UNIVERSITY OF OSLO

NCMM – Centre for Molecular Medicine Norway

# Annual Report NCMM 2023

NCMM

NORDIC **EMBL** PARTNERSHIP FOR MOLECULAR MEDICINE

UNIVERSITAS OSLOENSIS MDCCCXI

NCMM – From disease
mechanisms to
clinical practice

NCMM Co-Funders:

University of Oslo
The Research Council of Norway
Helse Sør-Øst

# Contents

# Welcome from the Director

Photo: Oda Hveem

Dear colleagues, friends, and supporters of NCMM. It is my great pleasure to welcome you to the 2023 NCMM Annual Report.

I would like to express my deep appreciation to our group leaders, researchers, students and staff for their dedication and hard work over the past year. Their achievements are demonstrated by the numerous publications reporting important discoveries as well as the multitude of initiatives undertaken throughout the year, some of which are detailed in this report.

I warmly congratulate Charlotte Boccara on receiving the prestigious Starting Grant from the European Research Council. Her innovative, interdisciplinary project, SleepCog, will open new avenues for understanding the role of sleep in brain development. I also wish to extend my congratulations to Biswajyoti Sahu, Marieke Kuijjer and Anthony Mathelier for completing a year of funding successes by securing three grants from the Norwegian Cancer Society's annual call.

I would further like to congratulate Sebastian Waszak on his new position as Assistant Professor of Life Sciences at the École Polytechnique Fédérale de Lausanne, starting in June 2023. His group continues working at NCMM with external funding.

NCMM remains dedicated to our vision of bridging the gap between basic science and translational and clinical medicine through multidisciplinary research. Our goal is to increase our understanding of molecular mechanisms of biology and to improve patient care and outcomes through precision medicine. Collaboration is key to achieving this and in 2023 we initiated two projects to encourage the development of new partnerships. NCMM launched the Joint Postdoctoral Program in Molecular Life Science, which aims to establish new collaborations between NCMM group leaders and partners in the Oslo area. The projects funded through this scheme will bring together research groups who have not previously collaborated, thus serving as a catalyst for novel and exciting research ideas.

Together with our Nordic EMBL partner centres, NCMM was awarded funds from NordForsk to support the NORPOD joint-postdoc program in 2023. The program aims to elevate the Nordic EMBL partnership collaborations by implementing joint projects across our borders that will tackle major research gaps in molecular medicine. The program will lay the foundations for a cross-Nordic community of early career researchers hosted by the four sites of the Partnership, thus facilitating the development of new competencies and promoting research excellence.

This year, we also celebrated the 10-year renewal of the Nordic EMBL Partnership, with an official signing ceremony in Helsinki. The renewal highlights the importance of cross-Nordic collaboration, and we look forward to strengthening our ties within the Nordics, EMBL and the wider EMBL partnerships. NCMM is also looking forward to hosting the annual Nordic EMBL Partnership meeting in September 2024. I am confident that this event will provide an excellent opportunity for scientific networking and knowledge exchange across the partnership.

Looking towards the future, we remain scheduled to relocate into our new spaces in the Life Science Building in 2026. The new building will result in the co-localization of leading university and hospital units within the life sciences, which in turn will be an opportunity for facilitating convergence, strengthening collaboration and identifying synergies between our research areas. NCMM will leverage the strengths of the EMBL model and the expertise of its academics to act as a node between research groups and across disciplines. This way, we will work to amplify efforts to develop new competencies and make important discoveries within molecular biology and health.

The coming years will bring changes and new exiting opportunities for the Centre to further develop and strengthen our impact on molecular biology and medical research. Our goal is to continue to act as an incubator for early career group leaders, and to promote excellence in research through collaborative efforts, both nationally and internationally.

March 2024

**Professor Janna Saarela**
Director, NCMM

# NCMM at a glance

## From disease mechanisms to precision medicine

NCMM's overall vision is to expand our molecular understanding of health and disease to enhance medical practice and promote innovation opportunities. Through basic research discoveries, we aim to provide a solid basis for development of improved diagnostics and more efficient and targeted therapies. As an international molecular medicine center, NCMM brings together multidisciplinary teams to combine basic and translational research approaches to tackle societally significant challenges. To embed this into our day-to-day activities, all our group leaders have affiliations or joint appointments within the faculties of natural sciences or medicine, or at hospital departments. In addition, our PhD students are hosted within both the natural sciences and medical faculties' doctoral programs. Translational research depends on close interactions between basic research, technology development, and hospital environments. Therefore, NCMM has established strong links to Oslo University Hospital (OUH) and other research organisations, such as SINTEF.

NCMM group leaders are outstanding, early-career researchers. Each has been recruited through a global, open call to a non-tenured 5+4-year position, with a start-up package to establish a research group. NCMM follows the European Molecular Biology Laboratory (EMBL) model for group leader recruitment and review, meaning that the final four-year extension of the group is determined by an international evaluation before the end of their first five-year period.

## The Nordic EMBL Partnership

NCMM is the Norwegian node in the Nordic EMBL Partnership for Molecular Medicine. The Partnership includes around 60 research groups and teams, with a staff of 600 employees and students across the four national nodes in Oslo, Helsinki, Umeå, and Aarhus. The Partnership has created a joint Nordic powerhouse for molecular medicine and translational research, with shared access to scientific infrastructures, including databases, facilities, and instrumentation as well as clinical materials and networks across the Nordic countries.



# Group leaders

From left to right: Biswajyoti Sahu, Anthony Mathelier (Associate Director), Janna Saarela (Director). Photo: Ine Eriksen/UiO

Irep Gözen. Photo: Oda Hveem

Sebastian Waszak. Photo: Oda Hveem

From left to right: Emma Haapaniemi, Marieke Kuijjer, Charlotte Boccara. Photo: Ine Eriksen/UiO

From left to right: Camila Esguerra, Nikolina Sekulic. Photo: Ine Eriksen/UiO

# Research excellence

Charlotte Boccara
Photo: Oda Hveem

# Systems neuroscience and sleep group

## Key expertise

- In vivo rodent models (mice and rats)
- In vivo electrophysiology
- Optogenetics and chemogenetics
- Immunohistology
- Cell culture, biology assays
- Computational methods
- Electronics and biosensors

### Research focus

Our core hypothesis is that poor sleep at critical developmental stages facilitates the emergence of neural and metabolic disorders. Currently, there is only correlative, but no causal evidence of this. To address this crucial gap in our knowledge from multiple angles, our team is composed of neuroscientists, molecular biologists, physicists, medical and computational scientists whose common goal is to elucidate some of the mechanisms at play during developmental sleep.

Because of this interdisciplinary approach, we have been in the unique position to pioneer in vivo miniature devices that allow us to record and decode neural activity from multiple brain areas of freely behaving rat pups as young as 9 days old. Together with the Institute of Basic Medical Sciences (IMB) and SINTEF, we were awarded a convergence grant in 2022 from the Research Council of Norway to make these recording devices wireless.

In parallel, we have started to use recent advances in viral, molecular and CRIPSR tools to interfere with sleep circuits to understand the impact of poor sleep during adolescence on healthy metabolic and cognitive development. Our long-term ambition is to reveal sleep as a prime target for therapeutics in developmental disorders.

### Major aims:

- Record and decode neural activity from multiple brain areas in freely behaving rat pups while they are learning tasks and while they sleep.
- Map how sleep architectures mature across development.
- Engineer rodent models of developmental sleep deprivation.
- Reveal the impact of sleep deprivation on healthy cognitive and metabolic development.
- Determine the underlying epigenetic mechanisms linking insufficient sleep during adolescence and the emergence of metabolic disorders (obesity, diabetes type II) during adulthood.
- Engineer new recording tools adapted for in vivo electrophysiology and optogenetics in developing rodents.
- Optimize computational methods to decode sleep oscillations.
- Establish tools to measure cognitive and social development in rodents.


**Illustration:** the Boccara group.

### Highlights in 2023:

- Charlotte Boccara was awarded a Starting Grant from the European Research Council for the project SleepCog: Map and manipulate sleep oscillations to reveal their role in healthy cognitive development. The project will start in 2024.
- The group is part of a collaborative project that received funding from Era-Net's call for Transnational Research Projects on Mechanisms of Resilience and Vulnerability to Environmental Challenges in Mental Health.
- Multiple new recruits joined our lab in 2023 (Sandra Bryne, Adrian Engberg, Mats Helmersen, Solveig Horn, Ane Gaupseth) and new individual fellowships (Mats: UiO MedFak Forskerlinje, Adrian: Dagmar Marshall Fonden + University of Copenhagen's Support Foundation for students of pharmaceutical science)
- Ruichi Saigal and Laure Gosse successfully defended their Master's theses.
- Our group presented at several international conferences: FENS (Paris), hippocampus conference (Verona), EMBL conference (Helsinki), Nordic Neuroscience (Copenhagen)
- We were joined by new associate lab members on the Smartsense project: postdoctoral fellows Jie Hou (Physics – w/ Ørjan Martinsen) and Damien Dufour (Molmed – w/ Nolwenn Briand)

### What are your goals for 2024?

During 2023, we collected a lot of developmental data both during sleep (Solomiia Korchinska, NCMM) and on metabolism (Damien Dufour, IMB) through our collaboration with Nolwen Briand and Philippe Collas. We also established several of our analytics tools and Brijesh Moodi (NCMM) led the work on automatic detection of sleep oscillation and sleep scoring. Our goal is to publish the results from these projects in 2024.

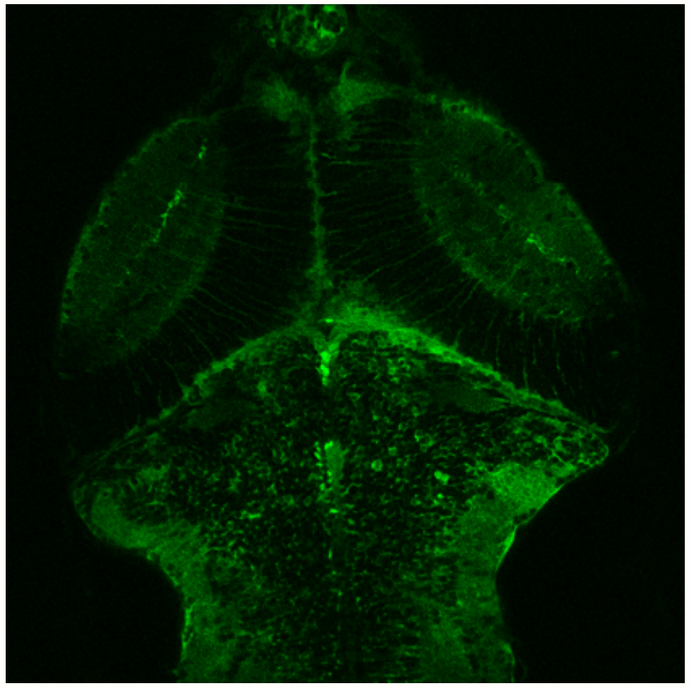
Thanks to our funding successes in 2022 and 2023, we will aim to recruit new lab members in 2024: 1-2 PhD students and 2-3 postdocs. They will work on the SmartSense and BrainChip projects awarded in 2022, as well as on newly awarded projects: autophagy & sleep (co-funded with Helene Knævelsrud) and Resilience (Era-Net).

One challenge for 2024 is our move to the newly refurbished animal facilities hosted at the Institute of Basic Medical Sciences. We are working closely with the department of comparative medicine and NCMM to equip several new recording rooms to accommodate our new and on-going projects.

We will also explore a more translational application of our work. To this end, Charlotte Boccara will assume a 20% position at the Oslo University Hospital, as well as start a collaboration with occupational health (STAMI) on shift workers.

Camila Esguerra
Photo: Oda Hveem

# Chemical neuroscience group



Two-photon microscopy image of a 5-day old zebrafish larval brain, showing active glial cells (green). The glial cells are modified to express a calcium-GFP reporter, making them fluoresce in green when they are activated.
Credit: the Esguerra group

## Key expertise

- Zebrafish disease models
- Automated behavioral assays
- Drug screening and toxicology
- Histology
- Imaging
- Brain recordings
- Robot-assisted tumor cell xenografting

### Research focus

The overarching aim of our group is to understand how genetic mutations and other lesions can lead to disturbances in brain development and homeostasis. We seek to elucidate the underlying genetic causes of drug-resistant epilepsies, neuropsychiatric disorders, and brain cancers by probing for novel disease-associated gene variants. To achieve this, we use genetically engineered zebrafish and pharmacological models. The zebrafish models allow us to perform efficient screening for novel disease pathways and drug candidates, as well as phenotypic analysis such as behavioral assays. These models and neuroactive small molecules will serve as valuable tools towards understanding the development, function, and diseases of the brain.

### Major aims:

- To study brain disorders by establishing and validating animal models of epilepsy (with a focus on severe, early-onset, refractory epilepsies), schizophrenia, autism, and brain cancers.
- To elucidate underlying disease mechanisms that can lead to the discovery of new therapeutic interventions.
- To screen for novel drug candidates.
- To understand drug mechanism of action.
- To test drug candidates for potential toxicities.

### Highlights in 2023:

- Our group published five papers in 2023. One publication, “Perinatal exposure to potential endocrine disrupting chemicals and autism spectrum disorder: From Norwegian birth cohort to zebrafish studies” (Desalegn et al., 2023), is of particular importance. It highlights how one can utilize the zebrafish model to validate environmental toxicants as risk chemicals for disease when combined with human cohort data. The publication of this paper led to an invitation to give a talk at EMBL Rome, as part of the *EMBL Human Ecosystems Transversal Theme Program.*
- The result of a successful drug repurposing study showed that a drug, previously used for the treatment of glaucoma and heart failure, was highly effective in attenuating seizures in both our zebrafish model and in patients with photosensitive seizures in the clinic.
- Our ongoing collaboration with Sebastian Waszak’s group to generate zebrafish models for diffuse intrinsic pontine gliomas (DIPG) is progressing. Xenografting of human DIPG tumor cells into the developing zebrafish brain was successful and initial tests show that tumors can be suppressed by a candidate drug about to enter clinical trials.
- A US patent application, where Camila Esguerra is a co-inventor, was granted on November 28, 2023 (Treatment for epilepsy; Patent number: 11826364).

### What are your goals for 2024?

We are aiming to complete several studies on zebrafish lines we have generated that carry patient mutations in genes encoding proteins of the SNARE complex. The SNARE complex is essential for neurotransmitter signalling and mutations therein lead to a spectrum of neurodevelopmental disorders. By combining structural biology and zebrafish disease modelling, we can assess genotype-phenotype correlations for patient mutations. We are also using several of these models for drug candidate testing and validation.

