UNIVERSITY OF OSLO

NCMM - Centre for Molecular Medicine Norway

Annual Report NCMM 2022

NCMM

NORDIC EMBL PARTNERSHIP FOR MOLECULAR MEDICINE

NCMM – From disease
mechanisms to
clinical practice

NCMM Co-Funders:

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

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Chapter 1

Welcome

Introduction from the Director

Dear friends, colleagues, and supporters of NCMM. It is my pleasure to welcome you to the 2022 NCMM Annual Report.

This was a year of optimism, and Norway was gradually able to open up again following the global pandemic. Despite some pandemic-related challenges persisting into the first quarter of 2022, NCMM was able to open up fully in the spring. One can say we had several post-pandemic "firsts" this year: first in-person retreat, first in-person SAB evaluation and several first in-person workshops, meetings and conferences replacing the already too familiar virtual interactions.

NCMM is now well into its third five-year period of operations (2020-2024). Importantly, the Nordic EMBL Partnership for Molecular Medicine agreement was renewed for a third 10-year period (2023-2033). An official signing of the agreement will take place in Helsinki in the spring of 2023. NCMM is excited to continue this fruitful and interdisciplinary partnership in translational molecular medicine together with our sister nodes. We look forward to the many opportunities for training, collaboration and education that this will create for our researchers at NCMM, and also wish to increase the awareness and invite all Norwegian researchers to benefit from the opportunities EMBL is offering to its member countries.

The overall vision for NCMM in the coming years is to continue to strengthen our position as a leading national centre for molecular precision medicine research. Following a successful evaluation by the Scientific Advisory Board, the group of Marieke Kuijjer was renewed for a second 4-year period in early 2023 – my very warm congratulations to Marieke! Two new group leaders recruited in 2022, Charlotte Boccara and Bishwajyoti Sahu, have now gotten a good start for building their research groups and programs at the Centre. During 2023, we aim to recruit two new group leaders with expertise in computational biology and novel technologies contributing to NCMM focus areas to replace the ones rotating out of NCMM this year. Together, our new and current group leaders will tackle NCMM's mission to shed light on the molecular mechanisms of health and disease to implement precision medicine.

NCMM aims to promote multidisciplinary collaborations that bring together basic and translational research. As part of this strategy, we are working on building stronger networks with the computational biology and bioinformatics research environments locally, nationally and internationally. We therefore recently appointed Anthony Mathelier as new associate director of NCMM, combined with joint affiliation as an adjunct Professor at the Centre for Bioinformatics, in March 2023. As group leader at NCMM, Anthony has proven to actively promote collaborations and mentorship both locally and with the wider bioinformatics community. This, combined with his expertise in computational biology, will be valuable for the future endeavours of NCMM.

The past 12 months, our groups have produced great scientific research and I want to thank our group leaders, researchers and staff for all their hard work and determination. I also want to thank our supporters and collaborators for working with us towards a shared goal of increasing our scientific knowledge and translating our findings into improved patient outcomes.

March 2023

Professor Janna Saarela
Director, NCMM

Photo: Oda Hveem

Anthony Mathelier appointed as the new Associate Director of NCMM

Photo: Oda Hveem

NCMM group leader Anthony Mathelier is the new Associate Director of the Centre, combined with a part-time Professor II position at the Centre for Bioinformatics.

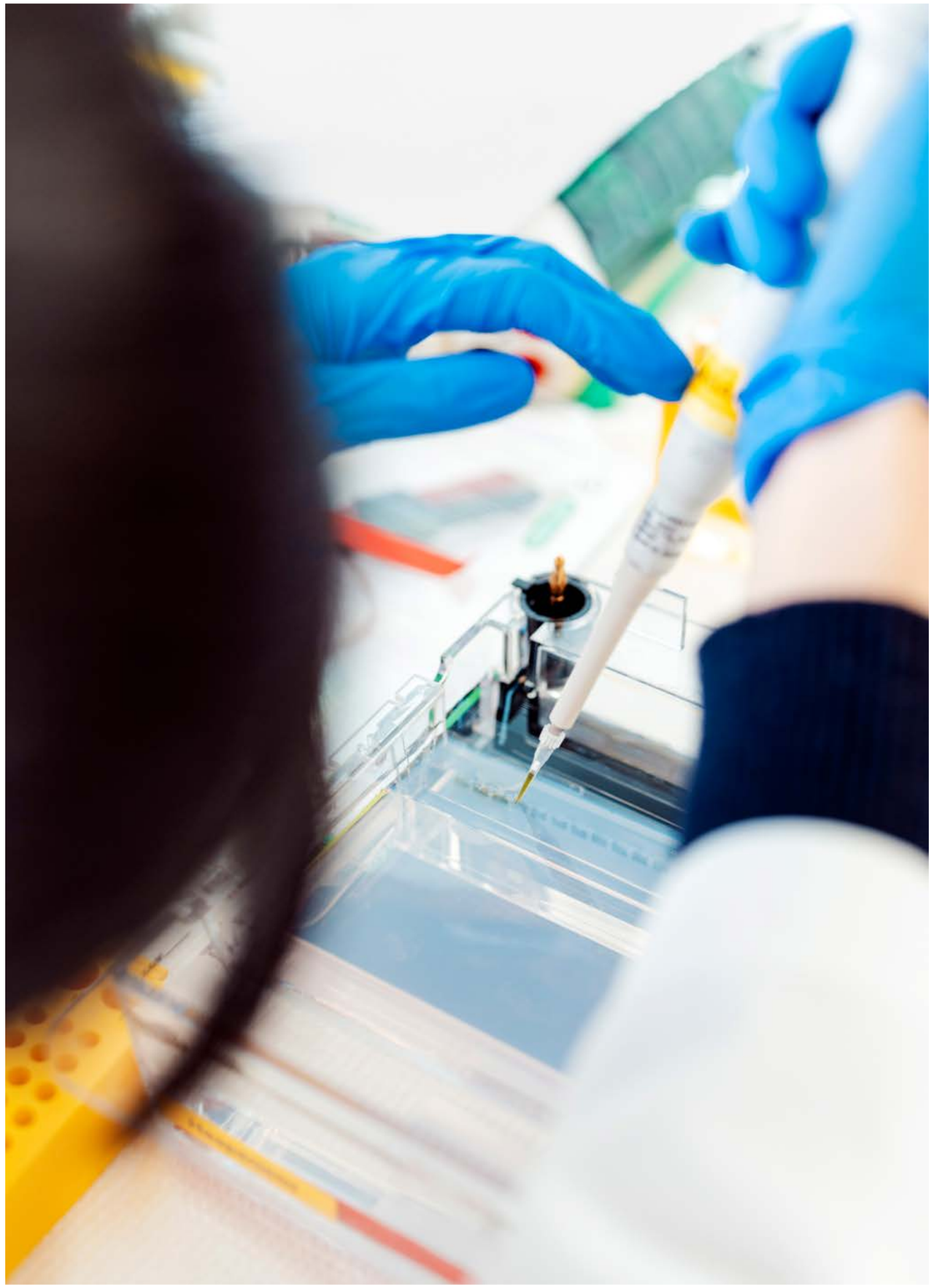
Mathelier currently leads the Computational Biology & Gene Regulation group at NCMM and will continue as group leader in addition to the position as Associate Director. Promoting a positive and collaborative working environment has always been a priority for Mathelier and will also be an important motivation for him going forward.

"I am excited to take on a new role at NCMM and will focus on promoting mentorship, enhancing interdisciplinary collaborations, and building a strong network for computational biology with translational capabilities. Through partnering with other institutions and organizing events I hope to create an active national bioinformatics society", says Mathelier.

As Associate Director, Anthony Mathelier will work closely with the Director of NCMM Janna Saarela.

