm on the surface of plastic beads and trained into microfactories for conversion of rest raw materials from the fish industry.
Water and lipid phases from spent medium will be collected and screened for potential products. Ultimately, our goal is to bring sustainable and natural products to the market quickly, and at relatively low costs.

Keywords

Moving Bed Technology, Recirculating Aquaculture System, metagenomics, metabolomics, microbial communities

MS03.3

Discovery and characterization of thermostable cellulases for degrading lignocellulosic biomass

Marianne Slang Jensen, Lasse Fredriksen, Alasdair MacKenzie, Phil Pope, Piotr Chylenski, Aniko Varnai, Gustav Vaaje-Kolstad and Vincent G.H. Eijsink

Department of Chemistry, Biotechnology and Food Science, NMBU-Norwegian University of Life Sciences, Ås, Norway

Lignocellulose is the most abundant biomass on Earth, and thus our largest organic carbon reservoir. Lignocellulosic byproducts from forestry and agriculture store considerable amounts of renewable energy accessible through enzymatic depolymerization, a process hampered by the recalcitrance of the biomass. Norwegian industrial actors are seeking sustainable biorefining strategies to utilize the entire biomass feedstock in value creation, whilst minimizing waste production. In the NorZymeD project, we aim to develop enzymes for large-scale biocatalysis of various Norwegian biomasses. Novel enzymes from natural biodiversities are discovered using (meta)genome mining and functional screening of fosmid libraries. Targeted biodiversities include various hot environments previously sampled by others, as well as deep sea hot vents of the Arctic mid-ocean ridge (AMOR), the Svalbard reindeer gut microbiome, gill symbionts of the wood-eating Arctic shipworm, and thermophilic enrichment cultures, which are being explored by NorZymeD partners. In the work presented here, approximately 20 putatively lignocellulose active enzymes have been selected for expression and several exhibit promising activity on industrial substrates at high temperatures. These enzymes are currently being characterized in detail and will be subjected to enzyme engineering to further optimize their performance. Simultaneously, efforts continue to discover additional cellulases to be used in enzyme cocktails tailored for Norwegian biomass at industrially relevant processing conditions.

MS03.4

Advanced CRISPR Genome Editing: Specific Sequence Changes and Whole genome screens

Marko Sankala

Sigma Life Science, Sigma-Aldrich Corporation

CRISPR endonucleases have recently taken the research world by storm with their elegant and simple mode of RNA-guided gene targeting. In this advanced CRISPR genome editing presentation we are going to cover plasmid and single stranded oligonucleotide donors. How to design CRISPR oligos and how extra chromosomes are changing the homologous recombination efficiency. Finally we are going to cover different library options for screening experiments.

MS03.5

Inactivation of Ku70 or p53 rescues perinatal lethality of XLF/DNA-PKcs double deficient mice

Valentyn Oksenych[1,2], Magnar Bjoras[2] and Frederick Alt[1]

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In our cells, DNA double-strand breaks (DSBs) are generated by environmental factors and physiologically, for instance, during the lymphocyte development. DSBs are recognized and repaired by distinct DNA repair pathways, including classical non-homologous end joining (C-NHEJ), where the Ku70/Ku80 heterodimer (Ku) is recruited to the DSB site and forms the DNA-PK protein kinase holoenzyme with the catalytic subunit DNA-PKcs. Then XRCC4/DNA Ligase4 ligates the DNA ends together. XLF is a C-NHEJ factor that directly interact with Ku and XRCC4. Deficiency of Ku70, Ku80, DNA-PKcs or XLF result in live mice that possess different levels of DNA repair defects, while deficiency of XRCC4 or Ligase4 leads to embryonic lethality. Recently, I found that combined inactivation of XLF and DNA-PKcs results in perinatal lethality in mice and increased genomic instability in cells. Deletion of *Ku70* or *p53* completely rescues perinatal lethality of XLF/DNA-PKcs double deficient mice. Mice with combined deficiency for Ku70, XLF and DNA-PKcs have body size and levels of genomic instability indistinguishable from that of Ku70-deficient littermates. Among other possibilities, our finding is consistent with a model where combined function of XLF and DNA-PKcs is required for C-NHEJ and that Ku70/Ku80 heterodimer blocks alternative DNA repair pathways causing, for instance, p53-dependent neuronal apoptosis

MS04.1

Structure-based design of riboswitch ligands

Thomas Wehler[1,2] and Ruth Brenk[2]

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Riboswitches are *cis*-acting gene regulatory elements that are mostly found in bacteria. They are located in the 5' untranslated region of mRNAs and consist of an aptamer domain that binds the ligand, and an expression platform that controls the expression of the downstream gene. The RNA can adopt one of several alternative conformations, the relative stability of which is determined by the binding of the ligand to the aptamer domain. Binding of the ligand directs folding of downstream elements in the expression platform that influence expression. The extent of the regulation of gene expression is controlled by the concentration of the small molecule ligand via the structure of the RNA. As such, they constitute novel targets for antibiotics. Crystal structures of several riboswitch classes have been determined, making this class of RNA amenable for structure-based drug design for hit discovery.

We will report on our efforts to validate RNA-ligand docking as a suitable tool for hit discovery for riboswitches, characterization of riboswitch binding sites in terms of druggability and on hit discovery for the FMN riboswitch, which is a target for antibiotics.

MS04.2

Structure-guided drug design for the antibiotic resistance enzyme OXA-48

Bjarte Aarmo Lund, Sundus Ahkter, Yngve Guttormsen, Tony Christopeit, Annette Bayer and Hanna-Kirsti S. Leiros

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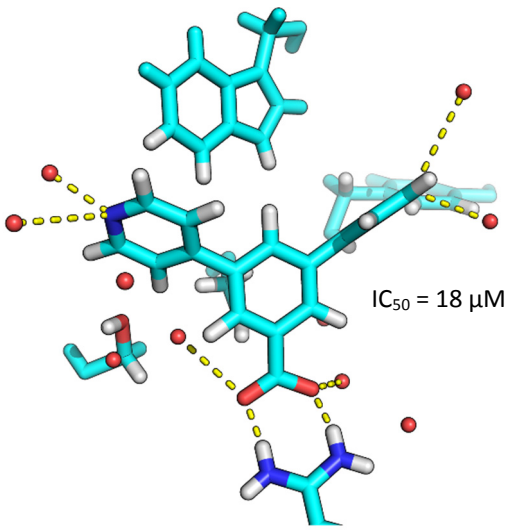
Antibiotic resistance shakes the foundation of modern healthcare. Antibiotic resistance enzymes such as the OXA-48 class D β-lactamase actively destroy antibiotics, making the bacteria resistant to penicillins and carbapenems.

To combat this threat, we are aiming at designing inhibitors towards these enzymes, so that the lifetime of the current antibiotics may be extended. We have performed a surface plasmon resonance (SPR) screen with 490 fragments to find inhibitor scaffolds for OXA-48. We have identified several interesting starting points for further optimization. By systematically varying the substitutions on the scaffolds we have identified the key interactions of these compounds. We were also able to use two alternate conformations from a X-ray crystallographic structure to design a merged compound with improved inhibitor potency. Our most potent compound has a K_D of 50 µM and an IC_{50} of 18 µM, and the compounds represent novel substructures for an important drug target involved in antibiotic resistance



MS04.3

Probing enzyme activation networks - structural and functional studies of flavoproteins in *Bacillus cereus*

Ingvild Gudim, Marie Lofstad, K. Kristoffer Andersson, Marta Hammerstad and Hans-Petter Hersleth

Department of Biosciences, University of Oslo

Many enzymes need to be activated by other proteins to perform their catalytic function. One such activating network in *Bacillus cereus* involves different flavin and iron-sulfur proteins. Here NADPH is used to deliver reducing equivalents to different ferredoxin/flavodoxin-NADP(H) oxidoreductases (FNRs), which deliver electrons to different flavodoxins (Flds) or ferredoxins (Fds), which finally activate different enzyme systems like ribonucleotide reductase or nitric oxide synthase. How selective, flexible and specific are these redox networks? Is one pathway more efficient or are they equally efficient, and what is the structural basis for the interaction between the different proteins? We are currently mapping this redox network, and have solved the crystal structure of several of the proteins [1-2]. We have initially shown that two of the FNRs can activate the Flds. Kinetic studies have indicated some differences in efficiency, while binding studies with microscale thermophoresis have indicated relative equally weak binding between the FNRs and Flds.

[1] Skråmo *et al*. (2014) *Acta Cryst*. F**70**, 777-780.

[2] Hammerstad *et al*. (2014) ACS *Chem. Biol*. **9**, 526-537.

MS04.4

A comparison of the dimanganese active sites of class Ib ribonucleotide reductase and manganese catalase by CD and MCD spectroscopy

Marie Lofstad[1], Lars H. Böttger[2], Åsmund K. Røhr[1], Hans-Petter Hersleth[1], Marta Hammerstad[1], Edward I. Solomon[2] and K. Kristoffer Andersson[1]

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Ribonucleotide reductases (RNRs) are enzymes that convert RNA building blocks into DNA building blocks. This reductive reaction requires a cysteine thiyl radical, which, in the case of class Ib RNRs, is initiated by an Fe^{III}_2- or Mn^{III}_2-tyrosyl radical (Y) cofactor in the NrdF subunit of RNR. During enzymatic turnover the cofactor is activated by oxygen, and generates a Y that is transported from the NrdF subunit to the NrdE subunit of RNR, where DNA building blocks are formed.

Manganese catalase (MnCAT) enzymes contain an active site that is similar in structure to the Mn^{III}_2 form of NrdF, characterized by a carboxylate-bridged Mn^{III}-O-Mn^{III} cofactor. However, it catalyzes a different reaction – the degradation of hydrogen peroxide to dioxygen and water. A still unresolved question is how these enzymes containing similar active sites can catalyze different reactions.

A variety of spectroscopic methods have been used to try to resolve this question. Samples containing NrdF with active Mn^{III}-O-Mn^{III} cofactor [1] have been prepared and studied by circular dichroism (CD) and magnetic CD (MCD) spectroscopy at Stanford University. The data show both similar and distinct features compared to MnCAT.

[1] Tomter, A.B. *et al*. *Coord. Chem. Rev.* **2013**, *257*, 3-26.

MS04.5

The structure of *Salinibacter ruber* Single-Strand Binding protein reveals a novel, octameric architecture of bacterial SSB proteins

Marcin Pierechod[1], Ulli Rothweiler and Taiana de Oliveira[2]

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DNA replication, recombination and repair requires unwinding of the double-stranded helix structure to allow the dedicated machinery to access the genetic information. These processes generate single-stranded DNA, which not only self-associates creating roadblocks to genome maintenance, but also is prone to chemical and nucleolytic attack. To prevent DNA damage, bacterial, archaeal and eukaryotic cells have evolved protective ssDNA-binding proteins (SSBs) that bind ssDNA with high affinity and specificity, maintaining it in an unfolded, linear form.

Salinibacter ruber is one of the few eubacteria that thrive in extreme salt level environments, owing to highly increased intracellular salt concentrations. Since ssDNA hairpin stability increases significantly in high-salt solutions, characterization of *S.ruber* SSB seems to be crucial for understanding mechanism of action of DNA maintenance systems that evolved to work in high salt concentrations.

The initial protein oligomer size estimation revealed that in contrast to the vast majority of bacterial SSBs that function as tetramers or homodimers containing 4 oligonucleotide binding folds (OB), *S. ruber* SSB contains as many as 8 OB folds. Therefore, we focused our efforts on structural characterization of both apo protein as well as the nucleoprotein complex. Analysis of the wt protein crystal packing not only revealed an atypical filament-like higher order structure, but also allowed us to design a surface entropy mutant that formed a nucleoprotein complex with 75 nucleotide long poly dT synthetic ssDNA. We have also visualized higher ordered structures of *Sr*SSB with the use of transmission electron microscopy (TEM).

MS05.1

Protein synthesis arrest and GADD34 are part of the anti-viral cellular tool box

Philippe Pierre

Centre d'Immunologie de Marseille-Luminy, France

Viral triggering of the innate immune response in infected cells aims at delaying viral replication and prevents tissue spreading. Viral replication is delayed by host protein synthesis inhibition and infected cell apoptosis on one hand, while infection spreading is controlled by the synthesis of specific proteins like type-I interferons (IFNs) and pro-inflammatory cytokines on the other hand. How do these two apparent conflicting responses cooperate within the same infected cells to mount effective defenses against pathogens? What are the molecules or the complexes resolving this contradiction over time? Some recent studies reveals unanticipated connections between innate immunity and stress pathways, giving important clues on how are orchestrated the cellular responses to limit efficiently infection.

MS05.2

Identification of adult hemogenic sinusoidal endothelial cells in adult bone marrow.

