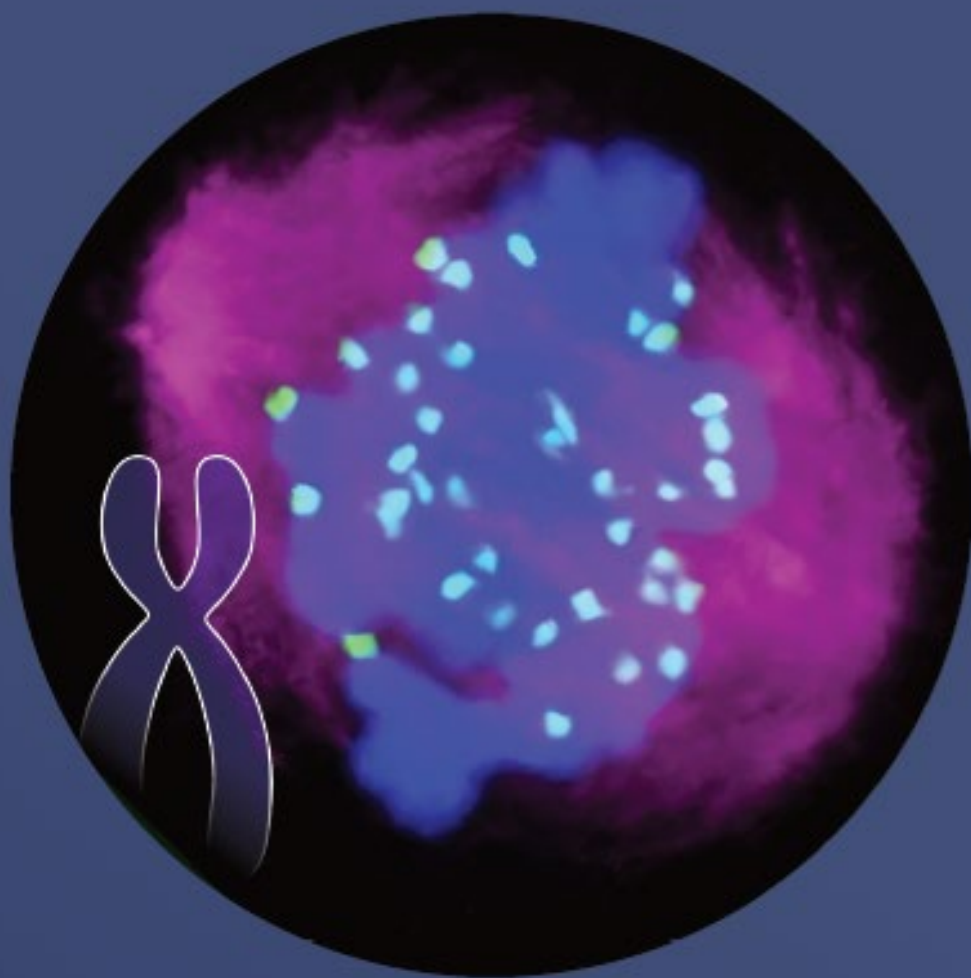


Centre for Embryology and Healthy Development

CRESCO



| 20
25
ANNUAL
REPORT

Front page design: Ellen Tenstad, Science Shaped
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Photos in
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UNIVERSITY
OF OSLO

Our Vision: Understand Healthy Embryo Development Across Species

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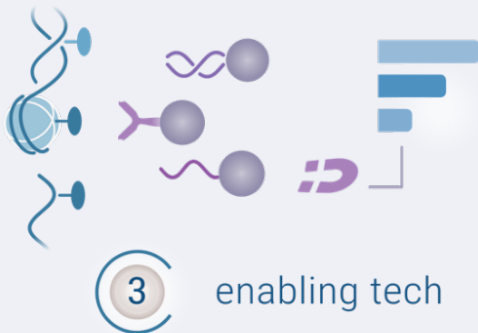
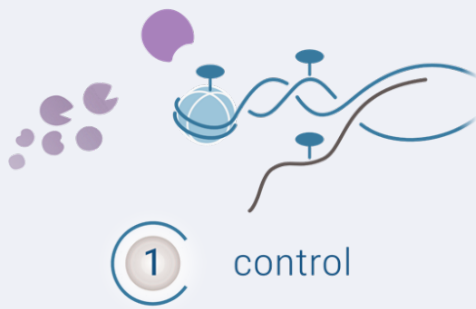
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CRESCO means "spring from"

HEALTH in the earliest stages of life

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The CRESCO PIs in Copenhagen. Back row, from the left: Mads Lerdrup, Elisabeth Kommisrud, Hilde Nilsen, Peter Fedorcsak, Arne Klungland and John Arne Dahl. Front row, from the left: Lorena Arranz, Magnar Bjørås and Pål Falnes.
Photo: Guro Flor Lien, UiO

CRESCO

Centre for Embryology and Healthy Development

Health in the earliest stage of life

CRESCO is a team of researchers that combine complementary expertise on epigenetic and epitranscriptomic modifications, DNA repair and genome (in)stability, single-cell and single-nucleotide analysis, embryology and healthy development.

Organization:

CRESCO, Centre for Embryology and Healthy Development, was founded by the Norwegian Research Council in 2023. The Department of Clinical Medicine, Medical Faculty at the University of Oslo (UiO) is our host institution. Consortium agreements regulate cooperation connecting UiO with Oslo University Hospital (OUS), University of Inland Norway (INN) and Copenhagen University (UCPH). Most of the activity at CRESCO is co-localised at SINTEF, Forskningsveien 1. In the beginning of 2027, we will move to the new Life Science Building. We consist of 9 research groups with complementary expertise.

Group leaders:

Arne Klungland, UiO and OUS

Lorena Arranz, UiO and OUS

Peter Fedorcsak, OUS and UiO

Elisabeth Kommisrud, INN

John Arne Dahl, OUS

Magnar Bjørås, NTNU and OUS

Hilde Loge Nilsen, OUS and UiO

Pål Falnes, UiO

Mads Lerdrup, UCPH

Management:

Arne Klungland, Centre Director 2023-2028

Lorena Arranz, Centre Director 2028-2033

Guro Flor Lien, Centre Manager

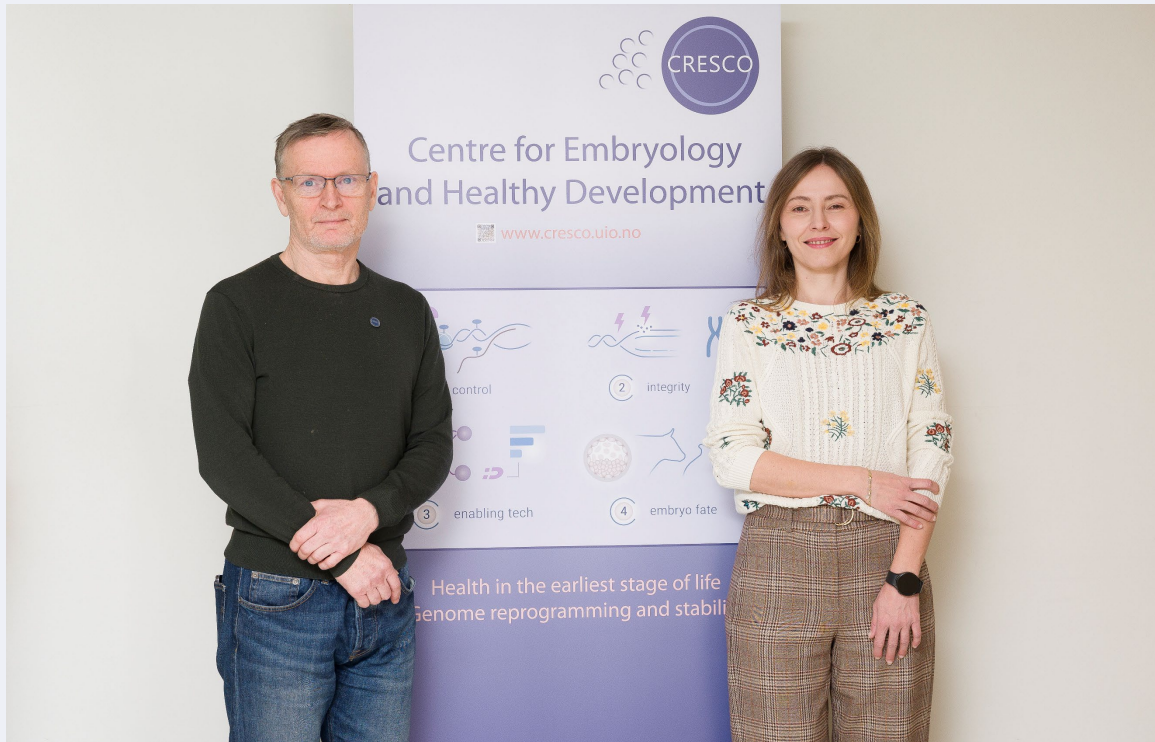


Arne Klungland, Guro Flor Lien and Lorena Arranz.
Photo: Birgit Solhaug, UiO



The move-in process for the Life Science Building is planned to begin in 2026, with a gradual phase-in towards 2027. The Life Science Building will serve as a shared facility for leading university and hospital environments in life sciences. The building will feature flexible solutions for research, diagnostics, innovation, and education, gathered in one site. It will foster extensive interdisciplinary collaboration, house technologically advanced equipment, and support the development of outstanding research environments across disciplines.

ABOUT CRESCO



Centre Director Arne Klungland and Deputy Director Lorena Arranz.

Photo: Birgit Solhaug, UiO

Some of the most profound events in the life of an organism, with far-reaching consequences for development and health, happen during the very early stages of existence. These include completion of meiosis, merging of parental genomes at fertilization, and reprogramming of chromatin during early embryo development.

CRESCO combines matching expertise on epigenetic and epitranscriptomic modifications, DNA repair and genome (in)stability, single-cell and single-nucleotide analysis, embryology and healthy development.

Despite its evolutionary conservation, human conception is associated with chromosome errors and an unexpectedly high frequency of pregnancy loss and congenital disorders.

In CRESCO, we propose to use cutting-edge technology to study in exquisite detail the roles of dynamic and reversible epigenetic

and epitranscriptomic modifications in oocyte and the early embryo, including their functions in genome stability, chromosome segregation and retrotransposon activity.

Our overarching goal is to understand the role of epigenetic and epitranscriptomic information in the passing of life from one generation to the next in the One Health perspective.

We are very grateful for the generous contribution to our research from the Norwegian Research Council (RCN), the Norwegian Cancer Society and the South-Eastern Norway Regional Health Authority that provide funds for several of our projects. Also, our hosts, University of Oslo, Oslo University Hospital and the University of Inland Norway, provide additional funding and infrastructures as well as smooth accounting and administrative support. We are looking very much forward to the years to come!

Arne Klungland, Director

Lorena Arranz, Deputy Director

CRESCO BOARD



The CRESCO Board photographed at our first board meeting. From left to right: Dag Kvale, Andreas Matussek, Lorena Arranz, Arne Klungland, Melinka Butenko, Marte Tøndel and Marit Lieng. Photo: Guro Flor Lien, UiO

CRESCO Board

Dag Kvale, Head of the Board, is Head of the Institute of Clinical Medicine at The University of Oslo (UiO) as well as a Professor at Oslo University Hospital (OUS), Dept. of Infectious Diseases.

Andreas Matussek is Head of the Division of Laboratory Medicine at OUS in addition to being a Professor at UiO.

Marit Lieng is the Director of Medical Science, Research and Education at OUS and a Professor at the Women's Division at UiO.

Melinka Butenko is a Professor at the Section for Genetics and Evolutionary Biology and Deputy Head of Department at IBV, UiO.

Marte Tøndel is the Research Director at University of Inland Norway.

Together, this team represents most of the institutions involved in the centre.

We want to express our gratitude to all of you for taking on this task!

SCIENTIFIC ADVISORY BOARD



Our SAB photographed during their first visit to CRESCO. Prof. Rob Klose was unfortunately unable to attend. From left to right: Professor Yang Shi, Prof. Nadia Mercader Huber, Prof. Primo Schär, Centre Director Arne Klungland and Deputy Centre Director Lorena Arranz. Photo: Guro Flor Lien, UiO

Scientific Advisory Board (SAB)

Prof. Primo Schär

Vice-Director of Research and Professor at the University of Basel. Prof. Schär's research delves into biological processes that influence genome plasticity, ensuring stability of genetic and epigenetic codes of cell identity.

Prof. Nadia Mercader Huber

Professor at the Institute of Anatomy and Head of Section for Developmental Biology and Regeneration at the Universität Bern. Her research explores cardiac regeneration in zebrafish, offering groundbreaking insights into regenerative biology.

Prof. Yang Shi

Professor of Epigenetics at the University of Oxford. His work focuses on identifying epigenetic regulators in cancer and translating these findings into innovative therapeutic strategies.

Prof. Rob Klose

Professor of Epigenetic Regulation of Chromatin Function at the University of Oxford. The Klose Lab is dedicated to understanding the influence of chromatin and epigenetic processes on gene expression.

We are grateful for the valuable insights and guidance from our SAB and look forward to continued collaboration!



Research Group Presentations



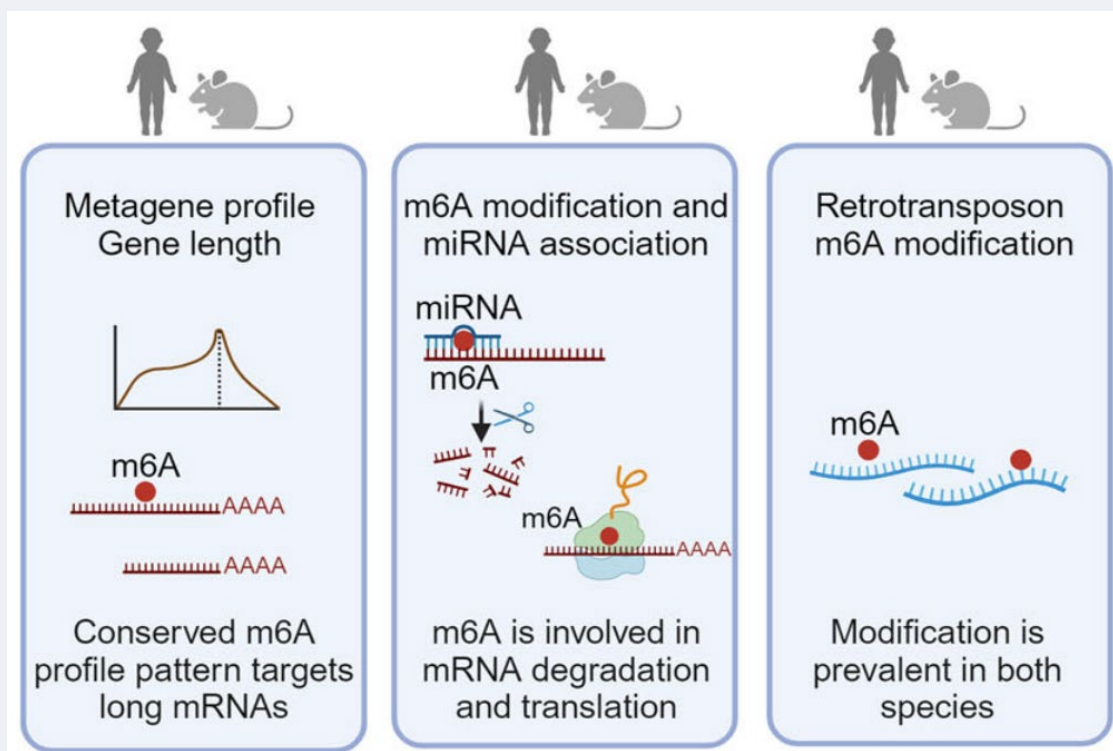
The Klungland group. Front row from left: Xuechen Wu, Ngan Huynh Bao, Felicia Kristiansen, Sophie Bresson and Aylin Cengiz. Back row from left: Yesim Bilmez, Sonia Perez, Yanjiao Li, Gaute Nesse, Arne Klungland and Dongjie Zhou. Photo: Guro Flor Lien, UiO

Klungland Group

Dynamic Gene Regulation

We aim to gain new insights into how molecular mechanisms of epigenetic and epitranscriptomic gene regulation contribute to meiosis and the development of a healthy embryo.





We have now completed the first studies on the RNA m6A methylome landscape during mouse and human oocyte-to-embryo transition, OET (Wang et al., 2024, Li et al., 2025).

Research focus:

While the core building blocks of our DNA, RNA and proteins were characterized decades ago, recent research has identified a remarkable diversity of chemical modifications that adapt the coding properties of bases in DNA and RNA and the activity and stability of proteins. The dynamic potential of many such chemical modifications provides a reversible gene-regulation mechanism that can also act on environmental signals. This level of gene regulation allows for reprogramming that is crucial during meiosis and early embryo development.

Our aim is to identify writers, readers and erasers of such marks to gain mechanistic understanding of their biological impact during meiosis and preimplantation embryo development.

We are particularly interested in the reprogramming of the human genome in meiosis and in the preimplantation embryo.

Current Projects:

- Identify molecular mechanisms underlying coding properties of methylated adenines in mRNA. Investigate gene-regulation during meiosis and maturation of sperm and egg.
- Study epigenetic and epitranscriptomic gene regulation during the maternal to zygotic transition. Gain novel mechanistic insight on epigenetic and epitranscriptomic gene regulation of cancer.
- Investigate how active matter principles operate during early mouse development (GENESIS convergence).

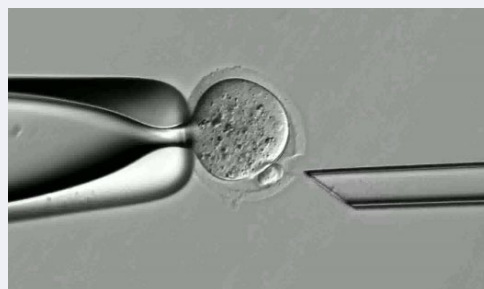
Highlights 2025:

- Li Y#, Wang Y#, Cengiz#.... Dahl JA*, Greggains G*, Au KF*, Klungland A* The RNA m6A landscape during human oocyte-to-embryo transition. EMBO J 2025, 44:4150–4180.
- Funding for new convergence environment, GENESIS. FRIPRO funding for Yanjiao Li to study the "Metabolism-Epitranscriptome Crosstalk: Novel Regulation in Embryo Development". AK receives the EMBO member diploma.

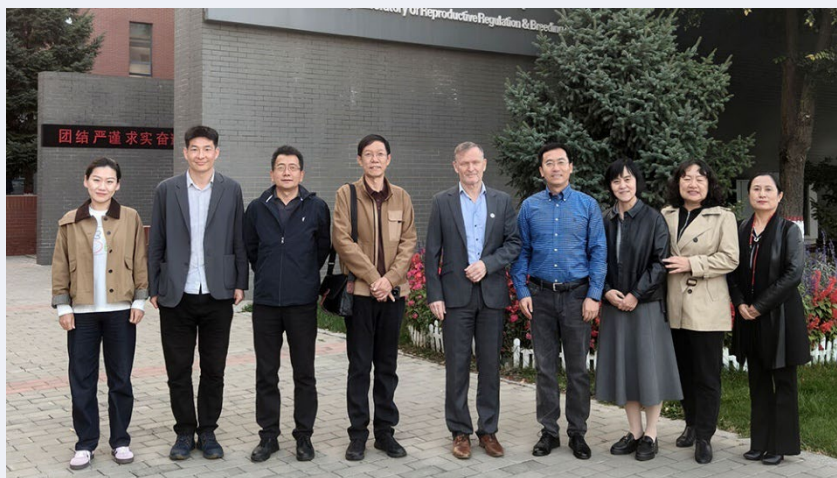
Everyday life in the group

Our everyday life in the laboratory focus around timely breeding, small-scale isolation and analysis of RNA, DNA and proteins from single oocytes or preimplantations embryos. Oocytes and embryos are also examined with advanced light microscopy to correlate (epi)genetic reprogramming with phenotypic traits and detailed localization on proteins and DNA during divisions. In collaboration with Reproductive Medicine at Oslo University Hospital and University of Inland Norway (both being active partners of CRESCO) such studies are also transferred to humans and livestock animals with a One-Health perspective. Additionally, we generate novel mutant models to get insight on the role of single genes in the reprogramming of meiosis and early preimplantation embryo.