"We at NCMM are pleased that Anthony Mathelier will take on the role of Associate Director. I very much look forward to working with him on further developing NCMM's research strategies, collaborative networks, and scientific excellence", says Saarela.

The position of Associate Director is combined with a part-time Professor II position at the Centre for Bioinformatics, under the Institute of Informatics at the University of Oslo. Mathelier will take up the position as NCMM's Associate Director from March 1st, 2023.



Chapter 2

Research

NCMM Group Leaders

Insert: Biswajyoti Sahu

From the left: Emma Haapaniemi, Nikolina Sekulic, Marieke Kuijjer, Anthony Mathelier, Janna Saarela, Camila Esguerra, Sebastian Waszak, Charlotte Boccara, Irep Gözen and Judith Staerk.

Charlotte Boccara

Systems neuroscience and sleep group

Photo: Oda Hveem

Key expertise

- In vivo rodent models
- In vivo electrophysiology
- Optogenetics and chemogenetics
- CRISPR
- Immunohistology
- Cell culture, biology assays
- Computational methods
- Electronics and biosensors

Research focus

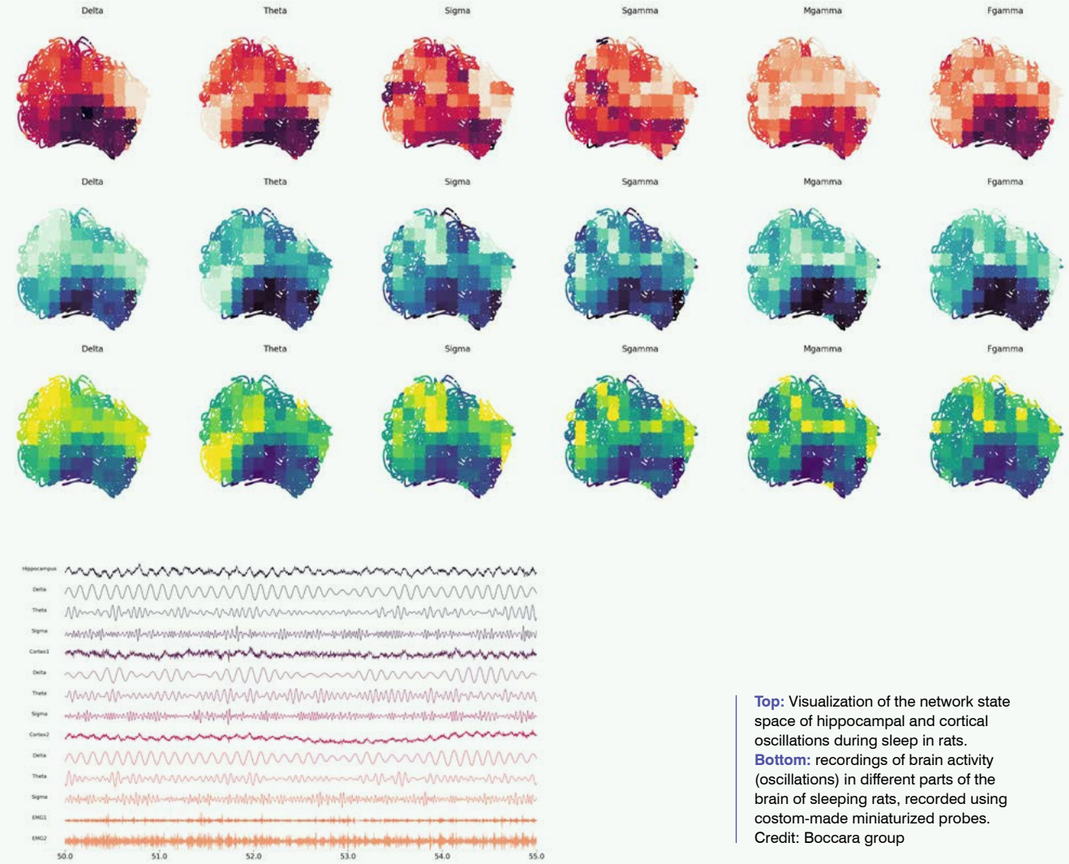
Our core hypothesis is that poor sleep at critical developmental stages facilitates the emergence of neural and metabolic disorders. As for now, there is only correlative, but no causal evidence of this. To address this crucial gap in our knowledge from multiple angles, our team is composed of neuroscientists, 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 12 days old. In 2022, we were awarded an NFR-convergence grant together with IMB and Sintef to harness innovations in technologies to make these 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 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



Top: Visualization of the network state space of hippocampal and cortical oscillations during sleep in rats.
Bottom: recordings of brain activity (oscillations) in different parts of the brain of sleeping rats, recorded using costom-made miniaturized probes.
Credit: Boccara group

Highlights in 2022:

- Postdoc Solomiia Korchinska used in vivo miniature devices to record and decode neural activity from multiple brain areas in freely behaving rat pups during sleep
- Scientia Fellow Postdoctoral Fellowship for Brijesh Modi, who joined our group in 2022
- Received NFR Technical Convergence grant – shared with Torkel Hafting IMB and Sintef – of 20m NOK
- Received NFR Large-Scale Interdisciplinary grant with collaborators Phillipe Collas and Nolwen Briand from the Institute of Basic Medical Sciences, UiO and Ørjan Martinsen from the Department of Physics, UiO, to decode metabolic and epigenetic disorders caused by adolescence sleep deprivation
- Publication of Nature Communication paper from former PhD Davide Spalla: Spalla D, Treves A, Boccara CN. Angular and Linear Velocity Coding in the Parahippocampal Circuits. Nature Communication (2022)
- VG, one of the biggest national newspapers in Norway, interviewed Charlotte about the results of the Nature Communications paper

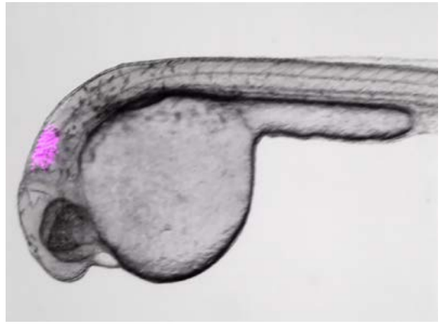
What are your goals for 2023?

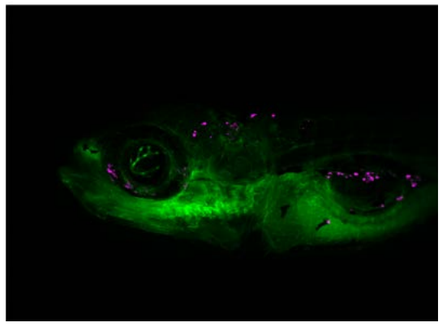
One of our goals for 2023 is to submit our results on the automatic detection of a sleep oscillation involved into memory processes and called sharp wave ripples. This work is spearheaded by Brijesh Modi and Eis Annavini and will be presented in Verona in May. Concomitantly with this work, we hope to build an online benchmarking platform that would be useful for the whole community. Later in the year, we also plan to submit our work on the maturation of sleep oscillations in rodents led by Solomiia Korchynska. We hope to develop good rodent models of sleep deprivation and advance on biosensor/recording devices development.