Peter A. McCourt, Ana Oteiza[1], Melonie Storan[2], Brenda Williams[2], Chad Heazlewood[2], Karen K. Sørensen[1], S Li[2], Christian Nefzger[3], Yoshiaki Kubota[4], Jose Polo[3], Susie Nilsson[2]

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Hemopoietic stem cells (HSC) reside in marrow niches, producing circulating blood cells. Interfacing blood and the niche are sinusoidal endothelial cell lined vessels. Bone marrow (BM) sinusoids have been identified as critical stem cell regulators and a key niche component. However, little is known about the characteristics or functional capacity of marrow endothelial cells. We have identified, prospectively isolated and characterized marrow scavenging sinusoidal endothelial cells with immense endocytic capacity, demonstrating a hierarchical organization and a sub-population highly enriched for endothelial sinusoidal stem cells (BM-ESSC) in endosteal BM with long-term serial transplant potential and revascularization of recipient marrow. In addition, we also demonstrate that BM-ESSC have hemogenic potential: giving rise to long-term multi-lineage reconstituting HSC. These findings represent a major advance in the understanding of marrow sinusoidal endothelial cells and HSC *in vivo*. Identification of human endothelial counterparts and their use in transplantation may lead to improved clinical outcomes.

MS05.3

Amnis Imaging Flow Cytometry: high speed, high content image analysis of cells in flow

Owen Hughes

Merck

Amnis imaging flow cytometers are automated, high speed microscopes that can numerically quantify cellular morphology and the intensity, location and co-localisation of fluorescent markers within hundreds of thousands of cells per sample. Optics comprise up to seven excitation lasers, brightfield illumination and twelve image detection channels ranging in wavelength from 420 to 800 nm. This uniquely powerful technology can be applied to analyse a wide range of phenomena in cell biology as well as a number of non-cellular particle applications. The key principles of the technology and their use in a range of objective and statistically robust cellular analysis applications, will be discussed.

MS06.1

Phylogenetic analysis of NAD biosynthesis and consumption

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The abundant cofactor NAD is best known for its role in redox reactions. In addition, NAD is substrate to many NAD-consuming reactions that are important in signal transduction and gene regulatory pathways, including DNA-damage repair as well as histone and enzyme modifications. All latter reactions produce Nicotinamide (Nam), an essential nutrient. NAD homeostasis is maintained by salvage pathways that recycle Nam to NAD. There are two such pathways that were earlier thought to be mutually exclusive. There is one with two enzymes starting with Nam phosphoribosyltransferase (NamPRT) and one with four enzymes starting with Nam deamidase (NADA). In addition to NamPRT and NADA, some higher organisms possess a third enzyme that uses Nam, the Nam-N-methyltransferase (NNMT). This enzyme methylates Nam and thereby removes it from recycling. The physiological role and evolutionary origin of NNMT is so far unclear. To address the question of the evolution of NAD biosynthesis and consumption, we performed a phylogenetic analysis of the distribution of NADA, NamPRT, and NNMT as well as ten NAD-consuming enzymes. We found that the two pathways using NamPRT and NADA can co-exist in certain species. We also found that a combination of NamPRT and NNMT is beneficial when the complexity of NAD consumption increases, whereas NNMT and NADA hardly occur together in the same organism. These findings may help understanding the role of NNMT in NAD homeostasis.

MS06.2

Open source data and utilities for protein target prediction of small molecules

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Large-scale cheminformatics databases, such as PubChem and ChEMBL, are now well-established sources for bioactivity data critical for medicinal chemistry. Many other protein-ligand interaction databases also exist, including the PDB. Programmable access to these databases has opened tremendous opportunities, for example machine learning for cheminformatics analysis.

In this study, we have utilized open and free Python tools to harness the potentials that exist in those databases to predict protein targets of our newly synthesized compounds. These compounds are potential leads that inhibit kinases involved in non-small cell lung cancer. The Bayesian models trained on activities and inactivity data on PubChem and ChEMBL were used to predict targets of these compounds, based on fingerprint similarities. Subsequent binding experiments by kinase profiling confirmed *in silico* predictions. We also identified possible chemical descriptors of these compounds by applying supervised machine learning methods and structure-based analyses.

Managing and analyzing “big data” in medicinal chemistry and drug discovery have become indispensible with the advent of public repositories of bioactivity data. Modern databases offer enhanced functionalities in addition to data by implementing web services, such as “REpresentational State Transfer” (REST). For coordinated access, Python has become one of the most useful “glue” programming languages with many external free libraries that are used by scientific community. This study shows some of the many potential uses of these databases and libraries.

MS06.3

Identification and analysis of genes in immediate-early response processes

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We present a well-curated consensus set of genes showing rapid activation of gene expression after different types of stimulation, also known as the immediate-early response (IER). The expression of such genes may reach a maximum very rapidly after activation, and it is therefore interesting to understand how they are regulated. The genomic locations of the identified IER genes are compared bioinformatically against genomic features known to be important for gene regulation, such as binding of transcription factors, insulators (CTCF) and cohesin, epigenetic properties of chromatin and DNA methylation. The analysis includes ChIA-PET data on chromatin interactions to analyse gene regulation through looping. We already know that immediate-early response genes often are in an epigenetic bivalent or poised state, where both active and repressive epigenetic signatures are found at the same time. These genes are initially repressed, but may rapidly be activated. The new analysis highlights the importance of interactions between IER gene promoters and strong distal enhancers for this gene activation, and how in particular cohesin and insulators may facilitate the process.

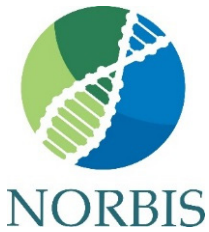
MS06.4

NORBIS – the national research school in bioinformatics, biostatistics and systems biology

Christine Stansberg

University of Bergen

NORBIS is the Norwegian research school in bioinformatics, biostatistics and systems biology. The school was funded by the Norwegian Research Council in 2015, and is a collaborative work between Norwegian universities and non-academic partners. NORBIS aims to provide a high quality PhD education through its network of excellent research groups in Norway, and will offer ten PhD courses during a period of two years, in addition to our annual conference, a summer school and other workshops. Since the beginning in April, we have successfully arranged our first annual meeting, as well as our first course, on multiple sequence alignment. The school will educate methods-oriented researchers, who will in the next round develop, teach, train, drive, and support use of bioinformatics, statistical genomics and computational biology within the wider area of molecular life science. NORBIS will be highly visible in the international research community in the field, in the society and among relevant industries. This new arena for research and research education will improve the PhD-education, increase the recruitment to this fast growing scientific field, and give an overall international perspective to the PhD-training.



MS06.5

MotifLab – a regulatory sequence analysis workbench

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MotifLab is a general workbench for analyzing regulatory sequence regions and discovering transcription factor binding sites and cis-regulatory modules. MotifLab can make use of well-established motif discovery programs to predict novel binding sites or scan DNA sequences for matches to known binding motifs. Additional information can be incorporated into the analysis to filter out likely false predictions, including information about e.g. gene expression, epigenetic marks, phylogenetic conservation, cooperative binding partners and identified ChIP-seq peaks. The latest version of MotifLab also has support for long-range chromatin interaction data which allows gene promoters to be linked to their distal enhancers for a more complete picture of the genomic regions involved in regulation. Users can record multi-step analyses into protocol scripts that can be rerun as automatic workflows on other datasets, and a host of interactive tools encourage visual exploration of data in the sophisticated internal sequence browser.

MS07.1

Development of a new validation method for identification of lysosomal proteins, and its application in therapy

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The traditional view of the lysosomes is as an end-point organelle of macromolecular degradation, conforming to the 50-60 lysosomal storage disorders, with a cumulative frequency of 1:8000 newborn, where the structure of the respective storage product is related to the deficient lysosomal hydrolase activity. As the lysosomes are also a part of the endosomal and autophagosomal systems, there is likely to be a larger variation of lysosomal proteins and more lysosome-associated diseases, than previously thought. Despite the invention of several methods enriching lysosomal proteins, the lack of robust validation procedures has prevented the construction of a lysosomal proteome. Here we show that the N-glycans of native lysosomal proteins from porcine and bovine brain are trimmed by lysosomal exoglycosidases to unique structures, that can be used to validate the lysosomal location of a protein. This validation method revealed that phospholipase D3 and adenosine deaminase 2, which were thought to be located in the endoplasmic reticulum and serum, respectively, are in fact both lysosomal proteins. The lysosomal location of these proteins is pivotal for understanding the pathophysiology and developing therapies of the congenital diseases associated with defects ofthese proteins. We anticipate that the novel validation method will enable the construction of a complete lysosomal proteome, which will be an invaluable tool understanding the dysfunctional lysosomal pathways in congenital lysosomal diseases.

MS07.2

METTL20 is a Novel Lysine-Specific Methyltransferase that Targets the Beta Subunit of Electron Transfer Flavoprotein (ETFβ) and Modulates Its Activity

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Proteins are frequently modified by methylation of lysine residues, catalyzed by *S*-adenosyl-L-methionine dependent lysine-specific (K) methyltransferases (KMTs). The methyltransferase METTL20 belongs to a group of ten established and putative KMTs. The protein is ubiquitously present in chordates and is also found in a subset of bacteria, *ex.* in *Rhizobiales* order of alpha-proteobacteria. We found that human (Hs) METTL20 was associated with mitochondria, and that recombinant HsMETTL20 methylated a single protein in extracts from human cells, which we identified as the β-subunit of the mitochondrially localized electron transfer flavoprotein (ETFβ). HsMETTL20 was found to specifically methylate two nearby lysine residues, K200 and K203, in ETFβ both *in vitro* and in cells. Interestingly, the residues methylated by HsMETTL20 partially overlap with the so-called 'recognition-loop' in ETFβ, which has been previously shown to mediate its interaction with several mitochondrial ETF-dependent dehydrogenases. Accordingly, we found that HsMETTL20-mediated methylation of ETFβ *in vitro* reduced ETF ability to receive electrons from the medium chain acyl-CoA dehydrogenase and the glutaryl-CoA dehydrogenase. In conclusion, our study establishes HsMETTL20 as the first human KMT localized to mitochondria, and suggests that it may regulate cellular metabolism through modulating the interaction between its substrate ETFβ and dehydrogenases.

MS07.3

Discovery of a potentially novel cellulolytic mechanism linked to the Bacteroidetes Por secretion system

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In the new bio-based economy, lignocellulosic biomass is thought to play a major role due to its massive and renewable energy stores. However, industrial biomass degradation is currently inefficient and requires a greater understanding of how this process ably occurs in nature. Obligate herbivores have evolved intricate symbiotic relationships with polysaccharide degrading microorganisms, making their microbial community interesting targets for enzyme-prospecting.

From a cow rumen metagenome dataset, we have discovered a potentially cellulolytic gene cluster. The cluster is novel in its arrangement, with *four* glycoside hydrolase family 5 (GH5) predicted cellulases, in addition to a GH3 beta-glucosidase and a GH94 cellobiose phosphorylase. Interestingly, three of the GH5 cellulases contain a C-terminal Por Secretion System (PorSS) tag, which is associated with allocation of proteins to the outer membrane. The Por, or type IX secretion system, has also been shown essential for gliding motility and the degradation of crystalline chitin and celluloseby several Bacteroidetes species. Since these observations suggest the presence of a novel cellulolytic machinery, we have synthesized and expressed glycoside hydrolases from this gene cluster to elucidate their functions. Here we report the biochemical characterization of these enzymes against cellulosic substrates, revealing several enzymes with strong endocellulase activity. Collectively, the computational and biochemical data suggests an as-yet undiscovered cellulolytic mechanism within the rumen microbiome.

MS07.4

Chitin degradation by *Cellvibrio japonicus*

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Cellvibrio japonicus is a Gram negative soil bacterium that is primarily known for its ability to degrade plant cell wall polysaccharides through utilization of an extensive repertoire of carbohydrate active enzymes (CAZymes). Several putative chitin-degrading enzymes are also found amongst these CAZymes, such as chitinases, chitobiases and lytic polysaccharide monooxygenases (LPMOs). We have examined the secretome of *C. japonicus* using a simple plate-based culturing technique. By combining this approach with label-free quantification, proteins secreted by the bacterium during growth on α- and β-chitin were mapped and quantified. Hierarchical clustering of the detected protein quantities revealed groups of up-regulated proteins that include all five putative *C. japonicus* chitinases as well as a chitin-specific LPMO (*Cj*LPMO10A). The latter enzyme was cloned, expressed and characterized both biochemically and structurally. The enzyme was active on both chitin polymorphs and the presence of a chitin-binding domain was important for activity. Structurally, *Cj*LPMO10A showed features shared by both chitin and cellulose active LPMOs. Finally, cultivation studies of *C. japonicus* deletion mutants showed that *Cj*LPMO10A is important for efficient utilization of chitin by the bacterium.