We can now dissect single cells, including polar bodies) with the CRESCO funded system for laser-assisted microinjection and manipulation – and analyse genetic, epigenetic and epitranscriptomic modifications in a single cell. In laser-assisted polar body biopsy, a laser is used to create a small opening in the zona pellucida surrounding the oocyte. Then, a fine pipette is introduced through this opening to gently remove the polar body, which can then be analysed molecularly or genetically. This enables insight on reprogramming in single oocytes, preimplantation embryos as well as on cancer heterogeneity. →



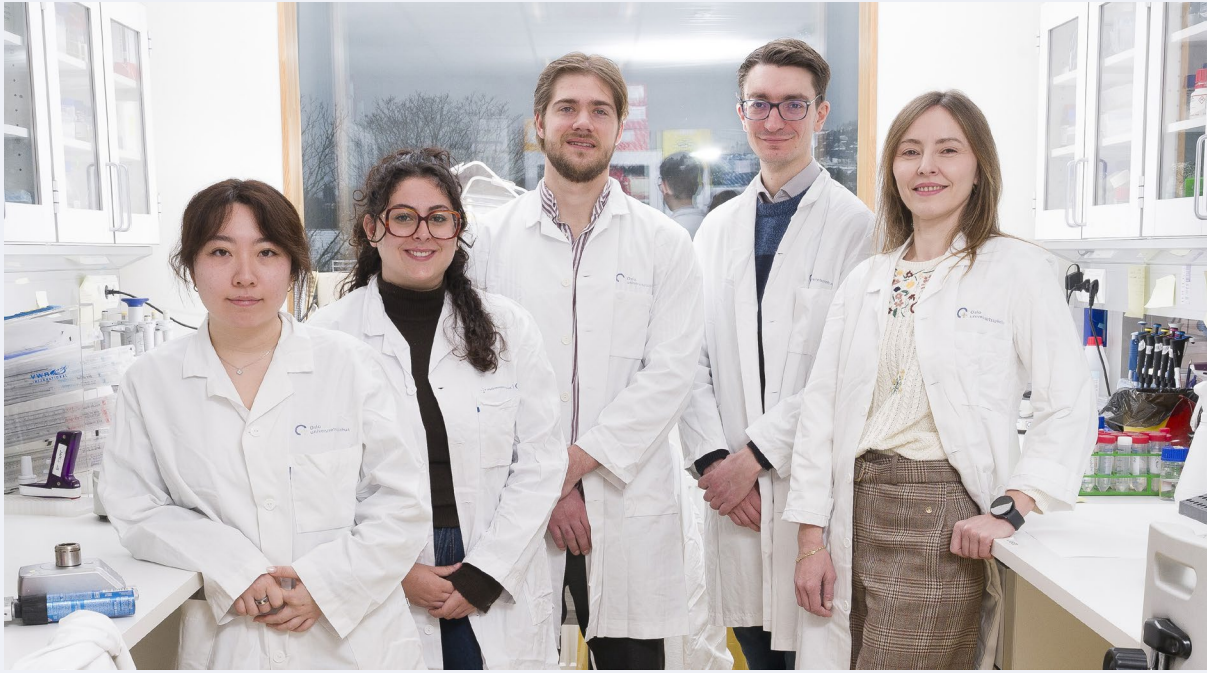
Picture with Arne Klungland in the middle and Yanjiao Li second from left, visiting the College of Life Sciences. On Arnes left hand side is Prof Cheng-Guang Liang, the MSc supervisor of Yanjiao Li, that is famous for his research on mammalian oocyte maturation and early embryo development, including chromosome aneuploidy related human infertility and disease. →



AK is interviewed by EMBO on how his interest in research on genetics started and developed. He also gives some advice for the young researchers.

←





The Arranz group has 5 members (here in the lab at Oslo University Hospital). From left: Yimeng Chen, Daniela Cabrera-Henríquez, Marcel Heugel, Vincent Cuminetti and Lorena Arranz. Photo: Birgit Solhaug, UiO.

Arranz Group

Stem cells Ageing & Cancer

We aim at understanding the mechanisms of stem cell malignant transformation in the context of the stem cell niche.





Vincent and Lorena examining images of bone marrow stem cell niches. Photo: Åsne Rambøl Hillestad, UiO

Research focus:

Stem cells self-renew and provide the source for replenishing mature cells in the organism throughout its life. These fascinating abilities ensure tissue regeneration but must be finely tuned regulated as their imbalance may contribute to failure in development, cancer and ageing.

Our research interest focuses on the processes that control stem cell behaviour. We aim at understanding the mechanisms of stem cell malignant transformation, using an integrative perspective that considers cell-autonomous alterations in the stem cell and remodelling of the stem cell niche.

Our goal is the identification of novel and efficient therapeutic targets of clinical interest that will improve survival rates and quality of life in patients.

Current Projects:

- Stem Cell Metabolic Dysfunction in Myeloid Leukaemia and its Therapeutic Targeting.
- Exploring the transformation potential of haematopoietic stem cells under niche pressure, and its therapeutic targeting.
- Imaging Ageing Endothelium at the nanoscale.
- NEUROTARGET: The nervous system as a druggable vulnerability in myeloid cancers.

Highlights 2025:

- Papers published in Nat Commun and Exp Hematol Oncol.
- Vincent received the Kick-off grant award at the European Hematology Association (EHA2025) congress in Milan.
- Marcel spent 1 month at Josep Carreras Leukaemia Research Institute funded by CRESCO.
- Francisca Ferrer-Marín spent 6 months in our lab funded by the Spanish Health Authorities.
- Marcel, Yimeng, Vincent and Lorena presented work at various venues.

Everyday life in the group

Our everyday life in the laboratory focus around monitoring animals, stem cell isolation and analyses of RNA, DNA and proteins. We also examine stem cells and their niches with advanced microscopy and spectral flow cytometry and complete their comprehensive characterization under health or disease with ex vivo and in vivo functional studies, including gold standard methods such as transplantation. In addition, we generate novel conditional and inducible mutant models to get refined insights into the role of single genes in selected cell types and conditions. Our on-going collaborations with the Department of Hematology at the University Hospital of North Norway and at the Hospital General Universitario Morales Meseguer (Spain), as well as our newly established network within the Department of Hematology at Oslo University Hospital, Akershus University Hospital and Fundación Jiménez Díaz University Hospital (Spain) allow us to explore the clinical impact of our findings and the potential of their therapeutic targeting.

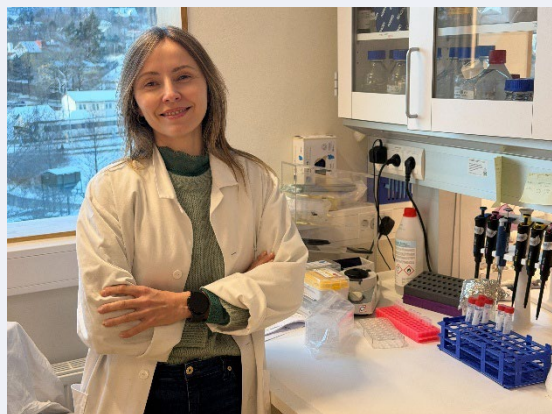


← Vincent receiving the Kick-off grant award at the EHA2025 congress in Milan (Italy). Photo: EHA.



↑ Yimeng and Lorena gave presentations at the 3rd Plenary Meeting of the ImAge-D MSCA-DN in Krakow (Poland). Photo: ImAge-D.

→ Our new project NEUROTARGET was featured by Blodkreftforeningen: Photo: Vincent Cuminetti.



↑ Our team members are active members of the community locally, nationally and internationally. Here, Yimeng participating in the panel discussion “PhD success in a changing research landscape” at the NorDoc PhD Summer School. Photo: Pascal Madeleine.



15 members of the Nilsen group: Nicola Montaldo, Veronica Morales, Petter Holland, Lisa Hubers, Jon Lærdal, Qindong Zhang, Yohan Lefol, Luisa Luna, Hilde Nilsen, Lene Alsøe, Francisco Naranjo, Alexander Myhr Skjetne, Laura Vinklerová, Torbjørn Rognes and Solveig Osnes Lund. Photo: Vincent Cuminetti

Nilsen Group

Genome instability in aging and disease

We study how DNA repair and genome stability maintain healthy cells and animals throughout their natural lifespan.

DNA repair enzymes have a unique ability to recognize rare chemical modifications in DNA and RNA. Some of these modifications are regulatory marks, others are damaged bases. We study how DNA repair proteins distinguish regulatory marks from DNA damage, and how modifications in RNA and DNA affect cells and animals throughout their lifespan.



Research focus:

Chemically modified nucleic acid bases are sources of genomic instability and mutations but may also regulate gene expression as epigenetic or epitranscriptomic modifications.

Depending on the cellular context, they can have vastly diverse impacts on cells, from mutagenesis or cytotoxicity to changing cell fate by regulating chromatin organisation and gene expression. The specificity and selectivity of the recognition of these modified bases relies on DNA glycosylases, which acts as DNA damage, or more correctly, as sensors of modified bases for the base excision repair pathway.

Our aim is to understand how DNA repair enzymes contribute to genomic regulation across the entire lifespan - from embryo to old age.

We study how ageing leads to a loss of coordination within the Base Excision repair pathway, which is essential for genomic integrity in mitochondria and nuclear DNA, protect us from cancer and neurodegeneration.

Current Projects:

- Genome stability in healthy aging.
- Genome instability as a driver of tumorigenesis and as a determinant of cancer therapy response.
- Genome instability in neurodegenerative diseases.

- Mitochondrial genome maintenance in Parkinson's Disease.
- DNA repair dependent chromatin dynamics as a basis of gene regulation during development and aging.

Highlights for 2025

- Nicola P Montaldo won a young research talent grant from the Research Council of Norway.
- Nicola P Montaldo won SPARK innovator award.
- Anwer D, **Montaldo NP, Nilsen HL, Polster A.** (2025) Longitudinal Assessment of DNA Repair Signature Trajectory in Prodromal versus Established Parkinsons Disease. *NPJ Parkinsons Disease*, 11(1):349. doi: 10.1038/s41531-025-01194-7.
- Rudolfova N, **Skjetne AM, Montaldo NP, Visnes T, Nilsen HL, Michel M** (2025) What's in a Name? Rethinking SMUG1 in Genome Maintenance. *NAR Cancer*. Dec 12;7(4):zcaf050. doi: 10.1093/narcan/zcaf050
- **Bordin DL, Lefol Y, Largartos-Donate M, Montaldo NP, Rolseth V, Tekin NB, Lirussi, L, Neurather C, Aman Y, Suganthan R, Sarno S, Zhang T, Alsøe L, Wang J, Bjørås M, Wong G and Nilsen HL.** (2025) *Nucleic Acid Research*, 53 (14), gkaf722, <https://doi.org/10.1093/nar/gkaf722>
- Zhang J, Wang H-L, Lautrup S, **Nilsen HL, Treebak JT, Watne LO, Selbæk G, Wu LE, Omland T, Pirinen E, Cheung TC, Wang J, Ziegler M, Tysnes OB, Zapata-Pérez R, Bruzzone S, Canto C, Deleidi M, Janssens GE, Houtkooper RH, Scheibye-Knudsen M, Koshizaka M, Yokote K, Verdin E, Bohr VA, Tzoulis C, Sinclair DA, Fang EF** (2025) Emerging strategies, applications, and challenges of targeting NAD⁺ in the clinic. *Nature Aging* 9th Sept, 10.1038/s43587-025-00947-6

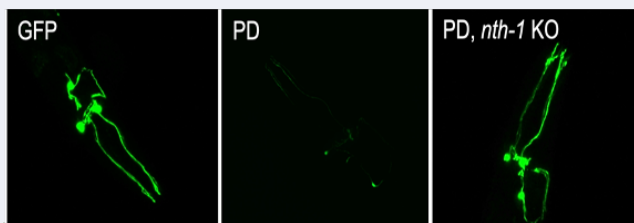
Everyday life in the group

Although our research focus is centred around DNA repair, and DNA-glycosylases in particular, we use many different experimental approaches.

We use the nematode *C. elegans* as a model system to understand how DNA repair enzymes promote healthy aging in general and how our neurons are protected during aging.

A grand challenge that we aim to tackle together with CRESCO colleagues is to map novel DNA modifications, including their writers, readers, and erases across lifespan. This work requires close collaborations between molecular biologists and bioinformaticians, and single cell sequencing is an important technology used in these projects.

→ Nicola P. Montaldo receiving the SPARK award. The spark team Zoe De Silva, Lisa Huber, Hilde Loge Nilsen, Alexander Myhr Skjetne, Nicola Montaldo, and Anders Fugelli. Francisco Naranjo was not present at the award ceremony. Photo: Jarli&Jordan/UiO



← We model human disease in the nematode *C. elegans* to learn how nuclear and mitochondrial DNA repair affect aging and age-related diseases. Here we show a *C. elegans* model of Parkinson's Disease (PD). Green Fluorescent Protein labels dopaminergic neurons so that we can monitor them inside a living animal throughout their lifespan. Using this system we have been able to show that Base Excision Repair can be a source of the genome instability (both mitochondrial and nuclear) is a cause of neurodegeneration under physiological aging. Over the last year Nico and his team have generated a human midbrain organoid system that we will use to study these mechanisms further.

Photo: Francisco Naranjo and Lisa Huber



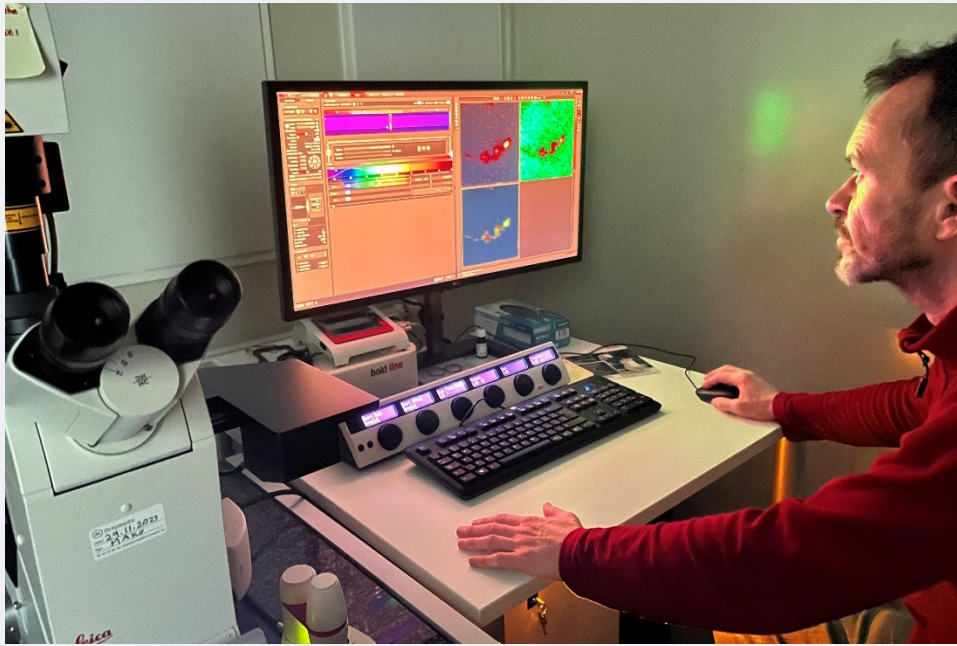
The Kommisrud group has 13 members Birgitte Narud, Teklu T. Zeremichael, Anne Hege Alm-Kristiansen, Cassandra Lax, Elina Holub, Frøydis D. Myromslien, Karina H. Johansen, Reina Jochems, Elisabeth Kommisrud, Valentina Krivenjeva, Asmita Shrestha, Erwan Yann Delbarre and Joanna Bremer. Photo: INN

Kommisrud Group

Biotech Livestock Repro

We aim to bridge the gap between basic science and practical livestock breeding applications through innovative embryology and cryopreservation approaches.





Confocal microscopy images of bovine immunostained blastocyst.
On the screen from left to right: DNA, immunostaining, merged.

Research focus:

Our research focuses on reproductive biology across livestock and aquaculture species, with emphasis on oocyte maturation, fertilization, and early embryo development. We are particularly interested in elucidating epigenetic and transcriptomic differences between gametes from individuals and between assisted reproductive technologies. Through PhD and postdoctoral projects, we apply e.g. metabolomics, epigenetics, and transcriptomics to uncover molecular mechanisms governing gamete biology and embryo development across species.

Our goal is to enhance reproductive success in livestock and aquaculture by identifying fertility biomarkers and understanding gamete biology. As fundamental pathways governing gamete development and fertilization are highly conserved across vertebrates, our findings in animal models could be expected to also contribute to a broader understanding of human fertility.

Current Projects:

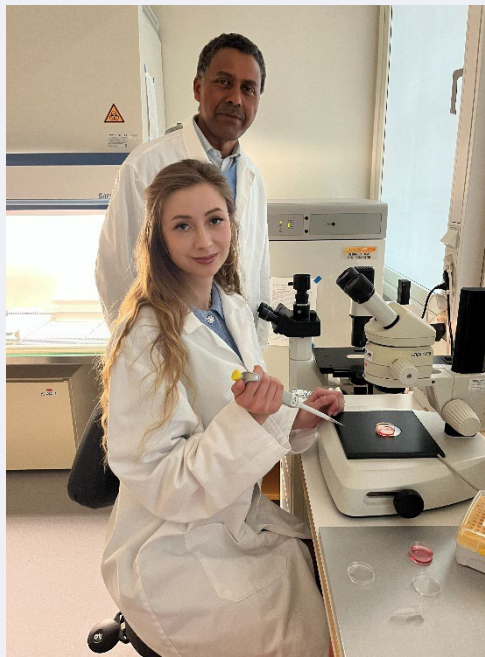
- AI and machine learning to explore sexual behaviour and maturity in beef bulls.
- Exploring egg quality in Arctic charr by AI.
- Bovine oocyte maturation times before IVF and their influence on embryo quality and survival.
- Exploring DNA epigenetic marks on maturing bovine and porcine oocytes and developing embryos.
- Infertility in beef bulls caused by a single-nucleotide deletion.

Highlights 2025:

- PhD dissertation by Asmita Shrestha on biomarkers for porcine sexual maturity.
- Elina Holub enrolled in the PhD program to study in vitro porcine embryo production.
- The new IVF lab for porcine embryo research operative.
- Presentations at CRESCO retreat at Hurdalsjøen.
- New partner TYR (beef cattle) in the Zygote project.
- Two new research projects to the group.

Everyday life in the group 🧪🔬

Analysis and characterization of sperm cells, oocytes and embryos form the core of our laboratory work. Flowcytometry and CASA analyses for sperm quality parameters are routinely performed. In our IVF laboratories we perform weekly experiments, starting with collection of ovaries at the slaughterhouse. Oocytes and embryos are examined by fluorescence and confocal microcopy and different staining procedures. In collaboration with the Bjørås, Klungland and Dahl groups we produce and prepare oocytes and embryos for comparative studies on epigenetics and epitranscriptomics across species. Our group also collect data in the field, e.g. on fish farms and at breeding companies premises.



Left: Teklu T. Zeremichael collecting oocytes from bovine ovaries obtained at the slaughterhouse.

Right: Teklu together with Elina Holub in the IVF lab.



↑ Meeting with scientist and industry partners (Geno, Norsvin, SpermVital, TYR and Klosser) in the Zygote project.



↑ Scrotal photoshoot at TYR's barn for beef bulls using everyone's familiar iPhone! Joanna Bremer and Team Bull's AI.



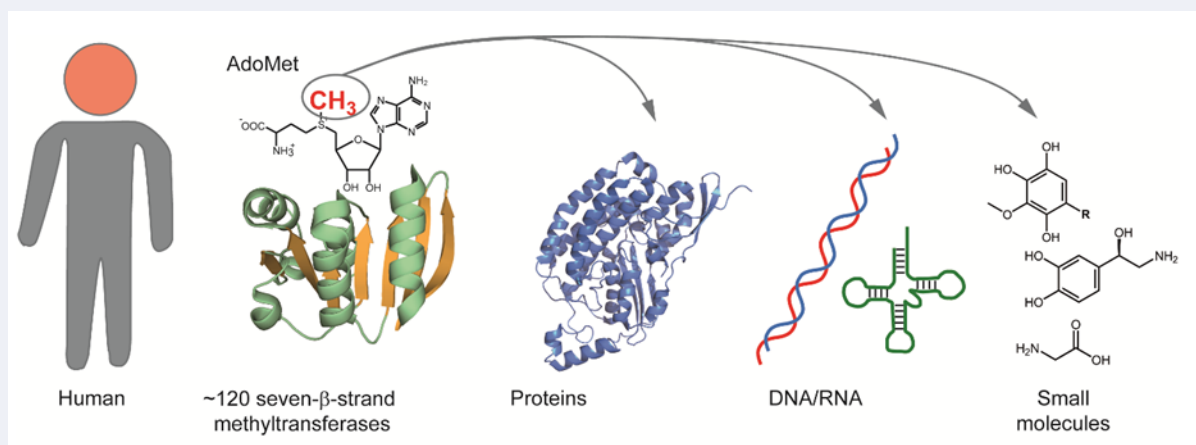
The Falnes group works closely with the group of Dr. Erna Davydova, who is also affiliated with CRESCO. The picture shows the two groups. From left: Jedrzej Malecki, Teqwa Zerouga, Pål Falnes, Klara Vladimir, Carmen Herrera, Marthe Lindahl Karlsen, Juan Jesús Martínez Gómez, Jawairia Kiran Chaudhry, Erna Davydova, Naveen Parmar. Photo: Åslaug Brynildsen, UiO.