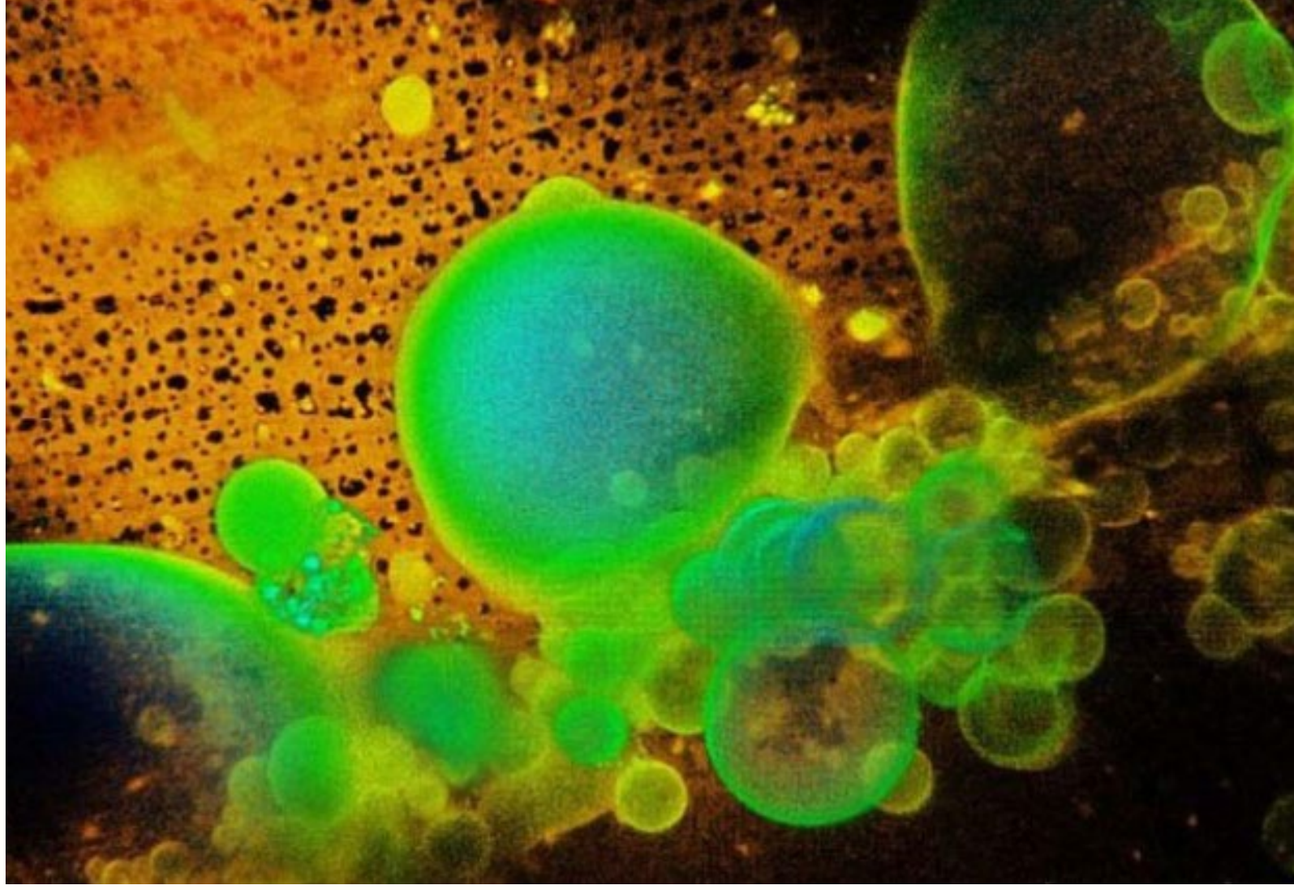
We will also wrap up our studies on 1) an ultra-rare genetic epilepsy and report our findings regarding potential drug candidates that are showing positive results in our fish model. 2) A ciliopathy candidate risk gene that we have modelled in zebrafish, (in collaboration with Eirik Frengen, Institute for Clinical Medicine, and Cinzia Progida, Department of Biosciences), and 3) a candidate risk gene for schizophrenia (in collaboration with Ole Andreassen, Institute for Clinical Medicine and Marianne Fyhn, Department of Biosciences).

We will continue our collaboration with Sebastian Waszak and his team to 1) delve further into refining our zebrafish DIPG models, to understand host-tumor microenvironment interactions (i.e., how do tumor cells trigger seizures? How do seizures modulate tumor growth?) and 2) continue drug testing – especially combinations of drugs, as we believe that this is key for killing aggressive tumor cells successfully.

A new study that we have started is the investigation of glial activity in zebrafish refractory epilepsy models, in collaboration with Rune Enger, head of the Glia lab at the Institute of Basic Medical Sciences.

Irep Gözen
Photo: Oda Hveem

# Bionano-technology and membrane systems group



## Key expertise

- Surface micro-/nano-fabrication and surface characterization
- In vitro assembly of biological soft matter
- Open-space microfluidics
- Laser scanning confocal microscopy
- Total internal reflection microscopy
- Differential interference contrast microscopy

### Research focus

Our research programs aim to understand the biophysical and materials science aspects of complex biological problems involving lipid membranes. We bring together biomembranes with solid interfaces as well as with micro- and nanotechnology, and observe the unique membrane interactions with high resolution microscopy. In all of our research lines, the common key structure is the membranes positioned on nano-engineered solid surfaces. Examples of our current research programs are synthetic cell and organelle engineering, primitive cell formation and development at the origin of life, biosensor development, and characterization of non-trivial biomembrane fractures.

### Major aims:

- Build structured synthetic cells and organelles from the bottom up.
- Construct artificial cells with increasing complexity and programmed functions.
- Development of lipid membrane-based biosensors of interest to medicine and pharma.
- Identify how surface-based pathways of primitive cell formation and development improve our understanding of the transition from non-animated matter to life.
- Find out the exact conditions leading to membrane fractures and their sealing, i.e., repair.

### Highlights in 2023 and Q1 of 2024:

- We have demonstrated how microbial colony-like membrane structures spontaneously form from artificial lipid assemblies on solid surfaces; the work was published in ACS Nano in international collaboration with researchers from Virginia Polytechnic Institute and State University, and Chalmers University of Technology.
- Two new manuscripts were completed/submitted, reporting on new morphologies and features of primitive cells.
- Our review on protocells was celebrated as one of the top downloaded and widely read articles in the journal *Small* (Gözen et al., 2022).
- Recent results were presented at invited talks, e.g. at the University of Strasbourg, and *the Origins Center Conference* in Groningen.
- Gözen was an invited panelist/panel leader at the *Life in the Universe Conference* in Boston.
- The group established international collaborations with researchers in the United Kingdom, Germany, and Canada on topics of sensing and protolife.

### What are your goals for 2024?

The current priority is to characterize the behavior of biomembrane assemblies on extraordinary surface samples from space in order to understand possible interactions of primitive cells which may have taken place on the early Earth. The next objective is to advance the recent experimental findings stemming from our collaborations in model protocell features and sensing. We have discovered a new surface spreading mode, which makes surface areas accessible to the internal space of protocells.

Confocal micrograph showing protocell colonies formed on cracks of the mineral oligoclase. Credit: Köksal et al., *ChemSystemsChem* 2022

Emma Haapaniemi
Photo: Oda Hveem

# Precision pediatrics and gene editing group

## Key expertise

- Standard CRISPR/Cas 9 gene editing
- Digital droplet PCR & single cell DNA sequencing
- In vivo NSG mice
- Isolation & expansion of primary cells and cell lines
- Flow cytometry
- Prime editing & lentivirus-derived prime editing

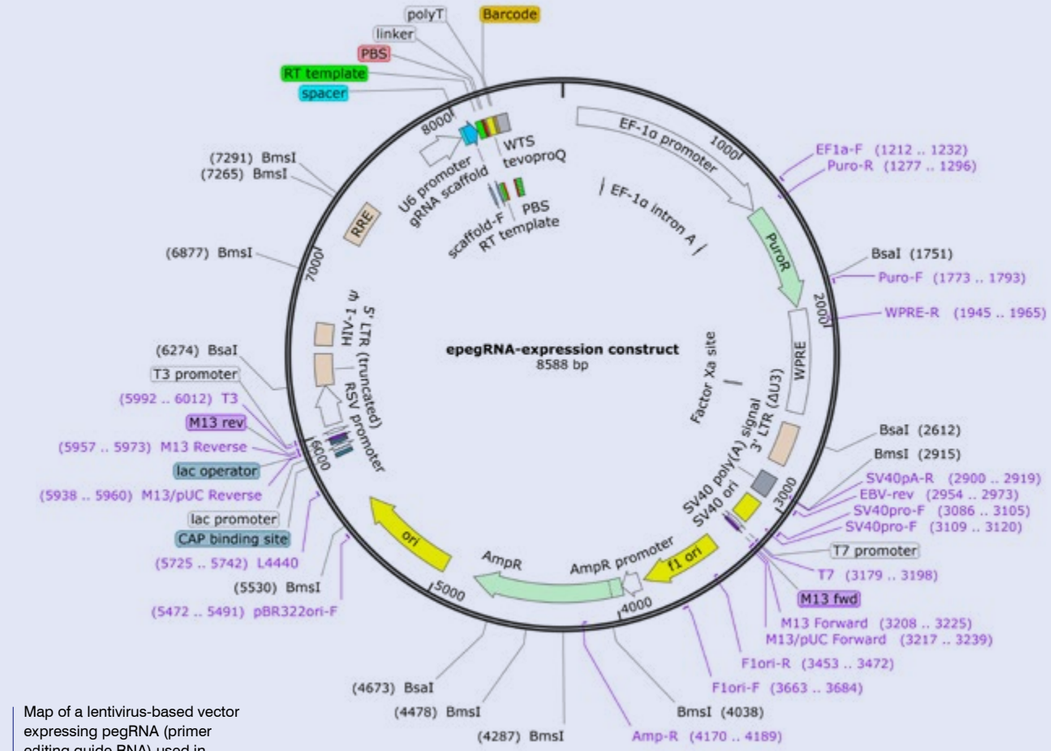
### Research focus

Our research goal is to build personalized gene therapy programs for inborn errors of immunity. Until now, we have mainly focused on Finnish founder immune diseases that serve as models for comprehensive technological analysis. Going forward, we are collaborating with Oslo University Hospital to develop gene-editing therapies for patients with STAT1 gain-of-function disease. However, our ultimate goal is to establish versatile gene-editing protocols that are disease-independent and can be tailored to a wide range of immunodeficiencies in a fast and efficient manner.

To achieve this goal, we are working to optimize the CRISPR-Cas9 gene editing tool and CRISPR-based technologies (Prime Editing) for use in personalized therapy. We are also working on optimizing high-throughput protocols for efficient gene editing in T cells and hematopoietic progenitor stem cells.

### Major aims:

- Establish a high-throughput platform for pooled CRISPR screening to find experimentally validated guides for personalized rare disease treatment.
- Scale up the successful gene editing protocols for clinical use: developing good manufacturing practices (GMP) and automatization of the editing protocol.
- Establish protocols to correct patient-specific STAT1 gain-of-function mutations and restoring physiological STAT1 signaling in T cells.
- Optimize methods for the evaluation of stem cell functionality.
- Identify homology-directed repair (HDR) enhancers to optimize the CRISPR gene editing platform for primary T cells and blood stem cells.
- Identify the efficient combinations of guides and repair templates for published STAT1 mutations and other monogenic T cell defects.




Map of a lentivirus-based vector expressing pegRNA (primer editing guide RNA) used in the Primer Editing system
Credit: Haapaniemi group
Created with SnapGene

### Highlights in 2023:

- We recruited several new lab members: one PhD student, one lab technician, and three MSc students.
- Zhuokun Li successfully defended her PhD thesis, titled: “Characterizing and improving CRISPR-Cas9 system with high-throughput methods”.
- Master students Ruchi Saigal, Sigrid Fu Skjelbostad, Oda Almåsbak Dønåsen and Tuva Sundell successfully defended their Master’s theses.
- We secured 100 000 NOK funding from Stiftelsen Astri og Birger Torsteds legater for Kreftforskning for the development of CRISPR-Cas9 gene therapy for ADA2 deficiency.
- We are part of Precision Immunotherapy Alliance “PRIMA”, a centre of excellence with funding from the Research Council of Norway, which had its official kick-off in 2023.
- Emma Haapaniemi was featured in Dagens Medisin (January 2023).
- We published a protocol for editing fibroblasts with in vitro transcribed Cas9 mRNA and profile off-target editing by optimized GUIDE-seq (Li, Z. et al. 2023, STAR Protocols)

### What are your goals for 2024?

We will test the safety of our gene editing protocols by looking at genomic integrity using different high-throughput methods (PacBio whole genome sequencing of edited cells, guide-seq). If the protocols pass the safety tests, we will scale them up to optimize them for use in humans, with the goal of editing enough T cells and hematopoietic progenitor stem cells (HPSCs) for use in clinical trials.

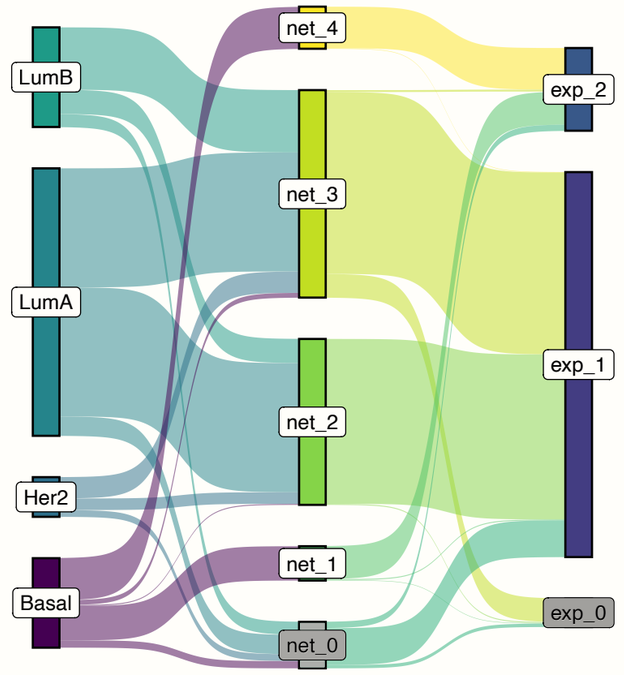
We will test GMP-grade reagents and start optimizing our protocol for GMP trials. In the first trial, we will give gene-edited T cells as a salvage therapy for infections and the model disease will most likely be STAT1 gain-of-function and cartilage hypoplasia. At the same time, we will advance ADA2 gene editing in HPSCs and test the efficiency of prime editing of ADA2 by lentivirus-derived vectors.

We also plan to establish an alternative animal model (humanized zebrafish) to facilitate our work on stem cells biology.

**Marieke Kuijjer**

Photo: Oda Hveem

# Computational biology and systems medicine group




This sankey diagram illustrates the relationship between molecular subtypes of breast cancer, as classified by the PAM50 gene signature, gene regulatory networks, and gene expression. Through this analysis, we've identified potentially novel breast cancer molecular subtypes based on information from gene regulatory networks, particularly two basal subtypes. Credit: Kuijjer group.

## Key expertise

- Computational tool development
- Bioinformatic and computational analysis
- Deep learning
- Single cell and spatial transcriptomics

### Research focus

Our group aims at understanding the molecular mechanisms that drive cancer development, progression, and heterogeneity. Our driving hypothesis is that the complex clinical phenotypes we observe in cancer cannot be adequately defined by individual layers of molecular data. Instead, we must consider the underlying network of interactions between the different biological components that can drive cancer phenotypes. To do so, we develop computational approaches that integrate knowledge of gene regulation with network science, allowing us to contextualize genomic data within large-scale regulatory networks and generate high-resolution maps of dysregulation in cancer. Ultimately, we hope that our research can impact the way we classify disease and suggest potential new targets for cancer treatment.

Our computational toolbox includes methods to model genome-wide regulatory networks, both on the level of transcriptional and post-transcriptional regulation, for individual patients and cell types. Applying these tools to large-scale cancer datasets has helped us identify important regulatory alterations in cancer. For example, we recently identified two new regulatory subtypes of leiomyosarcoma — an aggressive type of smooth muscle tumor — driven by different epigenetic programs.

### Major aims:

- Develop approaches to integrate multi-modal data.
- Construct spatially resolved and single-cell gene regulatory networks.
- Develop new methods to analyze genomic networks.
- Use network modeling and analysis to identify regulatory programs driving cancer development, progression, and heterogeneity.
- Use machine learning to detect new cancer cell subpopulations and the regulatory programs driving them.

### Highlights in 2023:

- Gabriel Stav successfully defended his Master's thesis within the Department of Biosciences.
- In the fall of 2023, the group was joined by three visiting students: Arturo Kenzuke Nakamura Garcia (PhD student) and Patricio López Sánchez (MSc student) from the National Autonomous University of Mexico (UNAM) and Anne Berge, PhD student from UiT - the Arctic University of Norway.
- Nolan Newman started his postdoctoral fellowship, focusing on network analysis in breast cancer; and Ine Bonthuis started her Master's thesis on deconvolution of gene regulatory networks.
- Our group received funding from the Krafttak mot Kreft program, Norwegian Cancer Society, to develop and apply network-based methods to identify regulatory drivers of breast cancer metastasis.
- The group published three new computational tools, including SNAIL (by Ping-Han), a normalization method that helps avoid false-positive associations in networks; PORCUPINE (by Tatiana), a network analysis tool that identifies heterogeneously regulated pathways in a patient cohort; and the NetZoo, an international collaboration that incorporates various of our network tools.
- Tatiana Belova co-organized a successful 2nd round of the Oslo Bioinformatics Workshop Week, and several group members contributed with workshops.