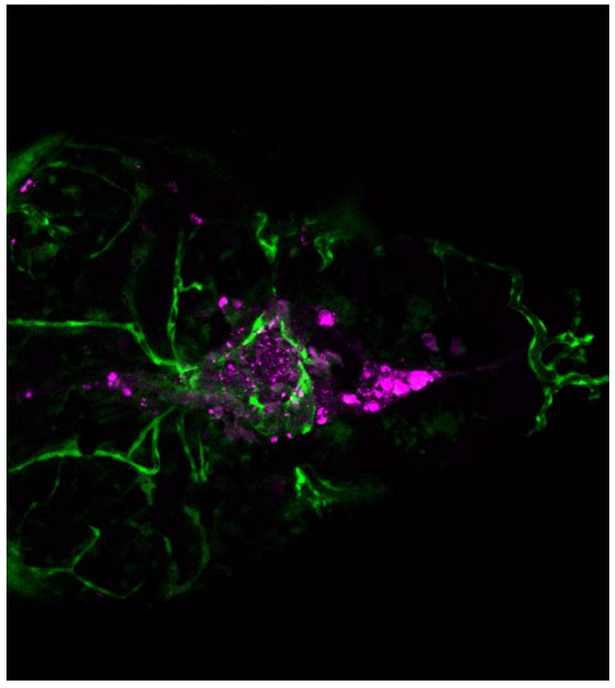
Camila Esguerra

Chemical neuroscience group

Photo: Oda Hveem







Zebrafish larva engrafted with fluorescent glioma cells (magenta) in the brain, with blood vessels in green. Images show immediately after engraftment (top left) and 5 days after engraftment (bottom left and right).
Credit: Esguerra group

Key expertise

- Zebrafish disease models
- Automated behavioral assays
- Drug screening
- 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, 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 2022:

Our group was awarded 3 new grants:

- EU Erasmus+ Key Action 2: The Virtual Innovative Biomedical Education in Science (VIBES) (01/02/2022 – 31/01/2025) (Esguerra partner PI)
- Norwegian Cancer Society Pioneer Grant: Zebrafish glioma avatars for disease modeling and combinatorial drug screening (01/01/2023-31/12/2024) (Waszak PI, Esguerra partner PI)
- Research Council of Norway IPN – Innovation Project for the Industrial Sector: EPITHERA: Clinical development of TQ-217, a novel drug candidate for treatment-resistant epilepsy (Esguerra partner PI)

What are your goals for 2023?

With the awarding of the EPITHERA innovation grant, we now have the funding to pursue mechanism of action studies of a drug lead that will enter clinical trials in 2023/2024.

We aim to publish a study describing genetically engineered zebrafish “avatars” for one of the SNARE complex proteins, which are critical for neuronal signalling. Our study has combined structural biology and in vivo modelling of epilepsy patient mutations in STX1B.

Parallel to ongoing drug screens in zebrafish, we will continue to test candidate small-molecules and natural product-derived compounds in equivalent or complementary rodent and fish models in collaboration with Assoc. Prof. Kinga Gawel and colleagues at the Medical University of Lublin, Poland.

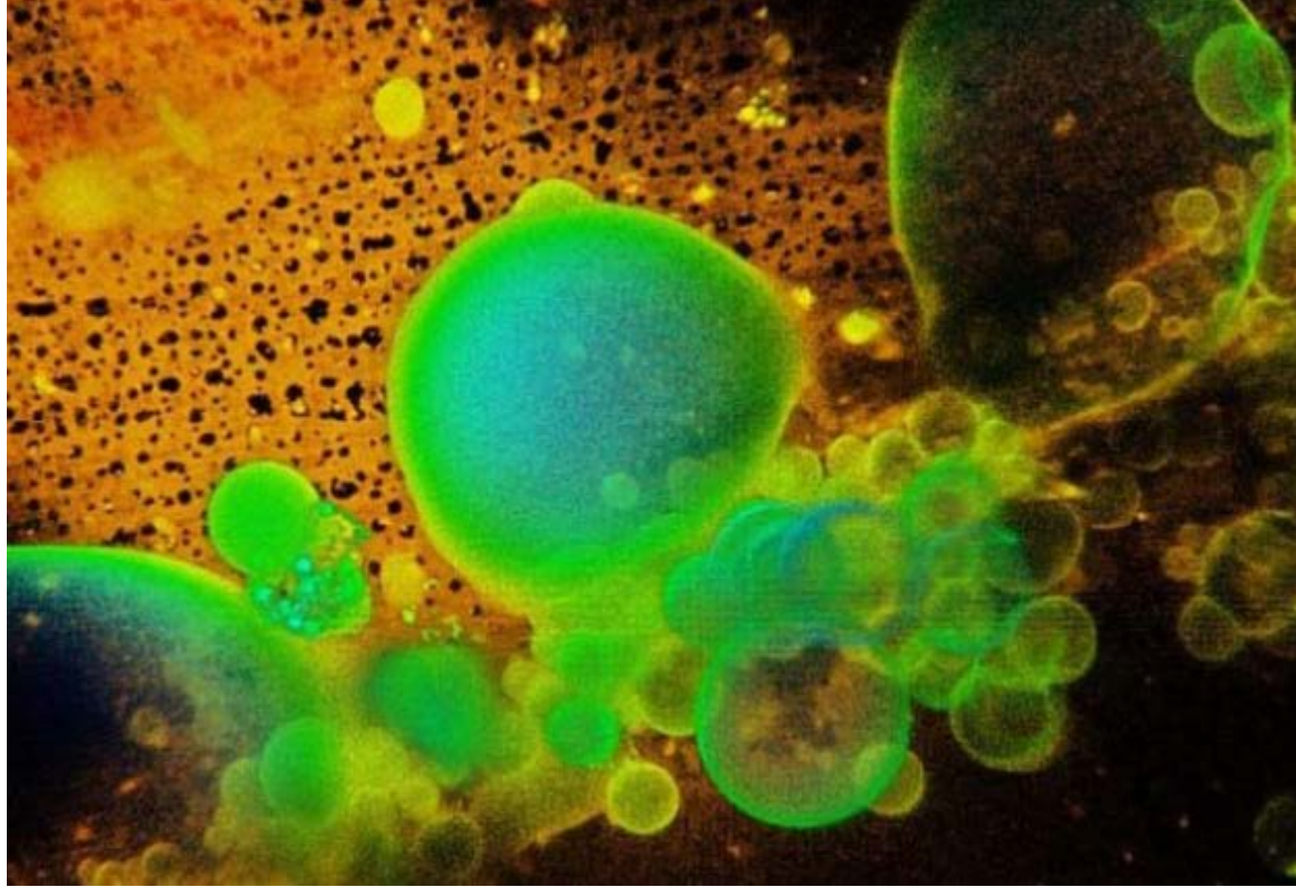
We will receive a new imaging robot in Oslo in 2023, which will open several possibilities for investigating xenografted tumors in zebrafish models. Our aim is to use this method to study how glioblastoma cells affect the host tumor microenvironment in developing zebrafish brains. The first step in 2023 is to optimize the robot for accuracy and efficiency for xenotransplantation.

The medium to long-term plan is to perform drug screens on both the xenografted tumor models and genetically engineered midline glioma models (the latter in collaboration with Sebastian Waszak and team).

Irep Gözen

Bionano-technology and membrane systems group

Photo: Oda Hveem



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 based on biomembrane-based fluorescent assays of interest to medicine and pharma
- Identify how surface-based pathways of primitive cell formation and development can make us understand 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 2022:

- Demonstrated how primitive cells on the early Earth may have communicated via lipid nanotubes, published in Nanoscale
- International news coverage on group's new findings from the Inverse, Phys.org, Notimerica, Newsaxes, Informacion, elPeriodico, La Nueva Espana, Faro De Vigo, La Opinion, Cordoba, Mediterraneo, Lavante
- Got approved funding for Marie Skłodowska-Curie Actions-Doctoral Networks project from the European Commission
- Master's thesis graduation of Maivizhi Thiyagaraja, project title: Thermo-responsive Artificial Cell Clusters

What are your goals for 2023?

We have recently established brand new international collaborations in the synthetic cell engineering and the origin of life projects and are hoping to advance experimental and theoretical findings in these areas. We want to follow up on our recent discoveries and extend our understanding of biomembrane interactions with rare extraterrestrial surface samples. My team will expand based on the recently obtained funding from the Norwegian Research Council and European Commission.