Falnes Group

Biological Methylation

Through identifying and characterizing the responsible enzymes, we aim at uncovering the biological roles of methylations on nucleic acids and proteins.





Numerous methyltransferase enzymes target a wide range of biomolecules in human cells. From: Falnes, PØ. *Nucleic Acids Res.* 2024, 52:11423-11441.

Research focus:

The nucleic acids (DNA and RNA) and proteins in our body are optimized and regulated through the attachment of methyl groups. A prime example of this is how methylation of DNA and histone proteins are important epigenetic regulators of many biological processes, including embryo development. The methylations are introduced by a number of highly specific "methyltransferase" enzymes. A strong focus of our group has been to identify and characterize methyltransferases that target non-histone proteins and RNA. This enables more focused studies on the biological significance of the methylations, and we also study the role of some of these methylations in the context of cancer. Moreover, we are interested in identifying proteins that interact with and "interpret" the methylations – so-called readers, as well as demethylases that act as erasers of the methylations.

Our aim is to identify mechanisms by which methylations on proteins and nucleic acids regulate and optimize key processes in human cells

Current Projects:

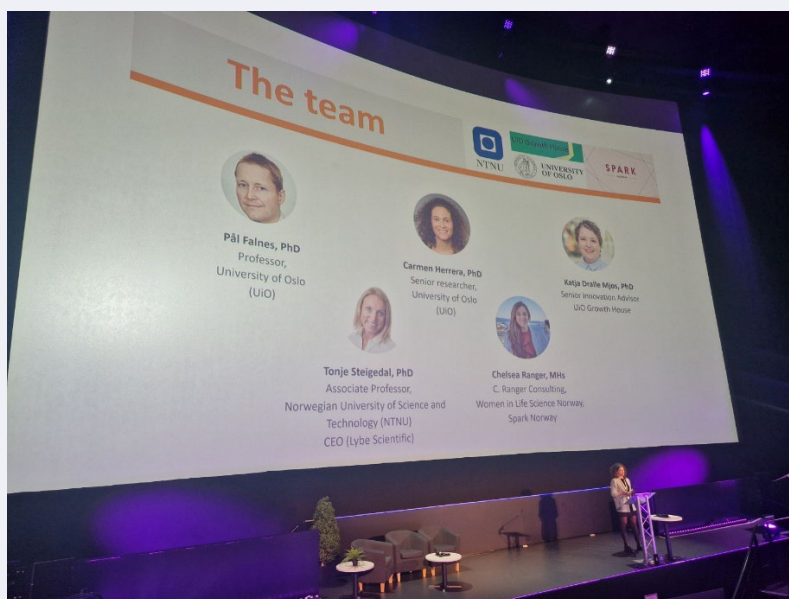
- Investigating the molecular mechanisms and functional significance of protein histidine methylation.
- Identification of novel methyltransferases, with a particular focus on protein methylation in muscle.
- Exploring the role of the methyltransferase METTL13 in cancer.
- Uncovering enzymes/proteins involved in tRNA modification.

Highlights 2025:

- Carmen was awarded grants both from the UiO Growth House and the Research Council of Norway, supporting cancer innovation activities based on the group's discovery of a novel human protein methyltransferase.
- We published an article describing our discovery and characterization of the novel protein histidine methyltransferase CARNMT1 (Malecki et al., *J. Biol. Chem.*).
- We published a research article on evolutionary, structural and enzymological aspects of the histidine methyltransferase METTL9 (Schroer et al., *J. Biol. Chem.*).

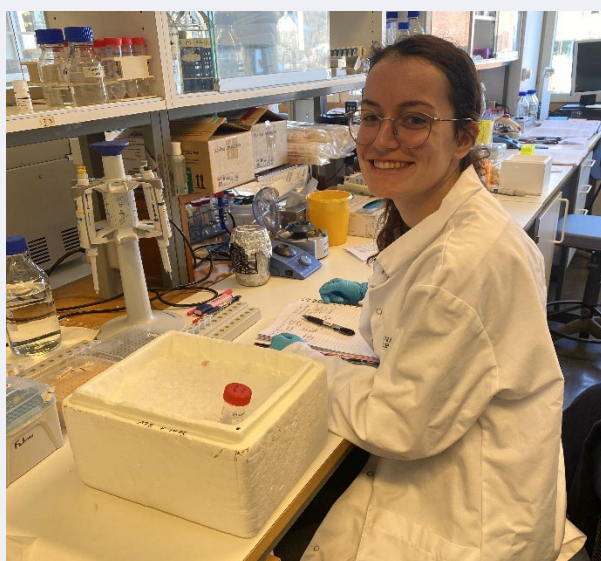
Everyday life in the group 🏠🔬

A large part of our work in the laboratory is centered around the biochemical investigations of various methyltransferases, as well as other relevant proteins. These are typically generated as recombinant proteins - expressed in and purified from bacteria. Human cell lines represent our main model system for studying in vivo methylation and its functional effects, and to assess the roles of specific methyltransferases, we use the CRISPR/Cas9 technology to abrogate their function. Also, we collaborate extensively with our department's proteomics facility to study protein methylation by mass spectrometry in vitro and in vivo. Currently, our key foreign collaborations are with groups from Germany, Switzerland and USA.



← Carmen presents her SPARK team's innovation research at the "SPARK Europe Showcase event" in Birmingham, UK.

↓ Master student Klara Vladimir prepares a biochemical experiment.



↓ Jędrzej and Pål at the annual meeting of the Norwegian Bioscience Society at Storefjell.



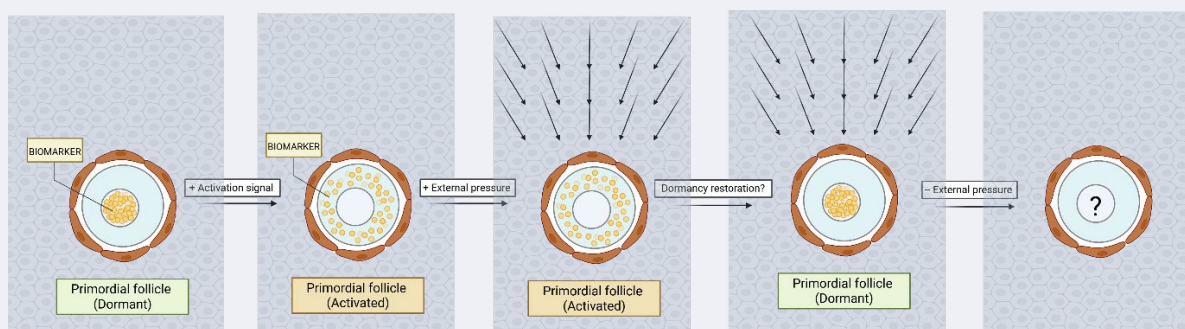


Research and innovation team at the Department of Reproductive Medicine (from left, Tomine Kalsvik, Maria Vera-Rodriguez, Peter Fedorcsak, Nadine Massiah, Eirin Aders. Not in the picture: Thea F. Mikkelsen. Photo: Ine Eriksen, UiO)

Reproductive Medicine Research in the Clinic

We investigate clinical fertility challenges through mechanistic laboratory research and translate biological insights into improved diagnostics and patient care.





One of our research questions explores whether follicle dormancy can be reversed through high-pressure exposure. To answer that, we will track some dormancy/activation-specific biomarkers.

Research focus:

The Reproductive Medicine Group investigates the biological mechanisms underlying reproductive disorders to translate discoveries into improved reproductive outcomes. Situated within the Department of Reproductive Medicine at OUS, the largest academic center for assisted reproduction in Norway, our work benefits from a high-volume clinical environment in which over 2,200 couples and single women received treatment in 2025.

Our research addresses reproductive potential as a continuous biological process, encompassing ovarian follicle reserve, embryo development, and endometrial receptivity. We investigate the decline and loss of ovarian follicles, a central mechanism underlying reproductive ageing and infertility, including after cancer treatment. In parallel, we study early human embryo development to understand why some embryos fail to progress or result in a successful pregnancy, and we examine endometrial function to improve the prediction of implantation.

Our main goal is to uncover the biological mechanisms that govern fertility, embryo development, and implantation, and to apply this knowledge to advance patient care, diagnostics, and fertility preservation strategies.

Current Projects:

- PRIME: Investigating how biomechanical properties of human ovarian tissue regulate follicle dormancy, activation, and spatial organization.
- FIN: Examining the molecular impact of uterine leiomyomas on endometrial receptivity and implantation potential.
- DECODE: Applying multiomic approaches to characterize discarded IVF embryos to identify molecular determinants of developmental competence and implantation failure.
- Fertility preservation in cancer: Identifying clinical, demographic, and regional disparities in access to fertility preservation services and reproductive outcomes.
- Digital oncofertility support tool: Developing a conversational AI-based platform to improve accessibility and implementation of fertility preservation guidelines.

Highlights 2025:

- Presentations at the CRESCO retreat and posters at the ESHRE 2025 conference.
- Purchased an advanced high-pressure culture system for ovarian tissue studies.
- Maria Vera-Rodriguez was elected as a member of ECR in CRESCO.
- Initiated collaboration with Igenomix Ltd, a global leader in preimplantation genetic diagnostics.

Everyday life in the group

The Reproductive Medicine Group is anchored by a core team, with frequent rotations of short-term students supporting ongoing projects. Close collaboration with clinical staff, including embryologists and doctors, ensures that clinically inspired ideas are integrated into research and that laboratory findings remain connected to patient needs, with many staff members ultimately becoming directly involved in projects. Daily life combines study design, grant writing, computational analysis, and manuscript development, reflecting the current stage of ongoing work. Although we are located separately from much of the CRESCO community, we greatly value and participate in the events and activities organized by the Centre, which foster collaboration, learning, and a shared sense of purpose.



↑ Members of the Reproductive Medicine Department, participating in daily 15-minute yoga sessions for a week to promote wellbeing and stress management.

↓ Thea Mikkelsen testing primers for her qPCR experiments, investigating the effect of leiomyomas on endometrial receptivity.



↑ The group's newly established clean laboratory, designed to maintain optimal conditions for working with human embryos and ovarian tissue.



The Dahl group members: Mette Istre, Arne Søråas, Gunhild Nyborg, John Arne Dahl, Sonja Hjellegjerde Brunvoll, Håvard Aanes, Michel Choudalakis, Anders Benteson Nygaard. Not present: Madeleine Fossli, Lina Suhaib Hamid el Rasheed and Olaug Marie Reiakvam. Photo: Guro Flor Lien, UiO

Dahl Group

Genome Regulation in Development, Ageing and Disease

The Dahl research group investigates molecular mechanisms of genome regulation in gametogenesis and early embryonic development, with particular emphasis on epigenetic and post-transcriptional control.



Research focus:

In oocytes, the genome is carefully prepared for the next generation through the placement of chromatin marks. These marks do not change the DNA sequence, but they influence its conformation, replication and transcription. As a result, instructions of genome regulation are transmitted from oocyte to embryo, helping to orchestrate normal early development.

The Dahl research group investigates genome regulation in early development and fertility, with a particular focus on epigenetic and post-transcriptional processes. A current central research area is how epigenetic regulation influences transposon activity and function, and how this contributes to epigenome establishment, genome stability and the control of gene expression.

The group also studies RNA modifications, chromatin structure, and histone marks that regulate maternal gene expression and the transition from maternal to zygotic genome regulation.

The work combines experimental approaches and sequencing-based analyses with bioinformatics. The research is relevant both to fundamental developmental biology and to clinical questions related to fertility.

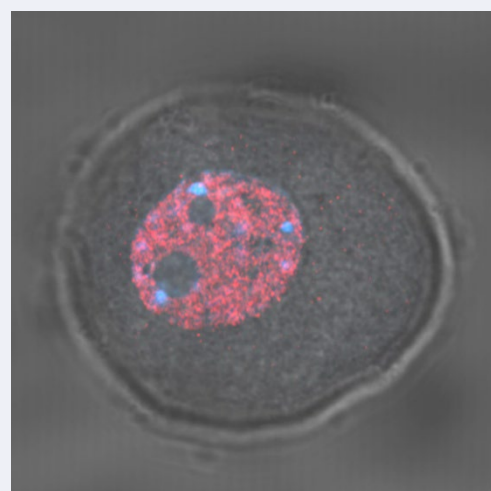
→ Oocyte collected from 10-day old mouse, stained for the histone variant H2A.Z (red) and for DNA (blue).

Current Projects:

- The dynamic establishment of histone marks during oogenesis and in the early embryo.
- Oocyte histone marks during genome wide transcriptional silencing in mammalian oocytes.
- Post-transcriptional regulation of RNA in Zebrafish oocytes and embryos.
- Multivalent readers of histone modifications.
- Cancer detection by ChIP-seq - CATCH.
- Regulation of transposable elements during development.

Highlights 2025:

- Norwegian Cancer society grant (8 M NOK), ChIP-Care
- Grant from Astri og Birger Torsteds legat til bekjempelse av kreft.
- Major waves of H2A.Z incorporation during mouse oogenesis and preimplantation embryo development, Fossli et al., Nature Communications, 2026.
- Broad H3K4me3 domains support oocyte genome silencing and maturation but are dispensable for repression in early embryos, Skuland T et al., Development.
- The RNA m6A landscape during human oocyte-to-embryo transition (Li Y et al., EMBO J).



Everyday life in the group 🏠🔬

Our everyday life in the laboratory focus around isolation and preparation of oocytes and preimplantation embryos at specific stages of development. We carry out epigenetic and epitranscriptomic analysis of these oocytes and embryos in order to generate a reference map of normal and healthy development. Furthermore, we assess perturbations that take place as a consequence of abnormal development, and/or resulting from overexpression or depletion of specific factors. We work with several different species, and collaborate with the University of Newcastle, University of Inland Norway, Department of Reproductive Medicine at Oslo University Hospital, Norwegian Transgene Center and NMBU to allow for this. We have several collaborative projects with the Lerdrup group at the University of Copenhagen. Some group members work on technology development, and some are specialists in computational analysis. Some group members have mostly a clinical focus, in particular regarding projects relevant for aging, COVID-19 and cancer. We have an extensive network of collaborators across several hospitals/campuses in the Oslo region, allowing e.g. to investigate if patients with mild cognitive impairment can benefit from plasma exchange with young plasma.



Michel Choudalakis in the process of selecting zebrafish embryos at the fish facility, Norwegian University of Life Sciences (NMBU).



The Lerdrup group has 6 members of 4 nationalities. From left: Erkut Ilaslan, Clara Petit Cabarrocas, Mirra Søegaard, Vilius Kasparavičius, Mads Lerdrup, Mika Zagrobelny.

Lerdrup Group

Decoding The Embryo Epigenome

We use computational tools and genome-wide data to explore how the enigmatic epigenome existing in mammalian oocytes and embryos regulate genome function and stability.





A highly productive morning during our August 'work camp' at Lysebu in Oslo where the H2A.Z manuscript is being revised and readied for resubmission.

Research focus:

We want to understand the causes for and consequences of the profound reshaping of the epigenetic landscape that take place during mammalian oogenesis and preimplantation embryo development. This has become a data-heavy science, and our group specializes in computational studies. Combined with the cutting-edge low input sequencing-based assays established by collaborating groups in CRESCO, this is a powerful approach to reveal how these epigenetic changes affect reprogramming of the embryo genome, DNA replication timing and genome stability.

Our aim is to decode and understand the ruleset that govern the epigenome in oocytes and early embryos and understand how it affects outcomes and functions in the genome.

In previous work, we showed that aberrant epigenetic reprogramming in mouse oocytes leads to failed embryo development, DNA-fragmentation and widespread perturbations

in the transcriptional programs needed for embryo development (Sankar, Lerdrup, Manaf et al, Nat. Cell Biol. 2020). This revealed a new link between chromatin states and errors in embryo development, and we are exploring if this acts through effects on DNA-replication and the widespread replication stress that occurs in mouse and human embryos during the first cell divisions.

Current Projects:

- Basic exploration and mapping of the unusual epigenome in mammalian oocytes and early embryos.
- Identification of instructive forces (genomic elements) that govern this epigenome.
- Charting the genome-wide interplay between chromatin states in embryos.
- Investigating the relationship between the epigenome and embryo development, and in particular zygotic replication and replication stress.

Highlights 2025:

- Fossli, Ilaslan, Skuland, Choudalakis, Søegaard, Halliwell, Khan, Indahl, Vera-Rodriguez, Manaf, Geijer-Simpson, Suganthan, Jermstad, Dalen, Eskeland, Kommisrud, Klungland, Bjørås, Fedorcsak, Greggains, Zagrobelny, Dahl, Lerdrup. Nature Communications, 2025, PMID 41331258. With this we presented high resolution genome-wide mapping of the histone variant H2A.Z, revealing an intricate and dynamic environment. Importantly, there are patterns of epigenetic information that can be inherited from the egg to the embryo, and this seems to regulate the architecture and function of the genome. The work capitalized on the highly collaborative environment within CRESCO and included authors from six groups in CRESCO.
- The group organized a PhD course in Analysis of genome-wide enrichment data, and the course was attended by several Norwegian PhD students who got admission-free access through the NorDoc initiative.
- Erkut was awarded the prize for the best poster at the yearly meeting in the department.

Everyday life in the group

Our key means of exploration are analytical and computational tools that we often develop ourselves. Modern day scientific progress is often limited by the abilities to handle, analyse, interpret, and understand the exponentially growing amounts of data that are generated. Our approach offers a useful complementary skillset within CRESCO, and we collaborate broadly and deeply with many of its groups. We are very keen on bridging the distance offered by our physical location in Copenhagen, and each week have multiple online meetings with our peers in Norway as well as frequent visits.



→ Erkut is awarded the prize for the best poster by HoD Ian Hickson during the annual department meeting.

← Erkut, Mika, and Mirra embracing Norwegian culture during one of the three visits to Norway in 2025.





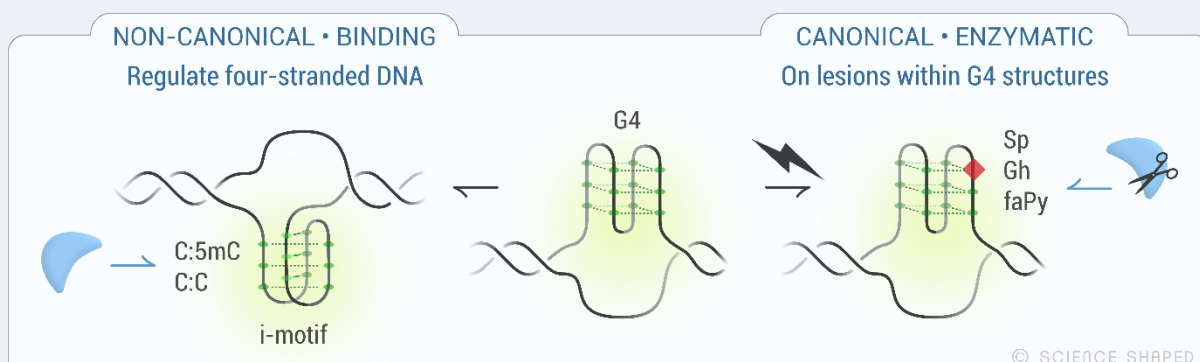
The Bjørås group. From the left: Eirin Starheim, Magnar Bjørås, Tekle A. Lobie, Ingrid Åmellem, Xiaolin Lin, Raji Suagnathan, Sigrid Aslaksen, Linda Ellevog-Skuggen and Parvin Horrieh. Not present: Adeel Manaf, Tine Neurauter and Gunn Hildrestrand. Photo: Guro Flor Lien, UiO

Bjørås Group

Cellular Responses to DNA damage

Our research focuses on the impact the interplay between oxidative stress, DNA repair, secondary DNA structures and epigenetics have for genome regulation.





Guanine quadruplex (G4) and intercalating-motif (i-motif) dynamics at G:C rich regions have impact on genome regulation (e.g., gene expression, telomere stability, replication)

Research focus:

Damaged or modified DNA can trigger apoptosis, cell senescence or changes in gene expression, inhibit cell division, or introduce mutations leading to the decay of genetic information, with deleterious effects for the development and functioning of organisms. Defects in the repair of DNA lesions have diverse manifestations, including degenerative disease and carcinogenesis. Base Excision Repair (BER) is the major pathway for repair of oxidative DNA damage, initiated by DNA glycosylases. Recent findings suggest roles of DNA glycosylases beyond BER, including regulation of secondary DNA structure dynamics (e.g., guanine quadruplexes, G4).

We aim to determine how non-canonical functions of DNA glycosylases, epigenetic marks and DNA secondary structures cooperate to regulate mammalian genomes.

In CRESCO we have a particular focus on the role of secondary DNA structures in reprogramming of the mammalian genome in early embryo development.

Current Projects:

- Aberrant Oxidative DNA Modifications and DNA Structures in Genome Regulation.
- Bacterial Toxin-Antitoxin peptides in biological responses to DNA damage.
- Modelling and testing treatment modalities in rare neurodegenerative diseases using patient-derived organoids.