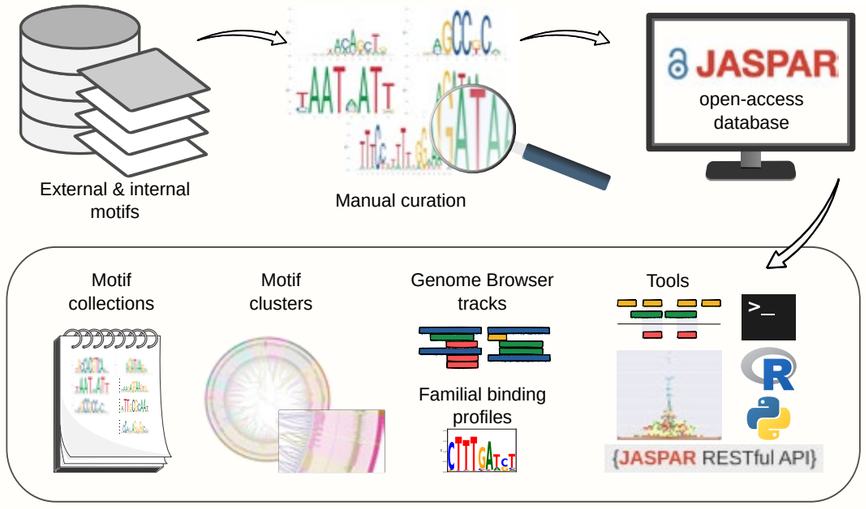
### What are your goals for 2024?

We are currently focusing on wrapping up five papers that we hope to make available in pre-print format in 2024. These include a tool to generate input data for network modeling, a pan-cancer network analysis, a deep learning-based approach to integrate and isolate variability in multi-modal single-cell data, an integrative analysis of networks with multi-omics data, and an analysis of whole genomes in osteosarcoma. Additionally, we have several exciting new methods and analyses that we hope to further develop, including new approaches to model fine-tuned networks for single-cell and spatial omics data, and various in-depth analyses of regulatory drivers of breast cancer heterogeneity.

Anthony Mathelier

Photo: Oda Hveem

# Computational biology and gene regulation group




Graphical abstract of the JASPAR 2024 publication depicting the data generation, curation, and release to the community. It provides an overview of the comprehensive database for transcription factor binding motifs, highlighting its curated content, advanced analytical tools, and integration with genomic resources. Credit: the Mathelier group.

## Key expertise

- Computational biology
- Machine learning techniques
- Transcriptomics assays
- Epigenetics
- Cancer genomics

### Research focus

Our research group is dedicated to improving our understanding of the non-coding portion of genomes. We are particularly interested in deciphering the cis-regulatory code that controls gene expression, as this knowledge can help us understand how gene expression can be disrupted in diseases.

Over the years, our group has developed several computational tools and resources to analyze in-house and publicly available multi-omics data. Key examples are our JASPAR and UniBind databases, which ELIXIR Norway has recognized as national resources. We have used our tools to study cancer patient somatic alterations in the non-coding portion of the human genome to predict alterations disrupting the regulatory program in cancer cells.

Moving forward, our group will continue to develop computational tools and resources to model and map genome-wide transcription factor (TF)-DNA interactions, study the interplay between transcription regulation and cancer somatic alterations, characterize DNA methylation patterns in cancer cells, and decipher patient-specific cis-regulatory activity. Our ultimate goal is to shed light on the molecular mechanisms underlying transcriptional dysregulation in cancers and deliver new knowledge in cancer research that will benefit patients in the future. We will combine experimental approaches and computational methods on patient samples to achieve this.

### Major aims:

- Improve the characterization of TF – DNA interactions through the maintenance and update of our key established resources (JASPAR and UniBind).
- Identify the molecular drivers of aberrant DNA methylation patterns in cancer cells and assess the cascading effect of gene expression deregulation.
- Reveal cis-regulatory signatures (i.e., sets of active DNA regulatory regions) associated with breast cancer subtypes and their underlying molecular drivers.
- Predict DNA regulatory regions that are critical for cancer cell survival
- Elucidate the interplay between RNA-DNA interactions and the regulation of gene expression.
- Provide a regulatory map of normal breast epithelium at single-cell resolution to better understand cancer initiation.

### Highlights in 2023:

- Our group received funding from the the Rosa Sløyfe scheme, Norwegian Cancer Society, to explore how TFs drive cancer development via aberrant DNA methylation patterns.
- We developed a tool, called COBIND, to identify TF co-binding patterns with functional relevance, validated by evolutionary conservation and empirical data (Rauluseviciute et al., 2023).
- The group celebrated the 20th anniversary of the JASPAR open-access database of transcription factor binding profiles with its 10th update (Rauluseviciute, Riudavets-Puig et al., 2023).
- A preprint identifying links between DNA demethylation and gene expression deregulation in cancer has been published (Ankill et al., 2023). This work was a collaborative effort led by Thomas Fleischer's group at the Institute for Cancer Research, uncovering common patterns of aberrant DNA methylation patterns across cancers.
- Anthony Mathelier became the Associate Director of NCMM on March 1st, 2023
- Anthony Mathelier co-organized the Regulatory and Systems Genomics session of the combined conference on Intelligent Systems for Molecular Biology and the European Conference on Computational Biology (ISMB/ECCB).

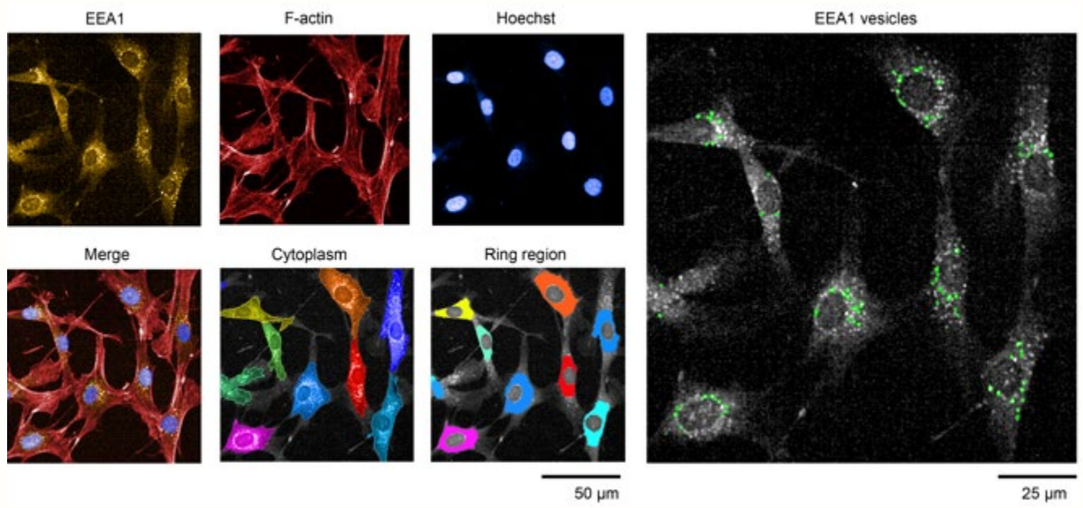
### What are your goals for 2024?

In 2024, our focus will remain on advancing our understanding of TF-DNA interactions, unraveling the molecular basis of cancer through studying DNA methylation patterns, and identifying critical regulatory regions affecting cancer progression. Our group is committed to enhancing our computational and experimental approaches, including introducing new assays and tools, to deepen our insights into cancer's molecular mechanisms. A key part of our mission is to foster a nurturing environment for our trainees, aiming to integrate our scientific endeavors with career development opportunities successfully. Importantly, we are dedicated to open science, adhering to the FAIR principles in developing computational software and resources to ensure our contributions are accessible, interoperable, and reusable. Ultimately, our efforts are geared toward generating knowledge that can significantly impact cancer research and patient care.

Janna Saarela

Photo: Oda Hveem

# Human immune disorders group




## Key expertise

- RNA, genome and exome sequencing and data analysis
- Genome-wide association studies
- Novel methods for anonymization and synthetization of health data
- CRISPR-edited cell models
- Functional immune cell assays
- Immunofluorescence analysis and live cell imaging

### Research focus

Our research goal is to identify and understand critical components of the human immune system and the mechanisms that lead to immune deficiency, autoimmunity and immune dysregulation. Specifically, we are focusing on rare inherited errors of immunity (IEI), rare hematological disorders and multiple sclerosis (MS). We draw on patient data, samples, and genome-edited cell models to identify genetic variants which underly monogenic diseases, or predispose to the development and severity of MS. This approach allows us to discern the disease mechanisms and shed further light on normal immune function. We then utilize this knowledge to enable molecular diagnostics and predict disease progression and beneficial treatment strategies. So far, we have developed a comprehensive map of the genetic landscape of MS susceptibility and identified the first genetic variant contributing to the disease severity and progression. This work was done in collaboration with the International MS Genetics Consortium and Multiple MS Consortium. We have also identified several novel genetic causes of severe human immune diseases, provided knowledge on their disease mechanisms, and contributed to international consensus guidelines for their treatment.

Finally, we are also working on developing methods for safe sharing of sensitive health data, which is critical for precision medicine research.

### Major aims:

- Identify novel genetic variants that cause rare, inherited immune diseases and study the functional consequences of the variants to understand disease mechanisms and normal immune function.
- Improve diagnosis of inherited errors of immunity by targeting noncoding variants through the utilization of novel genomic technologies.
- Identify dysregulated immune pathways which could be targeted by existing treatments in patients and predict disease activity.
- Develop novel personalized medicine approaches for MS patients by utilizing genetic, omics, MRI, and health and life-style data.
- Develop innovative tools for anonymization and synthesizing data for safe health data sharing.

### Highlights in 2023:

- In collaboration with the International MS Genetics Consortium and MultipleMS Consortium, we identified the first genetic variant associated with disease severity and progression in MS disease: Locus for severity implicates CNS resilience in progression of multiple sclerosis. (Nature, 2023).
- Contributed to develop multidisciplinary consensus statements for the evaluation and management of DADA2: Evaluation and Management of Deficiency of Adenosine Deaminase 2: An International Consensus Statement. (JAMA Netw Open, 2023).
- Applied novel genome sequencing methods to improve rare disease diagnosis by using linked-read sequencing for identifying haplotype information of large neuromuscular disease genes (Lehtonen et al. 2023, Scientific Reports).

Imaging-based analysis of cellular structures in fibroblasts taken from a patient with malformations of cortical development and immune dysfunction. EEA1 vesicles, cytoplasm, and ring region were identified by software analysis. Credit: the Saarela group

### What are your goals for 2024?

In 2024, we will focus on understanding the roles of novel IEI genes, ADA2, SIT1 and MAP4K1, in the regulation of the immune system. We will also use long- and short-read RNA sequencing methods to identify mono-allelic expression or aberrant splicing events in IEI. These methods will allow us to identify potential novel causes of IEI, which are not observable by current exome and genome sequence data analysis. Additionally, we aim to develop and apply novel methods for sharing sensitive health data across borders and diseases. This is part of the EU funded WISDOM project, which aims to utilize novel AI based tools enabling integration and safe sharing of medical and research data across borders and diseases for computational model building and validation. We will also study the risk factors and particularly the role of genetic variants in DNA repair genes in aging in a NordForsk funded collaboration study with researchers from Norway, Sweden and Japan.

Biswajyoti Sahu

Photo: Ine Eriksen/UiO

# Precision cancer epigenomics group

## Key expertise

- Chromatin biology and epigenetics
- Genome-wide omics methods (ATAC-seq, ChIP-seq, STARR-seq, HiChIP, PRO-seq etc)
- Single-cell multiomics (scRNA-seq, scATAC-seq)
- Lentiviral expression systems and CRISPR-Cas9 genome editing
- Long read nanopore sequencing for CpG methylation and GpC chromatin accessibility (NaNOME-seq)
- Bioinformatic analysis of omics datasets
- In vitro and in vivo assays for cell growth and tumorigenicity

### Research focus

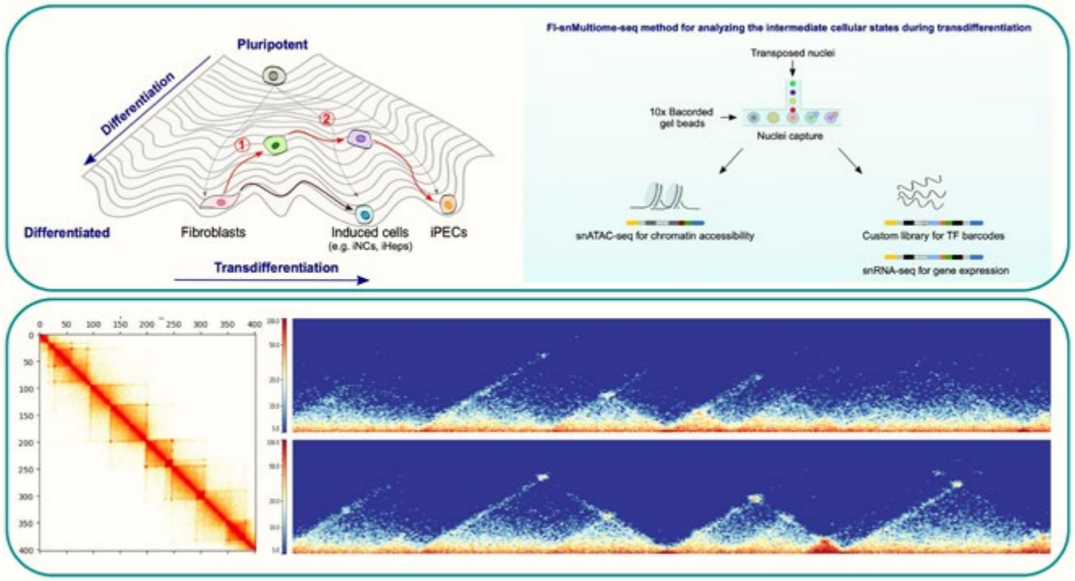
Our research focus is to understand the molecular mechanisms that lead to organ-specific cancer, with a special focus on the role of lineage-specific transcription factors (TFs) in early tumorigenic events. We utilize a systems biology approach with a plethora of cutting-edge experimental methods to study enhancer malfunction, genome plasticity and cancer-specific gene regulation. Our aim is to harness the developments in the field of cell fate conversion and transcription regulation by TFs to establish a molecularly defined genomics approach to understand the process of tumorigenesis. For this, we have already developed an experimental system to generate pancreatic ductal epithelial cells and a novel single-cell multiomics method to dissect the role of different factors in this process. Understanding such early tumorigenic events can be used to identify novel biomarkers or tissue-specific vulnerabilities for developing targeted therapies.

### Major aims:

- Establish a molecularly defined system to study the role of TFs and organ-cancer specific oncogenes in early stages of cancer development.
- Develop tools for cell fate conversion and high-resolution single-cell/nuclei multiomics.
- Delineate the human non-coding regulatory genome, the cis-regulatory logic and the role of transposable elements as enhancers.
- Understand how TFs modulate the gene regulatory networks and what are the sequence determinants of human gene regulatory elements.