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

Emma Haapaniemi

Precision pediatrics and gene editing group

Photo: Oda Hveem

Key expertise

- Standard CRISPR-Cas9 gene editing
- Digital droplet PCR (ddPCR) & single cell DNA sequencing
- In vivo NSG mice
- Isolation & expansion of primary cells & 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 the Oslo University Hospital to develop gene editing therapies for patients with so-called STAT1 gain-of-function disease. However, our ultimate goal is to establish versatile gene-editing protocols that are disease-independent and that can be effectively and fast tailored to a wide range of immunodeficiencies.

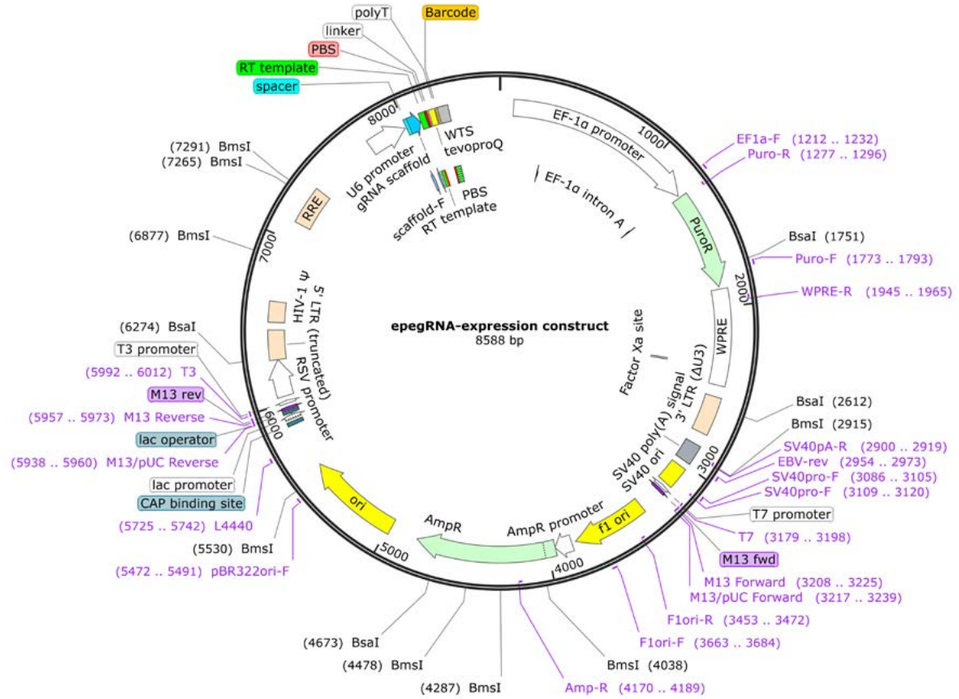
To achieve this goal, we are working to optimize the CRISPR-Cas9 gene editing tool for use in personalized therapy. We have made significant contributions to gene-editing protocols by screening the effect of 450 DNA repair protein-Cas9 fusions on editing outcomes. As a result, we identified that Cas9-POLD3 fusion enhances gene editing by speeding up the initiation of DNA repair. This allows for faster and more efficient gene editing. We have also worked on optimizing high-throughput protocols for efficient gene editing in T cells and hematopoietic progenitor stem cells (HPSC).

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 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 evaluation of stem cell functionality
- Identify HDR enhancers to optimize 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 defect

Highlights in 2022:

- Ganna Reint successfully defended her PhD thesis, titled: “Refinement strategies for CRISPR-Cas9 genome editing”
- Master students Frida Høsøien Haugen and Jacob Conradi successfully defended their master’s thesis
- In collaboration with Professor Eivind Valen from UiB we have received 19.9 million NOK grant from the Research Council of Norway to research personalized gene editing with the aim to advance gene therapy for primary immunodeficiencies (PIDDs)
- We received 19.9 million NOK funding from KLINBEFORSK for developing CRISPR-Cas9 gene therapy for STAT1 Gain-of-Function disease
- We are part of Precision Immunotherapy Alliance “PRIMA”, new Center of Excellence that received funding from The Research Council of Norway
- The Haapaniemi group’s research was featured in Aftenposten (June 22), Apollon research magazine (Nov 2022) and Dagens Medisin (January 2023)



Map of a lentivirus based vector expressing pegRNA (primer editing guide RNA) used in Primer Editing system.
Credit: Haapaniemi group

What are your goals for 2023?

We will test the safety of our gene editing protocols by looking at genomic integrity using different high-throughput methods. If the protocols pass the safety tests, we will scale them up to human size doses with the goal to edit enough T cells and HPSCs for use in clinical trials. We will finish in vivo experiments and then start the process towards clinical 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 efficiency of prime editing of ADA2 by lentivirus derived vectors.

Marieke Kuijjer

Computational biology and systems medicine group

Photo: Oda Hveem

Key expertise

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

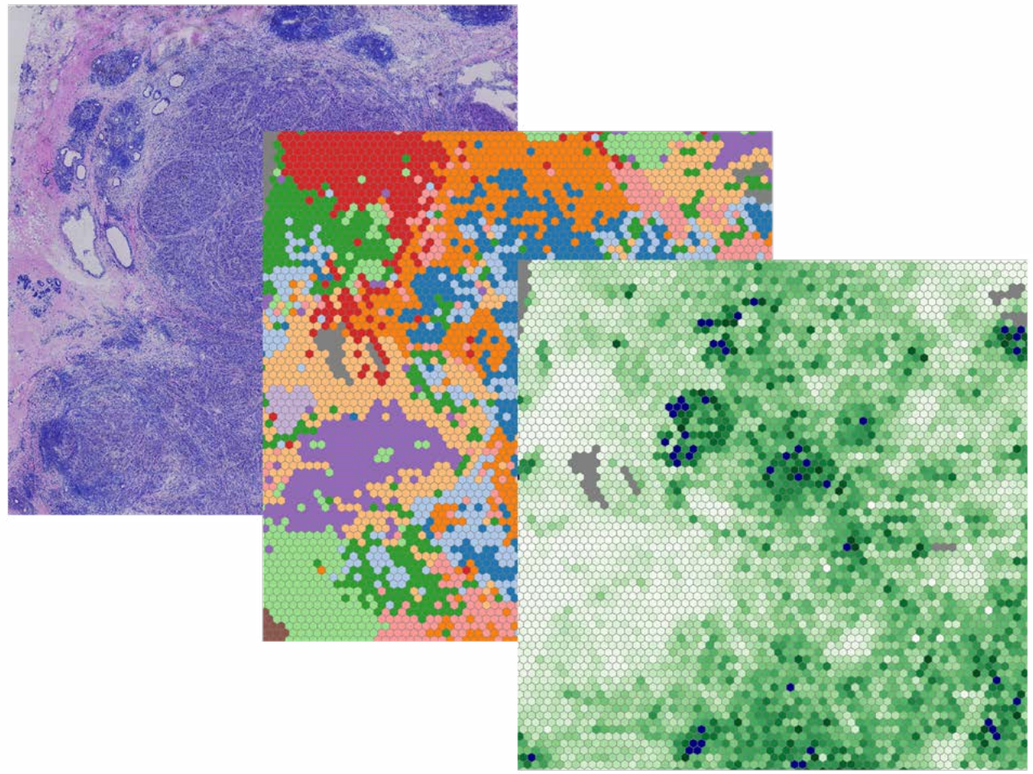
Research focus

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. This allows 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. Applying these tools to large-scale cancer datasets has helped us identify important regulatory alterations in cancer. For example, in glioblastoma—an aggressive type of brain cancer—we recently identified the regulatory network of PD1 signaling to be associated with prognosis.