- Applications of nanoparticle technology in genomics.
- DNA secondary structure dynamics in early embryo development.

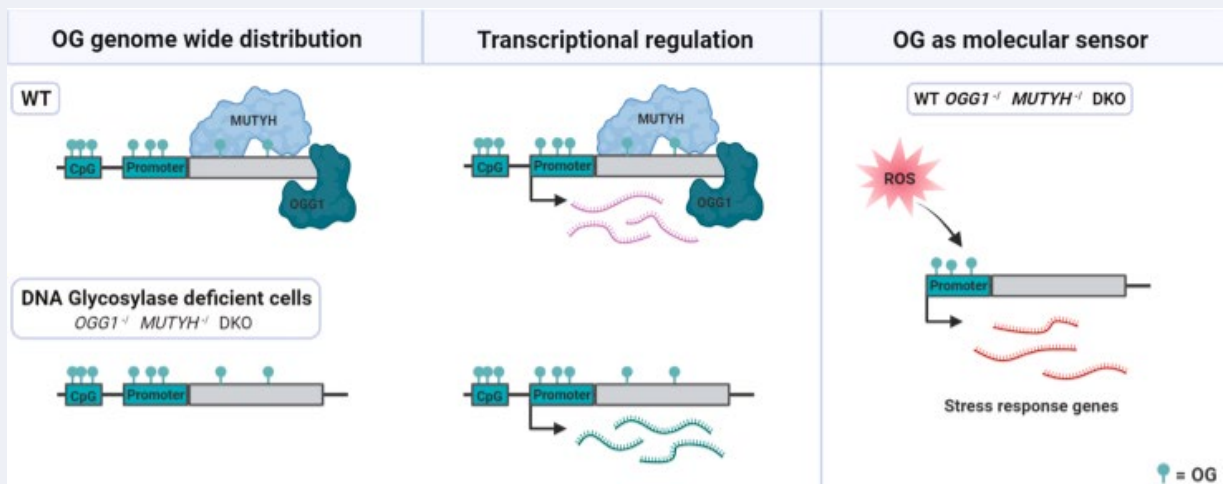
Highlights 2025:

- NEIL3 influences adult neurogenesis and behavioral pattern separation via WNT signaling (Cell Mol Life Science 2025).
- NEIL3 shapes hippocampal network dynamics and fear memory through modulation of PV+ interneurons (Prog Neurobiol 2025).
- Established single cell sequencing method for genome wide profiling of 5mC and 5hmC (Genome Biology 2025).
- Established methods for genome wide profiling of 8-oxoguanine and G4 structures (Redox Biol 2025).
- A preliminary evaluation of a fast, low-cost, and high-throughput nucleic acid extraction method for bacterial microbiota profiling in low-microbial biomass samples (Sci Rep 2025).
- Rapid DNA and RNA isolation from few or single cells using low-cost NAXtra magnetic nanoparticles (Sci Rep 2025).
- Early transcriptional responses reveal cell type-specific vulnerability and neuroprotective mechanisms in the neonatal ischemic hippocampus (Acta Neuropath 2025).

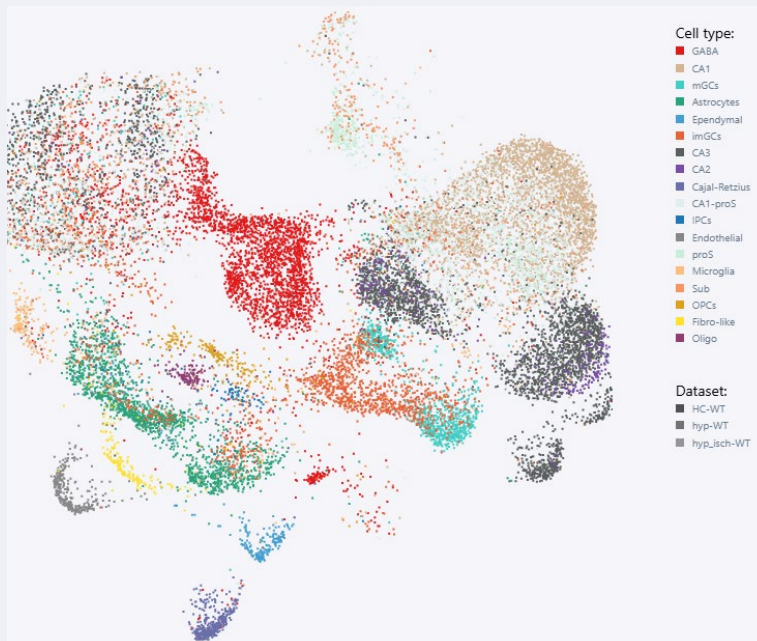
Everyday life in the group

Our everyday life in the laboratory focus around:

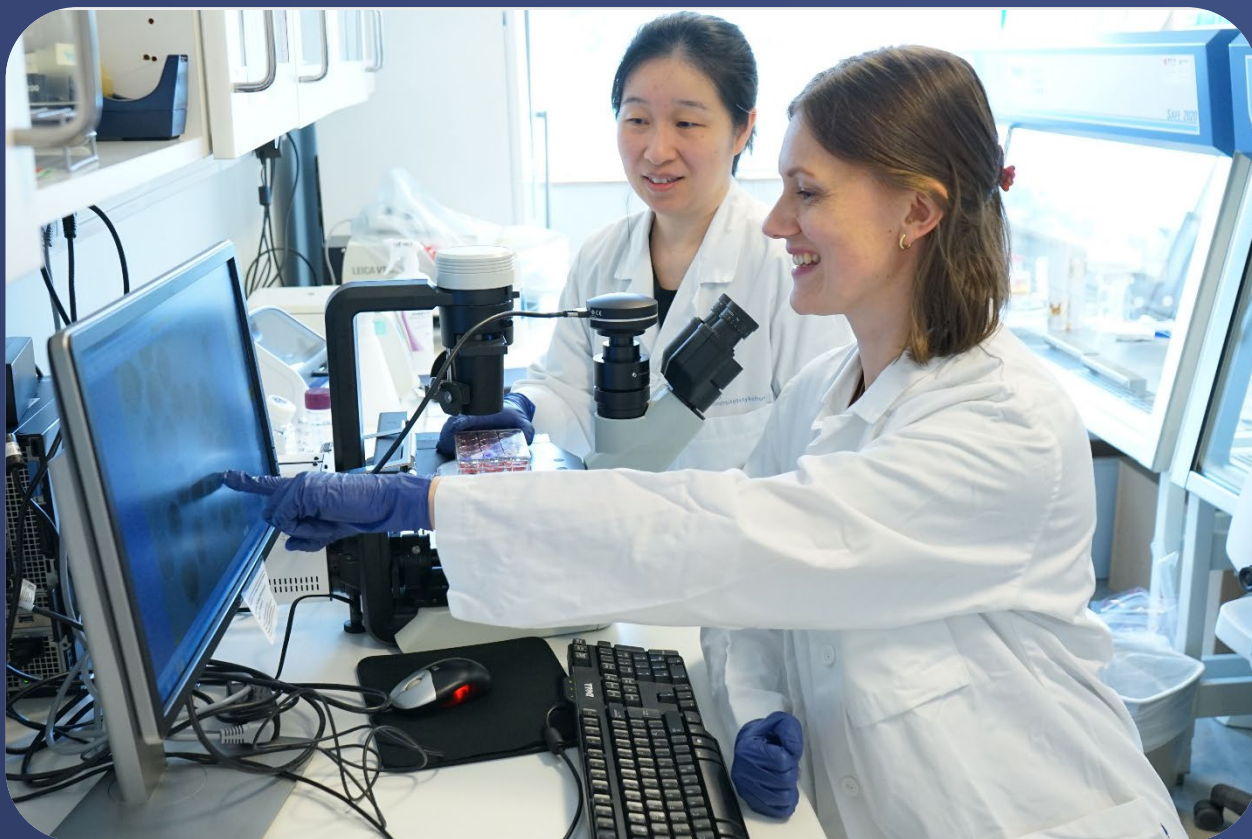
- Phenotyping of transgenic mouse models and human cell lines (DNA repair deficiencies).
- Generating human patient derived organoid models (brain, heart, lung and retina) for disease modeling and preclinical testing of gene therapies.
- Developing small cell numbers and singel cell genomewide profiles of epigenetic marks and secondary DNA structures utilizing magnetic nanoparticle technology.
- Measuring molecular interactions of recombinant proteins (e.g., switch sense and plasmon surface resonance).
- Hi gh and super resolution microscopy of tissue, 3D organoids and monolayer cell cultures.



8-oxoguanine genomic profiling: Genomic 8-oxoguanine modulates gene transcription independent of its repair by DNA glycosylases OGG1 and MUTYH (Redox Biol 2025)



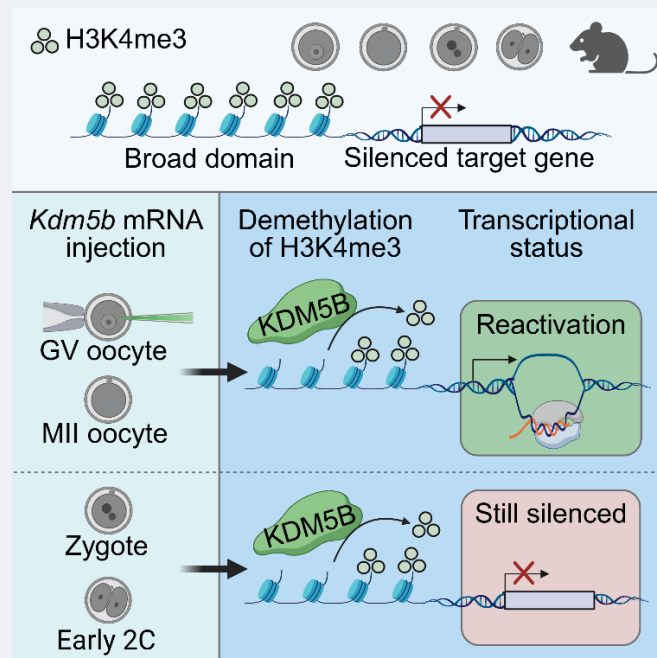
Neonatal hypoxic-ischemic (H-I) brain injury, a leading cause of neurodevelopmental disabilities, severely affects the metabolically active and neurogenic hippocampus. We constructed a comprehensive hippocampal cell atlas and developed a machine-learning classifier for precise cell type identification. Our analysis reveals early vulnerabilities in mature neurons and notable resilience in immature DG, GABAergic, and Cajal-Retzius cells following H-I. The integrated hippocampal atlas, post-H-I atlas, and machine learning classifier are available at <https://hippo-seq.org> (Acta Neuropat Comm 2025)



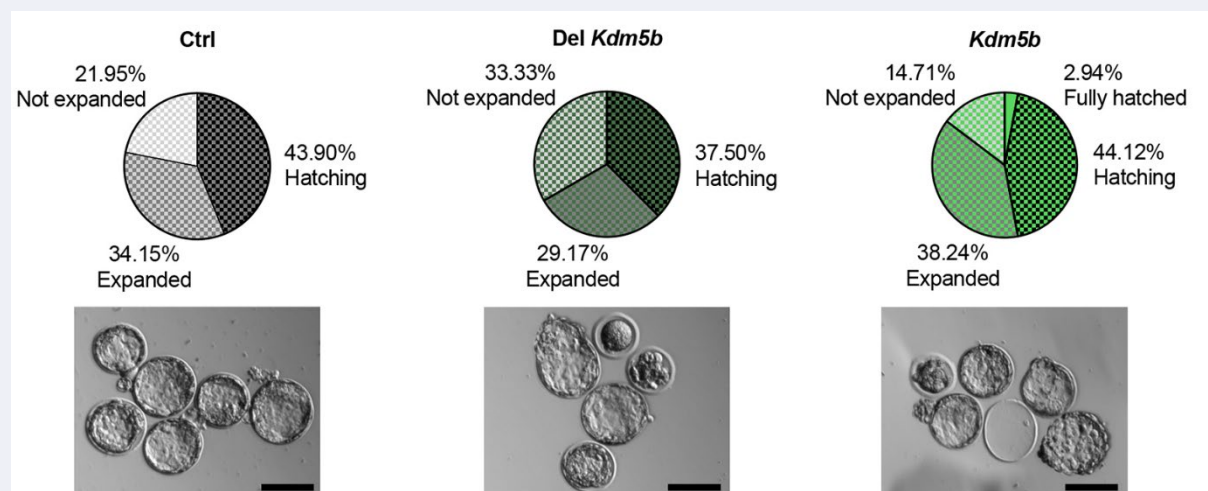
Research Highlights

Broad H3K4me3 domains support oocyte genome silencing and maturation but are dispensable for repression in early embryos

Skuland et al., Development | 2025 | 152: dev204638

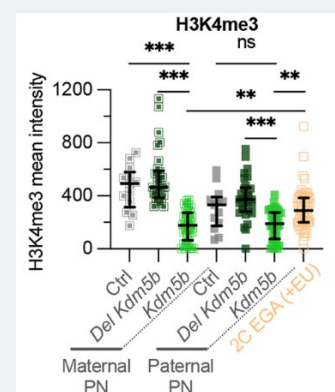


The genome of mouse oocytes is silenced by broad histone H3K4me3 domains, which are removed during embryonic genome activation (EGA) by KDM5B. We induced removal of H3K4me3 by injecting mouse oocytes with *Kdm5b* mRNA and observed transcriptional activation and impaired oocyte maturation timing. Premature depletion of broad H3K4me3 domains in zygotes or early 2-cell embryos did not alter the transcriptional program. We suggest that broad H3K4me3 domains are required for oocyte genome silencing, timely maturation and post-fertilisation silencing, but not for transcriptional repression pre-EGA.



↑ Comparable developmental progression until blastocyst stage by uninjected mouse zygotes (Ctrl) and zygotes injected with *Del Kdm5b-yfp* or *Kdm5b-yfp*.

→ Expression of H3K4me3 is reduced in both maternal and paternal pronuclei after injection of *Kdm5b-yfp* mRNA compared to control.

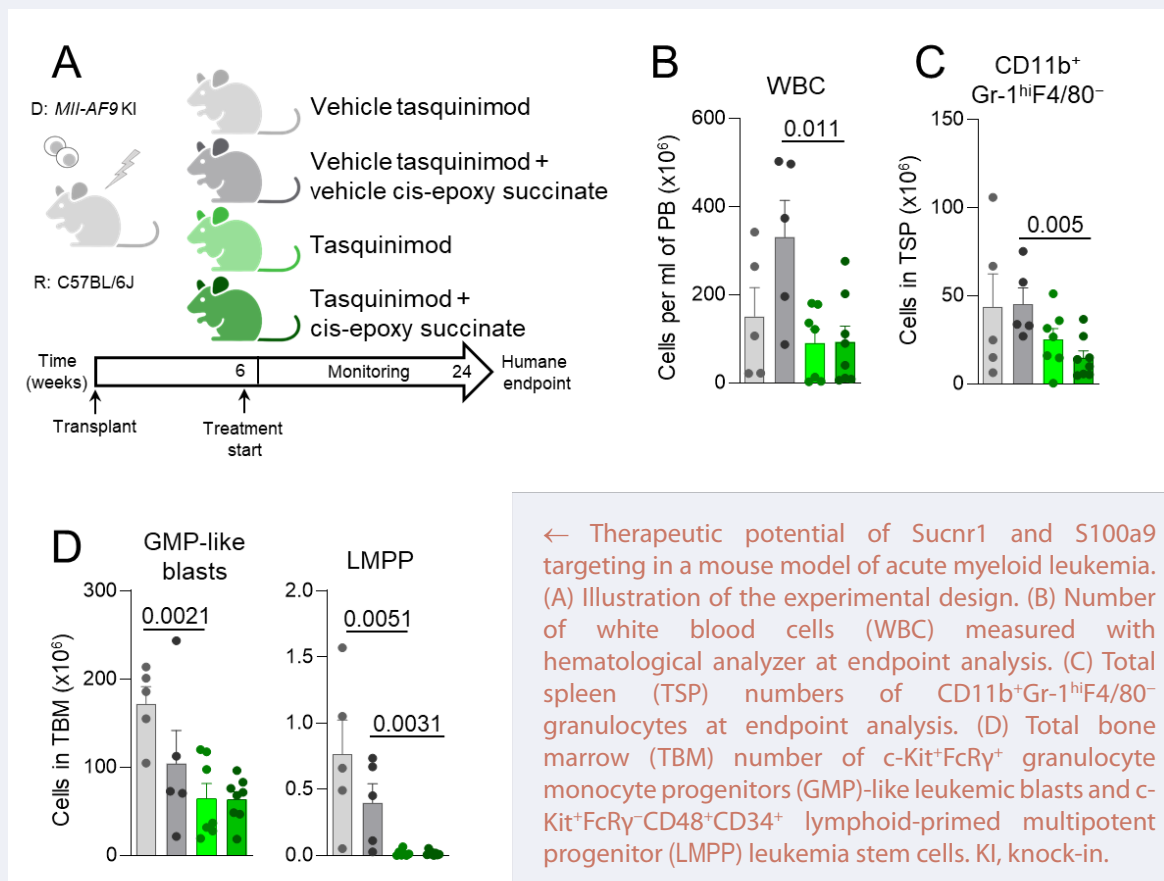


Succinate receptor 1 restricts hematopoiesis and prevents acute myeloid leukemia progression

Cuminetti et al., Nat Commun | 2026 | in press

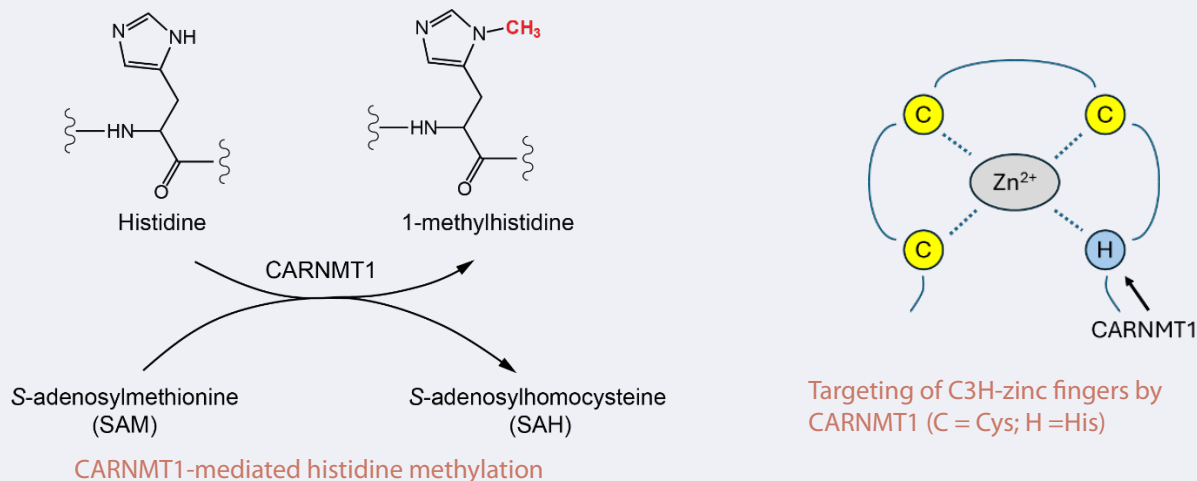
Succinate is an intermediate metabolite with pleiotropic intracellular roles involving epigenetics and hypoxia response, among others, but also extracellularly signaling through succinate receptor 1 (SUCNR1). Despite intriguing roles for Sucnr1 in inflammation, few studies have explored its role in stem cells and hematopoiesis.

Here, we show that low SUCNR1 represents a marker for reduced overall and progression-free survival in acute myeloid leukemia (AML) patients. Succinic acid, which displays Sucnr1-dependent and independent effects, promotes disease in mouse models of pre-leukemic myelopoiesis, AML and AML xenografts, expressing low SUCNR1. In vivo global or hematopoietic deletion of Sucnr1 induces expansion of hematopoietic stem and progenitor cells (HSPC) and hematopoiesis, whilst Sucnr1-tomato+ HSPC display restricted engraftment potential. Mechanistically, activation of Sucnr1 counterbalances the stimulatory effect of intracellular succinate in HSPC and preserves HSPC transcriptional programs via control of S100a8/S100a9. Blocking S100a9 with tasquinimod rescues the defects of Sucnr1 knock-out mice, and combined with a potent Sucnr1 agonist shows therapeutic value in AML mice. In AML xenografts, single-cell RNA-sequencing reanalyses confirm SUCNR1 as a therapeutic vulnerability in patients. Together, Sucnr1 signaling restricts hematopoiesis at least partially through HSPC and via control of S100a8/S100a9. Its dysregulation emerges as contributor to malignancy that opens therapeutic avenues for AML patients.