### Highlights in 2023:

- Biswajyoti Sahu started as a researcher in the Department of Cancer Genetics, Oslo University Hospital.
- Two major manuscripts from the Sahu group were published in high impact journals: First, in Fei et al. (published in Developmental Cell) we show the role of six defined TFs in controlling pancreatic ductal cell fate. In addition, we developed factor indexing single-nuclei multiome sequencing method for robust quantification of gene expression and chromatin state (FI-snMultiome-seq). Second, in Karttunen, Patel et al. (published in Nature Communications) we show the role of specific repeat elements in the human genome that can function as cancer-specific enhancers and be exploited by cell type-specific TFs in colorectal and hepatocellular carcinoma.
- Our research published in Nature Communications was also covered in Nature Reviews Cancer as an editorial highlight titled “Enhanced transposable elements”.
- Our group received funding from the Norwegian Cancer Society, to dissect epigenetic plasticity driving pancreatic cancer for precision genomics.
- The group also received a grant of 75 000 NOK from Astrid og Birger Torsteds legat.
- Two collaborating manuscripts were published: (i) Pihlajamaa et al. (Nature Biotechnology, 2023) reported a novel CRISPR/Cas9-based precision genome editing method; (ii) Gawriyski et al (eScience, 2023) characterized a function of LEUTX transcription factor during embryonic development.
- Our group started new collaborative projects with Professors Vessela Kristensen, Tero Aittokallio and Caroline Verbeke at Oslo University Hospital and the University of Oslo.




Top: Dissecting the mechanisms of direct cell fate conversion using transcription factors and their characterisation using high resolution multiomics (FI-snMultiome-seq) for gene expression and chromatin state transitions. Bottom: Delineating the epigenome reprogramming through altered promoter–enhancer interactions and 3D genome organisation in cancers cells. Credit: the Sahu group.

### What are your goals for 2024?

In the coming year, our goal is to establish a human cell transformation model together with the recently identified lineage-specific TFs controlling pancreatic cell identity. We are also employing machine learning-based approaches to understand TF dynamics in different stages of cancer using datasets from pancreatic cancer patients. In parallel, we will continue our research on TF-mediated gene regulation and the human non-coding regulatory genome to understand the cis-regulatory logic and the function of cancer-specific enhancers. The aim is also to establish an endometriosis model system to study epigenetic reprogramming in endometriosis-associated ovarian cancer. Furthermore, with new members joining the group, the goal is to expand our research into more translational areas. This includes studies on patient material and establishing new cutting-edge methods for studying epigenetic mechanisms at increased resolution and accuracy. The focus will be on securing external grants as well as on the training and career development of the recruited researchers in the group.

**Nikolina Sekulić**
Photo: Oda Hveem

# Structural biology and chromatin group

## Key expertise

- Protein expression and purification
- Cryoelectron microscopy (cryoEM)
- Hydrogen-deuterium exchange coupled to mass spectrometry (HDX-MS)
- Enzyme analysis
- X-ray crystallography

### Research focus

Our group seeks to understand the molecular determinants that ensure that chromosomes, the carriers of genetic information, are correctly distributed during cell division. To this end, we study the centromeres, i.e. the parts of the chromosomes that ensure that the chromosomes are evenly distributed to the daughter cells during each duplication and cell division. The stability of the genome is essential for life, yet the organization of centromeres varies between different types of organisms. We therefore aim to understand the factors that ensure correct distribution of chromosomes across different species. Our work also has implications for cancer research, as uncontrolled cell division is a hallmark of cancer.

### Major aims:

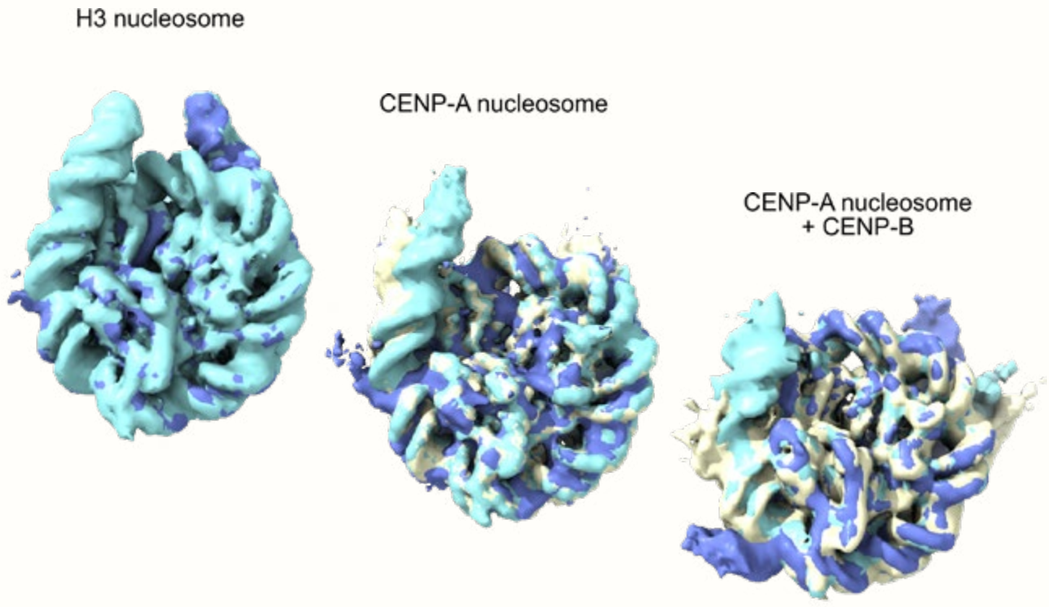
- Understand the organization of centromeres during cell cycle.
- Establish how centromeres recruit kinases and phosphatases that govern mitosis.
- Understand the molecular mechanisms regulating the activity of mitotic kinases and phosphatases.

### Highlights in 2023:

- Our work on the structural basis of the multi-step allosteric activation of Aurora B kinase was published in Elife (Segura-Peña et al. 2023, Elife).
- A collaborative project between our group and the Fierz' lab in Switzerland was published in Nature Communications (Nagpal et al. 2023, Nat Commun). The study demonstrated how CENP-A and CENP-B collaborate to create an open centromeric chromatin state.
- We contributed to a collaborative study showing that bi-allelic variants in SNF8 cause a disease spectrum ranging from severe developmental and epileptic encephalopathy to syndromic optic atrophy. (Brugger et al. 2024, Am J Hum Genet.).
- Nikolina Sekulic organized the mini-symposium "CryoEM and CryoET: From knowledge to cures" with several international experts in the field and coordinated the application for Norwegian national infrastructure on cryoEM.
- Three of our Master students successfully defended their theses.

### What are your goals for 2024?

In 2024, we will extend our research to the centromeres of other organisms, as centromere organization varies greatly among organisms. Given the rapid advances in genome sequencing and the development of AlphaFold, we believe now is the right time to explore a range of natural designs that ensure genomic integrity. We have also started several collaborations using HDX-MS technology to map epitopes and paratopes involved in mediating antibody-antigen interactions, which is highly appreciated in the dynamic Oslo immunotherapy community. Together with the IT team and the support of the Hanseatic Life Science Research Infrastructure Consortium (HALRIC), we are involved in a larger cross-border project with Sweden, Denmark and Germany. We are developing a Hanseatic Science Cloud to make it easier for scientists in the Oslo region to access and use the scientific infrastructures in the Øresund-Kattegat-Skagerak region. This will help Norwegian science to develop in parallel with its surroundings and pave the way for establishing national expertise in cryo-EM and other cutting-edge techniques that require expensive infrastructure. Finally, we continue to enjoy the privilege of doing science and educating the talented next generation of scientists.

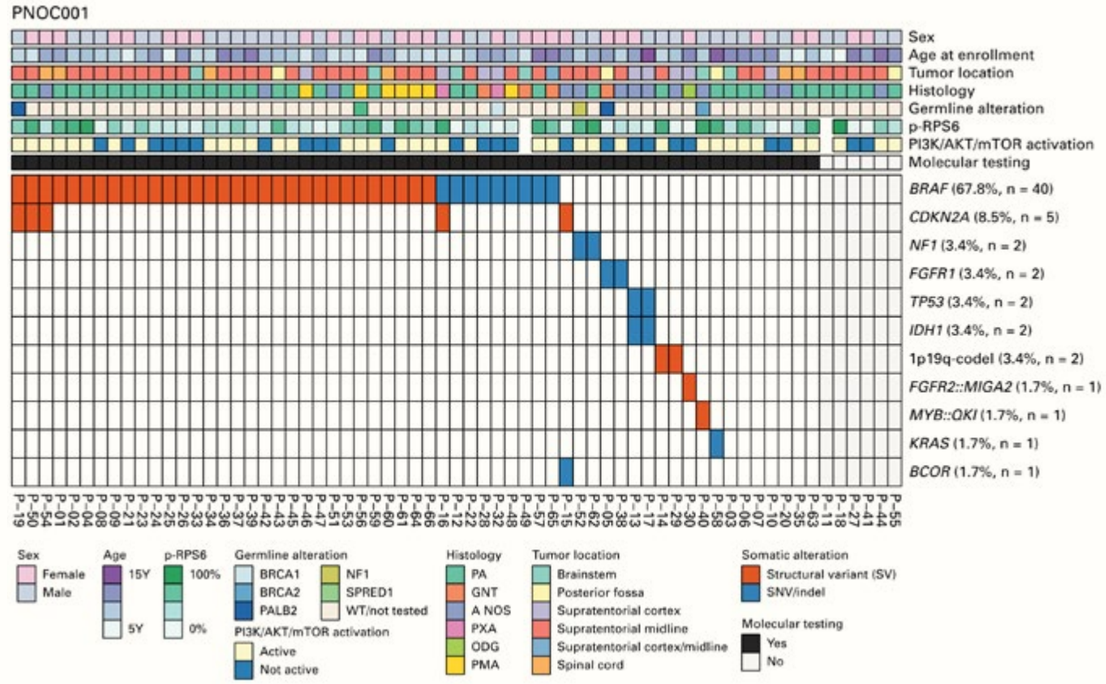



CryoEM density maps for H3 nucleosomes, CENP-A nucleosomes, and CENP-A nucleosomes in complex with CENP-B. For each sample, the maps with the most wrapped DNA (cyan), the partially unwrapped DNA (yellow) and the most unwrapped DNA (blue) are superimposed. It shows how the extent of DNA unwrapping increases from H3 to the CENP-A nucleosome and then further in the presence of CENP-B. Credit: Sekulić group.

Sebastian Waszak

Photo: Oda Hveem

# Computational oncology group




Genomic landscape of recurrent or progressive pediatric low-grade glioma. Credit: the Waszak group

## Key expertise

- Bioinformatics
- AI and machine learning
- Nanopore sequencing
- Statistical genetics
- Neuro-oncology
- Genomic medicine
- Cancer genomics

### Research focus

Our research group is dedicated to shedding light on brain tumors. We are particularly interested in understanding the biology of pediatric- and adult-type gliomas. To this end, we employ a multidisciplinary approach that combines AI/machine learning techniques with wet lab research. We develop new methods for the rapid and minimally invasive diagnosis and surveillance of brain tumors to guide treatment decisions and monitor disease progression. Another goal of our work is to advance clinical cancer genomics based on new technologies that improve our understanding of the genomic and epigenomic landscape of brain tumors. Our research aims to impact neuro-oncology by enhancing molecular diagnostics and improving our understanding of the molecular mechanisms underlying disease formation and progression.

### Major aims:

- To infer clinically actionable genomic alterations from digital brain tumor tissue slides.
- To develop novel approaches for rapid diagnosis and surveillance of brain tumors.
- To develop zebrafish as a model system for drug screening of pediatric brain tumors.
- To perform integrative analysis of germline and pediatric brain tumor genomes.

### Highlights in 2023:

- The results from the clinical trial of everolimus therapy for children with recurrent or progressive pediatric low-grade glioma was published in the Journal of Clinical Oncology (Haas-Kogan et al., 2024).
- The ONC201 therapy trial for children with primary or progressive H3K27M-mutant diffuse midline glioma was published in Cancer Discovery (Venneti et al., 2023).
- A Pan-cancer atlas of somatic core and linker histone mutations was published in npj Genomic Medicine (Bonner et al., 2023).
- Our group established long-read whole genome sequencing using nanopore technology of brain tumors and zebrafish lines at NCMM.

### What are your goals for 2024?

We are currently analyzing the first cohort of Nanopore whole genomes of pediatric brain tumors to uncover novel genetic and epigenetic driver mutations. With funding from the Norwegian Cancer Society and in collaboration with the Esguerra group, we're planning to initiate drugs screens using zebrafish models of pediatric-type diffuse glioma.

The digital pathology project, funded by the Ian's Friends Foundation, is in its final phase and we are validating our AI models with external patient cohorts and are preparing to publish our findings. Additionally, in partnership with the University of Heidelberg, we're preparing to publish our research on the genetic and genomic landscape of GNAS-associated medulloblastoma.

# Research Higlights

## Why do some patients experience faster progression of multiple sclerosis?

A large, international collaboration has led to the discovery of the first genetic variant associated with more severe disease progression in patients with multiple sclerosis (MS). MS is a disease that affects the central nervous system, meaning the brain and spinal cord. The severity of MS symptoms and the speed of disease progression vary from patient to patient, making it a highly unpredictable disease. Understanding the underlying causes of this is valuable to clinicians when determining the most appropriate and effective treatment regime for individual patients. To address whether the cause could lie in the patients' own genes, two large MS consortia came together to analyze genetic data from more than 22,000 MS patients from around the world. NCMM Director Janna Saarela contributed to the study by setting up and maintaining the largest harmonized, multi-modal data resources for MS to date. Using advanced statistical analysis, the authors were able to identify the first genetic variant associated with faster disease progression. This provides a new avenue for future studies aiming to understand the mechanisms of MS development and progression, and for exploring new drug targets.

International Multiple Sclerosis Genetics Consortium; MultipleMS Consortium. **Locus for severity implicates CNS resilience in progression of multiple sclerosis.** *Nature.* 2023

## Environmental pollutant increases risk of developing autism

Photo: Oda Hveem

The study is the result of a collaboration between Camila Esguerra's group at NCMM and the Norwegian Institute of Public Health. The researchers examined data from a large cohort study on human breast milk in Norway to identify pollutants in breast milk that could be harmful to the baby. The study found that an environmental pollutant, called β-Hexachlorocyclohexane (bHCH), increased the risk of the child developing autism spectrum disorder when present at high levels in the mothers' breast milk. The association between bHCH and an increased risk of developing autism was confirmed using zebrafish as model systems. bHCH derives from the broad-spectrum insecticide Lindane, which has been banned in Norway since 1992, and in the EU since 2008. However, the chemical is very stable and can persist in both the environment and in tissue for long periods of time. Furthermore, it is still used in other parts of the world, where it may contaminate into the oceans. The study highlights the need to prevent environmental contamination with bHCH, and awareness of the long-term effect pollutants can have in the population.

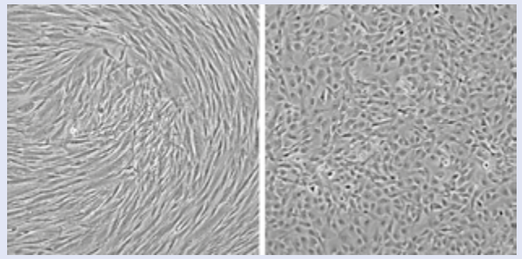
Desalegn AA et al. **Perinatal exposure to potential endocrine disrupting chemicals and autism spectrum disorder: From Norwegian birth cohort to zebrafish studies.** *Environ Int.* 2023

## Newest update of the JASPAR database marks 20-year anniversary

JASPAR is a comprehensive open-access database of curated, non-redundant transcription factor binding motifs. The database is an important resource for the field, with approximately 15 000 users accessing the database each month. The Mathelier group at NCMM and collaborators have now released the 10th update of the database, adding more motifs and functional updates. For 20 years, the JASPAR database has offered researchers access to experimentally defined transcription factor binding motifs and tools for their analysis and visualization of the data. Researchers utilize JASPAR for comparative genomics, understanding gene regulatory networks, and interpreting the impact of genetic variations. The database makes it possible to investigate how transcription factors interact with the DNA to control gene activities, and in identifying where these interactions occur in the DNA sequences.