MS08.1

Discovery of a Novel Covalent Inhibitor of the Metallo-β-lactamase NDM-1

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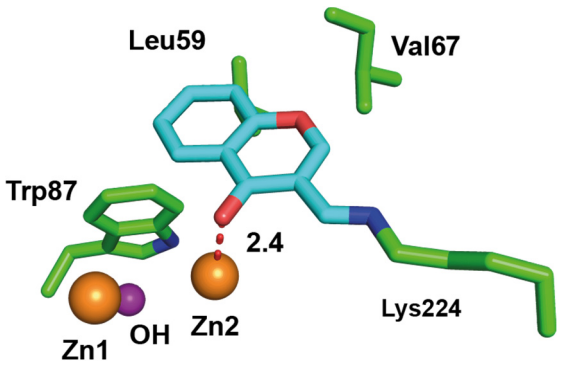
Metallo-β-lactamases (MBLs) are enzymes able to hydrolyze β-lactam antibiotics and render bacteria resistant to them. The co-administration of MBL inhibitors together with β-lactam antibiotics could restore their function, but so far there are no MBL inhibitors in clinical use. One of the most clinically relevant MBLs is the New Delhi Metallo-β-lactamase 1 (NDM-1).

We have established a fragment screening strategy combining a surface plasmon resonance (SPR) based assay and an enzyme inhibition assay to identify novel starting points for potent β-lactamase inhibitors.[1] The screening strategy was used for NDM-1 identifying four fragments inhibiting the enzyme. The fragment with the highest affinity was further investigated by determining the inhibition modality. Furthermore, structure activity relationships (SAR) were established, leading to the identification of a covalent reversible inhibitor. This inhibitor was further characterized using mass spectrometry, an SPR based biosensor assay and an enzyme inhibition assay, showing that the inhibitor specifically bound to the active site of the enzyme.
The identified inhibitor is the first example of a non-β-lactam compound covalently inhibiting a MBL and has a high potential to be further optimized into a potent inhibitor.



[1]Christopeit *et. al.*, (2015) Discovery of Novel Inhibitor Scaffolds against the Metallo-β-lactamase VIM-2 by Surface Plasmon Resonance (SPR) Based Fragment Screening. J. Med. Chem. 2015

MS08.2

The role of Nephronectin in breast cancer progression and metastasis

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Tumor progression requires interactions of cells (both tumor and stromal cells) with the extracellular matrix (ECM) via transmembrane receptors belonging to the integrin family. Nephronectin (Npnt) is an extracellular matrix protein previously shown to be involved in embryonic development of endocrine organs via interaction with the integrin α8β1 receptor with the three amino acid sequence RGD (Arg-Gly-Asp) in the Npnt protein. In a genomic analysis of a spontaneous model of breast cancer, several ECM proteins such as Npnt were identified and linked to tumor progression. It has also been previously shown that Npnt is upregulated in metastatic vs non-metastatic breast cancer cells.

We have showed that increased levels of Npnt in weakly metastatic breast cancer cell line 66cl4 cells leads to increase in metastasis. In this study, we injected variants of the 66cl4 cell line via tail-vein in wild type Balb/c mice and harvested lung tissues with various numbers of metastases. The aim of this study was to identify the integrin receptor (possibly integrin α8β1 or αvβ3) for Npnt and the downstream signaling pathways activated upon binding. Multi-color confocal images display (presence of two fluorophores in the same pixel) co-occurrence of Npnt and integrin α8. This accentuates the scope to investigate their biological correlation and mechanisms by which Npnt promotes breast cancer metastasis.

MS08.3

Significance of NFE2L2 Target Genes for Survival of Breast Cancer Patients: High Expression of NQO1 is Associated with Poor Clinical Outcome

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Breast cancer (BC) accounts for 14% of all cancer deaths. The major cause of death in BC patients is metastases. The transcription factor nuclear factor, erythroid 2-like 2 (NFE2L2) is activated by oxidative stress and directs the expression of genes involved in antioxidant pathways, such as the glutathione (GSH) and thioredoxin (TXN) pathways, NADPH production and iron sequestration. In established tumors activation of NFE2L2 is tumor promoting by protecting tumor cells from oxidative stress, stimulating cell proliferation and upregulating multidrug resistance-associated proteins (MRPs).

Here we study Nfe2l2 signaling in the murine mammary tumor cell lines 66cl4 and 67NR established from the same tumor. The metastatic 66cl4 display elevated Nfe2l2 activity compared to the non-metastatic 67NR. Knockdown of *Nfe2l2* in 66cl4 leads to impaired cell growth. Transcriptome analysis suggests that only a subset of Nfe2l2 target genes are upregulated. To determine which genes are most relevant for breast cancer metastasis we correlated expression level with survival using open access databases. We identified 10 NFE2L2 controlled genes whose high expression correlated with poor prognosis. Of these NQO1 and HMOX1 are upregulated in 66cl4. How these proteins may contribute to metastasis is incompletely understood.

MS08.4

How does the neonatal Fc receptor (FcRn) handle the transport of its two ligands, IgG and albumin, in the human placenta?

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The neonatal Fc receptor (FcRn) is a versatile receptor that binds and transports both immunoglobulin G (IgG) and albumin across cellular layers. In this study, we explore the use of an ex vivo human placenta perfusion model to study maternofetal transport of albumin and therapeutic human IgG variants. Specifically, we aim to understand the transport route of two clinically approved antibodies, the anti-C5 antibody Eculizumab (IgG2/4) and the anti-TNF-α antibody Infliximab (IgG1). Although albumin binds to the same receptor it is not transported across the placenta to the same extent as IgG. Methods and preliminary data will be discussed.

MS09.1

The neonatal Fc receptor (FcRn)-mediated recycling of IgG and albumin in endothelial cells

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Immunoglobulin G (IgG) and albumin are the two most abundant proteins in blood. While IgG is pivotal in protection against pathogens, albumin maintains the osmotic pressure and transports essential insoluble molecules, such as fatty acids and hormones. Despite functionally unrelated features, they share a unique long serum half-life caused by binding to a broadly expressed cellular receptor, the neonatal Fc receptor (FcRn). FcRn binds both ligands pH dependently, to non-overlapping binding sites, with strong binding at pH 6, but no detectable binding at pH 7.4. The long half-life is thought to rely on rescue from intracellular degradation due to binding of the ligands to FcRn localized to acidified endosomes, and FcRn-mediated recycling back to the cell surface where the neutral pH of the blood triggers release. Due to their important biological functions, and the fact that they are increasingly utilized in therapy, it is fundamental to understand in detail how FcRn transports its ligands in different cell types. We have established a human endothelial cell assay to study FcRn-mediated transport. The assay can be combined with imaging to elucidate the cellular events leading to efficient recycling of albumin and IgG.

MS09.2

Identification of a novel lysosomal degradation pathway acutely activated upon nutrient starvation

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Degradation of cellular components is essential for cell survival during nutrient starvation to provide metabolic building blocks and to implement cellular adaptations. Here we report a novel and highly acute degradation response to nutrient starvation, triggered independently of the classical and well-established nutrient sensing hubs. Using quantitative proteomics, we identified the changes in the proteomes of two different human cell lines (A549 and BJ) caused by acute nutrient starvation. The results reveal a surprisingly similar response in the two cell lines with a clear overlap of the most comprehensive changes suggesting that nutrient starvation triggers a highly specific and conserved degradation response. These changes take place as early as 30 minutes after nutrient removal and include re-localization and degradation of integral plasma membrane proteins regulating both morphology and metabolism. The degradation is mediated by the lysosome but is neither executed by mTOR deactivation nor mediated by canonical macroautophagy (e.g. ATG5, FIP200, VPS34). Instead, we found that the multivesicular body (MVB) pathway orchestrates this catabolic cascade as depletion of VPS4a/b impaired the acute degradation response. We hypothesize that this acute degradative response constitutes a unique cellular program serving two purposes. Firstly, to ensure immediate reinforcement of the pools of free amino acids needed to sustain protein synthesis. Secondly, to readily implement essential adaptations by cellular remodelling to cope with more prolonged periods of malnutrition.

MS09.3

CLEC16A is localized in Rab4a+ endosomes in Jurkat cells

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Multiple sclerosis (MS) is an inflammatory, demyelinating disorder of the central nervous system that develops in genetically susceptible individuals. More than 100 single nucleotide polymorphisms (SNPs) are associated with MS. SNPs in *CLEC16A* are associated with susceptibility to develop MS and other autoimmune diseases, and the risk genotype of an intronic SNP correlates with higher *CLEC16A* expression in human CD4+ T cells. *CLEC16A* encodes the C-type lectin like domain family 16A protein, which recently was shown to be important for endocytic transport and autophagy in *Drosophila Melanogaster*, in murine pancreatic β cells and thymic epithelial cells and for HLA-II expression in human dendritic cells. The role of CLEC16A in human T cells is currently unknown. By confocal microscopy we have shown that CLEC16A co-localizes with the recycling Rab4a+ endosomes and is in close proximity to the early Rab5+ endosomes. Whether CLEC16A affects the size and distribution of these endosomes in T cells, similar to what has been shown in *Drosophila*, is currently investigated by imaging flow cytometry.
Rab4+ endosomes mediates cargo recycling to the plasma membrane and have a role in the early events of autophagy. We are currently investigating CLEC16A's function in these processes.

MS09.4

FYCO1 Contains a C-terminally Extended, LC3A/B-preferring LC3-interacting Region (LIR) Motif Required for Efficient Maturation of Autophagosomes during Basal Autophagy

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FYCO1 is a transport adaptor that binds phosphatidylinositol 3-phosphate, RAB7 and LC3 to mediate transport of late endosomes and autophagosomes along microtubules in the plus end direction. Here we show that FYCO1 preferentially binds to LC3A and –B. By peptide array-based mutational scans of the binding to LC3B, we find FYCO1 to contain a C-terminally extended LIR. We determined the crystal structure of a complex between a 13-amino acid LIR peptide from FYCO1 and LC3B at 1.53 Å resolution. By combining structural information with mutational analyses, both the basis for the C-terminally extended LIR and specificity for LC3A/B binding were revealed. FYCO1 contains a 9-amino acid long F-type LIR motif. In addition to the canonical aromatic residue at position 1 and the hydrophobic residue at position 3, an acidic residue and a hydrophobic residue at positions 8 and 9, respectively, are important for binding to LC3B. The specificity for binding to LC3A/B is due to the interaction between D1285 in FYCO1 and H57 in LC3A/B. Knockout cells of FYCO1 reconstituted with GFP-FYCO1 WT and LIR mutant showed that FYCO1 with a functional LIR facilitates efficient maturation of autophagosomes under basal conditions, but not in starvation conditions.

MS10.1

Bioactive peptides from marine sources

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Marine organisms and material of marine origin that also include organic matter usable for food, have a huge potential for exploring novel bioactive components with activities that can be documented or exploited. In this context, peptides or proteins are very interesting.

The wide repertoire of biological functions covered by natural peptides makes them interesting for bioprospecting and drug discovery. Antimicrobial peptides (AMPs) are also important components of the innate defense in all invertebrate species investigated and are considered as evolutionary ancient weapons against pathogenic microorganisms.

Our aim is to study novel antimicrobial natural products (AMPs) from marine organisms, to explore their structure and mode of action. The organisms are collected from the Arctic or/and sub-Arctic region and can be very diverse covering biological resources from microalgae to invertebrates, but it might also be marine rest raw material. Extractions are made and novel bioactive compounds (peptides) are isolated and characterised by traditional bioassay-guided purification in combination with a genetic approach. A more extensive screening can be done in collaboration with the HTS platform, Marbio, UiT, and can be further developed in collaboration with the Arctic Biodiscovery Centre in Tromsø. Mechanisms of action studies are performed on promising AMPs to understand the activity and reveal the potential for different applications.

MS10.2

Controlled electron supply and site-directed mutagenesis give new insights into the catalytic mechanism of lytic polysaccharide monooxygenases

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Lytic polysaccharide monooxygenases (LPMOs) are recently discovered carbohydrate-active enzymes that are crucial for the degradation of recalcitrant polysaccharides like cellulose or chitin. LPMOs are copper-dependent and utilize a redox mechanism to cleave glycosidic bonds. Enzymatic activity depends on molecular oxygen and externally provided electrons supplied by various sources, such as chemical compounds or by proteins.

We show that a fungal cellobiose dehydrogenase from *Myriococcum thermophilum* (*Mt*CDH), can act as electron donor for the chitin-active LPMO, CBP21, from *Serratia marcescens*. Our results show that employing an enzymatic electron donor enables controlled supply of electrons to the LPMO that yield stable enzyme kinetics. Near equimolar concentrations of *Mt*CDH and CBP21 gave the most stable reaction profiles, whereas overdosing of electrons resulted in altered kinetics and lower yields. Excess of electrons were correlated with formation of reactive oxygen species that may influence enzyme stability. Analysis of CBP21 active site and substrate surface mutants using the controlled reaction conditions described above is ongoing. Preliminary results indicate that the catalytic activity of CBP21 is delicately tuned and that even minor changes to the active site surroundings may have deleterious consequences for activity.