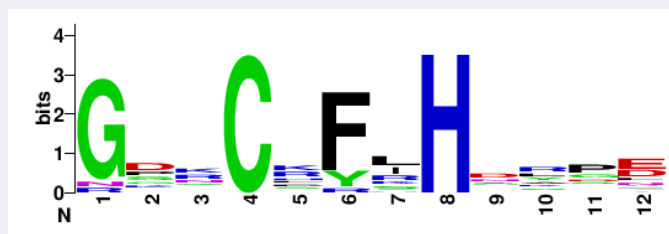


Identification of substrates and sequence requirements for CARNMT1-mediated histidine methylation of C3H zinc fingers

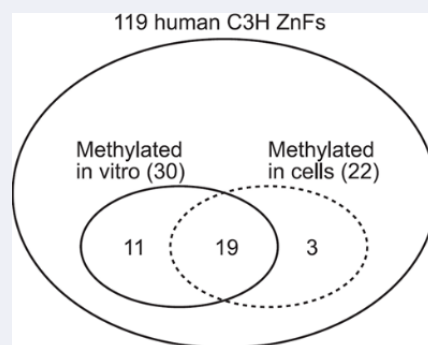
Malecki et al., Journal of Biological Chemistry | 2025 | 301: 11033542



It has recently been uncovered that protein histidine methylation is pervasive and functionally important. In the present study, we discovered that the human enzyme carnosine methyltransferase 1 mediates N1-methylation of histidines in a number of human proteins. The majority of the methylation sites are part of so-called C3H-zinc fingers (C3H-ZnFs; where three cysteine residues and one histidine coordinates a zinc ion), and many of them are found in proteins involved in mRNA splicing (e.g. U2AF1, RBM22 and RNF113A), supporting the notion that CARNMT1 regulates splicing. CARNMT1-mediated methylation was studied both in vitro and in cells. 119 human C3H-ZnF-derived sequences were tested as CARNMT1 substrates in vitro, and we found that only one fourth of these were methylated, indicating that only a subset of the C3H-ZnFs are regulated by CARNMT1. We also established several cellular CARNMT1 substrates, and found that in vitro methylation is a good predictor of cellular methylation. Finally, we also uncovered several CARNMT1 substrates in the nematode *Caenorhabditis elegans*, and several of them were orthologues of the ones discovered in human cells. In conclusion, this study uncovers CARNMT1 as a histidine methyltransferase, and C3H-ZnFs as robust and evolutionarily conserved CARNMT1 substrates, involved in the regulation of mRNA splicing.



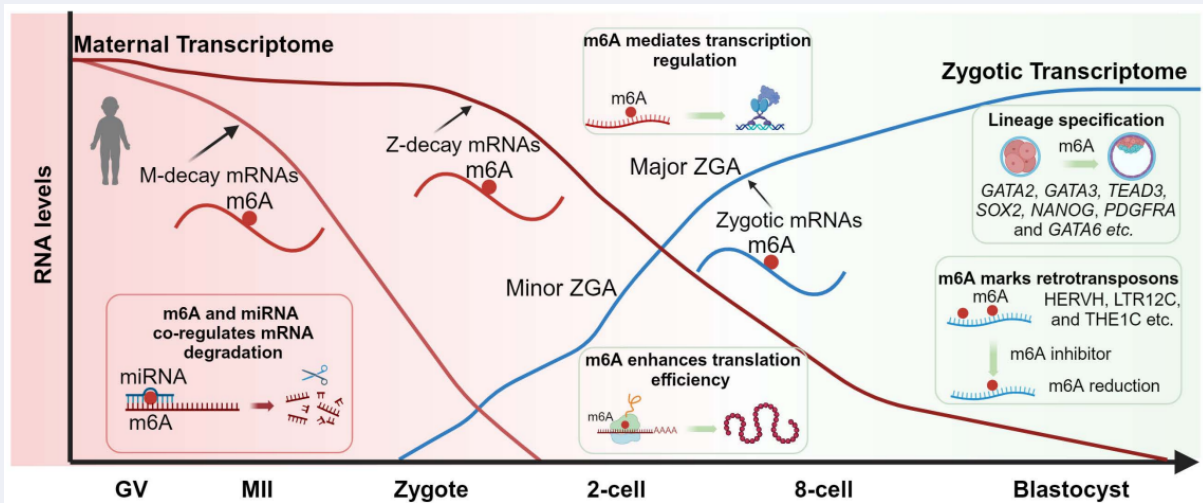
Sequence logo for CARNMT1-mediated histidine methylation of C3H-ZnFs, based on in vitro methylation of peptides



Summary of results data on CARNMT1-mediated methylation of C3H-ZnFs in vitro and in cells

The mRNA m6A landscape during human oocyte-to-embryo transition

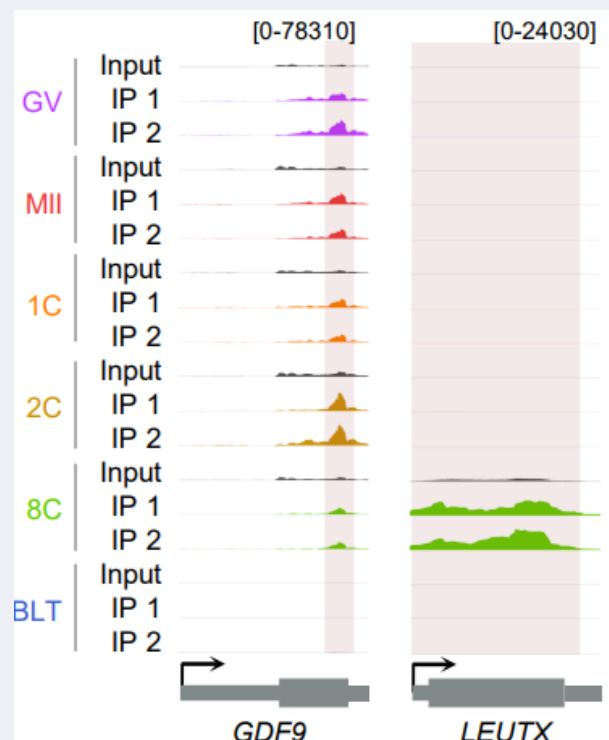
Li et al., EMBO j | 2025 | 44:4150-4180



↑ Summary of the RNA m6A methylome landscapes during human oocyte-to-embryo transition (OET). From Li et al., 2025

The reversible nature of m6A in RNA and its role in meiosis was documented more than 10 years ago. Recently, the first m6A RNA maps of mouse meiosis and embryo development was published by several research groups, including urs. In this study, the dynamic m6A profiles within human preimplantation embryos is presented.

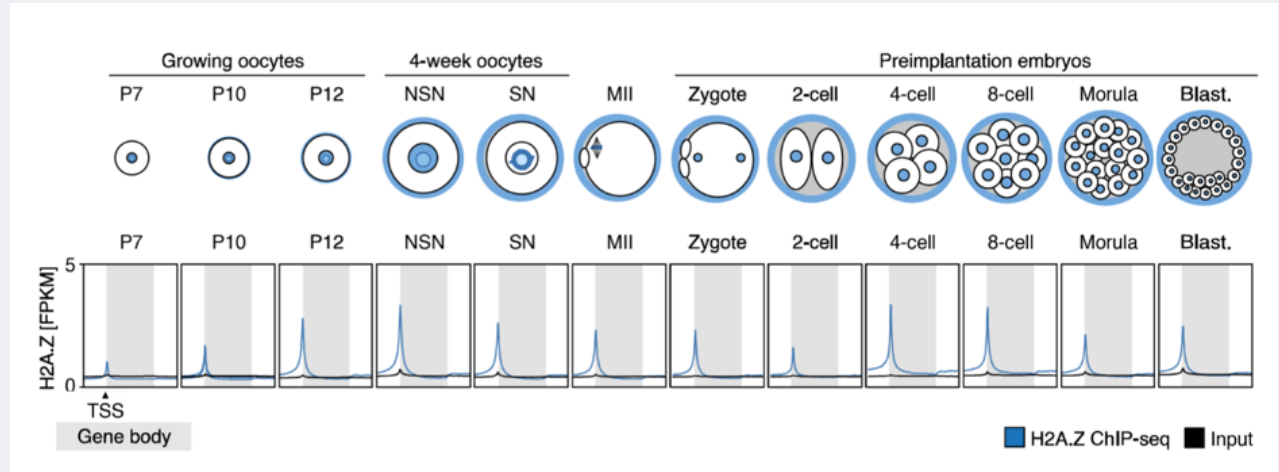
We reported the first RNA m6A landscape of single human oocytes and early preimplantation embryos. Comparison with the murine m6A landscape data reveal an intriguing variance during the zygotic genome activation. m6A-modified genes are involved in adjusting gene activity, while unmodified genes are mainly associated with basic metabolic processes. Maternal mRNAs genes demonstrate higher m6A modification levels, and these genes are targeted by micro RNAs for decay. m6A modified genes that are constantly expressed across all embryonic stages analysed demonstrate higher translation efficiency. Moreover, we found frequent m6A enrichment on embryonic stage-specifically expressed retrotransposons. m6A inhibition led to m6A erasure on retrotransposons. In summary, we provide a resource to broaden the knowledge on the roles of m6A during human embryo development.



Representative genome browser view of m6A picoMeRIP-seq signals. From Li et al., 2025 ↑

Major waves of H2A.Z incorporation during mouse oogenesis and preimplantation embryo development

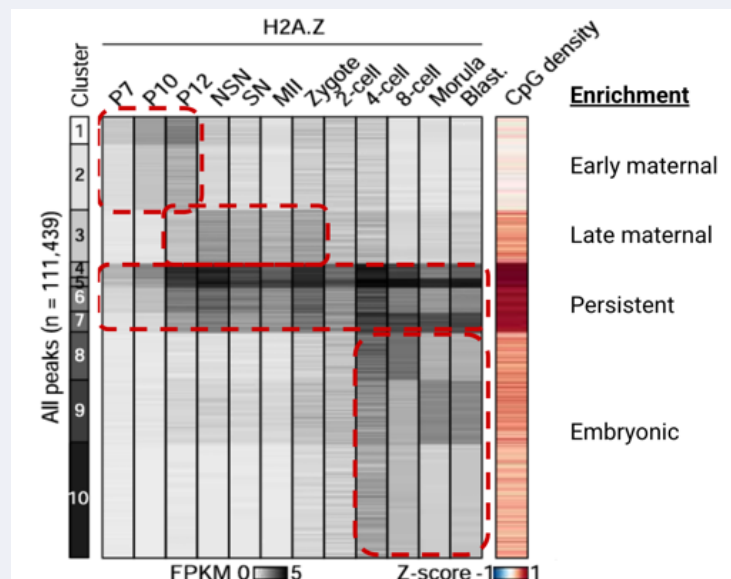
Fossliie and Ilaslan et al., Nature Communications | 2025 | 17:210



H2A.Z is incorporated both in mouse oocytes and pre-implantation embryos. Upper panel: Overview of the developmental stages that were sampled and analysed in this study. P, postnatal day; NSN, non-surrounded nucleolus; SN, surrounded nucleolus; MII, metaphase II; Blast., blastocyst. Lower panel: H2A.Z ChIP-seq signal in different developmental stages at gene bodies (shaded area, transcription start sites to the left), $n = 47,248$

Epigenomes of mammalian oocytes and early embryos undergo extensive reprogramming, yet how histone variants participate is incompletely understood.

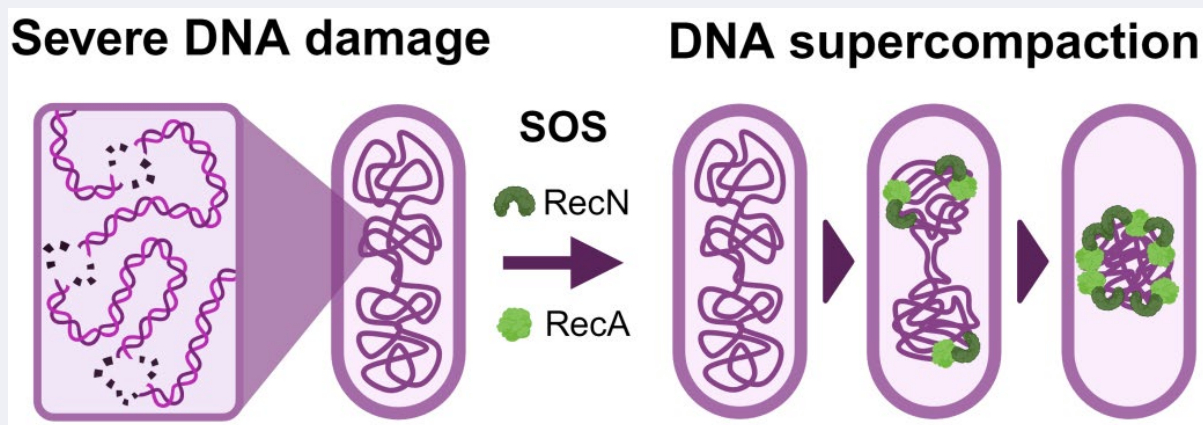
This study examines genome regulation during the transition from mouse oocyte to early embryo by mapping the dynamic distribution of the histone variant H2A.Z. We identify distinct waves of H2A.Z incorporation that form maternal, embryonic, and persistent enrichment patterns. Notably, late maternal H2A.Z is inherited by the zygote and closely associates with early replication and genome organization. Furthermore, persistent H2A.Z peaks are strongly linked to CpG sites, while stage-specific H2A.Z peaks are enriched at transposable elements. H2A.Z peaks span related stages and help preserve epigenetic information despite extensive remodeling, thereby defining how H2A.Z dynamics contribute to epigenetic reprogramming in early development.



H2A.Z incorporation in three major waves: i) Persisting and early maternal peaks, ii) late maternal peaks and iii) embryonic peaks. Heatmaps of H2A.Z enrichment at aggregated and clustered H2A.Z peaks.

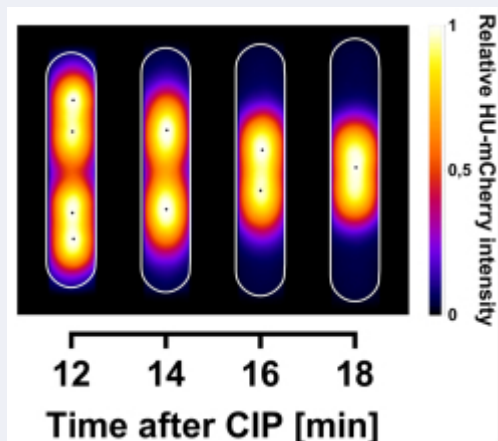
RecN and RecA orchestrate an ordered DNA supercompaction response following ciprofloxacin-induced DNA damage in *Escherichia coli*

Vikedal et al., Nucleic Acids Res | 2025 | 53:gkaf437



Fluoroquinolones induce double-strand breaks in bacterial DNA and trigger the SOS response, a major DNA damage pathway that promotes repair but also fosters the emergence and spread of antibiotic resistance. Fluoroquinolone resistance in *Escherichia coli* is an increasing global health concern, making it essential to understand how bacteria respond to these drugs at the DNA level.

In this study, we investigate DNA morphology in *E. coli* after exposure to ciprofloxacin (CIP). We show that CIP induces a stepwise reorganization of the nucleoid, culminating in a highly dense midcell structure, which we term DNA supercompaction. This response also occurs after treatment with other genotoxic agents. Using live-cell imaging, we demonstrate that RecN, an SMC-like protein, is required for DNA supercompaction, and that its dynamics and activity depend on RecA, with the two proteins frequently colocalizing at nucleoid-associated sites. Our findings indicate that RecN and RecA play active roles in DNA supercompaction following severe DNA damage, that this compaction forms part of a rapid, general survival response to double-strand breaks in *E. coli*, and that the degree of compaction scales with damage severity.



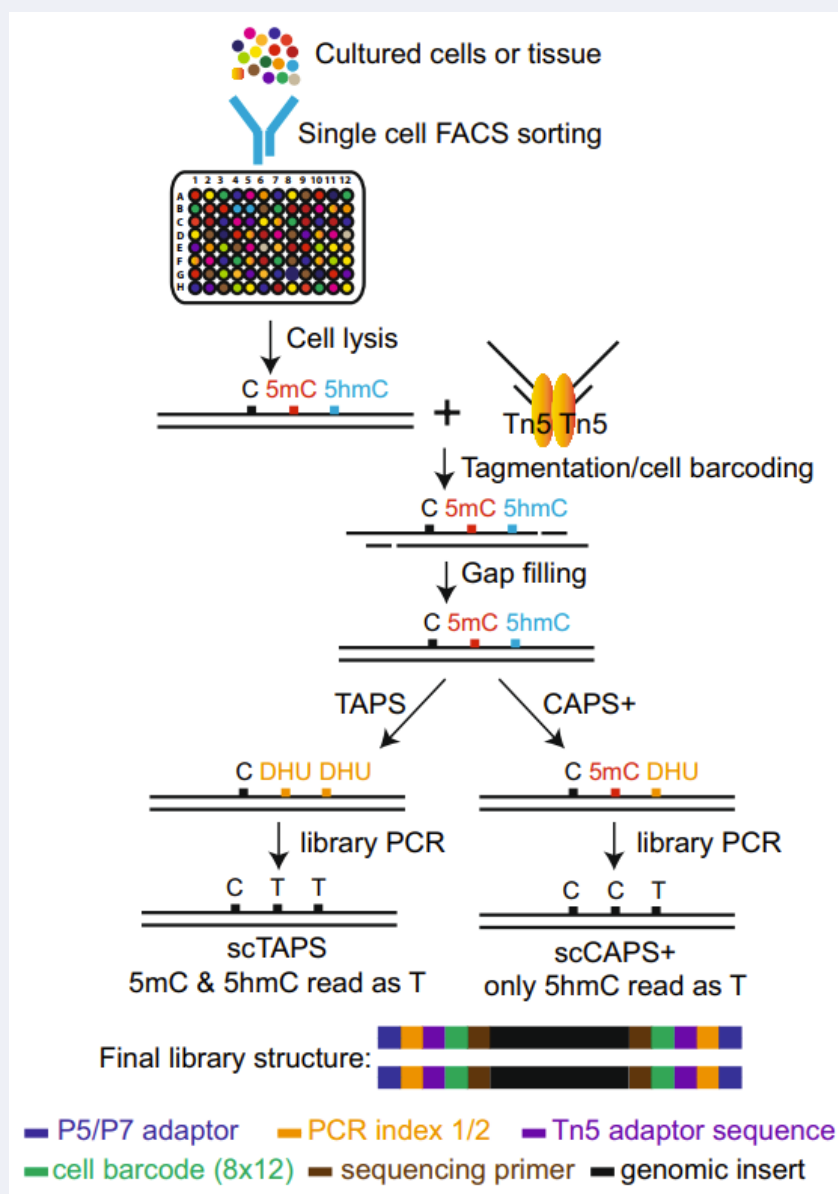
DNA supercompaction in wild-type *E. coli* cells (KV21) after CIP exposure. Cells were immobilized on agar pads and imaged using spinning disk microscopy. Results shown are from images captured 12, 14, 16, and 18 min after CIP exposure, averaged from 40 tracked cells from a single representative biological replicate. Figure show kymograph heat map of relative HU-mCherry intensity distribution over time.

Direct and bisulfite-free 5-methylcytosine and 5-hydroxymethylcytosine sequencing at single-cell resolution with scTAPS and scCAPS+

Chen et al., Genome Biology | 2025 | 26:44

DNA cytosine modifications such as 5-methylcytosine (5mC) and 5-hydroxymethylcytosine (5hmC) are key regulators of gene expression and cell identity. However, existing single-cell methods often lack direct, quantitative, and base-resolution detection of these marks, especially 5hmC.