Rauluseviciute I et al. **JASPAR 2024: 20th anniversary of the open-access database of transcription factor binding profiles.** *Nucleic Acids Res.* 2024

## New method makes it easier to research pancreatic cancer



The image to the left shows cells that can be found in our skin. The image on the right shows the same cells after they have been converted into pancreatic cells. Image: the Sahu group

Researchers in the Sahu group at NCMM have found a way to make pancreatic cells from completely different cell types. Pancreatic cells are difficult to obtain and grow in a laboratory, something that has been a limitation in pancreatic cancer research. Now that the Sahu group have found a way to generate the cells in the lab, this opens many doors to further study this cancer type. Specifically, the Sahu team identified six transcription factors that can alter gene expression to transform fibroblasts into pancreatic cells. The researchers will now use this new method to map the development of pancreatic cancer. By introducing various cancer-causing molecular changes as the cells transform, they can follow what happens to the cells and map the events that lead to the development of pancreatic cancer. In the long run, the Sahu group hopes to use this method to find new targets for the treatment of pancreatic cancer and uncover ways to detect the cancer earlier.

Fei L et al. **Single-cell epigenome analysis identifies molecular events controlling direct conversion of human fibroblasts to pancreatic ductal-like cells.** *Dev Cell.* 2023

## Cancer can be treated by blocking a central conductor of cell division

Main author of the study, Dario Segura-Pena (left) together with Nikolina Sekulic (right), head of the research group. Photo: Nikoline L. Rasmussen.

Researchers in the Sekulic group have uncovered the mechanisms behind the activation of Aurora B, a central conductor of cell division. When a cell divides, it happens through a series of carefully controlled steps at particular time points. Loss of control of cell division is a hallmark of cancer and results in uninhibited cell proliferation. In healthy cells, Aurora B is activated upon the initiation of cell division and ensures that the different steps of the process are executed correctly and in the right order. In this study, the Sekulic team uncovered the structural changes in Aurora B that leads to its activation. The goal is to use the knowledge of Aurora B activation as a basis for developing new cancer drugs that interfere with its activation. Blocking the activation of Aurora B in cancer cells will disrupt cell division and likely kill the cancer cells.

Segura-Peña D et al. **The structural basis of the multi-step allosteric activation of Aurora B kinase.** *Elife.* 2023

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# Funding Successes

## ERC Starting Grant to Charlotte Boccara

Charlotte Boccara was awarded 1.5 million euros from the European Research Council (ERC) for the project "SleepCog". The aim of the project is to determine the role of sleep in healthy brain development. The project will allow Boccara and her team to examine how poor sleep is linked to developmental disorders in children. They will develop innovative technology that enables researchers to measure sleep patterns in animals in a novel way. To achieve this, SleepCog brings together an interdisciplinary team with expertise from the fields of molecular biology through to physics and engineering. The unique collaboration will allow the research team to gain insights beyond what is possible with existing methods.

The SleepCog project also received attention in the media, and Boccara was interviewed in the Norwegian national news VG and in Khrono.


Khrono

Nyheter Debatt Student Nytt om folk

EU-MIDLER

**Hun er en av åtte forskere i Norge som sikrer seg millioner fra ERC**

Fem forskere ved Universitetet i Oslo, to ved NTNU og en ved Universitetet i Bergen ble i dag tildelt millioner fra Det europeiske forskningsrådet.


Charlotte Boccara ved Universitetet i Oslo får millioner til forskning på betydningen av søvn. Foto: Ola Nordal


Foto: iStockphoto

**Dårlig søvn: Kan ha sammenheng med ADHD og autisme**

VG+

Barn som får for lite søvn, strever oftere med å regulere følelser og er mer motorisk klumsete, viser studier. Nå mener forskere at det også kan være en sammenheng mellom ADHD og dårlig søvn hos små barn.

Av KAROLINE SKRØDER
Oppdatert 13. november

## Three NCMM projects awarded funding from the Norwegian Cancer Society

NCMM group leaders Marieke Kuijjer, Biswajyoti Sahu and Anthony Mathelier each received funding from the Norwegian Cancer Society in 2023. The Norwegian Cancer Society annually allocates funds to support cancer research in Norway. This year, all NCMM group leaders who applied were funded. The projects at NCMM are supported through different thematic categories: Mathelier's project is supported through 'Rosa sløyfe', Sahu receives funding through the open call for cancer research and Marieke Kuijjer's project is supported by 'Krafttak mot kreft'.

### Dissecting epigenetic plasticity driving pancreatic cancer for precision genomics

One of the non-genetic factors that is known to increase cancer risk is inflammation. The goal of Biswajyoti Sahu's project is to elucidate, on a molecular level, how inflammatory signals act alongside cellular regulatory pathways and oncogenic mutations to drive the development of pancreatic cancer.

### Precision Network Medicine for treatment stratification of metastatic breast cancer

Marieke Kuijjer's project aims to develop advanced computational tools that model the network of genetic interactions within individual breast cancer cells. These tools will be used to identify specific tumor cells with disturbances in their network interactions, and assess whether these disturbances lead to the development of breast cancer metastases.

### Characterization of transcription factors that drive deregulation of the gene regulatory program through aberrant DNA methylation patterns in cancer cells

Anthony Mathelier's project aims to create an innovative computational model validated by functional experiments to examine DNA methylation patterns in cancer cells. The goal is to elucidate the reconfiguration of gene regulatory networks driven by abnormal DNA methylation patterns, and potentially highlighting new biomarkers and therapeutic targets.

Photo: Oda Hveem

# The Zebrafish Core Facility

Zebrafish have several advantages as a model organism in biomedical research. Zebrafish and humans share genetic similarities, and many known developmental and disease-causing genes in humans can also be found in zebrafish. They have a high reproductive rate, which allows for efficient large-scale genetic studies and drug screens. Several tools exist for studying development and modeling disease in zebrafish, making them a cost-effective and efficient model.

The Zebrafish core facility team can assist researchers with performing experiments using zebrafish. The Zebrafish core facility offers access to fish housing, breeding and the use of several instruments specific for research on zebrafish. The team can assist in generation of disease models in zebrafish, including patient avatars for drug screening. They have experience within aqua culture, fish health, screening and characterization of new lines, GMO, 360° live-imaging of larvae, chemical screening, behavioral tracking, and microinjection (automatic/manual). Users can come to the facility to do their research, or they can buy services and analyses from the facility.

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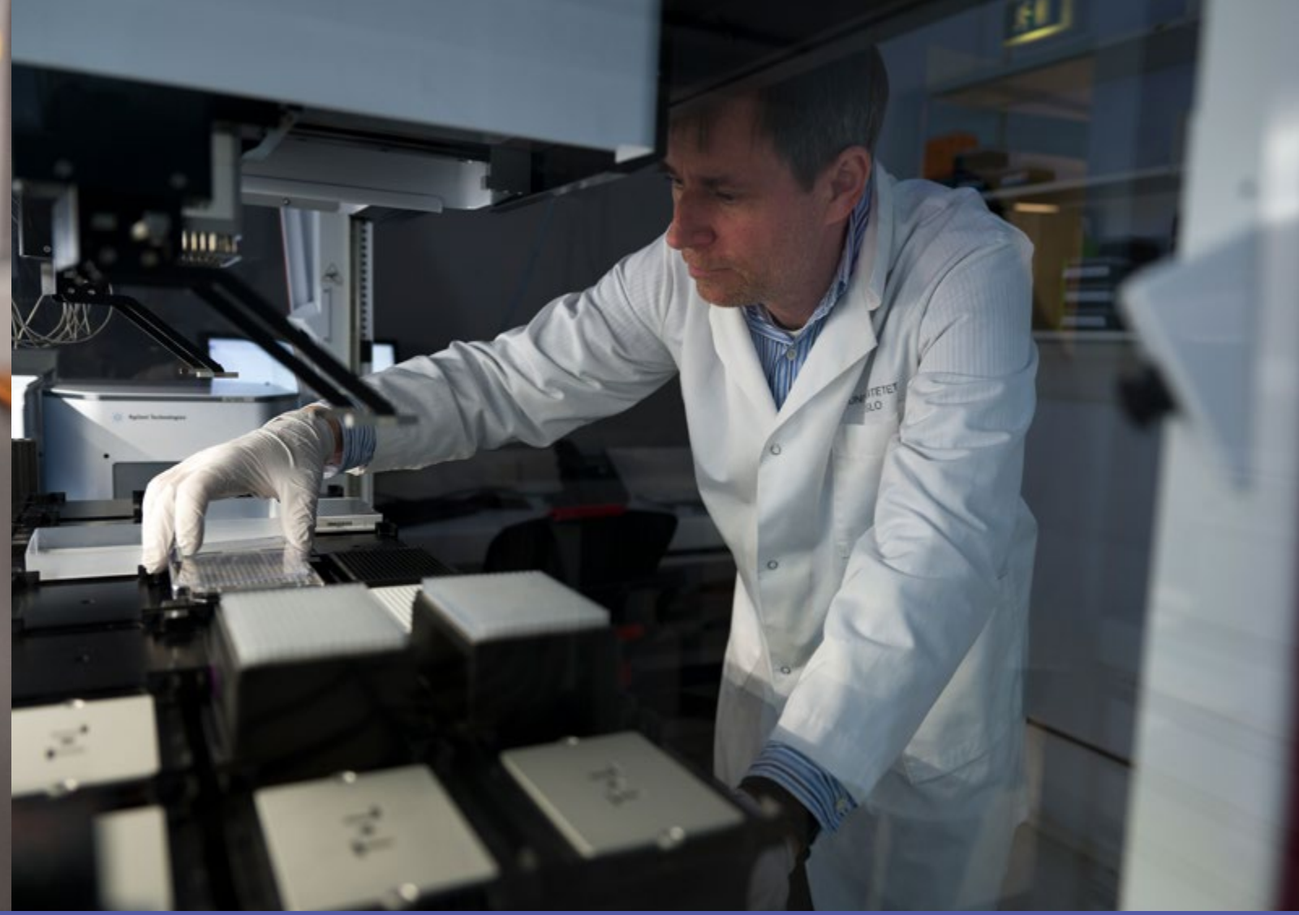

Photo: Ine Eriksen/UiO

# The High-Throughput Chemical Biology Screening Platform

The High-Throughput Screening (HTS) Facility offers expertise and services in the areas of chemical biology and small molecule-based HTS to academic users and biotech companies. It facilitates the discovery of small molecules to probe, explore and modulate biological systems. With its state-of-the-art instrumentation and an in-house screening collection of ~70 000 compounds, thousands of chemical substances can be screened on biological assays rapidly in a fully automated fashion to identify “hit compounds” that show the desired effects.

Applications can vary from blocking specific enzymatic activities to inducing distinct phenotypes in various cell types. Screening is therefore a standard first step in classic (small molecule-based) drug development campaigns. Together with other technologies, it can be applied in precision medicine approaches to guide treatment decisions e.g., for cancer patients, where biopsies are screened with a spectrum of clinically available drugs and drug combinations, to develop novel and more effective treatment strategies.

The HTS facility is part of the national research infrastructure NOR-OPENSCREEN which is the Norwegian node of EU-OPENSCREEN ERIC.

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# Research environment

# Introduction to Research Environment

by Associate Director
Anthony Mathelier

Research culture is a critical factor in our ability to produce high-quality research. A positive research culture and environment influence how research is done and directly impact the careers of the scientists and the supporting staff members. Such a culture enhances our research by emphasizing diversity, collaboration, and open science; all instrumental to the delivery of exemplary research. We strongly believe that better science is obtained when a research team comprises diverse people with different academic and cultural backgrounds. Everyone has a perspective, and combining all these perspectives can only benefit scientific inquiries.

At NCMM, we understand that our research culture is dynamic and continuously evolving. Our positive research culture attracts and supports the most talented individuals, enabling them to realize their full potential whilst with us. NCMM is a hub for excellent molecular medicine research and is an incubator for early-career group leaders and researchers. By adopting the EMBL model for early-career group leader recruitment and development, we strive to foster a creative environment where innovative ideas and individuals can develop.

Providing a diverse and inclusive work environment for all staff and students is vital for NCMM. Evidence consistently shows that caring about those we work with and providing them with a supportive work environment is fundamental to fostering team productivity and well-being. If team members are excited about their science, are provided with a good work environment, and have a supportive and collaborative team, then good science is very likely to follow. In science, we face both failures and successes in our work, so it is of utmost importance to have a team around you to support and help you in the difficult moments and to celebrate in the good ones.

Our efforts to develop our research environment are ongoing. We are committed to continuing to make progress in this area through meaningful and impactful changes.

In this section of NCMM's annual report, we highlight some of the initiatives we have undertaken over the last year to continue to build a fruitful and supportive research environment.



# Training and knowledge exchange

From left to right: Celina Wiik, Samuele Cancellieri, Vipin Kumar, Elham Shojaeinia, Oline Rio, Weiwei Li, Hemanga Gogoi. Photo: Ine Eriksen/UiO *(not in the photo: Ladislav Hovan).*

## NCMM Trainee Committee

The Trainee Committee at NCMM serves as a representative body for trainees (mainly PhD students, master students and post-docs), aiming to promote their engagement, well-being, and professional development within the Centre. The committee's primary purpose is to provide a platform for trainees to voice their ideas and concerns, fostering a supportive and collaborative environment. To achieve this, they organize a variety of activities for trainees and participate in arranging events involving the whole of NCMM. As of 2024, the NCMM Trainee Committee members are: Elham Shojaeinia (Esguerra group), Ladislav Hovan (Kuijjer group), Vipin Kumar (Mathelier group), Oline Rio (Haapaniemi group), Weiwei Li (Saarela group), Hemanga Gogoi (Sekulic group), Samuele Cancellieri (Sahu group), and Celina Wiik (Sahu group).

# PhD courses on precision medicine at NCMM

In 2023, NCMM hosted two PhD courses focusing on molecular medicine and multiomic data analysis, respectively. The courses are among the joint NordForsk-supported courses offered across the Nordic EMBL Partnership. Travel grants funded by NordForsk are also available for PhD students taking courses at the other Nordic nodes.

## Multi-omic data analysis and integration for precision medicine

The aim of this course is to teach students new approaches of multi-omic data analysis to study gene expression regulation in tissues. The course presents different computational methods to analyze multi-omic datasets in healthy and disease settings. Emphasis is given to the analysis and integration of datasets dedicated to the study of transcriptional gene regulation, systems biology, and cancer.

## National course in Molecular Medicine

The aim of this national course is to provide a comprehensive overview of selected topics in molecular medicine that are relevant to understanding disease mechanisms and development, aspects of translational medicine and the future of diagnostics and targeted therapies integrated to stratified, tailored, and personalized medicine. The lectures are given by national and international experts in the field, outlining state-of-the-art approaches and emerging trends.

## PhD defences in 2023 and Q1 2024

### Zhuokun Li
**Thesis title:** Characterizing and improving CRISPR-Cas9 system with high-throughput methods
**Supervisors:** Dr. Emma Haapaniemi, University of Oslo, Professor Hilde Loge Nilsen, University of Oslo, Professor Rafal Ciosk, University of Oslo

### Mateu Montserrat Canals
**Thesis title:** Molecular warfare: A structural biology view on pathogen weapons — GbpA from Vibrio cholerae — and host defences — Vg from the honey bee
**Supervisors:** Professor Ute Krengel, University of Oslo, Professor Hartmut Luecke, Nova School of Science and Technology, Professor Michele Cascella, University of Oslo, Associate Professor Reidar Lund, University of Oslo

### Flore Kersten
**Thesis title:** A double-edged sword. AB toxins as attack (cholera toxin) and defense (CCTX2) mechanisms
**Supervisors:** Professor Ute Krengel, University of Oslo, Senior Engineer Gabriele Cordara, University of Oslo

### Rafael Riudavets Puig
**Thesis title:** Deciphering transcriptional regulation and its role in cancer
**Supervisors:** Dr. Anthony Mathelier, University of Oslo, Professor Eivind Hovig, University of Oslo



Inês Almeida Lapa (left) and Veronica Careddu (right) at their stand at Teknisk museum. Photo: Øystein Horgmo/UiO

# Zebrafish at Forskningstorget 2023

The National Science Week in Norway, known as Forskningsdagene, is held to make science and research available to the public. As part of this, the Medical Faculty at UiO organized a Science Fair (Forskningstorg) at Teknisk museum in Oslo in September 2023. Researchers set up stands with various activities to showcase the research being done at the Medical Faculty. Up to 1000 students from various schools came by the stands on the first day. On the second day the museum was open for all and the stand was visited by people of all ages interested in science.