MS10.3

Structural and Bioinformatic Studies of the 'Lig E'Group of Bacterial ATP-Dependent DNA Ligases

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In addition to their replicative NAD-dependent DNA ligase, many species of bacteria possess accessory ATP-dependent DNA ligases (ADLs) some of which have a role in double-stranded break DNA repair. These bacterial ADLs (b-ADLs) vary considerably in size, ranging from minimal enzymes which include only the core catalytic domains, through to large multi-domain proteins with additional DNA modifying activities. Our work has focused on a group of minimal-type b-ADLs which include a putative periplasmic localization sequence, and we have delineated Lig E. Bioinformatic and structural studies indicate that members of Lig E differ from other groups of b-ADLs at the primary and tertiary structure levels, which together with their domain associations and distribution among bacterial species suggest that they were horizontally acquired by bacteria in a separate event to other b-ADLs, possibly from a bacteriophage. Here we present the results of these studies, together with our recently published structure of Lig E from the psychrophilic bacterium from *Psychromonas* sp. strain SP041 and introduce the BIOTEK2021 project 'Engineering efficient DNA ligases for improved Next-Generation-Sequencing'.

MS10.4

Towards a molecular-level theory of carbohydrate processivity in glycoside hydrolases

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Polysaccharide depolymerization in nature is primarily accomplished by processive glycoside hydrolases (GHs), which abstract single carbohydrate chains from polymer crystals and cleave glycosidic linkages without dissociating after each catalytic event. Understanding the molecular-level features and structural aspects of processivity is of importance due to the prevalence of processive GHs in biomass-degrading enzyme cocktails. Recent computational efforts have suggested that the processive ability of a GH is directly linked to the ligand binding free energy. In our studies, we offer the first experimental evidence confirming correlation of binding free energy and degree of processivity and evidence that both polar and aromatic residues are essential for maintaining processive ability.

MS11.1

Role of specialized hepatic scavenger cells in control of biodistribution of large molecule drugs and nano formulations

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When developing large molecule drugs or nanoformulations a major goal is to produce compounds that target the cell type where the wanted therapeutic activity is to be delivered. However, a great challenge in this development is the fact that the compounds frequently disappear by rapid uptake in the liver.

To solve the challenge of uncontrolled liver clearance it is necessary to understand the mechanism(s) of uptake. Large molecules and nanoparticles <200 nm, are cleared mainly by liver sinusoidal endothelial cells (LSECs), via specialized endococytosis receptors, whereas larger particles (>200 nm) are taken up in Kupffer cells (*Am.J.Physiol 2012,303:R1217*). The two cell types employ different types of scavenger receptors recognizing material to be cleared. Knowledge about these receptors and their ligand specificities is key to understand the mechanism of hepatic uptake. The uptake receptors of the LSECs represent a limited number of endocytosis receptor types that are uniquely expressed on this cell type; yet with these receptors the cells are able to clear all classes of macromolecules (polysaccharides, proteins, oligo/polynucleotides, lipids) from the circulation.

In conclusion, detailed knowledge about the scavenger function of hepatic scavenger cells and their receptors is mandatory to design strategies to reduce unwanted liver uptake of large molecule drugs and nano formulations.

MS11.2

Functional understanding of Ral signaling in *Drosophila melanogaster*

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The small GTPase Ral regulates important membrane trafficking events, including exocytosis, endocytosis and autophagy. In mammalian cells Ral is activated downstream of active Ras, which directly interacts with RalGEFs. Over the recent years it has become clear that Ral plays an important role in signal transduction leading to cancer formation and metastasis, both in Ras-dependent and independent manners. Yet, little is known about the Ral signaling network. To understand more about Ral signaling in development and carcinogenesis, we have characterized the effect of expressing constitutively active RalG20V and dominant negative RalS25N in various fly tissues, including wings, notum and eyes. Furthermore, we have analyzed the dependence of these phenotypes on known and predicted regulators and effectors of *Drosophila* Ral. Upon RalG20V expression we observed misorientation of bristles in the notum, wing vein defects and misaligned ommatidia. Conversely, expression of RalS25N led to loss of notum bristles, small and malformed wings and mild eye roughening. We further characterized the RalS25N-induced balding of the notum and found it to be suppressed by coexpression of the RalGEF Rgl or wild-type Ral or by reducing JNK signaling – a known downstream pathway negatively regulated by Ral signaling. In conclusion, we present fly models for Ral signaling amenable to genetic screening that will allow us to identify new components of the Ral signaling network.

MS11.3

CpG-induced exosome secretion from Atlantic salmon leukocytes

Dimitar Iliev, Guro Strandskog, Jorunn Jørgensen, Randi Olsen, Mehrdad Sobhkhez, Jack-Ansgar Bruun

Exosomes are nano-sized extracellular vesicles secreted by different cell types. Exosomes are generated in multivesicular bodies, through ESCRT-mediated mechanism and their endosomal origin is reflected in their protein composition. It has also been found that exosomes are enriched in ubiquitinated proteins; therefore, it has been speculated that autophagy or related mechanism/s may be involved in exosome formation. Due to their involvement in pathological conditions and their potential to be used as diagnostic and therapeutic tools, exosomes have been studied intensely in mammalian experimental systems. In contrast, knowledge about exosome composition, functions and biogenesis in lower vertebrates is scant. In the current project, we have been studying exosomes released from primary salmon leukocytes. Secretion of exosomes from primary salmon leukocytes isolated from head kidney (an immune organ analogous to mammalian bone marrow) can be greatly upregulated through *in vitro* stimulation with 2006T CpG oligonucleotides. Biochemical analyses indicate that protein composition of salmon exosomes is very similar to that of their mammalian counterparts. Our studies also demonstrate that ubiquitinated proteins and RNA (depleted of 18S and 28S rRNA) are enriched in CpG-induced exosomes and may serve as excellent markers for salmon exosomes. Interestingly, although typical ER markers, such as calnexin, are depleted from CpG-induced exosomes, considerable amounts of ER proteins involved in MHC-I antigen complex assembly, antigen processing and ERGIC components were found in exosome preparations. Moreover, low MW proteins derived from apoptotic bodies are also detected in exosomes indicating that these vesicles may originate from cross-presenting endosomes.

MS12.1

ELIXIR.NO - The national technology platform for bioinformatics

Nils-Peder Willassen[1], Lars Ailo Bongo[1], Finn Drabløs[2], Eivind Hovig[3,4], Dag Inge Våge[5], Inge Jonassen[6]

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ELIXIR.NO is the Norwegian part of the European ELIXIR infrastructure for bioinformatics. The purpose of ELIXIR is to construct and operate a sustainable infrastructure for biological information in Europe, in order to support life science research and its translation to medicine and the environment, the bio-industries and society.

A key component of ELIXIR.NO is a coordinated national help-desk. Here users can get advice and help, and the help-desk will also arrange and contribute to a lot of courses and workshops in bioinformatics, and develop software and databases for both end-users and trained bioinformaticians.

In addition, ELIXIR.NO is developing and providing pipelines for analyzing large-scale genomic data through Galaxy web interfaces installed at each node. The national e-infrastructure also allow users to efficiently and safely store data. Pipelines and data storage can be accessed through the Norwegian e-Infrastructure for Life Sciences (NeLS) portal (https://nels.bioinfo.no/).

Project management is at UiB, with Inge Jonassen as project leader, with nodes at UiO, NTNU, UiT and NMBU, thus involving all the main bioinformatics groups in Norway. By joining forces, ELIXIR.NO sets out to provide help in all areas of bioinformatics, including next-generation sequencing data, microarray data, protein structure analysis, statistical genomics, and access to useful databases and web services. Contact can be made by email to contact@bioinfo.no or by contacting the local ELIXIR nodes.

MS12.2

Norwegian Center for Digital Life

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Norwegian Center of Digital Life (Digital Life Norway; DLN) will be launched in 2016. DLN is a virtual centre hosting geographically distributed institutions and fostering collaboration across the scientific disciplines. DLN has ambitions to bring national biotechnology research and education to a higher level and to be internationally visible. DLN will be a dynamic and inclusive instrument for all relevant biotechnology research in Norway. Also, industry involvement will be central and DLN has ambitions to catalyze innovation in the biotechnology sector and related industries the coming years. Totally six research projects were recently funded in the initial call, and together these projects contribute a wide diversity in science, technology and transdisciplinarity. I will here present the goals and visions of DLN as well as updated status and plans for the initiation of this center.

MS12.3

Sequence assembly in the cloud, on the grid and in the basement

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Assembling short reads produced by NGS machines into longer sequences is important for the analysis we do in Meta-Pipe. This assembly must be parallelized to deal with the current and future data volumes, but due to the non-trivial nature of parallelizing assembly algorithms such as De Bruijn graph construction, it is not a given that such parallelization will scale. However, software packages such as Ray claim to scale well across multiple nodes. We have therefore investigated how Ray scales on three platforms utilized by academic users: a supercomputer (Stallo at UiT), our own commodity cluster (named ICE), and the Amazon EC2 cloud computing platform. These differ in three important ways: hardware infrastructure, cost and ease of use. For the evaluation, we have used a locally sampled metagenomic data set (Muddy). Our results show that Ray scales close to linearly on the three platforms. We see differences due to hardware, and that certain stages in the pipeline do not scale well with regards to memory use, which can limit scalability. The cost model of the three platforms are vastly different, but they provide similar performance while differing in ease of use.

MS12.4

GSuite tools: Efficient management and analysis of genomic dataset collections

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With the advance of genome-wide profiling techniques and the abundance of genomic data made publicly available, genomic investigations often involve genome-scale datasets (genomic tracks) related to many different molecules or cell types. The need for software tools that allow efficient management and appropriate methodologies for statistical analysis of such collections becomes obvious.

We present a broad selection of tools for creating, managing and performing analyses on collections of tracks. Collections are represented in a simple format, GSuite, which in the simplest case is just a list of URLs, and can be compiled efficiently from local files or public repositories. We also provide a range of descriptive statistics and present eight statistical tests for core questions related to collections of tracks. The software is available at: https://hyperbrowser.uio.no/gsuite.

Abstracts: Poster sessions

P1

Static and dynamic interactions between the glycine-rich loop of protein kinases and ATP site inhibitors

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Protein kinases are intensely studied, due to their roles in cell signaling processes via phosphorylation of other proteins, to their links to cancer and other diseases, and to their "druggability" as drug targets. The >518 protein kinases in the human genome share a conserved catalytic domain, while their activity is tighly regulated by diverse mechanisms. Most potential drugs target the ATP-binding pocket, between a mostly beta-sheet N-terminal lobe and a predominantly helical C-terminal lobe. Ligand binding depends on many structural features, such as flexibility, water structure, co-factor binding, and multiple binding sites. The subtleties of these phenomena challenge the usual assumptions of structure based drug design methods.
The glycine-rich loop, with the conserved motif glycine-x-glycine-x-aromatic-glycine (GxGxaG), covers the ATP binding site, and refolds in response to some inhibitors. Particularly notable among these is VX-680, an inhibitor first developed against Aurora kinases, but which also showed promise as an inhibitor of the drug resistant Abl kinase mutant T315I. In both targets, VX680 has pi-pi interactions with the aromatic side chain emerging from the refolded loop, although the glycine rich loop sequences differ significantly (GxGxFG vs GGGxYG). Some protein kinases, such as aPKC, have loop sequences lacking the third glycine, as in GxGxaA. Mutation studies of PKA with altered glycine-rich loop sequence characterize the roles of these glycine residues in inhibitor binding interactions.

P2

Production of sialic acids and derivatives by enzyme catalysis

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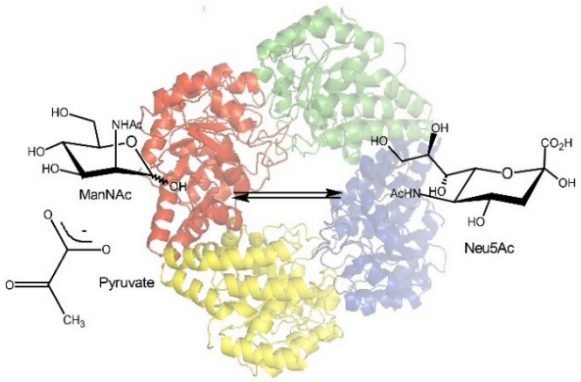
Sialic acids (Sias) are 9-carbon backbone sugars found on the surface of both prokaryotic and eukaryotic cells. The most well-known Sia, neuraminic acid (Neu), contains an *N*-acetyl modification at the 5-carbon position (Neu5Ac). The Sias are involved in the recognition and mediation of cellular adhesion processes, and different variants have the potential as anti-microbial and anti-viral drugs. Neu5Ac has a wide range of potential medical applications, such as anti-cancer, anti-adhesion and anti-inflammatory activities. Neu5Ac also has a huge potential as a food supplement, and its importance for brain development has made it an attractive component for infant formulas.