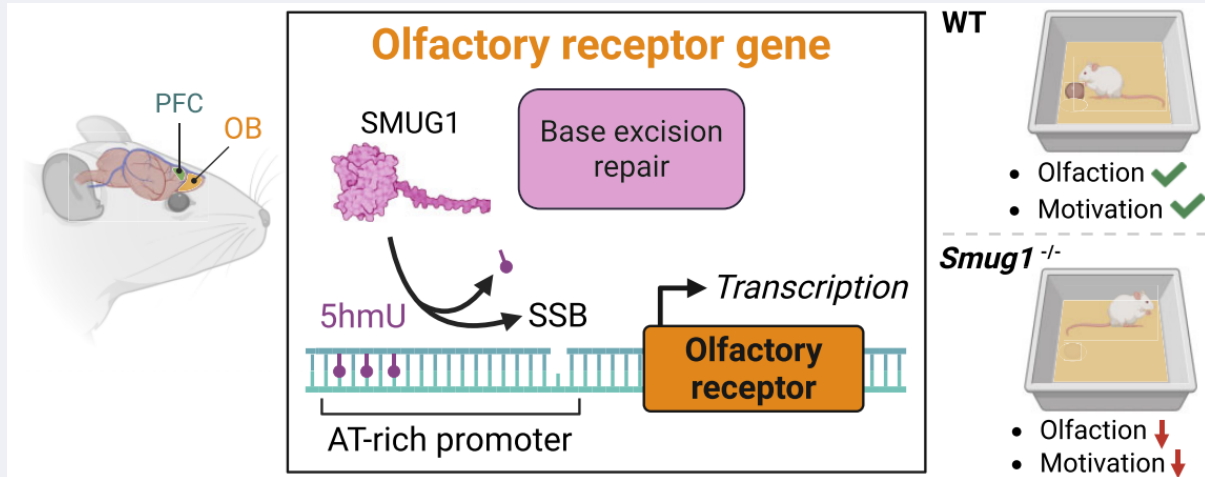
We present here two direct single-cell methodologies for sequencing: scTAPS for joint detection of 5mC and 5hmC, and scCAPS+ specifically for 5hmC, enabling quantitative and single-base resolution mapping of these modifications in individual cells. Our plate-based methods achieve approximately 90% mapping efficiency and accurately recover 5mC and 5hmC profiles in CD8+ T cells and mouse embryonic stem cells. Using scCAPS+, we further reveal a global increase in 5hmC across neuronal and non-neuronal cells in the hippocampus of aging mice. These technologies are readily compatible with high-throughput single-cell multi-omics and provide a robust platform for dissecting epigenomic dynamics in defined biological processes.



Overview of the scTAPS and scCAPS+ methodologies.

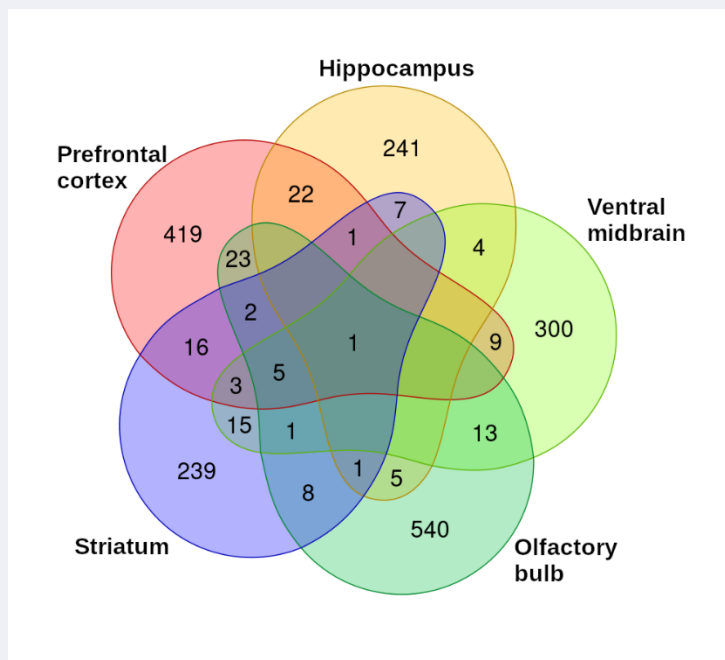
SMUG1 DNA glycosylase modulates reward behaviour through regulation of olfactory receptor gene expression

Bordin et al., Nucleic Acids Res | 2025 | 53: gkaf722



SMUG1 DNA glycosylase is the primary enzyme responsible for excising 5-hydroxymethyluracil (5hmU) from genomic DNA, with particularly high activity in the brain, suggesting an important role in controlling 5hmU levels in this organ. Although 5hmU has been proposed as an epigenetic mark, its regulatory functions and biological relevance remain poorly understood.

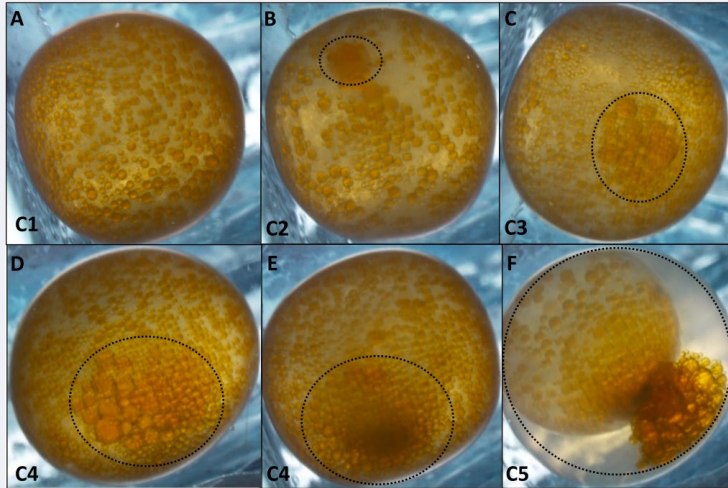
In this study, we show that loss of *Smug1* in mice causes accumulation of 5hmU and leads to widespread gene expression changes across multiple brain regions. Using chromatin immunoprecipitation, we demonstrate that SMUG1 is specifically recruited to AT-rich promoters of olfactory receptor genes, where it actively regulates 5hmU levels. Persistent 5hmU at these promoters results in impaired sensory perception of smell and altered reward-related behavior. These findings reveal a previously unrecognized, locus-specific role for SMUG1 in promoting transcription of olfactory receptor genes and establish a direct functional link between 5hmU removal and neuronal circuit function.



RNA sequencing analysis of *Smug1*^{-/-} versus WT brains. Venn diagram depicting the number of individual and overlapped differentially expressed genes (DEGs) in each brain region.

Lipid droplet distribution in Atlantic salmon (*Salmo salar* L.) oocytes is related to the fertilisation and developmental outcome

Kaththirarachchi et al., Aquaculture | 2025 | 596: 741759

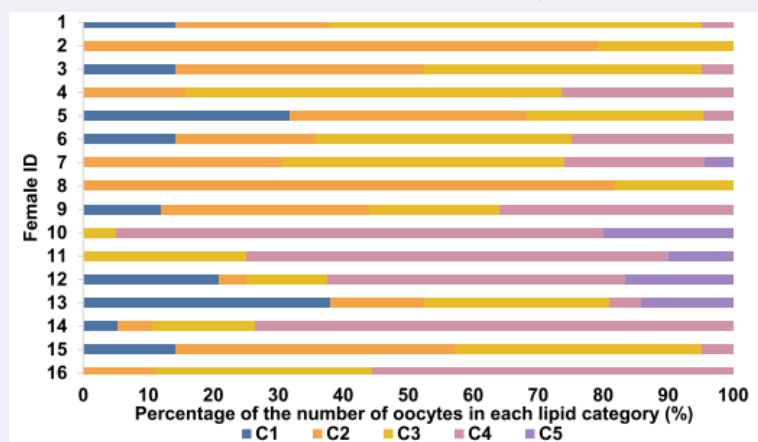


↑ Categories of lipid droplet distribution in Atlantic salmon (*Salmo salar* L.) oocytes. From Kaththirarachchi et al., 2025

The present study show that the categories of lipid droplet distributions hereby applied are predictive of fertilisation outcomes in Atlantic salmon. The lipid droplets content in mature oocytes, as the distribution and aggregation thereof, may be a determinant of the quality of oocytes. Our findings might facilitate developing a practical and cost-effective method to

predict oocyte quality for improved production efficiency in Atlantic salmon oocytes upon collection.

At present, there is no simple and practical applicable method to determine the quality of Atlantic salmon oocytes upon collection at the fish farm. Investigating oocyte lipid droplet patterns might be a tool for the aquaculture industry to predict oocyte quality in Atlantic salmon. While examining the lipid distribution in oocyte batches from 16 females of Atlantic salmon with a range in fertilisation rate (6–97 %), five categories of lipid droplet patterns were distinguished. In category 1, the lipid droplets were evenly distributed whereas in the remaining categories lipid droplets showed varying degree of coalescence. Categories 2, 3, 4 and 5 were distinguished based on the area of coalesced lipid droplets. The fertilisation rate was observed to be high (≥ 90 %), in females that had more oocytes from category 1, 2 and 3 whereas females with more oocytes from category 4 and 5 showed a low fertilisation rate (<90 %). A similar pattern was revealed between lipid droplet categories and eyed embryo and hatching success. Staining of salmon oocytes further confirmed the observed lipid droplet patterns, and different sizes of lipid droplets were present in almost all oocytes. The study revealed a significant association between lipid droplet category and fertilisation outcome in oocytes of Atlantic salmon that can be a practical tool for predicting oocyte quality.



↑ Categories based on the lipid distribution in oocytes (n = 20) from 16 females of Atlantic salmon (*Salmo salar* L.). From Kaththirarachchi et al., 2025



PhD Disputations

Metabolomics, transcriptomics, and sperm quality analyses to investigate biomarkers in boar semen related to sexual maturity

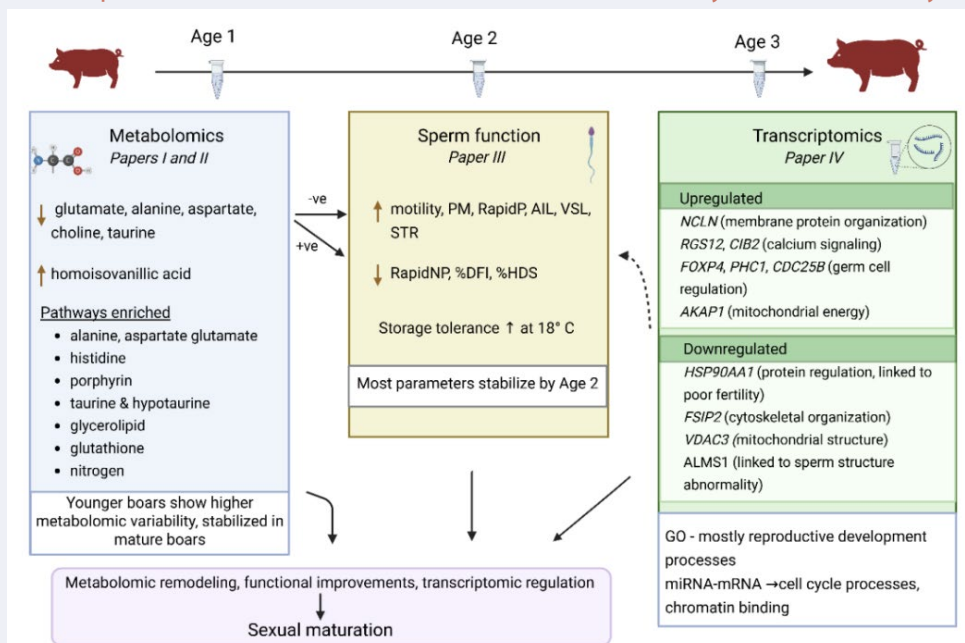
Faculty of Applied Ecology, Agricultural Sciences and Biotechnology, University of Inland Norway

This thesis longitudinally tracked Duroc boars from puberty to sexual maturity, combining targeted and untargeted metabolomics, sperm functional assays, and sperm transcriptomics to define molecular and functional maturation signatures. Key sperm metabolites — glutamate, alanine, aspartate, choline, taurine, and cystine — changed with age and correlated with improved motility, viability, acrosome and DNA integrity, and storage tolerance. Untargeted analysis highlighted enriched pathways (porphyrin, taurine/hypotaurine, glycerolipid metabolism). Transcriptomics identified 60 genes and six miRNAs with roles in spermatogenesis and revealed mRNA–miRNA regulatory networks. These results offer fundamental insights and potential biomarkers to optimize early semen use and accelerate genetic gain in pig breeding.



Asmita Shrestha

Main supervisor: Professor Elisabeth Kommisrud, University of Inland Norway.



Proposed integrated overview of sexual maturation in Duroc boars based on analyses of semen.



CRESCO

Early Career Researchers

CRESCO Young Investigator Grants 2025

To support the career development of Early Career Researchers (ECR) at CRESCO and our collaborators, we offer an annual grant call for amounts up to 250,000 NOK. Here are the recipients for 2025.

Name	Group	Project title
Adeel Manaf	Bjørås	Nanotools for high-resolution single cell epigenomics
Aylin Cengiz	Klungland	Genome instability in meiotic oocytes lacking m6A eraser ALKBH5
Birgitte Narud	Kommisrud	Factors affecting the development of gametes and embryos, and their relation to metabolomic and epigenetic
Cassandra Lax	Kommisrud	The effects of environmental factors on DNA-methylation in early stages of bovine embryo development
Dongjie Zhou	Klungland	Mapping of pseudouridylation in the mouse oocytes and embryos using picoPsiRIP-seq
Emma Lång	Bøe	Navigating the Tunnel - Uncovering Keratinocyte Dynamics in the Pathogenesis of Hidradenitis Suppurativa
Håvard Aanes	Dahl	Long-read sequencing of transcripts during early development for isoform specific detection of m6A
Kangxuan Jin	Klungland	Alkbh5 regulate oocyte development via MERVL retrotransposons
Marcel Heugel	Arranz	Exploring the transformation potential of hematopoietic stem cells with defects in <i>IL1RN</i> , and their therapeutic targeting
Michel Choudalakis	Dahl	Maternal UHRF1 and its association to H3K4me1-K9me2/3 in context of transposon regulation and heterochromatin establishment in developing oocytes and the early embryo
Parvin Horrieh	Bjørås	Deciphering the role of DNA secondary structures during oocyte maturation and early embryo development
Petra Santha	Pandey	A CRISPR/Cas9 based genome-wide screen to identify factors regulating transcription
Rujuan Zuo	Filipczyk	N 6 -Methyladenosine Safeguards Formative Competence for Lineage Entry – In Revision
Sara B. Markusson	Pandey	Establish the role of CDK12/CDK13 inhibition in regulating cell cycle and DNA replication
Vincent Cuminetti	Arranz	Studying Sucnr1 function on HSC in vivo in health and malignancy
Xuechen Wu	Klungland	Epitranscriptomic regulation and genome stability in primordial germ cells
Yanjiao Li	Klungland	NAD ⁺ -Capping: A New Mechanism for Metabolic Regulation of Zygotic RNAs in Early Embryos?
Yimeng Chen	Arranz	Transmission Electron Microscopy imaging of fenestrated endothelial cells in bone marrow



The Early Career Researcher (ECR) Committee 25-26: Maria Vera Rodrigues, Aylin Cengiz and Håvard Aanes.
Photo: Guro Flor Lien

CRESCO Early Career Researchers (ECR)



Motivation & Vision Statement

The Early Career Researcher (ECR) Committee 25-26 at CRESCO is driven by a shared motivation to create a vibrant, supportive, and empowering environment for PhD candidates, postdoctoral fellows, and all early-stage researchers in our community. As young researchers ourselves, we understand the challenges that come with navigating academic life from building a professional identity to finding a sense of belonging in a rapidly evolving scientific landscape. This committee was formed to address these needs and strengthen the ECR experience at CRESCO.

We are passionate about fostering an environment where early-career researchers feel supported both professionally and socially. Many of us have personally experienced the value of mentorship, collaboration, and peer support and want to ensure that all ECRs at CRESCO have access to similar opportunities. By building a strong network, we hope to reduce the sense of isolation that can come with research, encourage cross-disciplinary engagement, and create platforms where young researchers feel confident to share ideas, seek advice, and grow.

Committee goals

Our committee's mission is to strengthen the ECR community through career development, scientific exchange, and meaningful social interactions.

We aim to enhance the overall ECR experience by:

- Providing opportunities for professional growth through seminars, workshops, and career-focused events that support skill development and long-term career planning.
- Facilitating scientific discussions that allow ECRs to exchange knowledge, seek feedback,

and become active contributors to the scientific dialogue at CRESCO.

- Creating social spaces where researchers can relax, connect, and get to know each other beyond the confines of the lab, helping to cultivate a welcoming, collaborative community.

The CRESCO ECR committee invited two guest speakers in 2025:

- **Cécile Moroni**, “Edutainment” workshop on how to navigate a multicultural working environment in Norway.
- **Adine Dørum**, session on Transferable Skills. The session also included practical exercises, allowing participants to start applying the concepts during the seminar.

Plans for the coming year:

The ECR committee will continue organizing seminars, social activities and Language café, as well as provide some guidance for the arriving members at CRESCO.



Snapshots of our Early Career Researchers at the CRESCO Retreat. Photos: Guro Flor Lien

Highlights on Grants to CRESCO Early Career Researchers (ECRs)

Several of our ECRs have received national and international grants in 2025. We highlight the most relevant here.

Congratulations!

Vincent Cuminetti



Vincent receiving the Kick-off grant award at the EHA2025 congress in Milan (Italy). Photo: EHA.

European Hematology Association (EHA) Kick-off Grant in the group Stem Cells, Ageing and Cancer, supervised by Lorena Arranz.

Project title: **Succinate receptor 1 in the mesenchymal-adipocytic lineage of the HSC niche (MAdSuc).**

Yanjiao Li

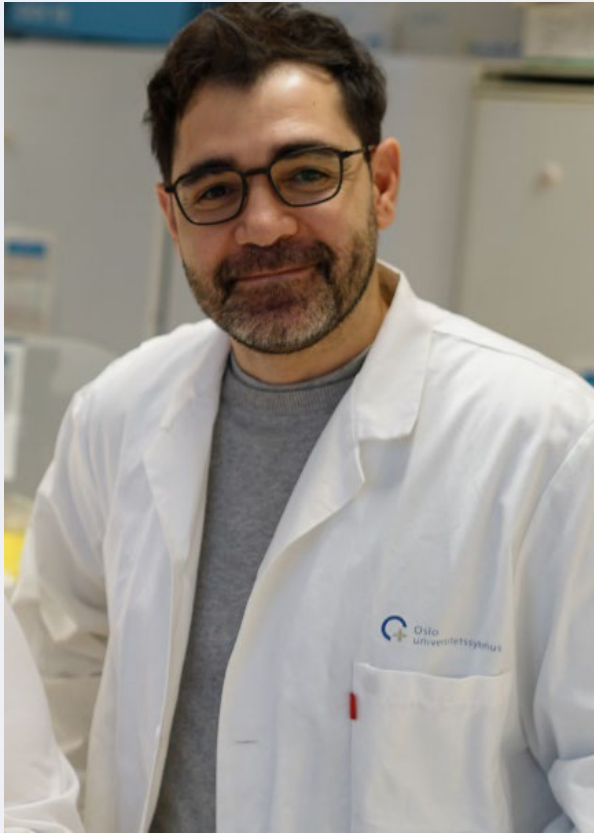


Researcher Project for Young Talents (FRIPRO) by The Research Council of Norway

Project title: **RNA modification in Early Embryo Development, Improving the outcome of IVF treatment**

Yanjiao Li. Photo: Guro Flor Lien, UiO

Nicola Montaldo

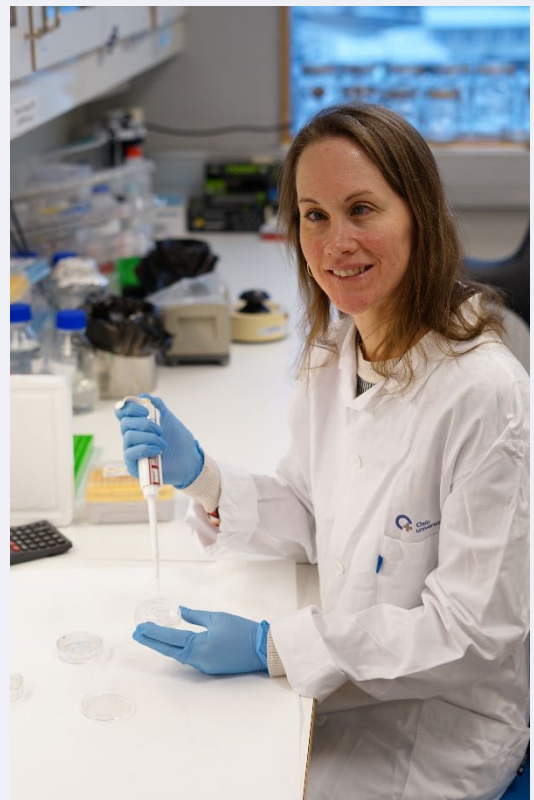


Nicola Montaldo in the lab. Photo: Guro Flor Lien

Research Project for Young Talents (FRIPRO) by The Research Council of Norway

Project title: **Mitochondria-Initiated Neuronal Defence against Parkinson's Disease.**

Emma Lång



Emma Lång in the laboratory. Photo: Guro Flor Lien

Helse Sør Øst Open Project funding

Project title: **Navigating the Tunnel: Keratinocyte Dynamics & Therapeutic Targeting of IL-17 in Hidradenitis Suppurati.**

Awards to CRESCO Early Career Researchers (ECRs)

Several of our ECRs have received national and international recognition to their outstanding work in 2025.

Congratulations!



Nicola Montaldo

Vaccibody Innovation Award 2025

The Vaccibody Innovation Award was established in 2020 when Agnete Fredriksen won the Research Council of Norway's Innovation Prize. Fredriksen donated the NOK 500,000 prize money to SPARK Norway, and for the past five years the NOK 100,000 award has gone to the most innovative SPARK Norway project among the graduated projects.