Major aims:

- Develop approaches to predict gene regulatory interactions
- Construct gene regulatory networks for single cells
- Develop new methods for genomic network analysis
- Establish tools to integrate patient-specific network models with multi-omics data
- Use network modeling and analyses to improve patient stratification



Visualization of total mRNA expression (right) and tissue classification (middle) of a breast cancer tumor sample (left), based on Leiden clustering of the filtered gene expression. Credit: Kuijjer group

Highlights in 2022:

- Ladislav was awarded a Marie Curie Scientia Fellowship. As part of his project, we also received funding from UNIFOR-FRIMED for spatial transcriptomics experiments
- Daniel Osorio (former Marie Curie Scientia Fellow) published a BioRxiv pre-print of "retriever," a method to predict drug combinations by integrating single cell data with large-scale perturbation screens. As part of this project, the group received funding from Familien Blix Fond for validation experiments (in collaboration with Vessela Kristensen's group at OUH)
- Tatiana Belova published a BioRxiv pre-print of the new network analysis tool PORCUPINE. The tool identifies pathways that are heterogeneously regulated in a patient cohort and thus can point to potential new ways of stratifying cancer patients
- Romana Pop contributed with a notebook to "NetBooks"—a resource of reproducible code and collaboration with the Quackenbush group (Harvard Chan School of Public Health). The work was published in Nature Methods and was highlighted in a Technology Feature in Nature
- Together with collaborator Salim Ghannoum (OUH), Tatiana Belova and Saikat Das Sajib received funding from the National Network for Breast Cancer Research for a collaborative project to investigate lymphocyte-breast cancer cell crosstalk
- Tatiana Belova co-organized the Oslo Bioinformatics Workshop Week
- The group co-organized a new PhD course in multi-omics data analysis and integration for precision medicine

What are your goals for 2023?

We are currently focusing on finalizing various applications of our network tools to different cancer types, including breast cancer, sarcomas, and pan-cancer approaches and will prepare these for BioRxiv submission. Additionally, we have several exciting new methods we are currently working on, including new approaches to integrate various types of single cell omics data, and to integrate networks with multi-omics data. We plan to use these to learn more on gene regulation in both healthy tissues and cancer.

Anthony Mathelier

Computational biology and gene regulation group

Photo: Oda Hveem

Key expertise

- Computational biology
- Bulk transcriptomics assays
- Single-cell ATAC-seq
- Machine learning techniques

Research focus

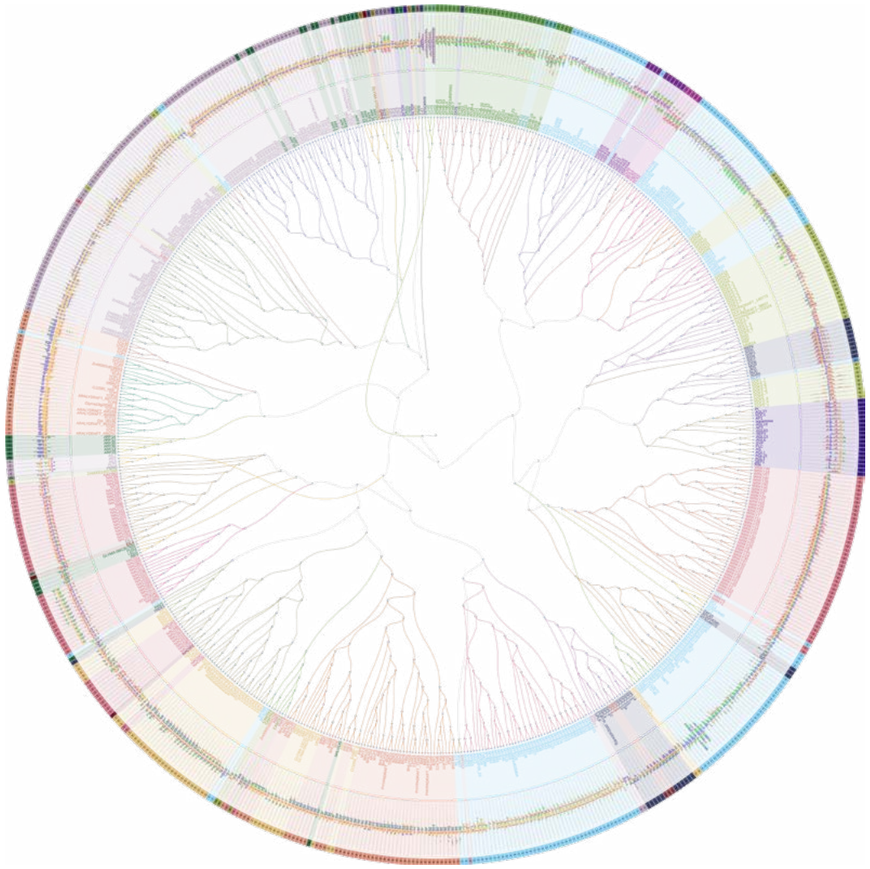
Our research group is dedicated to improving our understanding of the non-coding portion of genomes. We are particularly interested in deciphering the cis-regulatory code that controls gene expression, as this knowledge can help us understand how gene expression can be disrupted in cancers.

Over the years, our group has developed a number of computational tools and resources to analyze multi-omics data, including the JASPAR and UniBind databases, which are recognized as national resources by ELIXIR Norway. We have used these tools to study cancer patient somatic alterations in the non-coding portion of the human genome to predict variations that alter 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-DNA interactions, study the interplay between transcription regulation and cancer somatic mutations in 3D, 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. To achieve this, we will use a combination of experimental approaches and computational methods on patient samples.

Major aims:

- Improve the characterization of transcription factor (TF) – DNA interactions through the maintenance and update of our key established resources (JASPAR and UniBind) and the identification of TF co-binding partners using a novel computational model
- Study the interplay between transcriptional regulation and cancer mutations in 3D
- 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
- Provide a regulatory map of normal breast epithelium at single-cell resolution to better understand cancer initiation



Radial tree representing the clusterization of the DNA sequence patterns stored in the JASPAR database and that are recognized by plant transcription factors. Credit: the Mathelier group.

Highlights in 2022:

- Identified pioneer transcription factors that are associated with the modulation of DNA methylation patterns across cancers (Lemma et al., 2022)
- Developed a computational framework to predict cis-regulatory mutations that associate with transcriptional and post-transcriptional deregulation of gene regulatory programs in cancers (Castro-Mondragon et al., 2022)
- Ninth update of the JASPAR open-access database of transcription factor binding profiles (Castro-Mondragon, Riudavets-Puig, Rauluseviciute, et al., 2022)
- Anthony Mathelier was interviewed by the Medical Faculty to share his thoughts on good work environment, good interactions, and team building in research as part of the Inspirational leadership section
- Anthony Mathelier appointed as the Associate Director of NCMM
- Anthony Mathelier co-organized the first edition of the Norwegian Bioinformatics Days

What are your goals for 2023?

Our main objective is to create a great working environment for trainees so they can develop their skills and achieve their career goals. By doing so, we will be able to complete our ongoing scientific projects successfully. Importantly, we plan to improve the wet-lab aspect of our group by introducing a new experimental assay in Oslo. Additionally, we will develop new computational tools that will help us better understand the molecular mechanisms behind cancer.