Inês Almeida Lapa and Veronica Careddu from Camila Esguerra's group at NCMM participated with a stand on zebrafish. Over the course of the two-day Science Fair, they gave visitors insight into the everyday life of working with zebrafish.

"On the first day of the fair, we were very happy to see that the students were fascinated by the science, asking questions and wanting to participate in the experiments themselves. A big highlight was the fact that some of these children came back for the second day of the fair and brought their families along", says Inês Almeida Lapa, who found the experience very rewarding.

Summing up the event, she says: "We had visitors of all ages and backgrounds come by our stand and we were surprised by the amount of people who were interested in the science and wanted more in-depth explanations about the work of researchers. The biggest take away from this experience was that it is essential to have more events like this for young students and the general public to demystify, celebrate and encourage an interest in science and research. Because the people are definitely keen to listen, learn and be inspired".

Group photo of the participants at the NCMM Scientific Retreat in June 2023.

# NCMM Scientific Retreat 2023

Each year, NCMM organizes a retreat for staff and associated investigators to promote networking and knowledge exchange. In June 2023, NCMM and Associate Investigators gathered at Strömstad Spa, Sweden, for two days of excellent scientific talks and networking. The program included presentations from Associate Investigators, group leaders, postdocs, and PhD students, covering a range of topics within the field of molecular medicine.

In addition, the newly established NCMM Trainee committee organized a round table discussion on career development between trainees and NCMM alumni.

"Our first event was a round table discussion, where NCMM alumni presented their perspectives on career paths. The panelists offered an updated outlook on the variety of trajectories they experienced after they left the institute. Trainees welcomed the event and found the insights from the panelists' experiences quite enriching and thought-provoking", says Vipin Kumar, one of the committee members.

# Oslo Bioinformatics Workshop Week strengthens bio-informatic community

Ieva Rauluseviciute from NCMM hosting a workshop during OBiWoW 2023. Photo: Tatiana Belova.

The Oslo Bioinformatics Workshop Week (OBiWoW) is an initiative to build and strengthen the bioinformatics community in Oslo. The week consisted of several workshops organized and hosted by scientists experienced working with bioinformatics. The workshops were open to anyone within the scientific community interested in bioinformatics, regardless of background or experience. Several early career researchers from NCMM played a central role in organizing the event and hosted several workshops.

Ieva Rauluseviciute from NCMM participated as one of the instructors for the workshop: "Introduction to gene expression regulation by transcription factors and its computational analysis".

"It was a really nice experience because we had many great discussions throughout the workshop and a lot of engagement from the participants. We not only focused on how to perform the bioinformatic analysis, but also how to interpret the results. It gives people a broader understanding on how they can apply a bioinformatic tool or pipeline to their own work", says Rauluseviciute.



eatris NORWAY

EATRIS is a non-profit European Research Infrastructure Consortium (ERIC) that offers unique access to the academic expertise and high-end technologies required to advance new products through the translational process from target validation to early clinical trials. The infrastructure is open to both academic researchers and companies in need of support to advance biomedical innovations. NCMM coordinates the Norwegian participation in EATRIS and NCMM's Director, Professor Janna Saarela, is the EATRIS National Director of Norway and Anita Kavlie is the National Coordinator for EATRIS Norway.

EATRIS has five scientific platforms:

- Advanced Therapy Medicinal Products
- Biomarkers
- Imaging and Tracing
- Small Molecules
- Vaccine, Inflammation and Immune Monitoring

EATRIS offers a range of services which directly benefit Norway-based researchers. Key aspects of the services offered by EATRIS are: support for funding applications, including help in forming a consortium; EATRIS participating in research funding proposals as a full partner and providing various centralised services; supply a letter of support for research proposals; and taking a leading role in supporting the development and management of proposals coming from EATRIS member institutes.

EATRIS also offers an expert mentoring service for researchers investigating rare diseases, a matchmaking service to facilitate academic collaborations with industry, and educational and training offerings for the next generation of translational scientists.

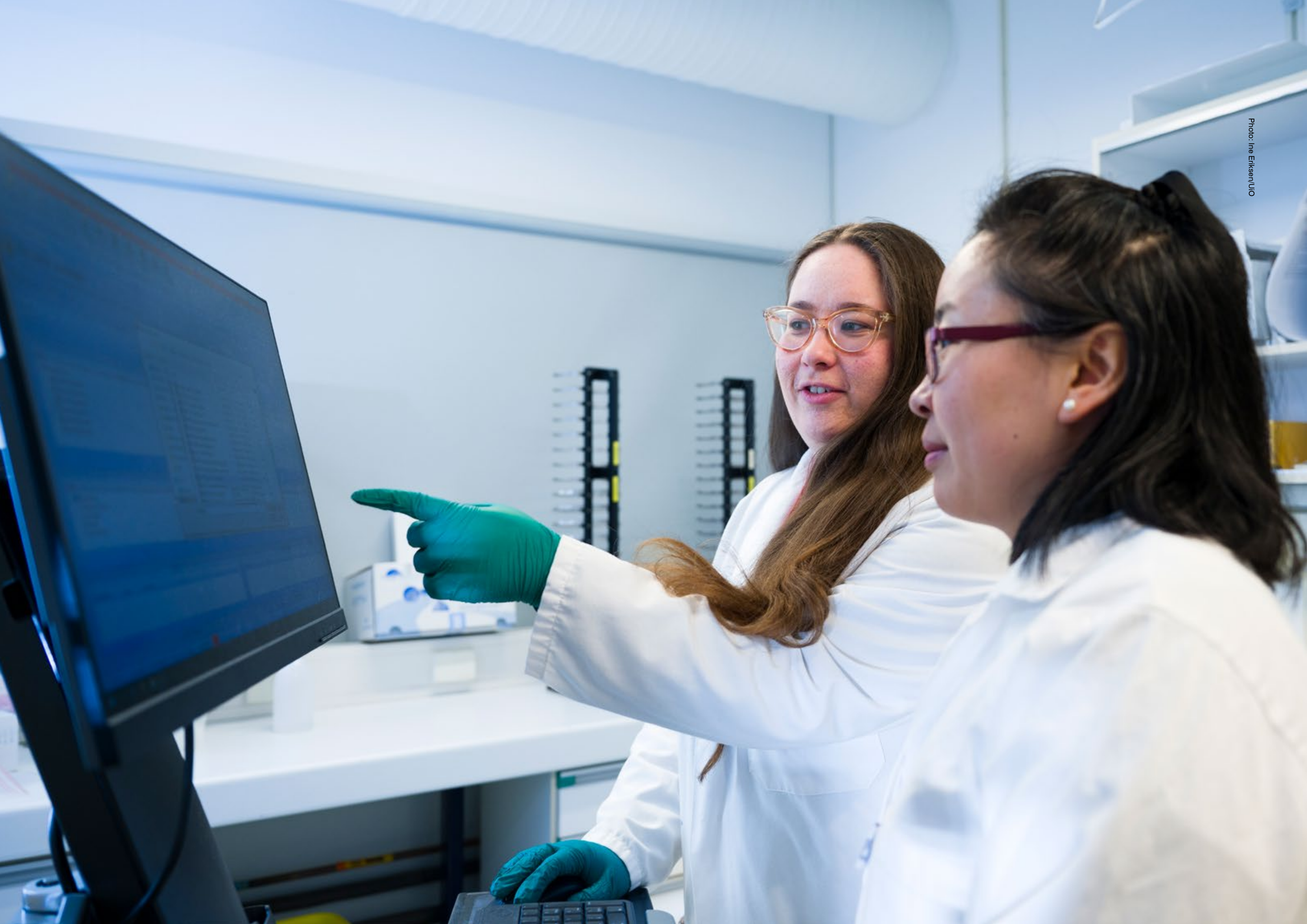


Photo: Ine Eriksen/UiO

# Collaborations

NCMM's objectives are to conduct cutting-edge research in molecular medicine and to facilitate the translation of discoveries in basic biomedical research into clinical practice. To enable translational research, NCMM has developed strong links across to UiO faculties and to South-Eastern Norway Regional Health Authority (HSØ) and its subsidiary Oslo University Hospital (OUH).

All NCMM group leaders have affiliations with UiO departments or institutes, both within the medical and natural sciences faculties, or at clinical or para-clinical departments at OUH. These affiliations help to facilitate clinical collaborations, giving Group Leaders better access to patient materials, biobanks, and clinical trials. They are also crucial for facilitating translational research. These research collaborations have already resulted in a number of joint publications.

**NCMM group leaders currently hold adjunct appointments at the following departments:**

UIO

School of Pharmacy

NCMM PI: C.V. Esguerra

UIO

Department of Chemistry

NCMM PI: N. Sekulic

UIO

Institute of Basic Medical Sciences

NCMM PI: C. Boccara

UIO

Department of Informatics

NCMM PI: A. Mathelier

OUH

Department of Medical Genetics

NCMM PIs: J. Saarela and A. Mathelier

OUH

Department of Pediatric Research, Division of Paediatric and Adolescent Medicine

NCMM PIs: E. Haapaniemi and S. Waszak

OUH

Institute for Cancer Research

NCMM PI: B. Sahu



Photo: Ine Eriksen/UiO

**Research affiliations at international universities:**

UCSF

University of California, San Fransisco, US, Dept. of Neurology

NCMM PI: S. Waszak

LUMC

Leiden University Medical Center NL, Dept. of Pathology

NCMM PI: M. Kuijjer

EPFL

School of Life Sciences, École Polytechnique Fédérale de Lausanne, Switzerland

NCMM PI: S. Waszak

FIMM

Institute for Molecular Medicine Finland

NCMM PI: J. Saarela

UOH

Faculty of Medicine, University of Helsinki

NCMM PI: B. Sahu

# Associate Investigators

NCMM continues to develop its scientific community through strong collaborative links with key scientists and research groups across Norway. These links and collaborations greatly support interdisciplinary research and networking.

NCMM's Associate Investigators are a group of outstanding scientists based in Norway. They bring expertise compatible with NCMM's research areas and are interested in collaborating with NCMM. NCMM Associate Investigators continue to work at their host institutions, but are credited an affiliation to NCMM and the Nordic EMBL Partnership for Molecular Medicine. They are eligible to apply for seed-funding grants for collaborative projects with NCMM group leaders, and are invited to participate in NCMM conferences, workshops and retreats. As of Spring 2023, NCMM has 47 Associate Investigators.

| Associate Investigators: | Institution |
|---|---|
| Professor Tero Aittokallio | Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital |
| Professor Ole A. Andreassen | Division of Mental Health and Addiction, Oslo University Hospital and Institute of Clinical Medicine, University of Oslo |
| Professor Thomas Arnesen | Department of Molecular Biology, University of Bergen and Department of Surgery, Haukeland University Hospital |
| Dr. Magnus Aronsen | Division of Physiology, Institute of Basic Medical Sciences, University of Oslo and Oslo University Hospital |
| Associate Professor Lorena Arranz | Centre for Embryology and Healthy Development (CRESCO), Institute of Clinical Medicine, University of Oslo |
| Professor Yvonne Böttcher | Department of Clinical Molecular Biology, Akershus University Hospital and Institute of Clinical Medicine, University of Oslo |
| Professor Simona Chera | Department of Clinical Science, University of Bergen |
| Professor Rafal Ciosk | Section for Biochemistry and Molecular Biology, Department of Biosciences, University of Oslo |
| Associate Professor Rune Enger | Institute of Basic Medical Sciences, University of Oslo |
| Professor Marianne Fyhn | Section for Physiology and Cell Biology, Department of Biosciences, University of Oslo |
| Professor Joel Glover | Institute of Basic Medical Sciences, University of Oslo |
| Associate Professor Victor Greiff | Institute of Clinical Medicine, University of Oslo |
| Professor Gunnveig Grødeland | Institute of Clinical Medicine, University of Oslo and Oslo University Hospital |
| Professor John-Bjarne Hansen | KG Jebsen – Thrombosis Research and Expertise Centre (TREC), Department of Clinical Medicine, UiT - The Arctic University of Norway, and University Hospital of Northern Norway |
| Professor Nils Halberg | The Department of Biomedicine, University of Bergen |
| Professor Guttorm Haraldsen | Institute of Clinical Medicine, University of Oslo and Department of Pathology, Oslo University Hospital |
| Associate Professor Helene Knævelsrud | Institute of Basic Medical Sciences, University of Oslo |
| Professor Arne Klungland | Department of Microbiology, Division of Diagnostics and Intervention, Oslo University Hospital and University of Oslo |
| Professor Vessela Kristensen | Department of Medical Genetics, Oslo University Hospital and Institute of Clinical Medicine, University of Oslo |
| Professor Dirk Linke | Section for Genetics and Evolutionary Biology, University of Oslo |
| Professor Karl-Johan Malmberg | Department of Cancer Immunology, Institute for Cancer Research, Oslo University Hospital and University of Oslo |
| Professor Hans-Peter Marti | Department of Medicine, Haukeland University Hospital, University of Bergen |
| Professor Hilde L. Nilsen | Department of Clinical Molecular Biology, Akershus University Hospital and University of Oslo |
| Professor Ragnhild A. Lothe | Department of Cancer Prevention, Institute for Cancer Research, Oslo University Hospital and University of Oslo |
| Dr. Alicia Llorente | Institute for Cancer Research, Oslo University Hospital |
| Professor Reidar Lund | Section for Chemical Life Sciences, Department of Chemistry, University of Oslo |
| Professor Espen Melum | Research Institute for Internal Medicine, Oslo University Hospital and University of Oslo |
| Professor Emmet McCormack | Department of Clinical Science, University of Bergen |
| Associate Professor June Myklebust | Institute for Cancer Research, Oslo University Hospital and Institute for Clinical Medicine, University of Oslo |
| Professor Pål R. Njølstad | KG Jebsen Center for Diabetes Research, University of Bergen and Haukeland University Hospital |
| Associate Professor Lynn Butler Odeberg | Department of Clinical Medicine, UiT - The Arctic University of Norway and the Karolinska Institute |
| Professor Jacob Odeberg | Institute for Clinical Medicine, UiT - The Arctic University of Norway and University Hospital of North Norway |
| Professor Johanna Olweus | KG Jebsen Center for Cancer Immunotherapy, Department of Cancer Immunology, Institute for Cancer Research, University of Oslo and Oslo University Hospital |
| Professor Cinzia Progida | Section for Physiology and Cell Biology, Department of Biosciences, University of Oslo |
| Professor Christine Hanssen Rinaldo | Department of Clinical Medicine, UiT - The Arctic University of Norway and University Hospital North Norway |
| Adjunct Professor Hege Russnes | Department of Pathology and Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital and University of Oslo |
| Dr. Even Holth Rustad | Akershus University Hospital and Institute for Cancer Research, Oslo University Hospital |
| Professor Axel Sandvig | Department of Neuromedicine and Movement Science, Norwegian University of Science and Technology (NTNU) |
| Professor Anne Simonsen | Institute for Cancer Research, Oslo University Hospital and Institute of Basic Medical Sciences, University of Oslo |
| Professor Rolf Skotheim | Department of Molecular Oncology, Institute for Cancer Research, Oslo University Hospital and University of Oslo |
| Dr. Asbjørg Stray-Pedersen | Norwegian National Unit for Newborn Screening, Oslo University Hospital and Institute for Clinical Medicine, University of Oslo |
| Professor Kjetil Taskén | Institute for Cancer Research, Oslo University Hospital and University of Oslo |
| Dr. Alfonso Urbanucci | Institute for Cancer Research, Oslo University Hospital |
| Professor Eivind Valen | Section for Biochemistry and Molecular Biology, Department of Biosciences, University of Oslo and Department of Informatics, University of Bergen |
| Associate Professor Marc Vaudel | Department of Clinical Science, University of Bergen |
| Professor Emre Yaksi | Kavli Institute for Systems Neuroscience/Centre for Neural Computation, Norwegian University of Science and Technology (NTNU) |

Photo: Oda Hveem

# NCMM Joint Postdoctoral Program

To promote the establishment of new collaborations, NCMM announced the NCMM Joint Postdoctoral Program in Molecular Life Science in 2023. The program will support joint supervision of postdoctoral researchers between NCMM group leaders and partners from the Oslo arena through 2-year postdoctoral fellowships. An important criterion for the program is that the group leaders and partners have not collaborated on grants or publications within the past 5 years. NCMM will provide financial support for one year, while the partner will support the remaining year.