Nicola Montaldo and Agnete Fredriksen Photo: Photo: Jarli&Jordan/UiO.

Krister Vikedal

Prize for outstanding research article (OUS)

The awards for outstanding research articles are distributed twice a year based on more than 2,400 scientific articles published annually by OUS. The division's research committees nominate the articles and an external committee evaluates and finally selects the six worthy winners.

Article: **RecN and RecA orchestrate an ordered DNA supercompaction response following ciprofloxacin-induced DNA damage in *Escherichia coli***, Nucleic Acids Research, 2025; 53

Krister Vikedal at the award ceremony receiving flowers and a diploma. Photo: Tekle A. Lobie.



Erkut Ilaslan



Prize for the best poster (ICMM-KU)

During the annual meeting of the Department of Cellular and Molecular Medicine at the University of Copenhagen, posters presented by postdoctoral fellows and PhD students are nominated by attendees for the Best Poster Prize. In 2025, the award was given to Erkut Ilaslan for the poster titled **"Identification of RNA-binding Proteins Safeguarding the Oocyte Epigenome."**

Erkut Ilaslan receiving the Best Poster Award from Head of Department Ian Hickson at the annual departmental meeting.

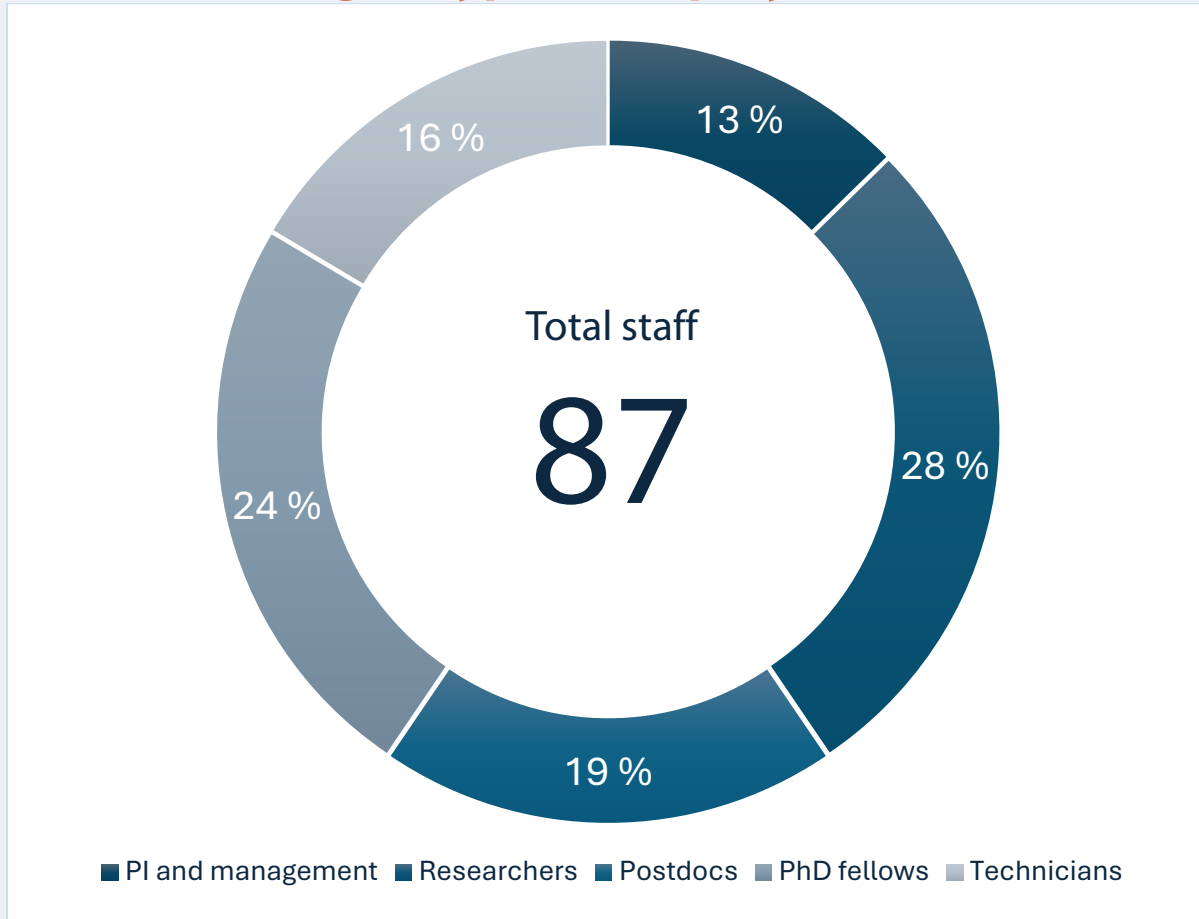


CRESCO In Numbers

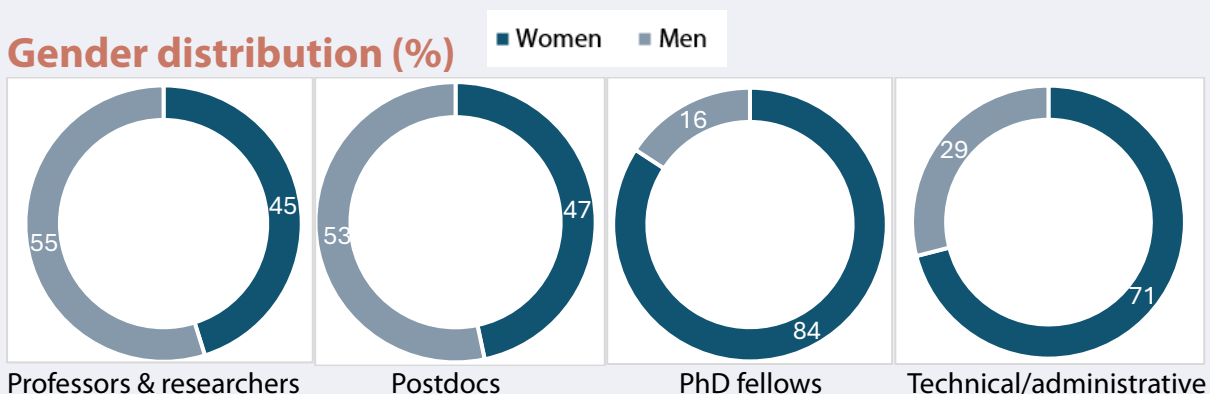
CRESCO in numbers

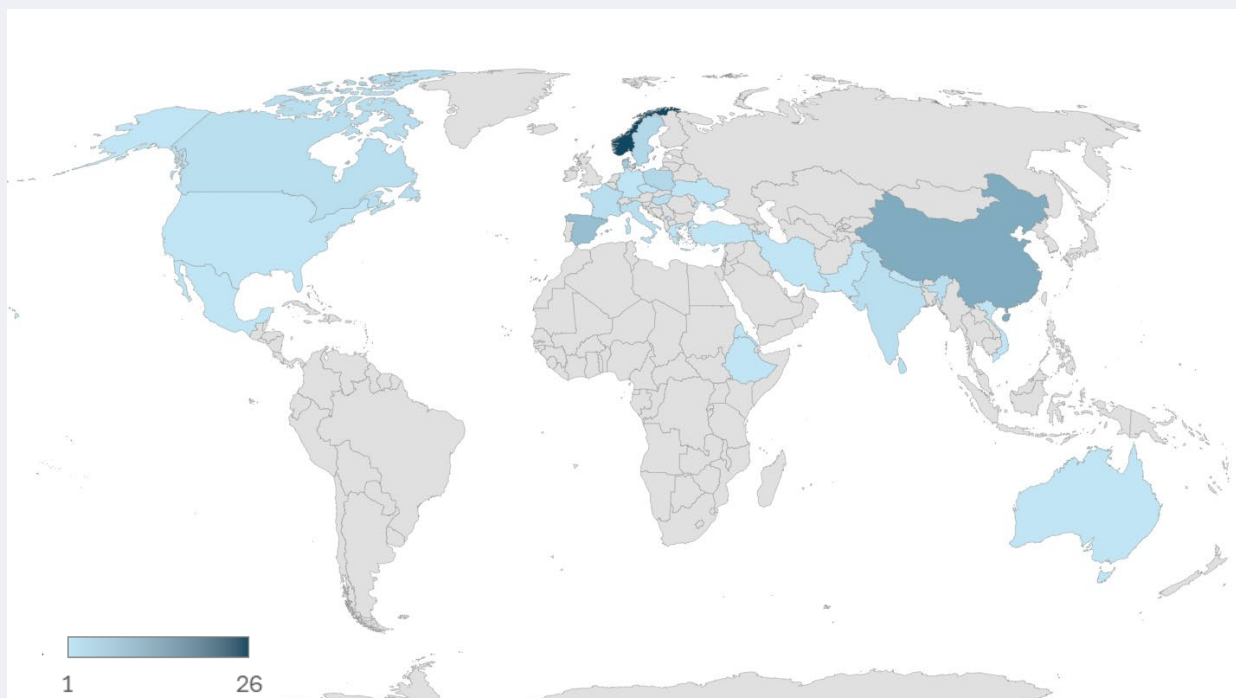
2025

Staff according to type of employment (%)



Gender distribution (%)



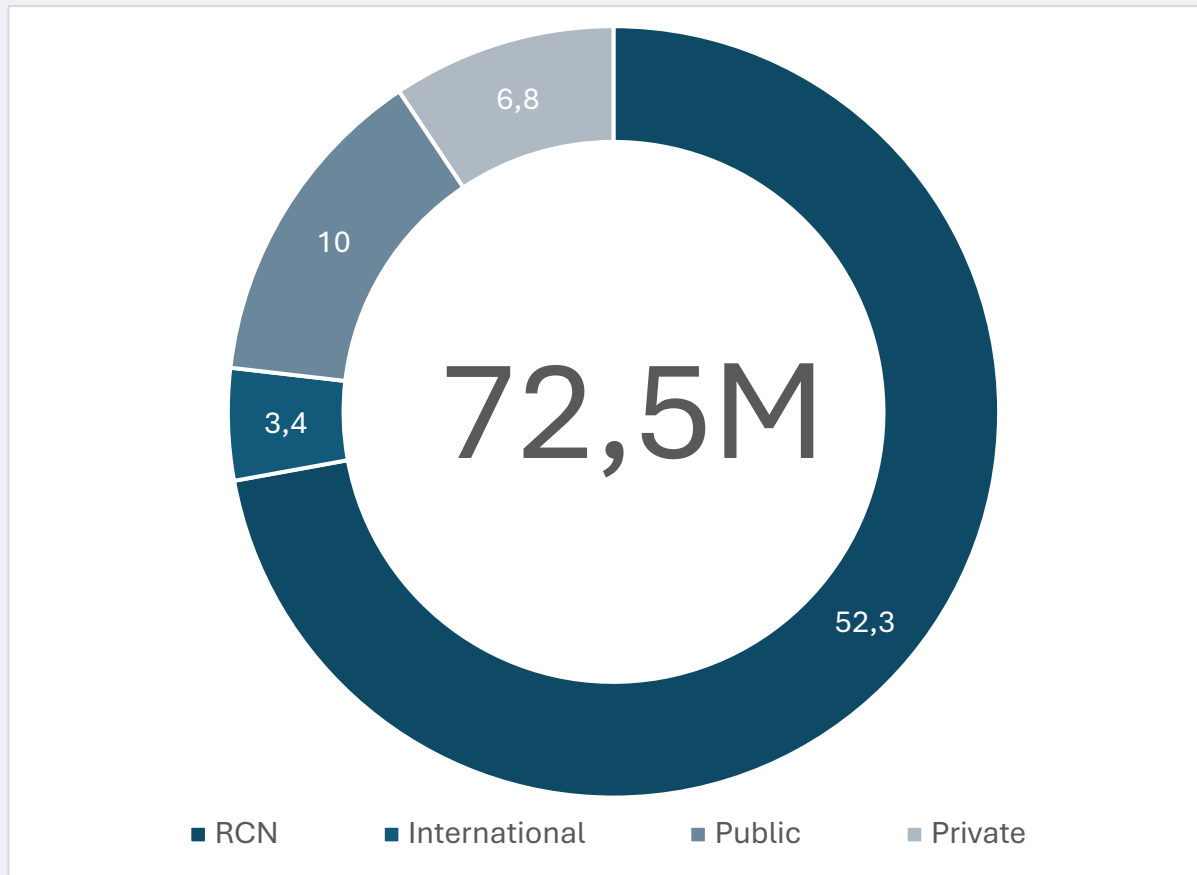


CRESCO staff represent 28 different countries.

Staff working on CRESCO projects in 2025

Adam Filipczyk	Erwan Yann Delbarre	Lisa Anne Hubers	Qindong Zhang
Adeel Manaf	Felicia Kristiansen	Lisa Lirussi	Rajikala Suganthan
Alba Soto Fuertes	Francisca Ferrer Marin	Lorena Arranz	Rujuan Zuo
Alexander M. Skjetne	Francisco J. N. Galindo	Lukasz Wyrozemski	Sara B. Markusson
Anna Lång	Gaute Nesse	Madeleine Fosslie	Sigrid Aslaksen
Anne Hege Alm-Kristiansen	Gunn Hildrestrand	Mads Lerdrup	Solveig Osnes Lund
Arne Klungland	Guro Flor Lien	Magnar Bjørås	Sonali Kaththriarachchi
Asmita Shrestha	Hilde Nilsen	Marcel Heugel	Sonia Pen Perez
Aylin Cengiz	Håvard Aanes	Maria Vera-Rodriguez	Sophie E. Bresson
Birgitte Narud	Ingeborg Austli Grov	Marthe Lindahl Karlsen	Stig ove Bøe
Carmen Herrera	Ingrid Åmellem	Michel Choudlakis	Tekle Airgecho Lobie
Cassandra Emilia Lax	Ingvill Sæbø	Mika Zagrobelny	Teklu T. Zeremichael
Charlotte Krog	Jedrzej M. Malecki	Mingyi Yang	Valentina K. Sinani
Christine Gran	Jingwei Li	Mirra Søegaard	Veronica S. Morales
Deo Pandey	Joanna Bremer	Nadine Massiah	Vincent Cuminetti
Dongjie Zhou	John Arne Dahl	Ngan Huynh Bao	Xiaolin Lin
Eirin J. Starheim	Kamilla Børve Nygård	Nicola Montaldo	Xuechen Wu
Elina Holub	Kangxuan Jin	Parvin Horrieh	Yanjiao Li
Elisabeth Kommisrud	Lara Gherz Eddin	Peter Fedorcsak	Yesim Bilmez
Emma Lång	Laura Vinklerová	Petra Sántha	Yimeng Chen
Erkut Ilaslan	Lene Alsøe	Preeti Jain	Yohan Lefol
Erna Davydova	Linda Ellevog Skuggen	Pål Falnes	

Funding in NOK



CRESCO economy

CRESCO-supported PIs currently receive national and international funding for around 30 projects that align with and complement the CRESCO initiative, totalling 72,5 million NOK annually, including the RCN CRESCO funding. We also enjoy strong support from our host Institutes.

SpermVital is a company created by CRESCO PI Elisabeth Kommisruds, and the company secured a three-year Innovation Project from RCN. SpermVital is a company developing ActPack, a novel bovine semen packaging technology for large-scale, sustainable artificial insemination. ActPack uses a natural alginate gel to temporarily trap sperm cells. After insemination, the gel dissolves gradually over about 24 hours, releasing sperm over time. This extends the fertile window, reduces dependence on perfect heat timing, and supports well-documented, high-quality semen production.

spermvital

Zenit Science, a company founded by CRESCO PI and professor at NTNU, Magnar Bjørås, has received 10 million NOK in funding for its innovative project focused on the development of organoids. These mini organs, created from human cells in 3D, have the potential to replace animal testing in important research areas such as disease modeling and the testing of drugs, chemicals, and gene therapy.



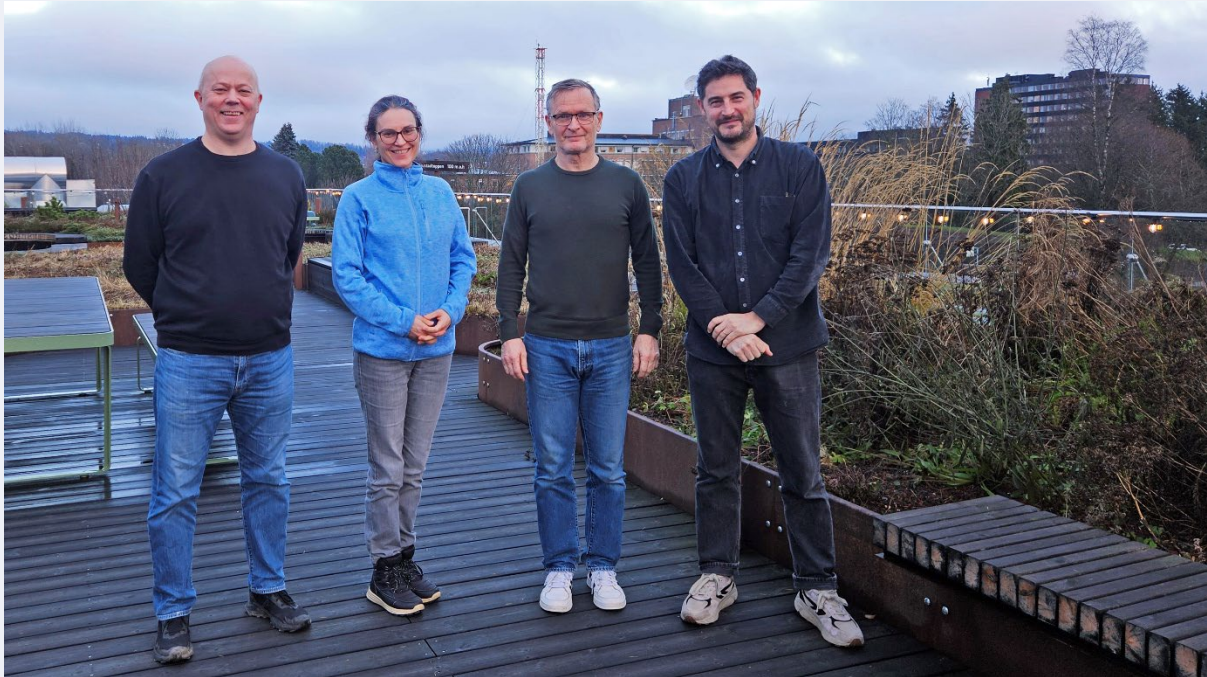
New projects funded in 2025

Nicola Montaldo	Mitochondria-Initiated Neuronal Defence against Parkinson's Disease	10 000 000
Anne Hege Alm-Kristiansen	Advancing Livestock Reproduction for Sustainable Breeding Through Integrative Functional Analysis of Gametes	12 906 000
Arne Klungland	Innovative Technology for Identification and Detection of Cancer Markers	500 000
Arne Klungland	Epitranscriptomic regulation of Bladder Cancer	6 750 000
Arne Klungland/ Sig Ove Bøe	GENESIS	8 750 000
Deo Pandey	Decoding addiction	4 250 000
Elisabeth Kommisrud	ActPack – Novel sustainable technology for large scale production of immobilized bull sperm doses	8 250 000
Emma Lång	Navigating the Tunnel	9 000 000
Francisca Marin/ Lorena Arranz	Identification of novel mechanisms that predispose to clonal hematopoiesis and/or myeloid neoplasm	236 000
John Arne Dahl	CATCH - CAncer deTection by CHip-seq	8 000 000
Lorena Arranz	NEUROTARGET	9 000 000
Magnar Bjørås	Advancing Organoid Technology	15 000 000
Magnar Bjørås	Advancing organoid technology – implication for personalized medicine	750 000
Vincent Cuminetti/ Lorena Arranz	Succinate-receptor 1 pathway in hematopoietic stem cell niche remodeling in AML	322 000
Yanjiao Li	Metabolism-Epitranscriptome Crosstalk: Novel Regulation in Embryo Development	10 000 000
Yanjiao Li	Deciphering a Century-Old Puzzle: Warburg effect in Cancer Cells	6 400 000



CRESCO
Convergence

GENESIS: Gene-Epigenome-Active Matter Nexus in Early Embryogenesis



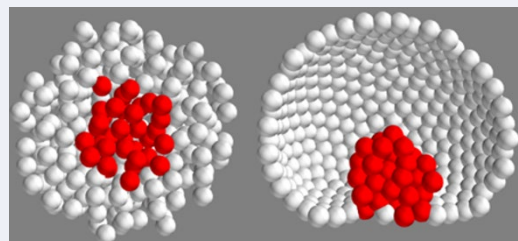
The GENESIS consortium (from left): Stig Ove Bøe, Department of Microbiology, Division of Laboratory Medicine (KLM), OUH, Luiza Angheluta, Department of Physics, The Faculty of Mathematics and Natural Sciences, Arne Klungland, Department of Clinical Medicine, the Medical Faculty and CoE CRESCO, and Alvaro Köhn-Luque, Institute of Basic Medical Sciences, Oslo Centre for Biostatistics and Epidemiology, Faculty of Medicine and CoE Integreat . Photo: Torunn Vistnes Espe.