Janna Saarela

Human immune disorders group

Photo: Oda Hveem

Key expertise

- RNA sequencing
- Genome and exome sequence analyses
- CRISPR edited cell models
- Functional immune cell assays

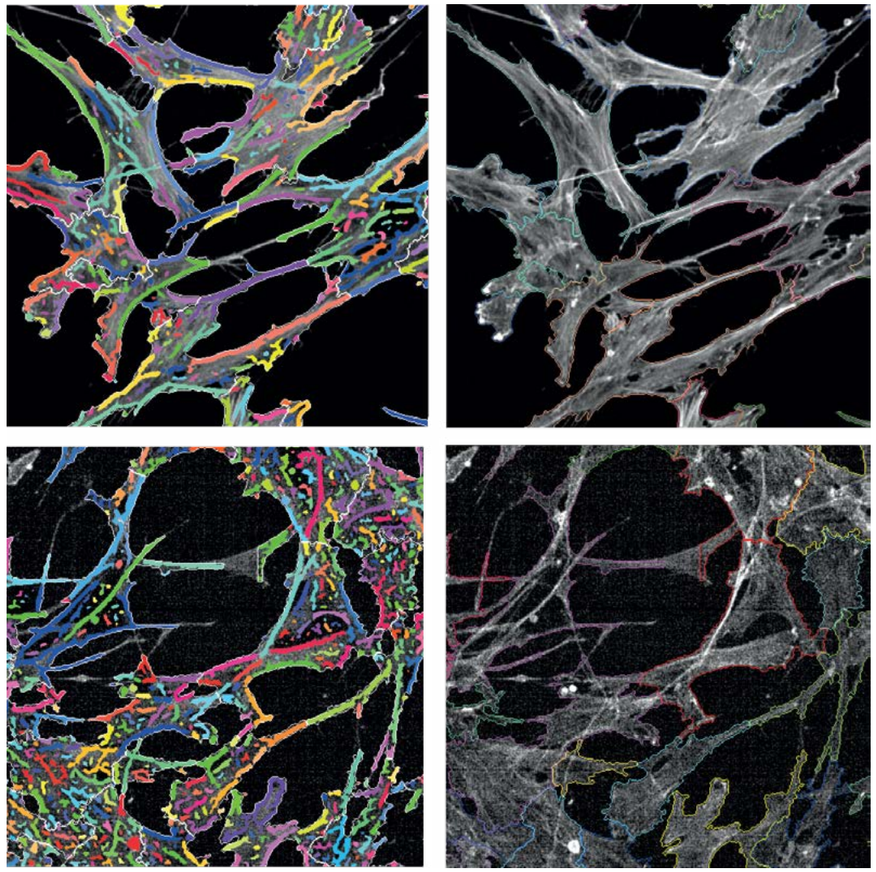
Research focus

Our research goal is to identify and understand the mechanisms that cause immune deficiency, autoimmunity and immune dysregulation. Specifically, we are working to elucidate the biological pathways and pathogenic mechanisms behind rare inherited errors of immunity (IEI) and multiple sclerosis (MS). Access to patient data and samples allows us to study the underlying genetic variants that predispose to the development of MS or cause monogenic IEIs, to discern the disease mechanisms, and to use this knowledge to predict disease progression and beneficial treatment strategies. So far, we have developed a comprehensive map of the genetic landscape of MS, in collaboration with the International MS Genetics Consortium. We have also identified several novel genetic causes of severe human diseases presenting with immune dysregulation and immunodeficiency.

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 utilizing novel genomics technologies
- Identify dysregulated immune pathways which could be targeted by existing treatments in patients and predict disease activity
- Develop novel personalised 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



Top: actin filament and cytoplasm quantification in patient
Bottom: Control fibroblasts
Credit: Saarela group

Highlights in 2022:

- Received grant from South-Eastern Norway Regional Health Authority of 9 mNOK to set up a Functional genomics platform for discovery of regulatory genetic variation and mechanisms in immune disorders
- Our review article together with colleagues from the International Multiple Sclerosis Genetics Consortium describing the current knowledge of genetic map of MS disease susceptibility in Lancet Neurology
- Identification of the first genetic variant associated with disease severity in MS disease – collaboration manuscript of the international IMSGC consortium submitted

What are your goals for 2023?

During 2023 we will focus on understanding the roles of novel IEI genes, ADA2, SIT1 and MAP4K1, in the regulation of the immune system. We will further use RNA sequencing methods to identify mono-allelic expression or aberrant splicing events that may be novel causes of IEI, which are otherwise not observable by current exome and genome sequence data analysis. In the complex disease projects we aim to shed light on MS pathogenesis and identify subgroups of patients by identifying dysregulated immune pathways. For this, we will use RNA sequencing data of a prospective cohort of 500 newly diagnosed patients. 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 research from Norway, Sweden and Japan.

Biswajyoti Sahu

Precision cancer epigenomics group

Photo: Oda Hveem

Key expertise

- Transdifferentiation using lentiviral expression systems or CRISPR-Cas9
- Single-cell multiomics
- Chromatin-based genomics assays (ATAC-seq, ChIP-seq, STARR-seq, HiChIP etc.)
- Bioinformatic analysis
- In vitro and in vivo assays for cell growth and tumorigenicity

Research focus

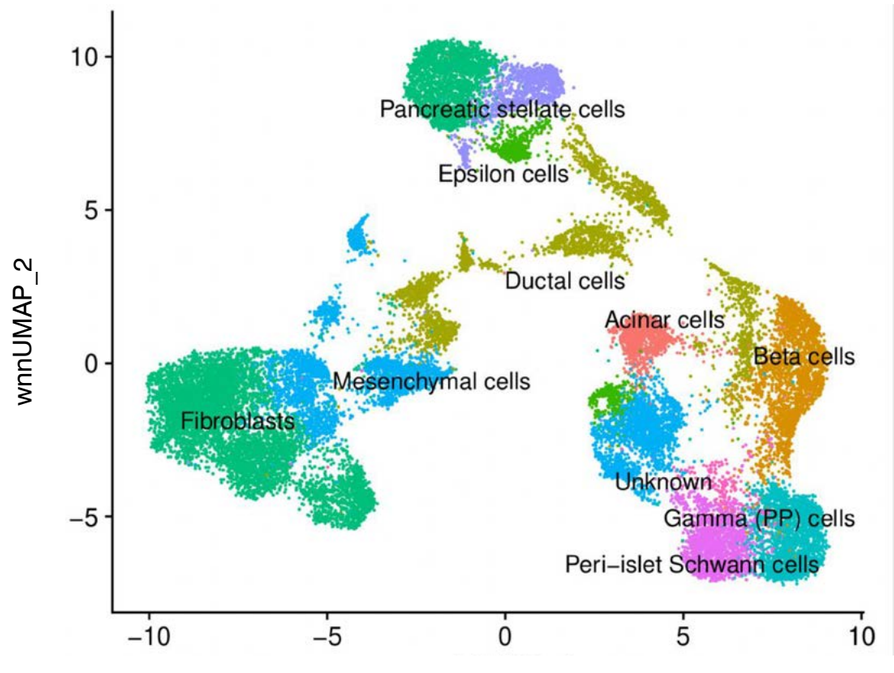
Our research focus is to understand the molecular mechanisms that lead to organ-specific cancer, with a special focus on the role of lineage-specific transcription factors (TFs) in early tumorigenic events. We utilize a systems biology approach with a plethora of cutting-edge experimental methods to 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 established a molecularly defined system to generate pancreatic ductal epithelial cells and a novel 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
- Develop tools for cell fate conversion and high-resolution single-cell/nuclei multiomics
- Delineate the human non-coding regulatory genome with special focus on the transposable elements
- Understand how TFs modulate the gene regulatory networks and what are the sequence determinants of human gene regulatory elements

Highlights in 2022:

- Started as group leader in precision medicine at NCMM
- First two major projects completed from my lab and manuscripts under revision: (i) We identified a pool of six defined transcription factors that enable generation of pancreatic ductal cells (Fei et al) and (ii) revealed specific repeat elements in the human genome that can function as cell type-specific gene regulatory elements (Karttunen, Patel et al.)
- Ville Tiusanen finished his Master's thesis and started his PhD studies in my group
- Published three papers: (i) Sahu et al (Nat Genet 2022:54:283-294) revealed sequence determinants of human gene regulatory elements using massively parallel reporter assays; (ii) Pihlajamaa et al (Nat Biotech 2023:41:197-203) reported a novel CRISPR-Cas9-based precision genome editing method; (iii) Gawriyski et al (iScence 2023:26) characterized a function of LEUTX transcription factor during embryonic development
- Started project on nanopore analysis of adduct generation with Dr. Esa Pitkänen, FIMM, University of Helsinki, Finland



What are your goals for 2023?