Neuraminic acid lyase (NAL) catalyzes the reversible reaction between *N*-acetyl mannosamine (ManNAc) and pyruvate and Neu5Ac. By identifying and characterizing targets from marine sources and couple this with structure determination using crystallography, the hope is to discover novel NALs. These may then be used in an enzyme catalyzed reaction for the production of Neu5Ac and derivatives.



P3

Towards an optimal Tyrosine Hydroxylase

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Tyrosine hydroxylase (TH) catalyzes the rate-limiting step in the synthesis of catecholamine neurotransmitters and hormones and its dysfunction thus leads to a range of neurological and motoric problems. TH has a tetrameric, multi-domain structure with each subunit having a flexible N-terminus that has phosphorylation sites and establishes regulatory interactions with the active site, other subunits, protein partners and membranes. The flexible, complex structure of TH makes it vulnerable to proteolysis and to date not amenable to crystallization in a full-length form. Several protocols for purification of recombinant TH exist, but in this work we have investigated the effect of fusion partners and purification resins to make a pure, stable and active human TH with intact N-terminus. We found that TH obtained via a 6xHis-MBP-TH purified on amylose resin is optimal for functional studies of TH as it has iron in its active site, shows relatively high stability and activity and can be stabilized by its natural feedback-regulator dopamine. A 6xHis-ZZ-TH purified on cobalt-containing resin is precursor for the TH that is most promising for structural studies as inhibitory cobalt from the resin appears to confer stability and defer denaturation and aggregation. Using SAXS-based rigid body modelling we have determined the full-length structure of TH in solution.

P4

Structural Insight into the Function of Ribonucleotide Reductase

Marta Hammerstad, Hans-Petter Hersleth, Ane B. Tomter, Åsmund K. Røhr and Kristoffer Andersson

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Class Ib ribonucleotide reductases (RNRs) use a dimetal-tyrosyl radical (Y•) cofactor in their NrdF subunit to initiate ribonucleotide reduction in the NrdE subunit. Contrary to the diferric tyrosyl radical (Fe^{III}_2-Y•) cofactor, generation of the active Mn^{III}_2-Y• cofactor requires the flavoprotein NrdI. Here we report the crystal structure of *Bacillus cereus* Fe_2-NrdF in complex with NrdI. Compared to the *Escherichia coli* NrdI-Mn^{II}_2-NrdF structure, NrdI and NrdF bind similarly in *B. cereus* through conserved core interactions. This suggests similar NrdI-NrdF binding in class Ib RNRs, with a protein-protein association unaffected by metal ion type bound in NrdF. However, the Mn^{II}_2-NrdF and Fe_2-NrdF structures show conformational flexibility of residues surrounding the metal ion site. The movement of one metal-coordinating carboxylate seems to be linked to the metal type present at the di-metal site. This conformation is likely vital for the water network connecting the NrdF di-metal site and the flavin in NrdI, suggesting metal-dependent variations in carboxylate coordination geometries during active Y• cofactor generation. Additionally, we show that binding of NrdI to NrdF could structurally interfere with the suggested $NrdE_2$-$NrdF_2$ holoenzyme formation, leaving the interaction mode between NrdI, NrdF and NrdE during cofactor generation and catalysis still not fully understood.

Hammerstad M, *et al*., *ACS Chem. Biol*. ***9*** **(2)**, 526–537 (2014)

Boal AK, *et al., Science*. **329**, 1526 (2010)

P5

A structural and functional investigation of Ribonucleotide reductase Class III in *Bacillus cereus*

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All known cellular life forms to date store their genetic information as DNA by utilising an arrangement of four different nucleotides. It is well known that ribonucleotide reductase (RNR) is solely responsible for the first committing step of DNA synthesis by producing deoxyribonucleotides from its ribonucleotide precursors[1]. Because RNR is vital for DNA synthesis it is an important target for anticancer, antibacterial and antiviral agents. The RNRs are divided into three classes, each consisting of two units, one catalytic subunit and a radical initiator unit. The RNR class III is only active during strict anaerobic conditions due to an oxygen sensitive glycyl radical in the catalytic subunit (NrdD) and an iron-sulphur cluster, which is inactivated by oxygen on the radical initiator unit (NrdG). The main aspect of this project will be to understand both the activation of NrdD by NrdG, and the re-activation of NrdG by a more general redox network in the model organism *Bacillus cereus*. Currently, both NrdD and NrdG have been successfully expressed and purified, and to understand the activation of NrdD, a combination of structural and spectroscopic studies will be performed in addition to binding and kinetic studies.

1. Andersson, K.K., *Ribonucleotide reductase*. Molecular Anatomy and Physiology of Proteins, ed. V.N. Uversky. 2008: Nova Science Publishers, Inc. Hauppauge, N.Y. USA.

P6

Nucleotide binding and hydrolysis of heat shock protein HSP70 as probed by biophysical and crystallographic studies of the nucleotide binding domain.

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The chaperone function of HSP70 assists the survival of cancer cells, which otherwise may be too destabilized to avoid apoptosis. HSP70 binds misfolded proteins via the substrate binding domain (SBD), while ATP hydrolysis at the nucleotide binding domain (NBD) powers refolding. HSP70 protein complexes possess various drug targeting sites, but the NBD may have the most druggable pocket. Despite this, few inhibitors have been described, possibly due to unique properties of ATP binding. We therefore investigated properties of HSP70-NBD crystals and binding site interactions, using site-directed mutagenesis, TLS protein dynamics and surface plasmon resonance (SPR), with an eye toward drug discovery applications.

We study how mutations of key adenine binding residues of the NBD influence the binding and hydrolysis of substrate (ATP). SPR experiments show the variations of affinities and kinetics of ATP (and analog) binding to wt, R272K, and E268Q/R272K variants of HSP70-NBD. High-resolution crystallography reveals the structural properties underlying the SPR results, and may shed light on the physiological mechanisms of cross-talk between the the NBD and SBD domains via changes between "open" and "closed" conformations of the nucleotide binding domain. Ensemble and TLS refinement applied to the HSP70-NBD structures reveal variabilities of dynamic structures relevant to ligand binding.

P7

Residue profiling of antibiotic resistant OXA-beta-lactamases through mutagenesis, enzyme kinetics and 3D structures

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Background: OXA-beta-lactamases are enzymes that hydrolyze beta-lactam antibiotics like penicillins, cephalosporins and carbapenems, thus studying the structure and activity of these enzymes are important steps in the search for OXA-beta-lactamase inhibitors. The aim of this project is to study three different mutations of the OXA-48 enzyme to gain further insight into inhibitor and substrate binding, and the dimerization of the protein. The full project also includes work on the related enzymes OXA-23 and OXA-24.

Methods: Site-Directed Mutagenesis was performed on the bla_{OXA-48} gene to create the mutations S118G, R206A and R250A. The mutants were expressed in competent *E. coli* cells in a large-scale, with subsequent purification and crystallization. Further work will include enzyme kinetics and size-exclusion chromatography studies on the mutants, in comparison with the wild-type OXA-48.

Expected results: The S118G mutant is thought to promote deacetylation of the protein-Avibactam complex, and cause resistance to the beta-lactamase inhibitor Avibactam. The R206A mutant is expected to disturb the dimerization of the protein. Lastly, the R250A mutant is thought to disrupt the binding of fragment hits, but may also disrupt binding of substrate.

Future perspectives: Hopefully this study will bring some new insights into the activity and mechanisms of the OXA-48 enzyme with respect to dimerization, and inhibitor and substrate binding.

P8

Binding of the lytic polysaccharide monooxygenase CBP21 to chitin – a computational approach

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Nature has evolved a battery of hydrolytic enzymes that can cleave polysaccharides into smaller units that are interesting for industrial applications; however, one of the main bottlenecks when degrading recalcitrant polysaccharides is that their tight packing limit the access of the hydrolytic enzymes to their substrate. Recently, a novel class of oxidative enzymes named lytic polysaccharide monooxygenases (LPMOs) was discovered to act as perforators, cleaving the microcrystalline polysaccharide chains, making them available for the hydrolytic enzymes. These enzymes can boost the efficiency of enzyme mixtures working on recalcitrant polysaccharides, being key candidates for development of cheaper and applicable biorefining processes.

Here we present a computational study focusing on binding of the AA10 LPMO CBP21 on crystalline chitin. We discuss the differences of CBP21 interacting with beta-chitin dihydrate and alpha-chitin, and compare our results with previous experimental work investigating the CBP21-chitin interaction.

P9

Regulatory interactions between the J- and UBA domains of NBR1 enable a switch between membrane binding and protein aggregation

Steingrim Svenning, Hallvard L. Olsvik, Andreas Brech, Johan Isaksson, Elenaz Naderkhani, Tom Egil Hansen, Sebastian W. Schultz, Trond Lamark and Terje Johansen

NBR1 is an ubiquitin binding selective autophagy receptor that has been implicated in degradation of a diverse set of cargoes including misfolded proteins and peroxisomes. NBR1 harbors a C-terminal ubiquitin- associated (UBA) domain for interaction with ubiquitin preceded by an amphipathic a-helix (AH) that mediates interaction with cellular membranes. Here, we have investigated the regulation of ubiquitin- and membrane binding by NBR1. We find that the AH is responsible for intramolecular inhibition of ubiquitin binding by NBR1, and that membrane and ubiquitin binding events are not mutually exclusive. Membrane binding by NBR1 might be negatively regulated by TANK-binding kinase 1 (TBK1)-mediated phosphorylation. We also find that p62 affects NBR1-containing structures by introducing aggregate forming potential. Hence, our data suggest that the interaction between the AH- and UBA domains regulates the ability of NBR1 to interact with membranes versus protein aggregates during selective autophagy.

P10

Crystallization of *Arabidopsis thaliana* SnRK2-interacting Calcium Sensor, the kinase inhibitor containing EF-hand motifs

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NF1-related protein kinases 2 (SnRK2s) are key signaling elements regulating response to environmental stresses and abscisic acid (ABA)-dependent plant development. A recently discovered SnRK2-interacting Calcium Sensor (SCS), found in all higher plants, is able to inhibit the kinase activity in the presence of calcium ions. Elucidation of this process at molecular resolution is critical for our understanding of plant stress signaling and other abscisic acid-dependent plant development pathways. In Arabidopsis thaliana, the SCS inhibitor is present in two forms, SCS-A and SCS-B, which contain either two or one EF-hand type calcium binding motif(s), respectively. There are no 3D structural data available for SCS besides the fact that it contains EF-hand motif(s), and the variability of such structures prevents reliable prediction. We have focused our efforts on elucidation of the structure of SCS-B protein, containing one, non-classical EF-hand calcium binding motif. Using PondrFit (http://www.disprot.org/), the protein classifies as intrinsically disordered, indicating likely problems with crystallization. Studies of dynamic folding stability using nuclear magnetic resonance (NMR) and hydrogen-deuterium exchange (HDX), coupled with mass spectrometry, have guided the choice of protein constructs for protein production and crystallization trials. Here we present initial results of our SCSB crystallization studies. This work was funded by Norway Grants (POL-NOR/203156/70/2013)

P11

Structure-function study of LsbB family leaderless bacteriocins.

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LsbB is a leaderless lactococcal bacteriocin targeting only *Lactococci*. It uses the membrane-bound protease RseP as a receptor on target cells. NMR structure study showed that LsbB had N-terminal α-helix while the C-terminal part was unstructured. Truncated peptides representing only the C-terminal part inhibited activity of whole LsbB molecules, indicating that the C-terminal part is likely to contain the receptor binding domain. The leaderless enterococcal bacteriocins, EntQ, EntEJ97 and EntK1, show significant sequence homology to LsbB at their C-terminal halves where all contain a KxxxGxxPWE motif. However, these three enterococcal bacteriocins have much wider inhibition spectra including species of *Lactococci*, *Enterococci* and *Bacilli*. Truncated peptides with sequences derived from the C-terminal regions of LsbB, EntK1and EntEJ97 could inhibit activity of any of the three bacteriocins, supporting the idea of the same receptor for these bacteriocins. It was also shown that NMR structure of EntK1 is very similar to LsbB but with a longer N-terminal helix.

When *E. faecalis rseP* was expressed in resistant to LsbB bacteriocins *S. pneumoniae*, the strain became sensitive to EntK1 and EntEJ97. Moreover, it was shown that *E. faecalis* RseP active site is not responsible for EntEJ97/EntK1 activity, since substitution of RseP conserved active site residues (HExxH) with alanines did not lead to resistant phenotype appearance.