**Following the call, 7 projects were supported and are expected to start in 2024:**

### Integrative modelling and single-cell analysis of pancreatic lineage-specific transcription factors in pancreatic cancer treatment resistance

Participating PIs:

- Dr. Biswajyoti Sahu
  – *Centre for Molecular Medicine Norway (NCMM), University of Oslo*
- Prof. Tero Aittokallio
  – *Institute for Cancer Research, Oslo University Hospital*

### Mechanisms of Epileptogenesis after traumatic brain injury: The search for new therapeutic strategies

Participating PIs:

- Dr. Camila Esguerra
  – *Center for Molecular Medicine Norway, University of Oslo*
- Prof. Erik Taubøll
  – *Dept. of Neurology, Oslo University Hospital*

### CRÊPE: Cis-regulatory elements for prostate carcinogenesis

Participating PIs:

- Dr. Anthony Mathelier
  – *Center for Molecular Medicine Norway, University of Oslo*
- Dr. Alfonso Urbanucci
  – *Institute for Cancer Research, Oslo University*

### Gene regulatory networks of tumor heterogeneity and metastatic progression in colorectal cancer

Participating PIs:

- Dr. Marieke Kuijjer
  – *Center for Molecular Medicine* Norway, University of Oslo
- Dr. Anita Sveen
  – *Institute for Cancer Research, Oslo University Hospital*

### Autophagy as a phylogenetically conserved mediator of sleep benefits

Participating PIs:

- Dr. Charlotte Boccara
  – *Center for Molecular Medicine Norway, University of Oslo*
- Dr. Helene Knævelsrud
  – *Institute of Basic Medical Sciences, University of Oslo*

### Non-invasive assessment of placental function & gene correction for inborn blood diseases

Participating PIs:

- Dr. Emma Haapaniemi
  – *Center for Molecular Medicine Norway, University of Oslo*
- Dr. Trond Melbye Michelsen
  – *Department of Obstetrics and Gynecology, Oslo University Hospital*

### Improved analysis tools for identifying functional and clinically relevant transcript isoforms from short and long-read RNA data

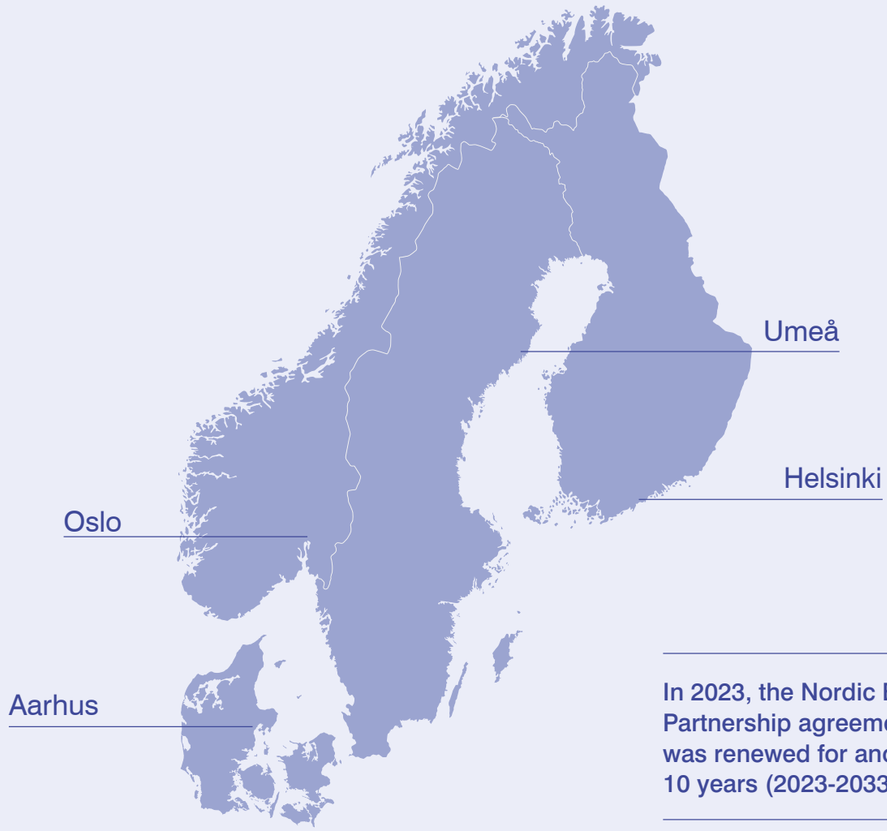
Participating PIs:

- Prof. Janna Saarela
  – *Center for Molecular Medicine Norway, University of Oslo*
- Prof. Dag Undlien
  – *Department of Medical Genetics, Oslo University Hospital*

# Nordic EMBL Partnership

The Nordic EMBL Partnership for Molecular Medicine is a major strategic player within Europe, focusing on increasing the molecular understanding of disease mechanisms. The Partnership benefits from the complementary nature of the research conducted, the availability of outstanding research infrastructures, and industry collaborations.

The Partnership was founded in 2008 as a collaboration between the EMBL (European Molecular Biology Laboratory) and FIMM (Institute of Molecular Medicine Finland) at the University of Helsinki, MIMS (Laboratory for Molecular Infection Medicine Sweden) at Umeå University, NCMM (Centre for Molecular Medicine Norway) at the University of Oslo and DANDRITE (Danish Research Institute of Translational Neuroscience) at Aarhus University. In addition to the Partnership between the Nordic nodes, each of the research centres collaborate locally and nationally with their host universities, public health institutes, hospitals, and research councils. This has resulted in a strong and far-reaching Nordic network for molecular medicine.




In 2023, the Nordic EMBL Partnership agreement was renewed for another 10 years (2023-2033).




The signatories of the renewed agreement for Nordic EMBL Partnership for Molecular Medicine, from left to right: Janna Saarela (NCMM Director), Svein Stølen (Rector University of Oslo), Edith Heard (EMBL Director General), Poul Nissen (DANDRITE Director), Eika Berit (Prorector Aarhus University), Hans Adolfsson (Rector Umeå University), Oliver Billker (MIMS Director), Mark Daly (Outgoing FIMM Director), Sari Lindblom (Rector University of Helsinki). Photo: Veikko Somerpuro.

# Renewal of the Nordic EMBL Partnership for a further 10 years

The Nordic EMBL Partnership for Molecular Medicine gathered in Helsinki in May 2023 to celebrate the signing of a renewed 10-year agreement between EMBL and the Universities of Oslo, Helsinki, Aarhus and Umeå. The directors from each node of the Nordic EMBL Partnership, the EMBL Director General, and the rectors of the hosting universities signed the agreement in the University Great Hall of the University of Helsinki. NCMM Director Janna Saarela and UiO rector Svein Stølen signed on behalf of NCMM and UiO.

Reflecting on the importance of the Nordic EMBL Partnership in Molecular Medicine, NCMM Director Janna Saarela noted:

"The Nordic EMBL Partnership is a unique network sharing a common vision of implementing excellence in research. The partnership units operate as greenhouses for talented young scientists to foster collaboration and impactful research in Molecular Medicine within their host environments and across nodes. NCMM looks forward to a further 10 years with our sister nodes and to the many opportunities for training, research collaboration and education that are to come."

NORDIC **EMBL**
PARTNERSHIP FOR
MOLECULAR MEDICINE

# Forging collaborations across the Nordics: the 2023 annual meeting of the Nordic EMBL Partnership for Molecular Medicine

*Adapted from the originally published article on the Nordic EMBL Partnership website*

The Finnish Nordic EMBL partner node, FIMM, hosted the 12th annual Nordic EMBL Partnership meeting in Helsinki 11-14 September 2023. The annual meeting strategically connects Nordic- and EMBL-based researchers. The event facilitates the expansion of knowledge through scientific presentations and discussions, while also providing opportunities to broaden networks and spark future collaborations.

Over 200 participants travelled to Aalto University's main building, Dipoli. The building's organic architecture, once a radical design trend, set the ideal atmosphere for nurturing collaborations that will push the boundaries in addressing current challenges in molecular medicine.

Introducing a fresh concept for the Partnership meeting this year, tandem talks showcased cutting-edge technologies that facilitate research collaborations across the nodes. Four examples highlighted successful cross-node collaborations on gut microbiota and metabolomics (MIMS-FIMM), long COVID (FIMM-MIMS), Zebrafish model for neurological diseases (DANDRITE-NCMM), and phenotyping rare neurological disease variants with high content analysis (NCMM-FIMM).

This year's meeting featured two additional program components that took place in advance of the main meeting. The 2023 Young Investigator Meeting (YIM) embraced "Sailing into the unknown: building bridges and forging collaborations". The second addition was the half-day Group Leader satellite workshop. Its primary emphasis was knowledge sharing and identification of new collaboration opportunities.

Oliver Billker, Speaker of the Nordic EMBL Partnership and Director of MIMS, concluded the event, saying "Many of the research projects presented during the meeting would not have been possible without Nordic collaborations. Our partnership is evolving, each node is involved in several research areas which drive today's molecular medicine research forward. I see us collaborating more and more in these areas, using our complementary strengths in different new ways, already exemplified in the ongoing tandem projects across the nodes".

## Nordic EMBL Partnership was awarded NordForsk funding for a postdoc program in molecular medicine

The Nordic EMBL Partnership for Molecular Medicine was awarded 20 million NOK for five years (2024-2028) by NordForsk as part of their Nordic University Cooperation initiative. The funding will support the program entitled "NORPOD - A collaborative postdoc program of the Nordic EMBL Partnership for Molecular Medicine", which will launch at the beginning of 2024. NORPOD is set up to promote direct collaborations between groups at different nodes in the Nordic EMBL Partnership, through joint postdoctoral fellowships.

# Governance

# NCMM Board

The NCMM Board, in collaboration with the Director, is responsible for the Centre's overall coordination and progress. The Board steers and supervises NCMM's activities and finances as well as approves the Centre's strategic plans, objectives, and budget.

The Board's decisions contribute to promoting excellence in the Centre's recruitments, research, collaborations, and translational value. The Board consists of the Chair and five members representing NCMM's host, the University of Oslo, and the consortium partner Health South-Eastern Norway Regional Health Authority (HSØ), as well as a national representative.

**Chair**

Professor
**Jens Petter Berg**
University of Oslo / Oslo University Hospital

**Members**

Professor
**Ola Myklebost**
University of Bergen
(national representative)

Professor
**Melinka Alonso Butenko**
University of Oslo

Professor
**Hilde Nilsen**
University of Oslo

Head of Research and Diagnostics
**Lars Eikvar**
South-Eastern Norway Regional Health Authority (HSØ)

Special Advisor
**Torunn Berge**
South-Eastern Norway Regional Health Authority (HSØ)

**Deputy Members**

Professor
**Magne Børset**
Norwegian University of Science and Technology (NTNU)
(deputy national representative)

Special Advisor
**Randi Vad**
South-Eastern Norway Regional Health Authority (HSØ)

Professor
**Arnoldo Frigessi**
University of Oslo



# A message from the Chair of the Board of NCMM, Jens Petter Berg:

Dear NCMM Employees, Colleagues, and Friends,

As Chair of the Board, I am very proud of NCMM's commitment to excellence during the past year, providing a cutting-edge environment for molecular medicine research. During their visit in 2023, the Centre's Scientific Advisory Board (SAB) also commended the Centre for attracting top international talent and fostering multidisciplinary research that bridges the gap between discovery science and clinical application. The Board extends its profound appreciation for the generous financial backing from our consortium partners: The Research Council of Norway, The South-Eastern Norway Regional Health Authority, and The University of Oslo.

I am happy that the NCMM leadership team has been reinforced by the appointment of Associate Director Anthony Mathelier. Anthony brings a wealth of experience that will enhance NCMM's mentorship and social cohesion efforts, something the SAB has encouraged us to fortify.

In focusing on the development of future scientists, the newly formed NCMM trainee committee will be a crucial link between our trainees and the NCMM leadership. I'm excited to see the committee's innovative plans unfold, further strengthening NCMM's scientific community.

During 2023 NCMM has taken strategic steps to promote collaboration through the establishment of the joint Postdoctoral Program in Molecular Life Sciences. This initiative has been endorsed by funding seven joint postdoc projects and promises to enhance partnerships across the Oslo research landscape and advance NCMM's scientific endeavors.

I would like to congratulate group leader Marieke Kuijjer for renewal of her research group and for her commitment to computational biology and systems medicine. I extend my gratitude to group leader Sebastian Waszak, for his valuable contributions to NCMM and offer my best wishes in his new position.

During 2023 there have been some changes in the Board. I would like to thank Bente Halvorsen and Arne Klungland for their invaluable efforts and dedication as members of the NCMM Board. I am pleased to welcome Lars Eikvar, Melinka Butenko, and Torunn Berge as new ordinary Board members, and Randi Vad as new deputy member to the NCMM Board. I look forward to a positive and collaborative relationship with each of them and the other Board members.

On behalf of the Board, it is with great satisfaction that I acknowledge the considerable strides and successes NCMM has made in basic and translational research over the past year. I am very grateful for the collaboration with and applaud the efforts of NCMM Director Janna Saarela and all NCMM employees. Your work has culminated in significant research funding and important scientific achievements.

19th March 2024

Warm regards,
**Jens P. Berg, Prof., MD, PhD**
Chair of the Board, NCMM

Photo: Øystein Horgmo, UiO

# Scientific Advisory Board (SAB)

The SAB's main mission is to offer academic and strategic advice, as well as benchmark the performance of NCMM's research groups and the Centre internationally. The SAB meets with NCMM core members every 18-24 months. These meetings allow for the review of recent progress and advice on future strategies. The most recent SAB visit took place in February 2023, when Marieke Kuijjer was evaluated and recommended for extension.