In the coming year, the goal is to continue working on the human cell transformation model and develop it further to understand the role of oncogene-TF nexus in the origin of pancreatic cancer. We also aim to utilize our expertise in understanding the TF-mediated gene regulation and the human non-coding regulatory genome to probe for enhanceropathies affecting human health in conditions other than cancer. The goal is to initiate novel projects within the laboratory in NCMM or in collaboration with other interested research groups. The focus will be on the training and career development of the recruited researchers in my group.

Pancreatic cell types generated from human fibroblasts using a transdifferentiation approach and visualized using uniform manifold approximation and projection (UMAP).
Credit: Sahu group

Nikolina Sekulic

Structural biology and chromatin group

Photo: Oda Hveem

Key expertise

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

Research focus

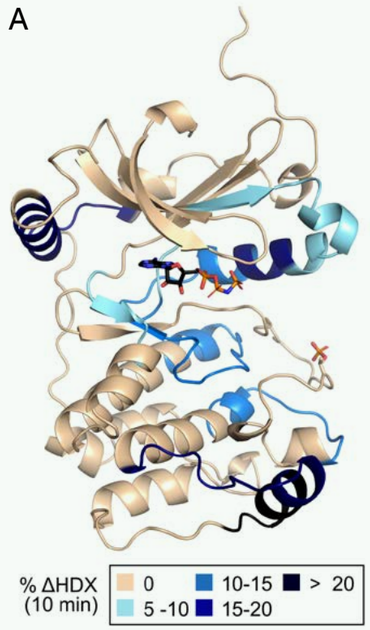
Our group seeks to understand the molecular determinants that ensure that chromosomes, the carriers of genetic information, are distributed evenly during cell division. To this end, we study human centromeres, which are the parts of chromosomes that ensure that the chromosomes are divided evenly among daughter cells with each duplication and cell division. Our work is of great importance for both basic research and cancer research because uncontrolled cell divisions, in which chromosomes often segregate incorrectly, are the hallmark of cancer.

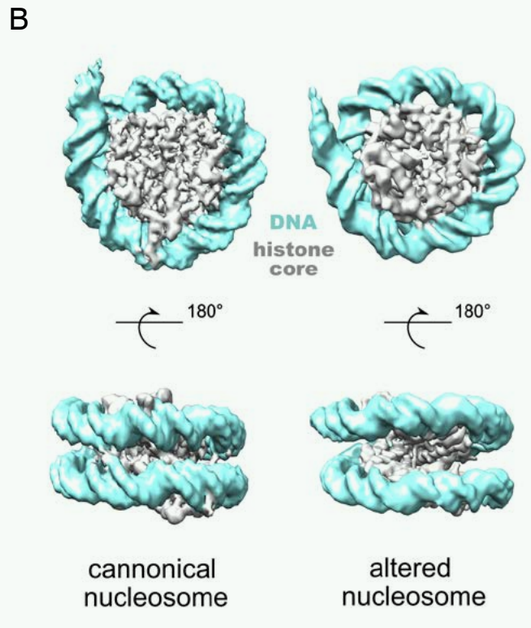
Major aims:

- Understand how the human centromere is organized
- Establish how centromeres recruit effector proteins that regulate mitosis
- Determine how Aurora B, an important mitotic kinase, is regulated at the molecular level

Highlights in 2022:

- Received 14,9 mil NOK from NFR FRIPRO for our project “Determining the molecular architecture of centromeric chromatin”
- Published 2 papers: (i) Segura-Peña D, et al. The structural basis of the multistep allosteric activation of Aurora B kinase. bioRxiv (2022), and (ii) Dorraji E, et al. Development of a high-affinity antibody against the tumor-specific and hyperactive 611-p95HER2 isoform. Cancers (Basel) (2022)
- Organized 2 international events in Oslo: Mini-symposium “Molecular structures in action” and the EMBO Dynamic kinetochore workshop
- Co-organized the Oslo epigenetics symposium with Prof. Eskeland and Dr. Pandey
- New collaborations with NCMM Associate Investigators Victor Greiff (Department of Immunology, UiO and OUH) and Cinzia Progida (Department of Biosciences, UiO) using NCMM seed funding
- Nikolina Sekulic has coordinated UiO participation in HALRIC, a Southern Scandinavian and Norther Germany alliance of hospitals, universities, research infrastructures and regional governments that was awarded 11,2 million EUR for developing cross-border collaborations
- HDX-MS hosted in our lab was highlighted as an innovative technology by the Nordic EMBL partnership





What are your goals for 2023?

In 2023, we would like to increase the visibility of the structural biology technologies in our lab: CryoEM and HDX-MS. We are the only lab in the Oslo region that has all the expertise and resources for these powerful technologies, and we hope to attract more local and national collaborators to take advantage of this opportunity. We are also expanding the scientific scope of our research to include centromeres from other organisms. Our work on Aurora B has shown that there is potential for therapeutic application, and we look forward to exploring how we can leverage our discovery in this direction. Finally, we will continue to enjoy the privilege of doing science and training young and talented new generations of scientists.

(A) Crystal structure of Aurora B kinase showing differences in hydrogen-deuterium exchange between the active and inactive form, revealing mechanisms of kinase activation.
(B) CryoEM maps showing different nucleosome types present at centromeres. DNA is in cyan and histone core is in gray.
Credit: Sekulic group

Sebastian Waszak

Photo: Oda Hveem

Computational oncology group

Key expertise

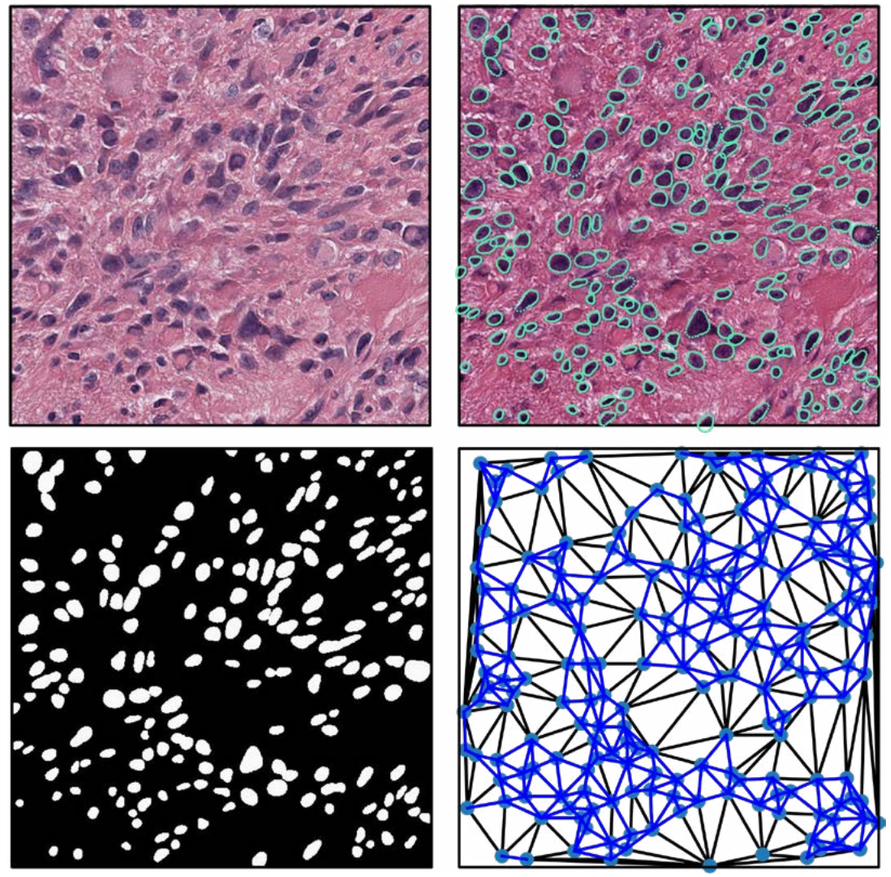
- Cancer genomics
- Cancer epigenomics
- Digital neuropathology
- Computational biology