P12

STED microscopy of ASC speck inflammasome formation in mouse macrophages

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A large number of molecules and structures, including crystals, can activate a signal complex of the innate immune system resulting in formation of NLRP3 inflammasome containing ASC specks (apoptosis-associated speck-like protein containing a caspase recruitment domain [CARD]) and pro-caspase-1. This further leads to caspase-1 mediated activation and release of proinflammatory cytokines. In non-activated macrophages ASC is distributed throughout the cell. Upon inflammasome activation the vast majority of ASC is aggregated into single dense specks in the cytoplasm. To study the formation of ASC specks, mouse macrophages C57 black/6 (B6) were stable transfected with ASC fused with the fluorescent protein mCherry or mCerulean and then stimulated with nigericin or cholesterol crystals. To investigate this process a Leica TCS SP8 STED 3X microscope equipped with 3 depletion lasers was used. We observed a clear difference in the dynamics leading to the formation of ASC specks dependent on the activation stimuli. Treatment with nigericin induced speck formation after ~30min and gave rise to a large number of cells containing accumulated specks. In contrast, CCs induced specks at a slower rate and resulted in fewer specks in total. STED nanoscopy enabled us to visualize the detailed filamentous structures within single ~1-2µm ASC specks in greater detail than achievable by conventional diffraction limited microscopy.

P13

Moving Tolls - novel interactors of TLR9 trafficking

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Toll-like receptor 9 (TLR9) is an important mediator of the innate immune response. The receptor binds foreign DNA and activates inflammatory and antiviral responses. TLR9 normally resides in the endoplasmic reticulum, but is trafficked to endolysosomes where it is cleaved, followed by ligand binding and activation. The mechanisms regulating this translocation are not well described, and we therefore set out to identify regulators of this trafficking. Based on data from a mass spec analysis of proteins interacting with the TLR9 adaptor protein Unc93B1, we designed a small siRNA screen and measured the effect of knockdown on TLR9 signaling. 3 interesting proteins were identified as possible regulators of TLR9, including the small Rab GTPase Rab39a. This protein has been reported to be involved in maturation of phagosomes and fusion of phagosomes with lysosomes. We will now further study the expression of this protein by confocal microscopy, to elucidate its function in TLR9 signaling.

P14

Delivering Biotherapeuticals: Challenge of unwanted liver uptake

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In spite of the great therapeutic potential of biologics and nano delivery systems, and the increasing amount of resources that are being spent on their development, the progress in this field has been limited when it comes to biodistribution control. However, testing in animal models have often resulted in the disappointing observation that the compound disappear by uncontrolled rapid uptake in the liver.

To solve the challenge of uncontrolled liver clearance of biologics and nano delivery systems it is necessary to understand the mechanism(s) of uptake. Large blood borne molecules are removed in the liver primarily by specialized scavenger cells via their specific uptake receptors. Unlike the hepatocytes that make up more than 90% of the liver volume, the scavenger cells represent only a minor part of the liver mass, but yet make up about a third of the cell number. These scavenger cells line the minute liver sinusoids that make up the vasculature of the liver and are exposed to the large molecule blood constituents entering the liver vasculature. Any molecule recognized by these cells as foreign will be effectively endocytosed and metabolised. A detailed knowledge about the scavenger function of these cells and their receptors are a prerequisite to design strategies to avoid unwanted hepatic uptake. Of note, this same knowledge will enable strategies to target biologics and nano therapeuticals to selected types of liver cells.

P15

Secretome of the liver sinusoidal endothelial cell

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Background: Liver sinusoidal endothelial cells (LSECs) line the wall of the hepatic sinusoid, where they regulate and survey the traffic of molecules and cells between blood and hepatocytes. These specialized endothelial cells are important scavenger cells responsible for removal of potentially dangerous macromolecules from blood, and they are increasingly acknowledged as important players in liver immunity. Morphological changes in LSECs are associated with fibrotic liver disease, and old age. Despite the importance of LSECs in liver host defense and homeostasis, little is known about their production and secretion of molecules.

Aim of study: To investigate the profile of proteins secreted by primary rat LSECs under normal and proinflammatory conditions, using Stable Isotope Labeling by Amino acids in Cell culture (SILAC) technology.

Results: A major challenge with LSEC secretome studies using SILAC technology is the rapid dedifferentiation of cells in culture. Following isotope labeling of cells for 3-5 days, cell-associated proteins and supernatants were resolved by one-dimensional SDS-PAGE electrophoresis, in-gel digestion of proteins, and analysis in tandem with LC-MS/MS (liquid chromatography/double mass spectroscopy). Validation of results by Western Blot, and qPCR are ongoing. We present here the major proteins secreted by LSEC in culture and discuss their possible roles for the liver microenvironment.

P16

Gastrin induces autophagy in gastric adenocarcinoma cells directly and via an autocrine loop

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Gastric cancer is one of the most common causes of cancer-related deaths worldwide. *Helicobacter pylori* infection followed by inflammation has been characterized as a risk factor for gastric adenocarcinoma development. Gastrin is a hormone secreted in the gut, involved in proliferation, invasion and migration of cells. However, it is still debated whether gastrin is involved in the development of gastric adenocarcinoma. Sustained gastrin treatment has been linked to increased ER stress in adenocarcinoma cells. High levels of autophagy, amongst others induced by ER stress, have been described in several cancer types and are commonly reported together with therapy resistance. It is important to further investigate the role of gastrin in adenocarcinoma and its role in autophagy induction. This could help to reveal new targets for therapy.

We have found that gastrin activates autophagy via the STK11-AMPK-ULK1 pathway in AGS-GR and MKN45 gastric adenocarcinoma cells. Activation of autophagy has been linked to increased survival of these cell lines upon cisplatin treatment. The aim of this study is to further investigate the signaling pathway of gastrin induced autophagy and whether, this could be regulated via an autocrine loop.

P17

Regulation of ErbB2 receptor tyrosine kinases by ERM proteins

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The members of the ERM protein family have been associated with a large variety of cellular functions such as signal transduction, protein trafficking, cell proliferation and migration. Dysregulation of ERM proteins has been described to correlate with carcinogenesis of different cancer types. Here, we demonstrate a functional interaction between ERM proteins and the ErbB2 receptor tyrosine kinase in breast cancer cells. We show that not only are the ERM proteins ezrin and radixin associated with ErbB2 at the plasma membrane, but depletion or functional inhibition of ERM proteins also destabilizes the interaction of ErbB2 with ErbB3, Hsp90 and Ebp50. Furthermor, ErbB2 becomes ubiquitinated and binds to c-Cbl, followed by rapid internalization of ErbB2 and ErbB3 receptors into intracellular vesicles protein degradation of ErbB2 and ErbB3. As a consequence of ERM inhibition and degradation of ErbB2 and ErbB3, signal transduction via Akt- and Erk-dependent pathways is reduced. Thus, our data demonstrates a regulatory role for ERM proteins in the membrane localization and complex stabilization of ErbB2 receptors and the oncogenic downstream signaling pathways.

P18

The multiple sclerosis susceptibility genes *TAGAP* and *IL2RA* are regulated by vitamin D in CD4+ T cells

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Multiple sclerosis (MS) is an inflammatory, demyelinating disorder of the central nervous system that develops in genetically susceptible individuals. The majority of the MS-associated gene variants are located in genetic regions with importance for T cell differentiation. Vitamin D is a potent immunomodulator, and vitamin D deficiency has been suggested to be associated with increased MS disease susceptibility and activity. Vitamin D acts through its vitamin D receptor (VDR), which binds vitamin D response elements (VDRE) within regulatory regions of its target genes, thereby affecting gene transcription. In CD4+ T cells, we have analyzed *in vitro* vitamin D responsiveness of selected VDRE-containing MS-associated genes. We identify *IL2RA* and *TAGAP* as novel vitamin D target genes. The vitamin D response was observed in samples from both MS patients and controls, and was not dependent on the genotype of MS associated SNPs in the respective genes. From published VDR chromatin immunoprecipitation-sequencing data, we have now selected eight more MS-associated genes to be analyzed for vitamin D responsiveness in CD4+ T cells.

P19

In vivo proteolytic activity assayed by subcellular localization switching

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Recombinant labelled proteins expressed in mammalian cells may or may not maintain their native activity. Therefore, suitable testing systems are advantageous. Presently, an approach to assay proteolytic activity *in vivo* by altering the subcellular localization of a labelled substrate was demonstrated. The assay included a protein shuttling between different cellular compartments and a selected protease. The shuttle protein used was the human immunodeficiency virus type 1 (HIV-1) Rev protein fused to the enhanced green fluorescent protein (EGFP) and the red fluorescent protein (RFP), while the protease was the site-specific protease from the herpes simplex virus type 1 (HSV-1). The fluorescent proteins in the Rev fusion protein were separated by a cleavage site specific for the HSV-1 protease (VP24). When co-expressed in COS-7 cells proteolysis was visualized by fluorescence microscopy as a shift from a predominantly cytoplasmic localization of the fusion protein Rev-EGFP to a nuclear localization while the RFP part of the fusion protein remained in the cytoplasm. It was also confirmed by Western blot analysis that VP24 cleaved the fusion protein. These results suggest that the activity of recombinant expressed proteases can be assessed by protease-mediated change in shuttling activity of fusion proteins containing a specific protease cleavage site.

P20

Identification of a novel lysosomal degradation pathway acutely activated upon nutrient starvation

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Degradation of cellular components is essential for cell survival during nutrient starvation to provide metabolic building blocks and to implement cellular adaptations. Here we report a novel and highly acute degradation response to nutrient starvation, triggered independently of the classical and well-established nutrient sensing hubs. Using quantitative proteomics, we identified the changes in the proteomes of two different human cell lines (A549 and BJ) caused by acute nutrient starvation. The results reveal a surprisingly similar response in the two cell lines with a clear overlap of the most comprehensive changes suggesting that nutrient starvation triggers a highly specific and conserved degradation response. These changes take place as early as 30 minutes after nutrient removal and include re-localization and degradation of integral plasma membrane proteins regulating both morphology and metabolism. The degradation is mediated by the lysosome but is neither executed by mTOR deactivation nor mediated by canonical macroautophagy (e.g. ATG5, FIP200, VPS34). Instead, we found that the multivesicular body (MVB) pathway orchestrates this catabolic cascade as depletion of VPS4a/b impaired the acute degradation response. We hypothesize that this acute degradative response constitutes a unique cellular program serving two purposes. Firstly, to ensure immediate reinforcement of the pools of free amino acids needed to sustain protein synthesis. Secondly, to readily implement essential adaptations by cellular remodelling to cope with more prolonged periods of malnutrition.

P21

Regulation of macropinocytosis by PI3P-binding proteins

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Macropinocytosis is an endocytosis mechanism that leads to the formation of large vesicle filled with extracellular fluids and soluble macromolecules. Formation of macropinosomes is a stochastic process that happens in areas of the cell that exhibit high levels of membrane ruffling. Membrane ruffles can collapse and pinch off by yet unknown mechanisms to form large vesicles. The transition of membrane ruffles to vesicles is controlled by a phosphoinositide cascade, in which phosphatases metabolize the lipid PtdIns(3,4,5)P3 to PtdIns(3,4)P2 and PtdIns(3)P. Inhibition of this cascade leads to defects in macropinosome formation. We have identified the protein Phafin2 as novel effector of PtdIns(3) during macropinocytosis. Using live cell and superresolution imaging, we could show that Phafin2 localizes to forming macropinosomes prior to recruitment of early endocytic markers, suggesting that Phafin2 is localized to the plasma membrane prior to scission of the nascent vesicle. Cells lacking Phafin2 show strong defects in macropinocytosis and increased membrane ruffles, suggesting that Phafin2 is required for the transition from plasma membrane ruffles to vesicles. Mechanistically, this is probably due to defects in actin organization, since cells depleted for Phafin2 show strong defects in actin organization. Taken together, this data suggests that Phafin2 is a critical regulator of membrane and actin organization during macropinosome formation.

P22

Catching the tubule – Analyzing the role of the PtdIns3P-binding protein WDFY2 in retrograde endocytic transport

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Phosphoinositides play a critical role in regulation of membrane trafficking. During their maturation, endocytic vesicles undergo a change in phosphoinositide composition that allows them to recruit different effector proteins that are involved in sorting decisions and in cellular signaling events. During endocytic trafficking, Rab5-containing vesicles acquire phosphatidylinositol-3-phosphate (PtdIns3P) and PtdIns3P-binding proteins, allowing them to mature and fuse with early endosomes.
The PtdIns3P-binding FYVE domain containing protein WDFY2 is localized to early endosomes. The precise function of WDFY2 in the endocytic pathway is not fully known, but it is believed to take part in coordination of the interaction between compartments with PtdIns3P and other WD40 binding proteins in the early steps of endocytosis.
Live-cell microscopy showed that WDFY2 localizes to the tubular part of early endosomes and that this localization requires a functional FYVE domain. Since little was known about its role and interaction partners we performed a mass-spectrometry analysis to identify novel interaction partners. This yielded several interaction partners that have been associated with the retromer complex. Further microscopic analysis showed that WDFY2 colocalizes with markers of the retromer complex on tubules, suggesting that WDFY2 could play a role in retrograde transport. Our current studies focus on the functional role of WDFY2 during retrograde transport and sorting.