**Chair**

Professor
**Richard Treisman**
Research Director, Francis Crick Institute London, UK

**Board**

Dr.
**Alvis Brazma**
EMBL Senior Scientist & Senior Team Leader EMBL-EBI Hinxton Cambridge, UK

Professor
**Olli Kallioniemi**
Director SciLifeLab Karolinska Institute Stockholm, Sweden

Professor
**Titia Sixma**
Head of Division for Biochemistry Netherlands Cancer Institute Amsterdam, The Netherlands

Professor
**George Vassiliou**
Professor of Haematological Medicine, Wellcome-MRC Cambridge Stem Cell Institute, University of Cambridge, UK

Dr.
**Judith Zaugg**
Head of the Personalised Genomics to Study Genetic Basis of Complex Diseases group, EMBL Heidelberg, Germany

Photo: Oda Hveem

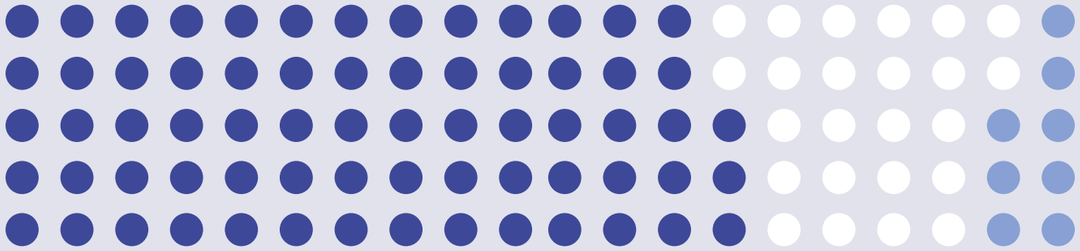
# Funding

54
mNOK
per year in core funding for 2020-24

30
mNOK
in competetive funding spent in 2023

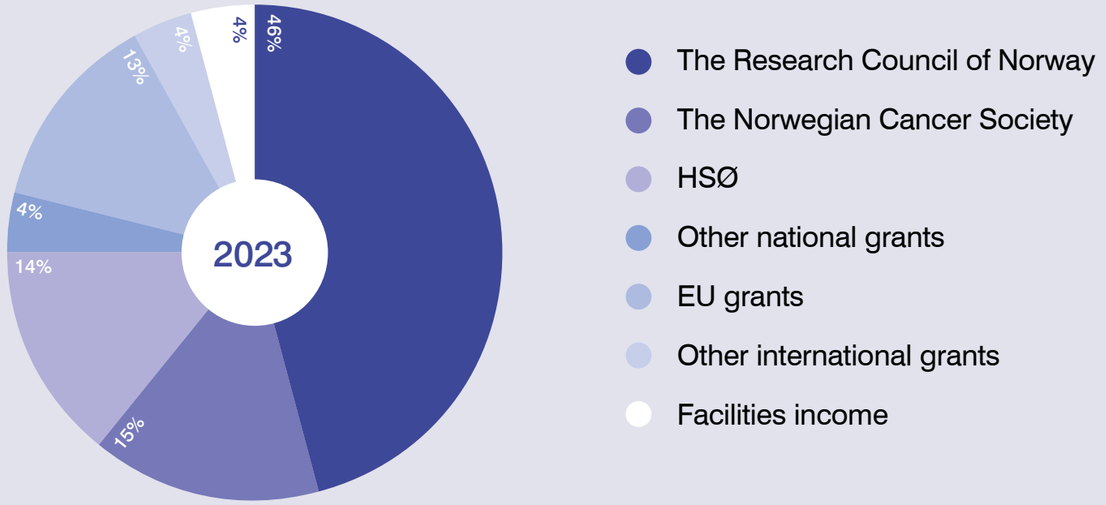
293
mNOK
in competitive funding for 2015-2023

## Core funding




The core funding for NCMM in the period 2020-2024 is 54.5 million NOK per year from the three consortia partners UiO, the Research Council of Norway (RCN) and South-Eastern Norway Regional Health Authority (HSØ). Overhead income from core facilities and production-based income comes in addition.

## Competetive funding

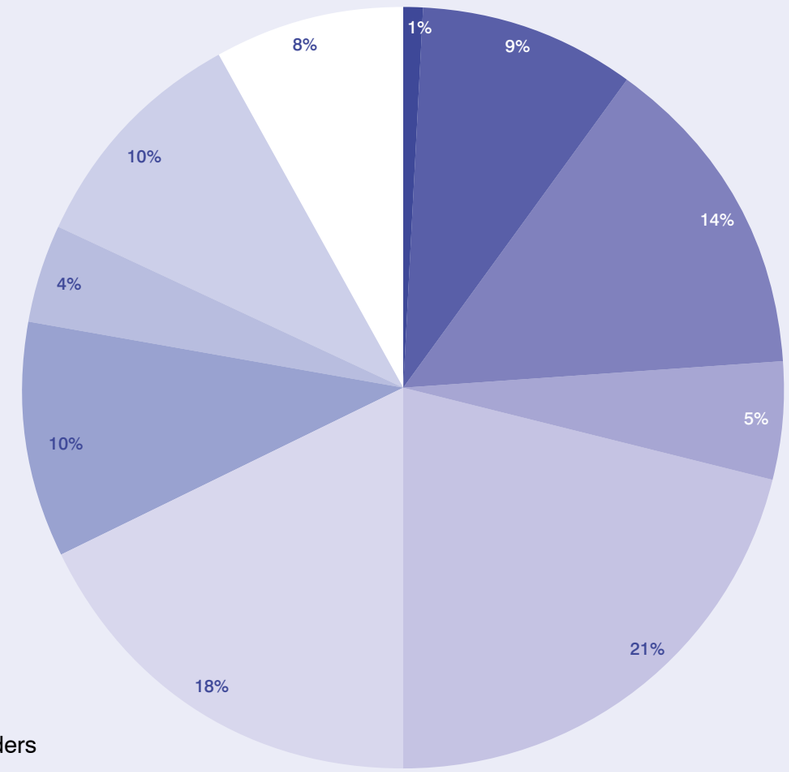



In 2023, the amount of competetive funding used by the research groups reached 30 million NOK. This funding includes grants from the Research Council of Norway, the Norwegian Cancer Society, South-Eastern Norway Regional Health Authority, the European Commission, the Swiss National Science Foundation Sinergia and private foundations and organizations.

# Personnel statistics

in 2023 and Q1 2024

## Staff according to type of employment (%)

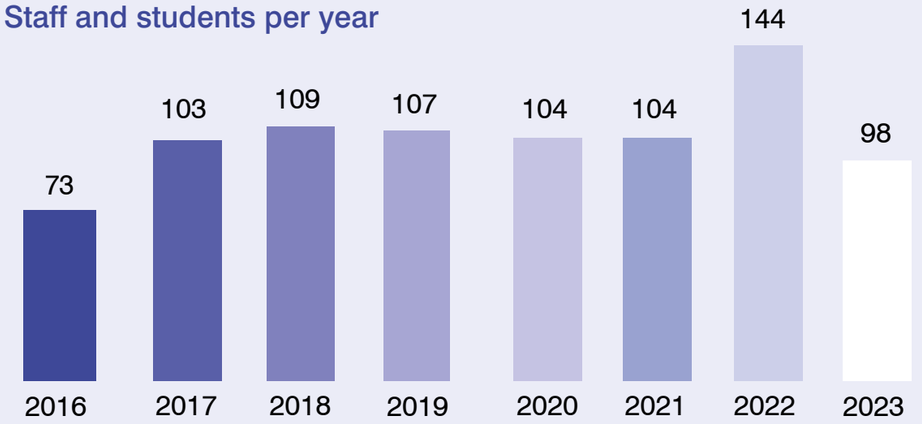



- Director
- Group leaders
- Researchers
- Postdocs
- PhD fellows
- Students
- Administration
- IT
- Engineers
- Research assistants

**98**

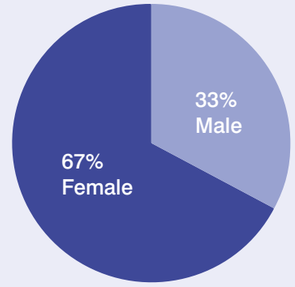
NCMM had 98 staff members and students in 2023. 86% of these are research and research technical staff.

## Staff and students per year

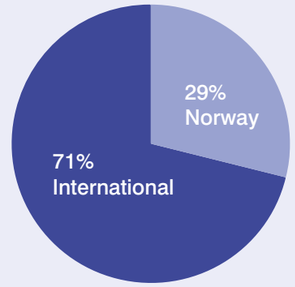



- 2017 represents NCMM after the merger with the Biotechnology Centre of Oslo
- 2022 saw an increase in students, an after-effect of the Covid-19 pandemic

## Staff gender balance




## International staff



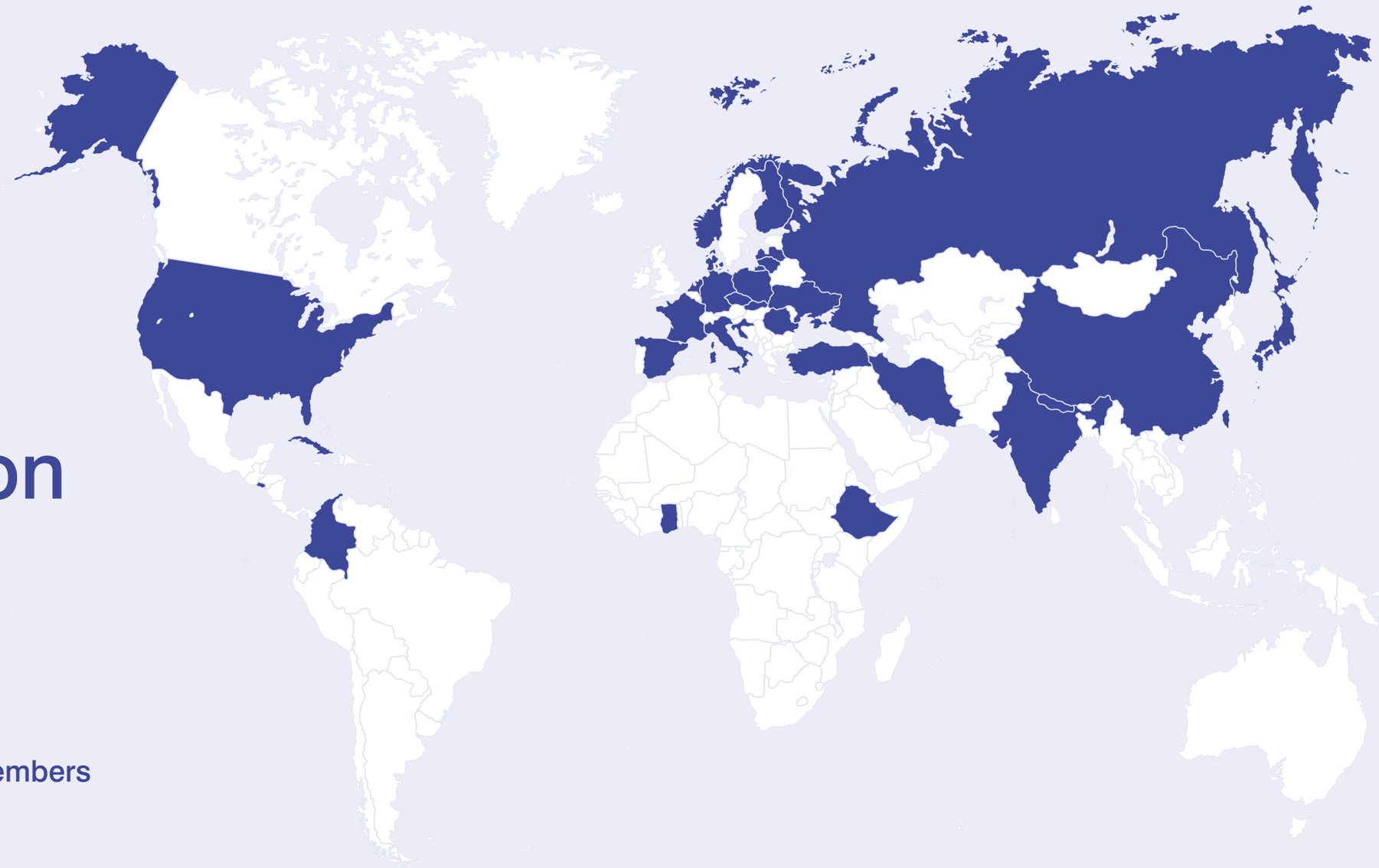

## Group leader gender balance

**7 out of 10 group leaders are female**

# Distribution of staff

As of Q1 2024

- 30 nations in total
- 59 international staff members



**1**
person

**Countries represented:**
Colombia, Croatia, Cuba, Czech Republic, El Salvador, Etiopia, Ghana, Italy, Japan, Latvia, Lithuania, Romania, Russia, Slovakia, Taiwan, Ukraine, Nepal, Denmark

**2**
people

**Countries:**
Iran, Netherlands, Turkey

**3**
people

**Countries:**
Germany, India, Poland, USA

**5**
people

**Countries:**
China, Spain

**7**
people

**Countries:**
Finland, France

**24**
people

**Countries:**
Norway

# Personnel at NCMM

## in 2023 and Q1 2024

### Director and administration

**Director**
Janna Saarela

**Associate Director**
Anthony Mathelier

**Chief Administrative Officer**
Ingrid Kjelsvik

**Head of Section for Research Strategy, Communication and International Relations**
Elizabeth Smethurst
*(from February 2024)*

**Financial Officers**
Mette Kvernland
Anita Elisabeth Skolem
*(until May 2024)*

**Human Resources Officer**
Nina Modahl

**Communications Officers**
Nikoline L. Rasmussen

**EATRIS Coordinator**
Anita Kavlie

**Higher Executive Officer**
Carlos Romeo Rodriguez

**IT Team**
Harold Gutch
Melaku Tadesse
Torfinn Nome
Pavel Zarva

**Administrative Officer**
Larissa Lily *(until December 2023)*

**Senior Strategic Officers**
Ragni Indahl *(from May 2023)*
Marie Goua *(from October 2023)*

### Laboratory Operations and Core Facilities

**HSE Coordinator**
Sissel Eikvar *(from August 2023)*

**General Lab Manager**
Xian Hu (Edna) *(until August 2023)*
Rasma Gutsmite *(from September 2023)*

**Senior Engineer**
Gladys Tjørhom

**Research Technician**
Luis Alberto Quintero Linares

**Chemical Biology Core Facility**
Johannes Landskron
*(Platform manager)*
Alexandra Gade *(HTS Scientific Officer, Screening & Chemistry)*
Eirin Solberg *(HTS Scientific Officer, Screening & Robotics)*

**Zebrafish Core Facility**
Camila V. Esguerra
*(Core Facility Leader)*
Alejandro Pastor Remiro
*(Fish facility technician)*

## Research groups

### Human immune disorders

**NCMM Group Leader**
Janna Saarela

**Head Engineer / Lab manager**
Monika Szymanska

**Postdoctoral Fellow**
Yasaman Padakman *(until July 2023)*

**PhD Fellows**
Johanna M. Lehtonen
Ragnhild Selvig Braathen
Weiwei Li
Pu Chen

**MSc Students**
Sanne Iversen Lurås
Tuva Sundell *(shared supervision with Emma Haapaniemi)*

### Computational Biology and Gene Regulation

**NCMM Group Leader**
Anthony Mathelier

**Researchers**
Roza Berhanu Lemma

**Postdoctoral Fellow**
Vipin Kumar

**PhD Fellows**
Rafael Puig Riudavets
Ieva Rauluseviciute
Katalin Terézia Ferenc

**Lab Engineer**
Dina Ruud Aronsen

**MSc Students**
Sebastian Mørch

**BSc Students**
Joel Rodriguez Herrera
(co-supervised with Marieke Kuijjer)

**Interns**
Stefanie Mantz
Ilayda Altinönder
Villads Winton

### Structural Biology and Drug Discovery group

**Principal Engineer**
Rasma Gutsmite
*(until September 2023)*

**Postdoctoral Fellows**
Javier Gutierrez *(until August 2023)*
Marta Sanz Gaitero *(until July 2023)*

### Precision pediatrics and gene editing

**NCMM Group Leader**
Emma Haapaniemi

**Head Engineer**
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Ruchi Saigal *(shared supervision with Charlotte Boccara)*

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### Chemical Neuroscience

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### Structural Biology and Chromatin

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### Bionanotechnology and Membrane Systems

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### Computational Biology and Systems Medicine

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Giulia Schito *(until July 2023)*
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### Precision Cancer Epigenomics group

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Maivizhi Thiyagaraja
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## NORDIC EMBL PARTNERSHIP FOR MOLECULAR MEDICINE:

FIMM
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Nordic EMBL Partnership for Molecular Medicine

MIMS
Molecular Infection Medicine Sweden
Nordic EMBL Partnership for Molecular Medicine

NCMM
Centre for Molecular Medicine Norway
Nordic EMBL Partnership for Molecular Medicine

DANDRITE
Danish Research Institute of Translational Neuroscience
Nordic EMBL Partnership for Molecular Medicine

EMBL
European Molecular Biology Laboratory

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