The first days of life, from fertilization to the pre-implantation embryo, are when the basic body plan of a mammal is set up. In the mouse, the single-cell zygote divides and rearranges to form a blastocyst, a small ball of cells that will later implant in the uterus. During this time, cells move, polarize, and begin to adopt distinct fates, laying down body axes and the first specialized tissues.

These processes can be viewed through the lens of “active matter” – systems made of many energy-consuming units that move and organize themselves, such as flocks of birds, cytoskeletal filaments inside cells, or groups of cells in a tissue. Active matter theory provides a framework for understanding how such systems spontaneously form patterns and structures. Yet we still do not fully understand how active matter-like behaviors in cells and tissues shape the self-organization of early mammalian embryos.

In this project, we will investigate how active matter principles operate during early mouse development, from fertilization to blastocyst formation. We will combine high-resolution live imaging and spatially resolved gene expression data with theoretical and computational models of active matter. By linking physical self-organization with gene regulation, we aim to reveal how evolution has tuned gene-controlled processes to harness active matter dynamics during the earliest stages of life.

Snapshots from simulations of blastocyst formation (Luiza Angheluta). →



Decoding addiction

Unravelling Individual Variability to guide Prevention



The Decoding addiction convergence (from left): Siri Leknes, Department of Psychology, Faculty of Social Sciences, Koen Vervaeke, Department of Basal Medicine, Faculty of Medicine, Deo Pandey, Department of Microbiology, Division of Laboratory Medicine (KLM), OUH, Osman Gani, Dept. of Pharmacy, Faculty of Mathematics and Natural Sciences.

Addiction is one of the most pressing public health challenges of our time. Yet individuals differ dramatically in their vulnerability to opioid dependence, treatment response, and relapse risk. A central biological player is the μ -opioid receptor, encoded by OPRM1, which mediates the rewarding and analgesic effects of opioids. Genetic variation in OPRM1 is associated with altered drug sensitivity, but the mechanistic consequences of specific mutations remain poorly understood across molecular, cellular, circuit, and behavioral levels.

Decoding addiction convergence focuses on a functionally significant OPRM1 variant (Arg181Cys) to understand how a single amino acid change can reshape receptor signaling, neuronal communication, and ultimately addiction-related behavior. We integrate four complementary levels of analysis: (i) human behavioral and pharmacological studies; (ii) in vivo mouse circuit analysis using biosensors, optogenetics, and real-time monitoring of dopamine and calcium dynamics; (iii) molecular and cellular dissection of signaling pathways in human and mouse neural stem cell-derived neurons; and (iv) computational modeling of ligand–receptor interactions and downstream G-protein versus β -arrestin signaling bias.

By bridging psychology, systems neuroscience, molecular biology, and structural pharmacology, Decoding addiction creates a true convergence framework. Our goal is to move from mutation to mechanism—and from mechanism to precision intervention—laying the foundation for individualized prevention and treatment strategies for opioid addiction.



CRESCO Patient Involvement

Patient day at MIK/CRESCO

Strengthening collaboration between patients and researchers



All the patient representatives, patient advocates, and researchers in physical attendance at the Patient Day.
Photo: Guro Flor Lien, UiO

First Patient Day at MIK/CRESCO

On 21 August 2025, **Dr Lorena Arranz**, Deputy Centre Director at CRESCO together with **Dr Anita Kavlie** from EATRIIS Norway, organized and hosted the first Patient Day at MIK/CRESCO, bringing

patient representatives and patient advocates, infrastructure, and researchers into the same room to explore how patient involvement can be strengthened across all stages of research.



Opening of the workshop at the Patient Day by Lorena Arranz and Anita Kavlie.
Photo: Guro Flor Lien, UiO

Patient Involvement

The morning program focused on experiences with patient involvement in both basic and clinical research, on how collaboration can shape project design, clinical trials, and communication of results:

- We listened to valuable patient voices from representatives from Kreftforeningen, Blodkreftforeningen and Blærekreftforeningen (Norwegian Bladder Cancer Society)
- Patient advocates were represented by the Acute Leukemia Advocates Network
- Researchers at Universitetet i Oslo (UiO) and Sykehuset Asker og Bærum HF shared their point of view into the topic and own experiences.



Anita Nymo, representing Blodkreftforeningen (the Norwegian Blood Cancer Society). Photo: Guro Flor Lien, UiO

Resources

The program followed with a resource session highlighting key national and European initiatives:

- Folkehelseinstituttet on patient engagement in medical devices
- EUPATI and their training of patient experts and open classroom resources
- Forening for sjeldne Neuroutviklingslidesler on the role of rare disease patient organizations in collaboration and data sharing, and their use of resources
- EATRIS introducing the Patient Engagement Resource Centre (PERC)
- REMEDI4ALL on drug repurposing with strong patient involvement at its core, and a concierge service for both patients and researchers

Round table discussions

In the afternoon, round table discussions brought researchers and patient representatives together in small groups. Early Career Researchers and Group Leaders briefly presented their scientific projects, followed by an open dialogue on how and when patients can best be involved. These lively conversations surfaced both opportunities and challenges.



Round table discussions with researchers and patient representatives. Here from Lorena Arranz' group. Photo: Guro Flor Lien, UiO

A clear message from the day was the strong enthusiasm to **make the Patient Day an annual tradition**, creating a dedicated arena for collaboration, learning, and mutual inspiration.

We extend a heartfelt thank you to all speakers, patient representatives and advocates, and researchers at MIK/CRESCO who made this day possible, and to all participants for their contributions.

We look forward to continued collaborations.

See you next year!



CRESCO
Innovation

Highlights on CRESCO SPARKees

Several of our ECRs have SPARK projects ongoing or received SPARK projects in 2025.

Congratulations!

Carmen Herrera



From left: Carmen Herrera and Pål Falnes (team member). Photo: Jarli&Jordan, UiO

Blood-Based test for monitoring lung cancer.

Timeline: 2024-2027 Our team is developing a non-invasive test to monitor lung cancer using a novel biomarker with high sensitivity and specificity, based on a newly identified human protein methyltransferase. This novel, blood-based test aims to monitor lung cancer and could potentially be integrated into standard patient screenings and annual checkups.

Milestones: Technology development (achieved); Validation of the blood biomarker (in progress).

Yanjiao Li

Advanced Technology for Identifying and Detecting RNA Modification–Based Cancer Markers.

Timeline: 2025-2027

RNA modifications are emerging as critical regulators of tumor initiation and progression, but robust and scalable technologies for detecting clinically relevant RNA modification signatures remain limited. This SPARK-supported project aims to develop innovative technologies for the identification and detection of RNA modification–based cancer biomarkers. By integrating sensitive RNA modification profiling methods with translational assay development, we seek to enable future diagnostic and prognostic applications in oncology.

Milestones: Data collection (in progress); Intellectual property (IP) strategy (under discussion).



Photo: Private

Nicola Pietro Montaldo



Photo: Private

Novel targets for attenuating Parkinson's disease progression.

Timeline: 2024-2025

This innovation project investigates whether regulation of a specific target protein can protect dopaminergic neurons from α -synuclein-dependent neurodegeneration, a key pathological mechanism in Parkinson's disease. Building on strong genetic and mechanistic evidence, we are translating these findings into a therapeutic strategy by developing a small-molecule aimed at modulating the target's activity in a clinically relevant manner.

Milestones: Established and validated in vitro models of α -syn-driven neurodegeneration; Demonstrated that regulation of the target protein confers neuroprotection in dopaminergic neurons; Identified and initiated optimization of small-molecule candidates (all achieved).

PROTAC-ting Against N6-Methyladenosine Addicted Cancers.

Timeline: 2024-2025

Recent studies show that cancer advancement involves increasing dependencies on ever higher abundances of the RNA modification N6-methyladenosine (m6A). We designed and synthesized a novel PROteolysis-Targeting Chimera (PROTAC) drug named EPITAC. Our drug is designed to firstly block the enzymatic cleft of the m6A methyltransferase enzyme METTL3. Its second property is an inbuilt linker and E3 ligand which sequesters the prostate cancer cells' own E3 ubiquitin ligase enzyme. The resulting polyubiquitination of METTL3 marks it for degradation by the proteasome, disabling m6A deposition on RNA. This design promises an increased potency and efficacy of EPITAC, reducing the possibility for off-target effects and drug-resistance mechanisms in clinical trials.

Milestones: Successful purification of EPITAC by November 2025, after 46 chemical synthesis and optimization steps (achieved); Testing and characterization of EPITAC in cancer models is ongoing (in progress).

Adam Filipczyk



Photo: Private

Awards to our PIs

Trønder of the Year 2025

Magnar Bjørås has been named Trønder of the Year by Adresseavisen and NRK!

Bjørås receives the award for his work in researching rare diseases, such as childhood dementia.



His biotech company Zenit Science works closely with his research groups in both Oslo and Trondheim.

Magnar Bjørås receiving his award in Olavshallen in Trondheim.

Innlandet Innovation Award 2025

Elisabeth Kommisrud was presented with The Innovation Award 2025! The award ceremony took place during the Agenda Innlandet Conference in Lillehammer on February 19th 2026. The Innovation Award is presented to entrepreneurs, companies, development organizations, or community actors who have contributed to business development in Innlandet through sustainable innovation.

Elisabeth Kommisrud, second from the left, together with County Mayor Thomas Breen (center) and the other award recipients.

Photo: Arne Klungland





CRESCO Events

CRESCO Guest Lectures

We are very happy with our continued series of guest speakers that are invited by our Principal Investigators or by our Early Career Researchers (ECR).

As part of our CRESCO guest lectures, in 2025, we have welcomed several international researchers at all career stages, expert in various topics relevant to us.



12.02.2025 Prof. **Lars Dyrskjød**, Professor at the Department of Clinical Medicine - Department of Molecular Medicine (MOMA), Aarhus University, Denmark. His research group performs translational bladder cancer research, Liquid biopsy analysis, biomarker validation and understanding disease biology, tumor subtypes and tumor evolution

Lecture title: **Tumor Characteristics and Systemic Immunological Profiles in Bladder Cancer: Correlations with treatment response and outcomes.**

24.02.2025 Dr. **Yungui Yang**, Director of the Beijing Institute of Genomics, Chinese Academy of Sciences and Director of the China National Center for Bioinformation (CNCB). His research interest is to dissect the roles and biological significance of RNA modification.



Lecture title: **Role of dynamic RNA methylation in gene expression regulation and introduction to CNCB**



11.04.2025 Dr **Victor Kalbskopf** Senior Engineer at the Bioinformatics Core Facility, Cancer Institute Radium Hospital, Oslo. Bioinformatics Core Facility have expertise in RNA-seq analysis, short and long read genomics and transcriptomics analysis, single-cell and spatial-omics, data management, and offer help with experimental design.

Lecture title: **Bioinformatics Core Facility: Getting Insights from Data.**

GUEST SPEAKERS

12.05.2025. Virtual International Journal Club through the EHA Specialized Working Group on Stem Cells. Dr. **Bong Ihn Koh** presented his work published in Nature in 2024.



Lecture title: **Adult skull bone marrow is an expanding and resilient haematopoietic reservoir.**



20.05.2025 Dr. **Marcus Buschbeck**, Senior Group Leader at the Josep Carreras Leukaemia Research Institute (IJ), Spain. In their basic research, his group dissects molecular mechanisms of chromatin regulation and evaluates if this knowledge has an application in cancer. The group has a long-standing interest in histone variants with macrodomains. In their more applied projects, the group screens for novel drug targets for blood cancers and to understand their molecular mode of action.

Lecture title: **Mining the chromatin regulatory space for drug targets in myeloid malignancies.**

27.05.2025 Dr **Sebastian Leidel**, Professor for Cellular RNA Biochemistry at the University of Bern. The focus of his work is RNA modifications and how they affect mRNA translation and RNA metabolism as a whole. To address these questions, the Leidel lab uses different experimental models from baker's yeast to zebrafish. Furthermore, they apply quantitative high throughput methods like ribosome profiling and RNA mass spectrometry.



Lecture title: **RNA modifications and the two sides of the coin in health, disease and development.**



17.06.2025 Prof. **Kenn Gerdes** is a distinguished microbiologist renowned for his pioneering research in bacterial genetics, stress response, and cell division mechanisms. He is now retired as a Full Professor while at the Department of Biology at the University of Copenhagen. His lab became one of the global leaders in this area. His contributions to the field have been recognized with numerous accolades, such as the EMBO Membership in 2005 and the American Academy of Microbiologists in 2009.

Lecture title: **Prokaryotic toxin-antitoxins: phylogeny and biological roles.**

GUEST SPEAKERS

22.08.2025 Dr. **Leo Kurian**, Professor at Goethe University Frankfurt, Germany. Their study examines context-specific splicing decisions in the heart, focusing on a key cardiac splicing factor. Although ubiquitously expressed, its loss uncouples cardiogenesis from sarcomere formation and function. They show that this factor stabilizes spliceosome complexes at weak 5' splice sites in mRNAs essential for cardiac function, ensuring splicing fidelity. Its loss disrupts the cardiac splicing code, causes nuclear retention of aberrantly spliced mRNAs, and yields a sarcomere-free, non-beating heart.



Lecture title: **A Pre-mRNA Splicing Program Decouples Cell Fate Decisions from Function During Cardiac Development.**



16.09.2025. Prof. **Mathew Coleman**, Professor at the University of Birmingham, UK. His group focuses on protein hydroxylases that target the protein synthesis machinery. In 2017 his team was awarded a CRUK Programme Foundation Award to investigate the role of histidine, arginine, and lysine hydroxylases in cancer. A less well-known sub-family of protein hydroxylases are characterised by the presence of a Jumonji-C (JmjC) catalytic domain and emerging roles in tumour cell biology. These enzymes are attracting interest as targets of hypoxia and oncometabolites and for their potential for developing novel therapeutics.

Lecture title: **Jumanji Jumonji: Emerging roles of protein hydroxylases in tumour cell biology.**

02.10.2025 Dr. **Bennett van Houten**, Richard M. Cyert Professor of Molecular Oncology at the University of Pittsburgh, where he co-lead the Genome Stability Program at the UPMC-Hillman Cancer Center until June 2024. He is recognized for his significant contributions to the study of DNA repair proteins in both bacterial and human cells, and his lab focuses on real-time single-molecule research of DNA repair protein dynamics, supported by a NIEHS RIVER Award



Lecture title: **Watching DNA repair at the single molecule level in real-time: seeing is believing.**

GUEST SPEAKERS



20.11.2025 Prof. Dr. **Saffet Öztürk**, Associate Professor at Department of Histology and Embryology, Akdeniz University School of Medicine in Antalya, Türkiye. Accumulating evidence indicates that both DNA and histone methylation patterns undergo age-associated alterations, which are closely linked to the progressive decline in fertility. Considering the interplay between these two epigenetic mechanisms, further investigations are warranted to clarify the molecular pathways underlying ovarian aging, particularly in the context of GV and MII oocytes

Lecture title: **The Relationship Between Female Fertility Loss During Ovarian Aging and DNA/Histone Methylation Changes**



Professor Leo Kurian giving his CRESCO guest lecture in our seminar room. Photo: Guro Flor Lien

CRESCO retreat at Hurdalssjøen



The retreat participants outside of Hurdalssjøen Hotel, in between two rain showers.
Photo: Guro Flor Lien, UiO

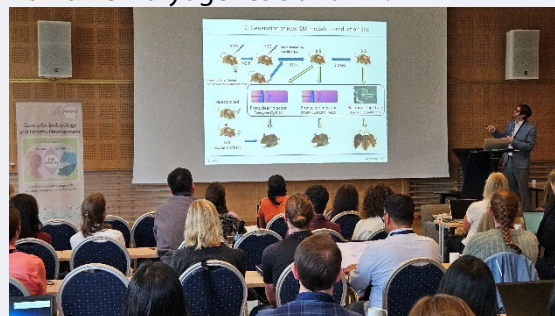
Our annual CRESCO retreat held at Hurdalssjøen Hotel focused on fostering collaboration, innovation, and knowledge exchange among senior researchers, early career scientists and Core Facilities. With an engaging program filled with presentations and ample networking opportunities, the retreat proved to be a vital platform for exploring cutting-edge research and establishing meaningful connections within the Centre.

Day 1: An experimental approach to CRESCO

CRESCO Principal Investigators (PIs) took to the stage to present their ongoing and future research projects in the first session. Each PI had five minutes to share insights into their ongoing work and future perspectives, allowing attendees to gain an overview of the diverse research within CRESCO.

Following the PIs, Knut Tomas Dalen from the University of Oslo (UiO) introduced the Transgene Core Facility, which plays a crucial role in supporting innovative genetic research.

After an enjoyable lunch, attendees were immersed in a series of experimental-focused presentations. This afternoon segment featured CRESCO PIs Elisabeth Kommisrud, who discussed livestock embryogenesis, and Peter Fedorcsak, who shared insights on human embryogenesis and IVF.



Knut Tomas Dalen introducing the Transgene Core Facility. Photo: Guro Flor Lien, UiO

Participants were also introduced to essential Core Facilities available to them. Leonardo Meza-Zepeda from OUH presented on the Sequencing Facility, discussing its role in enhancing genetic research capabilities. Stig Ove Bøe, also from OUH, followed with insights into Advanced Light Microscopy.

Representing NTNU, Cathrine Broberg Vågbø shared the key resources available at the DNA/RNA Core, which supports essential molecular research. The session concluded with Eirin J. Starheim from NTNU addressing the NAXtra magnetic nanoparticles, which provide a low-cost and efficient method for isolating nucleic acids from tissues, single cells, and cell-free body fluids. This segment underscored the vital contributions of core facilities to collaborative scientific advancements.



Participants mingling between sessions. Photo: Guro Flor Lien, UiO

The day concluded with opportunities for relaxation and social interaction, where attendees engaged in activities like kayaking, spa/sauna and wine tasting, before enjoying a wonderful dinner.

Day 2: Centre for Fertility and Health and our Early Career Researchers

The second day of the retreat began with a talk from the Centre Director of Centre for Fertility and Health, Siri Eldevik Håberg. The Centre primarily focuses on understanding fertility and reproductive health exploring various factors that influence fertility, including lifestyle, environmental, and biological factors. The centers research complement CRESCO's research focus.

The program continued with three sessions with CRESCO Early Career Researchers (ECR) presenting their work.



Siri Eldevik Håberg presenting the Centre for Fertility and Health. Photo: Guro Flor Lien, UiO

Elina Holub opened the morning session with her work on optimizing in vitro embryo production techniques in pigs, followed by Mika Zagrobelny's insights on histone variant incorporation during mouse oogenesis and Maria Vera-Rodriguez's PRIME study on reproductive health outcomes. Sonali Kaththiarachchi also discussed oocyte quality parameters in Atlantic salmon, emphasizing their relevance for aquaculture.

Following a coffee break, the second session continued with Kangxuan Jin addressing ALKBH5 deficiency in meiosis and Dongjie Zhou exploring pseudouridine dynamics. Yohan Lefol presented his findings on Smug1 in the murine olfactory system, linking genetic insights to broader biological contexts.

In the afternoon, Solveig Lund covered the role of GTF2H3 in Cockayne Syndrome and Erna Davidova discussed histidine methylation and zinc in the context of reproductive health. Parvin Horieh analyzed DNA secondary structures during oocyte maturation, while Vincent Cuminetti connected metabolic pathways to hematopoiesis and leukemia.

The outgoing Early Career Researchers (ECR) Committee officially transferred their responsibilities to the new committee and was presented with a gift in recognition of their great effort over the past year. The CRESCO retreat was a success, emphasizing the importance of collaboration and innovation in scientific research.

We extend our heartfelt gratitude to all participants, presenters, and organizers who contributed to this experience!

Our presence in social media

Follow us on LinkedIn, Instagram, Facebook or X to stay updated on our new publications, events, social activities and more!

LinkedIn



Instagram



Facebook



X



Social Activities in 2025

At CRESCO we strive to have an inclusive and social workplace where we get to know each other across research groups and locations. This year's social activities included hammock camping at Vettakollen, Holmenkollstafetten, our annual summer party, canoe trip to Fjorda and scientific crafts session for Easter and Christmas!



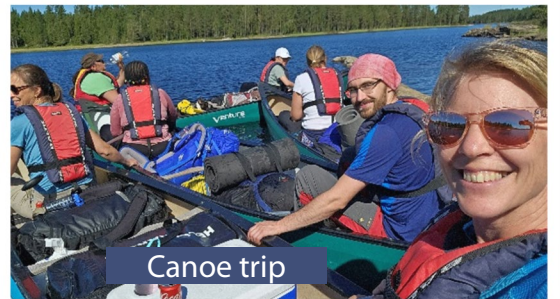
Summer party



Holmenkollen relay race



Science crafting



Canoe trip



Hammock camping



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