P23

Bmp4 and Grem1 in breast cancer tumor-stroma communication

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Breast cancer (BC) is a complex disease with very different individual progression. Fatal outcome is closely associated with metastasis. The ability to metastasize depends on both acquired cell intrinsic properties and interactions with the microenvironment.

To identify acquired mechanisms for metastasis we used a syngeneic mouse BC model. This model (4T1) consists of five cell lines isolated from one spontaneous tumor. All five cell lines form primary tumors in BALBc mice but display different metastatic potential. Transcriptome analyzes found Bone Morphogenic Protein 4 (Bmp4) and its antagonist Gremlin-1 (Grem1) upregulated in the metastatic 66cl4 cells compared to the non-metastatic 67NR in culture and tumors. Meta-analysis identified a clear correlation between high Grem1 mRNA levels and poor prognosis in BC patients. Thus, we asked if Bmp4 and Grem1 is secreted from the metastatic 66cl4 and may control fibroblasts and macrophages in tumor stroma, contributing to aggressive tumor development.

We found that 66cl4 secrete more Bmp4 and Grem1 compared to 67NR. Macrophages and fibroblasts respond to recombinant Bmp4, activating Smad1/5/9, counteracted by Grem1. This suggests that the metastatic cells have acquired the ability to secrete compounds that can control the microevironment.

Understanding how Bmp4 and Grem1 influence stromal cells could help to generate more specific therapies for aggressive BC.

P24

The role of the extracellular matrix protein Nephronectin in breast cancer progression and metastasis

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During tumor progression tumor cells and stromal cells interact with the extracellular matrix for survival, proliferation, differentiation, migration and invasion. Extracellular matrix proteins interact with various integrin receptors for cell adhesion and downstream signaling upon stimulation.

Nephronectin (Npnt) is an extracellular matrix protein known to be involved in development of endocrine organs via interaction with integrin receptor α8β1 and αvβ3. It has previously been shown that Npnt is upregulated in metastatic vs non-metastatic breast cancer cells and increased Npnt levels is correlated with poor outcome of breast cancer in patients.

In this study, we have been working with a weakly metastatic breast cancer cell line 66cl4 to study the role of Npnt during breast cancer metastasis. We have made four variants of the 66cl4 cell line for stable overexpression of the Npnt protein and mutated variants of the Npnt protein. These cells are denoted 66cl4- EV (empty vector), 66cl4- Npnt (wild type), 66cl4 -RGE (mutated RGD domain) and 66cl4 -RGE-AIA (mutated RGD-EIE domain).

The aim of this study is to identify the integrin receptor of Npnt during breast cancer metastasis and to characterize the downstream signaling mechanisms induced by Npnt. We are investigating three signaling pathways: the serine/threonine kinase Akt, also known as protein kinase B (PKB) or Phosphoinositide 3-kinase (PI3K), focal adhesion kinase (FAK) and extracellular signal-regulated kinase (ERK), also known as Mitogen activated protein kinase (MAPK). The overall goal is to understand the detailed mechanisms by which Npnt promote breast cancer metastasis.

P25

Hunting for proteins binding to the RUN and GOLD domains of FYCO1

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Autophagy is an evolutionary conserved degradative pathway where damaged or surplus cytosolic components degraded by lysosomes. Hence, protein aggregates, long-lived proteins and damaged cytosolic components, including organelles, are sequestered by a crescent shaped double membrane structure, the phagophore, that grows and closes upon itself to form the autophagosome. The sequestered content is degraded when the autophagosome fuses with the lysosome. Autophagy is activated as a protective response following exposure to cellular stress such as hypoxia, nutrient or growth factor deprivation, protein aggregates, reactive oxygen species, damaged organelles, intracellular pathogens or DNA damage. Autophagy depends on transport of autophagosomes to fuse with lysosomes. One of the proteins involved in this transport process is FYVE and Coiled-coil [CC] domain containing protein 1 (FYCO1). FYCO1 is involved in transporting autophagosomes and late endosomes along microtubules, in the plus-end direction, by interacting with kinesin. FYCO1 interacts with phosphatidylinositol-3 phosphate via its FYVE domain, with RAB7 via the coiled-coil, and with LC3 via the LIR. No binding partners for the N-terminal RUN domain and the C-terminal GOLD domain have been identified yet. Interestingly, the mutation L1376P in the GOLD domain is detected in patients with autosomal-recessive congenital cataracts suggesting a linkage between FYCO1 and human lens development and transparency. The aim of this project is to identify new binding partners for FYCO1`s RUN- and GOLD domains by GST-pulldown in extracts from human cell lines. Novel interaction partners for RUN and GOLD will be identified by LC-MS/MS and their roles explored in functional analyses.

P26

The long non-coding RNA NEAT1 is upregulated in epithelial-mesenchymal transition and is abnormally expressed in breast cancer

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Long non-coding RNAs (lncRNAs) are regulatory transcripts longer than 200 nucleotides. Aberrant expression of many lncRNAs is associated with human diseases including cancer.

NEAT1 (Nuclear Enriched Abundant Transcript 1) is a highly abundant transcript that localizes to and is essential for the formation of specific nuclear bodies called paraspeckles. Several studies have demonstrated that the number and sizes of paraspeckles increase in response to different cellular stresses. There are two distinct but overlapping transcript of NEAT1, NEAT1 and NEAT1_2. NEAT1 can regulate the expression of specific genes by sequestering specific mRNAs and proteins into paraspeckles, or by epigenetic regulation of target gene promoters. Moreover, high levels of NEAT1 are associated with poor clinical outcome both in breast and prostate cancer.

We have profiled by RNA-sequencing the expression of lncRNAs in MCF10A cells induced to go through epithelial-mesenchymal transition, and in epithelial and mesenchymal human mammary epithelial cells (HMLE). Interestingly, we have found NEAT1 to be upregulated in EMT and found the transcript to be highly expressed in certain subtypes of breast cancer.

P27

n-3 PUFAs modulate SQSTM1 and dampen pro-inflammatory CXCL10 in human macrophages

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Inflammation is crucial in defense against infections but has to be tightly controlled to avoid detrimental activation. If regulation fails, chronic inflammation might promote cardiovascular, neurodegenerative or autoimmune diseases. Nutrition can influence the inflammatory state of the body and omega-3 polyunsaturated fatty acids (n-3 PUFAs) have acknowledged anti-inflammatory effects beneficial for patients with inflammation-related diseases. A better understanding of how n-3 PUFAs modulate signaling might contribute to rebalance inflammatory processes and prevent diseases.
Here we propose a model in which the n-3 PUFA docosahexaenoic acid (DHA) induces a transient increase in protein levels and cytosolic speckles of the autophagic cargo receptor sequestosome 1 (SQSTM1/p62) in macrophages. SQSTM1-bodies co-localized with polyubiquitinated proteins and formed dense structures that might be removed by lysosomal degradation. Further, screening of 500 inflammation-related transcripts identified C-X-C motif chemokine 10 (CXCL10) among the LPS-induced signaling substances with the clearest decrease by DHA pretreatment. Surprisingly, SQSTM1 seemed necessary for proper induction of CXCL10. In addition, MS-analysis of proteins that associate with SQSTM1 in a DHA-dependent manner identified several established regulators of inflammation. Thus, we speculate that DHA triggers formation of SQSTM1-bodies providing a signaling platform where positive and negative regulators merge to control the output of inflammatory signaling.

P28

DNA polymerases from the Arctic

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The Arctic is inhabited by a vast diversity of life despite its harsh environmental conditions. In order for the organisms to cope with the detrimental effect of low temperature adaptation mechanisms must be in place. Utilizing cold-adapted enzymes is one of the strategies to counteract the decreased reaction rates at low temperature. These enzymes possess a range of structural features that are necessary to perform their activity at low temperature. They are in general more catalytically efficient and more thermolabile compared to their mesophilic counterparts.

The main focus of our research team is to identify DNA polymerases from the marine Arctic environment and further characterize and develop them for use in molecular diagnostic applications. The targets are submitted to a state of the art protein production pipeline including recombinant protein production, purification, biochemical/biophysical characterization and 3D-structure determination. Interesting candidate enzymes are further developed through rational protein design and/or molecular evolution studies. We are, in addition, interested in gaining further insight into the molecular basis for cold adaptation, and the structure-function relationships of these complex enzymes.

P29

Cool catalysts for biomass conversion

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Enzymes from organisms capable of efficient biomass conversion at low temperatures are scarcely studied. In this work, we have sequenced DNA from bacterial enrichment cultures using BALI-cellulose (Borregaard) and α-chitin as sole carbon sources. The inoculum used was Shipworm (*Psiloteredo megotara*) and Atlantic Wolffish (*Anarhichas lupus*) intestinal content respectively. New enzymes degrading lignocellulose and chitin has been discovered by sequence comparison. Additionally we have sequenced several Cyanobacteria (*Nostoc* sp.). Two Cyanobacterial epimerases has been recombinantly expressed and structural & functional characterization is ongoing. The enzyme is a piece of a larger effort to enable efficient conversion of GlcNac to different sialic acids.

P30

Enzyme Innovations from the Marine Arctic

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Our group is located in the far north of Norway at the Department of Chemistry at UiT – The Arctic University of Norway. As part of the MabCent-SFI (Centre for Research-based Innovation) program our main goal was to identify and develop enzymes for use in industrial and/or biotechnological applications. Our main research efforts have throughout the last 8 years been on characterizing cold-adapted DNA-modifying enzymes like DNA polymerases and nucleases. This research has been performed in close collaboration with biotechnological industry and innovation focused. Throughout the years we have deepened our knowledge about these enzyme classes and established methods to analyze and characterize them in detail. An innovation project based on the results from our research got granted by the BIOTEK 2021 program providing us with the possibility to continue our work on these commercially interesting enzymes after the MabCent-SFI program. To date we have submitted four Disclosures of Invention to UiT and one patent has been filed. Already one of the innovations has led to a license agreement with biotechnological industry.

P31

Maximizing the value of marine by-products

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The focus on Bioeconomy and the strategy of production of renewable biological resources in EU and Norway has led to the establishment of several biotechnology projects on marine by-products with the aim to maximize the value and to increase the use and outcome of commercial products. By-products define part of the fish or other marine organisms that is not the main product and can be as much as 70%.

To maximize the production yield and value, the aim is to use 100% of the biomass of marine resources. Even if this is not very likely, it is essential to explore the potential of marine biomasses and characterize the composition in terms of chemical composition, characteristics and features like biological interesting activities detected. In this ongoing master project, snow crab (*Chionoecetes opilio)* by-products are analyzed and different processing methods are compared. Traditionally there are several bioprocesses that can be used in combination with hydrolysis. Most rest raw material from fish production is utilized for fishmeal and oil, but other resources are not used as effectively. The most valuable bioprocessing is where the material can be used for food or high value products. The processes and possibilities will be presented at the meeting.

P32

Bioactive peptides from marine sources

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Marine organisms and material of marine origin that also include organic matter usable for food, have a huge potential for exploring novel bioactive components with activities that can be documented or exploited. In this context, peptides or proteins are very interesting.

The wide repertoire of biological functions covered by natural peptides makes them interesting for bioprospecting and drug discovery. Antimicrobial peptides (AMPs) are also important components of the innate defense in all invertebrate species investigated and are considered as evolutionary ancient weapons against pathogenic microorganisms.

Our aim is to study novel antimicrobial natural products (AMPs) from marine organisms, to explore their structure and mode of action. The organisms are collected from the Arctic or/and sub-Arctic region and can be very diverse covering biological resources from microalgae to invertebrates, but it might also be marine rest raw material. Extractions are made and novel bioactive compounds (peptides) are isolated and characterised by traditional bioassay-guided purification in combination with a genetic approach. A more extensive screening can be done in collaboration with the HTS platform, Marbio, UiT, and can be further developed in collaboration with the Arctic Biodiscovery Centre in Tromsø. Mechanisms of action studies are performed on promising AMPs to understand the activity and reveal the potential for different applications.

P33

A novel expression system specialized for psychrophilic enzymes

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In recent years, commercial interest for enzymes originating from extremophiles has increased due to their highly specialized properties. For example, psychrophilic (cold-loving) enzymes often show high catalytic efficiency at low temperature and heat-lability gives susceptibility to heat inactivation at relatively low temperatures. These characteristics can be highly desirable in molecular applications, such as work that involves nucleic acids (RNA in particular). However, lack of specialized expression systems hampers the psychrophilic enzyme development. Typically, low expression, misfolded/non-functional protein and inclusion bodies hinders successful protein production.

To address this issue we are developing a new protein expression system. A marine bacterium naturally adapted to cold conditions, hence well suited to express psychrophilic enzymes, was selected from a collection of natural isolates from the Arctic/sub-Arctic region. The bacterium grows fast to high density at 4-16^{o}C in culture media without expensive supplements. The complete sequence of the genome is the basis for bioinformatic analyses. Further, vectors for genetic manipulations and stabile plasmids are efficiently introduced. In addition to commonly used inducible systems (e.g. ITPG/T7RNApol) for activating protein production, we are developing a new system especially adapted to our novel expression host.

P34

Quorum sensing in *Aliivibrio wodanis* 06/09/139: N-acyl homoserine lactone synthesis and transcription profiling

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Moritella viscosa is the primary pathogen that causes winter ulcer, a cold-water associated disease that affects Atlantic salmon when the sea temperature is lower than 8°C. However, *Aliivibrio wodanis* is repeatedly co-isolated together with *M. viscosa* from the infected fish. Although their co-existence apparently signifies their interaction, little is known about the role of *A. wodanis* in winter ulcer. In a recent study, it was shown that *A. wodanis* has some impeding effect on growth and gene expression of *M. viscosa*. Therefore, it is hypothesized that these two bacteria may use quorum sensing (QS), a cell-to-cell communication system and other factors to compete, infect the fish, progress the disease and cause mortality [1]. N-acyl homoserine lactones (AHLs) are the most common QS signaling molecules used by Gram-negative bacteria to control activities such as biofilm, luminescence and virulence. *A. wodanis* 06/09/139 produces only one AHL (3-OH-C_{10}-HSL) and encodes the AinS/AinR and LuxS/LuxP QS systems. AinS in other aliivibrios are known to produce AHLs, and the signaling cascade is known to activate LitR, a master transcriptional regulator. In order to study the function of these genes in AHL synthesis, Δ*ainS* and Δ*litR* mutants have been constructed. Since winter ulcer is a temperature regulated disease, the wild type, mutants as well as complementary strains will be cultivated at different temperatures, and samples for transcription analyses and AHL profiling will be collected at different cell densities. AHLs will be analyzed using HPLC-MS\MS and expression profiling using RNA_seq. The knowledge from this research might be helpful for improving vaccination strategies for winter ulcer disease.

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P35

Characterization of an evolutionarily conserved lysine-specific eEF2 methyltransferase

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Many components of the protein synthesis machinery, such as ribosomal proteins and translation factors, may be methylated on specific lysine residues. For the most part, neither the function of such modifications nor the responsible methyltransferases are known. We have identified the methyltransferase, EEF2KMT, which methylates a specific lysine residue in eukaryotic translation elongation factor 2, eEF2. We show that eEF2 is close to fully trimethylated at this residue in yeast, as well as in several mammalian cells and tissues, with the exception of the rat brain where eEF2 methylation levels appear to be lower, indicating that this modification may be subject to regulation in certain mammalian organs and tissues. In addition, we identify the *S. cerevisiae* functional homologue of the EEF2KMT enzyme and show that the corresponding yeast knockout strain is hypersensitive to the translation inhibitor sordarin and displays increased -1 ribosomal frameshifting, suggesting that EEF2KMT-mediated methylation may be required for optimal eEF2 function, with a possible role in the maintenance of translational accuracy.

P36

Regulation of Promoter Activity of the Human Oncovirus Merkel Cell Polyomavirus Variants MCC350 and 16b by Large T-antigen

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Merkel cell polyomavirus (MCPyV) is a human virus that is common in skin where it is found in an episomal state in host cells. The virus is not harmful in healthy individuals, but it is involved in the pathogenesis of Merkel cell carcinoma (MCC) in elderly and immunosuppressed individuals. Approximately 80% of all examined MCC specimens are virus-positive. Two hallmarks of MCPyV-positive MCCs are integrated viral genome and expression of truncated large T-antigen (LTAg). The MCPyV genome is functionally divided into: (i) early region encoding the oncoproteins LTAg and small t- antigen, 57 kT, and the ALTO protein, (ii) late region encoding the capsid proteins, and (iii) the non-coding control region (NCCR) encompassing the origin of replication and the promoters controlling the expression of the early and late genes. The NCCRs of most MCPyV isolates are quasi identical to the reference strain MCC350. However, the NCCR of MCPyV isolated from healthy skin (strain 16b), feces (strain HB039C), and a Kaposi's sarcoma sample (strain TKS) is ~20 bp longer due to a repeated sequence. The aim of this study was to compare the activity of the MCC350 and 16b strains and to monitor the effect of full-length and truncated LTAg. Transient transfection studies in HEK293 cells with a luciferase reporter plasmid demonstrated that the early 16b is stronger than the early MCC350, while their late promoters have similar activity. Full-length as well as truncated large T-antigen repressed early MCC350 and 16b promoter activity.

P37

MotifLab – a regulatory sequence analysis workbench

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MotifLab is a general workbench for analyzing regulatory sequence regions and discovering transcription factor binding sites and cis-regulatory modules. MotifLab can make use of well-established motif discovery programs to predict novel binding sites or scan DNA sequences for matches to known binding motifs. Additional information can be incorporated into the analysis to filter out likely false predictions, including information about e.g. gene expression, epigenetic marks, phylogenetic conservation, cooperative binding partners and identified ChIP-seq peaks. The latest version of MotifLab also has support for long-range chromatin interaction data which allows gene promoters to be linked to their distal enhancers for a more complete picture of the genomic regions involved in regulation. Users can record multi-step analyses into protocol scripts that can be rerun as automatic workflows on other datasets, and a host of interactive tools encourage visual exploration of data in the sophisticated internal sequence browser.

P38

Comprehensive detection and classification of circular RNAs in starlet sea anemone

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Recent studies reveal that circular RNAs (circRNAs) are abundant, stable and ubiquitous molecules in eucaryotes representing a class of noncoding RNAs rather than byproducts of splicing as thought previously. We use existing computational tools to predict circular RNAs in total RNA-Seq libraries of two developmental stages of *Nematostella vectensis* (Starlet sea anemone). We compare the genomic features of circRNAs across several species and characterize the deeply conserved ones.

P39

META-pipe – Pipeline annotation, analysis and visualization of metagenomic data

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Sequenced DNA from environmental samples is becoming increasingly abundant within the different fields of biology. The introduction of next generation sequencing technology, generating a vast amount of metagenomic data, requires not only extensive amounts of computation power, but also novel software to process and analyze data on a much larger scale than before. Here we introduce Meta-pipe, a pipeline for storage, analysis and visualization of metagenomic data. Meta-pipe runs on the supercomputer Stallo, and is integrated with Galaxy, an open web-based workflow manager. The modular annotation pipeline Meta-pipe provides a framework to include any command line prediction or annotation tool, running the analyzes in parallel to reduce runtime drastically. Meta-pipe offers a number of attractive analysis outputs, among them a tabular output imported to METAREP, a web based open source tool for visualization. METAREP allows viewing, querying, browsing and comparing datasets with built in tools such as statistical tests, multidimensional scaling and heatmaps. Meta-pipe is currently in development, where functionality is added as we see fit. Expected impacts will be easy access to, and more efficient exploration of metagenomic data for new applications in biotechnology.

P40

Practical Applications of Informatics Tools to Identify Drug Targets for Novel Compounds from Bio- and Chemoprospecting

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A relatively low-risk strategy of incrementally improving known binders of conventional drug targets dominated late 20th century drug discovery. In this century, good generic drugs, the natural development of resistance to some conventional therapies, and modern research into disease mechanisms have shifted much of the focus to new targets. However, it is often observed that even detailed structural knowledge of targets does not enable rapid drug design, due to target flexibilities and the subtleties of target ligand interactions, and *in vitro* effects often do not translate to *in vivo* activities. Thus, bio- and chemoprospecting approaches using cell based assays and phenotypical screening have found renewed acceptance in the pursuit of new therapeutics. Successful hit finding in these two approaches often leads to difficult target-finding challenges. Fortunately, the large and growing databases of compound properties, including especially target-ligand interactions, may be mined to form good hypotheses to explain bioactivities and facilitate progress into target-based design cycles. We present here examples of uses of informatics tools, especially based on similarity analyses on biological targets, physicochemical descriptors of compounds, compound-target interactions and cell-based or phenotypic activity patterns, to guide the search for mechanisms underlying the observed bioactivities.

P41

Next generation deep sequencing of rat liver sinusoidal endothelial cell and Kupffer cell transcriptomes suggests functional complementarity

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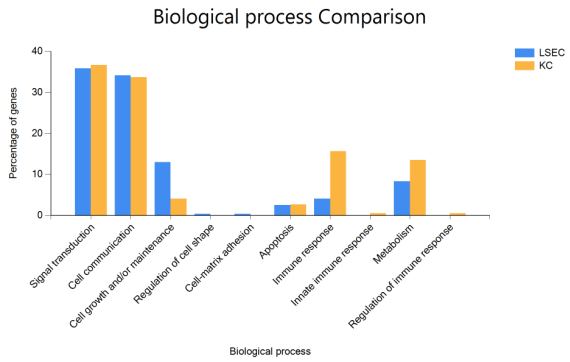
Liver sinusoidal endothelial cells (LSECs) and Kupffer cells (KCs) have important roles in liver homeostasis and host defense. LSECs form the fenestrated lining of the hepatic sinusoids and regulate the traffic of cells and molecules between luminal blood and parenchymal cells. KCs, also present in the sinusoids, are professional phagocytes. Both cells express distinct sets of scavenger receptors and demonstrate efficient receptor-mediated endocytosis both in vivo and in vitro. Together they form an effective waste-clearance system for exogenous and physiological substances, in which LSECs endocytose soluble molecules and nanoparticles, including virus, and KCs take care of bacteria, and dead/dying cells. The present study is an endeavor to acquire more evidences illustrative of the characteristics and functions of LSECs and KCs using high throughput RNA-Seq techniques (Ion Torrent). The study detected 8963 genes with expression above 5 RPKM. Among those, 648 and 465 genes are differentially expressed in LSECs and KCs.

Most of the differentially expressed genes of LSEC are genes involved in development and maintenance of blood vasculatures whereas those of KCs are involved in development and regulation of the immune system (Figure1).



P42

The structure of a dual-specificity tyrosine phosphorylation-regulated kinase 1A-PKC412 complex reveals disulfide-bridge formation with the anomalous catalytic loop HRD (HCD) cysteine

Marina Alexeeva, Espen Åberg, Richard A. Engh and Ulli Rothweiler

Dual-specificity tyrosine phosphorylation-regulated kinase 1A (DYRK1A) is a protein kinase associated with neuronal development and brain physiology. The DYRK kinases are very unusual with respect to the sequence of the catalytic loop, in which the otherwise highly conserved arginine of the HRD motif is replaced by a cysteine. This replacement, along with the proximity of a potential disulfide-bridge partner from the activation segment, implies a potential for redox control of DYRK family activities. Here, the crystal structure of DYRK1A bound to PKC412 is reported, showing the formation of the disulfide bridge and associated conformational changes of the activation loop. The DYRK kinases represent emerging drug targets for several neurological diseases as well as cancer. The observation of distinct activation states may impact strategies for drug targeting. In addition, the characterization of PKC412 binding offers new insights for DYRK inhibitor discovery.

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P43

The 5-hydroxymethylcytosine Level Increases During Rat Sertoli Cell Differentiation

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The role of the DNA base modification 5-hydroxymethylcytosine (5-hmC) is not yet fully elucidated. There is evidence that it regulates the expression of genes and that it can be an intermediate in the demethylation of 5-methylcytosine. Sertoli cells are nurse cells present in the seminiferous tubule that create and maintain the spermatogonial stem cell niche and support the developing germ cell through spermatogenesis. The Sertoli cells supply the germ cells with nutrients, hormones and other chemicals and are required for male sexual development. Using mass spectrometry we found that the global level of 5-hmC increases significantly in rat Sertoli cells during the maturation of the testis. This shift in 5-hmC level is concurrent with the cessation of Sertoli cell proliferation and beginning of its commitment to nurture the developing germ cells to mature sperm. These results were confirmed by quantitative immunofluorescence assays, measuring the relative increase in 5-hmC in testis sections throughout puberty. The change in 5-hmC abundance during Sertoli cell differentiation offers further insight into the potential role of 5-hmC as gene expression regulator.

P44

Confocal microscopy studies of human stem cell growth on dental implants

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Confocal microscopy can provide a wealth of information about cell health, location and differentiation, as well as protein dynamics and localization when used at higher spatial resolution. However samples such as cell culture monolayers are more amenable to confocal microscopy than others such as 3D cultures or those involving opaque cell scaffold substances. At the Institute of Clinical Dentistry we are developing methods for imaging human mesenchymal stem cells (HMSCs) colonizing dental implant surfaces such as titanium coins, hydroxyapatite, and cleaned sterilized human dentin. We find that the Leica SP8 confocal microscope can be used in reflectance mode to provide good images of the surface of the opaque scaffolds, but the detection of cells growing on the dentin surface is challenging due to autofluorescence from dentin collagen. HMSCs growing on titanium coins can be imaged after staining with acridine orange or DAPI, whereas far-red fluorophores such as DRAQ5 may be more appropriate for dentin-containing samples.

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