Research focus

Our research group is dedicated to shedding light on one of the most challenging medical conditions affecting children and young adults: brain tumours. Specifically, we are interested in understanding the biology of diffuse midline gliomas (DMG) and diffuse intrinsic pontine gliomas (DIPG), a type of brain tumor that arises in the midline structures of the brain and spinal cord. Despite recent advances in brain tumor research, diffuse midline gliomas and many other pediatric-type gliomas remain poorly understood, and treatment options are limited, leading to poor survival rates. To achieve our goals, we employ a multidisciplinary approach that combines molecular techniques and computational biology with clinical data analysis. We aim to identify critical molecular changes that initiate and drive tumor growth by investigating the cellular origin and somatic evolution of brain tumours. We also develop new technologies for rapid and minimally invasive diagnosis and surveillance of brain tumors, which can help guide treatment decisions and monitor disease progression. In addition, we strive to advance clinical cancer genomics research based on new computational and experimental techniques that improve our understanding of the genomic and epigenomic landscape of brain tumours. Our research group aims to impact pediatric neuro-oncology by enhancing molecular diagnostics of brain tumours 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 technologies for rapid diagnosis and surveillance of brain tumors
- To identify the cellular origin of childhood brain tumors at single cell resolution
- To develop zebrafish glioma avatars for disease modeling and drug screening



Digital pathology in neuro-oncology
Credit: Waszak group

Highlights in 2022:

- First biopsy-driven and biology-based combination therapy trial for children and young adults with diffuse intrinsic pontine glioma published in Clinical Cancer Research
- GPR161- and ELP1-related medulloblastoma predisposition syndromes recognized as novel entities in the Inaugural WHO Classification of Genetic Tumour Syndromes
- Pioneer Project Award of 2mNOK from the Norwegian Cancer Society to develop zebrafish DIPG avatars
- Anne Martina Kraus defended her MD thesis titled “Deciphering the genomic and epigenomic role of p53 in H3K27-altered diffuse midline glioma”
- Sebastian Waszak and his team received the Children’s Brain Tumor Network Global Inclusion Award for their research on pediatric brain tumors
- Sebastian Waszak became a member of the DIPG/DMG National Tumor Board (dmgnationaltumorboard.org)

What are your goals for 2023?

We received in 2022 funding from NCMM to sequence the complete genome of pediatric brain tumors with Nanopore sequencing. This project will uncover complex sequence alterations and hopefully pave the way towards clinical implementation of long-read cancer genome sequencing. Our newly funded IFF project “Digital pathology in pediatric neuro-oncology” is up and running and we are excited to expand this project with new international collaborators. We will also present results that summarizes the therapeutic, molecular, and biomarker outcomes of PNOC001, a phase 2 study of the mTOR inhibitor everolimus for recurrent/progressive low-grade gliomas in children.

NCMM Alumni

NCMM operates under the EMBL model and serves as a greenhouse for young, talented researchers within the fields of molecular medicine, biotechnology and translational research. The Centre prides itself on providing an environment that allows all of our staff to develop and grow so that, when they are ready for their next challenge, they are equipped with the experience and skills needed to succeed. Over 2022, we caught up with some of our former researchers to find out more about what they are working on now.

Group Leader Alumni

Dr. Judith Staerk, the Stem cell group

Photo: Oda Hveem

Dr. Judith Staerk has been Head of the Stem cell group at NCMM since 2011. She was successfully externally evaluated and renewed for a second period of four years from 2017. During the fall of 2022, she rotated out of NCMM.

While at NCMM, Judith Staerk and her research group used human pluripotent stem cells to understand the interplay between the cells' metabolism and gene regulation during stem cell renewal and blood cell differentiation. In developmental biology a major focus is to identify key events that govern cell fate decisions, including how stem cells renew and differentiate into more specialized cell types but also how somatic cell types are reset to the pluripotent state. By studying metabolic and epigenetic regulation in human pluripotent stem cells, the Staerk group uncovered several molecular events that are involved in driving stem cell renewal and differentiation to the hematopoietic lineage.

Photo: Øystein Horgmo, UiO

Dr. Kinga Gawel

Dr Kinga Gaweł was a a Postdoctoral Fellow in the Esguerra group from 2018 to 2020. She is currently an Associate Professor at the Medical University of Lublin, Poland. At NCMM, Kinga worked with zebrafish as a model system, and still use them in her daily work. About her time at NCMM, Kinga comments: "My postdoc in Camila's lab definitely pushed my career. When I returned to my mother university (Medical University of Lublin, Poland), I was promoted to the position of Associate Professor. During my stay in NCMM, I was quite efficient in terms of publications, and some of them were included into my second doctorate thesis (docent) - which is now under evaluation. Apart from this, I gained a lot of knowledge and new skills which I am still using in Poland. Not to mention all the collaborations which were established during my time at NCMM."

Rønnaug Steen Kolve

Rønnaug Steen Kolve joined NCMM in 2015 and together with colleagues built the Zebrafish Core Facility, a research platform at the Faculty of Medicine. She ultimately became the manager of the facility. She then embarked on a career in research funding, first at the Norwegian Research Council, and currently at the Norwegian Cancer Society.

About her time at NCMM, Rønnaug comments: "It was challenging work, a steep learning curve - and I love learning. I figured out during my studies that being challenged regularly is really important for me. I get bored if I'm not actively learning. Camila, my colleagues at NCMM, and the visiting scientists had different skills and a lot of knowledge for me to pick up. This, along with the analytic work I did on my own, kept me motivated. In addition, I learned about Norwegian laws and regulations regarding keeping research animals and having a proper research lab. I also got to teach for the first time, which I enjoyed a lot!"

Photo: Rønnaug Steen Kolve

Servicing a Research Centre:

NCMM's administration, IT team and core facilities

NCMM is a diverse and multidisciplinary research environment, requiring a team of specialists to support and manage everyday functions, as well as to help develop and grow the Centre and its research groups.

Administration
NCMM has in-house administration team that includes dedicated HR, financial, strategic, communications, and research administration support. Also included under the administration umbrella is an in-house media kitchen, autoclaving, and laboratory technicians - all of whom provide a vital service that allows the research groups to operate effectively and efficiently.

Information Technology (IT)
NCMM has an in-house IT team that is responsible for the development and maintenance of the scientific computing infrastructure and for providing scientific computing support at NCMM, as well as general everyday IT assistance. NCMM's IT team also collaborates closely with the University of Oslo's IT department, USIT, thus providing a close connection to further expertise and support when needed.

Core Facilities

NCMM is home to two core facilities: the High-Throughput Chemical Biology Platform and the Zebrafish Core Facility.

The High-Throughput Chemical Biology Screening Platform
The Chemical Biology High-throughput Screening (HTS) facility offers staff and technologies that enable researchers and biotech companies to discover small molecules to probe, explore, and modulate biological systems.

The HTS facility offers rapid, automated testing of thousands of chemical substances on biological systems to identify so-called "hit compounds" that show a desired effect. The biological system can vary from blocking specific enzymatic activity to inducing distinct phenotypes in certain cells. Screening is therefore a standard first step in drug development campaigns.

The HTS facility is part of the Norwegian chemical biology network NOR-OPEN-SCREEN which is the Norwegian node of EU-OPENSCREEN.

For further information contact:

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chembio@ncmm.uio.no

The Zebrafish Core Facility
The zebrafish core facility team can help other researchers without the necessary expertise to perform 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.

For further information contact:

Camila Vicencio Esguerra
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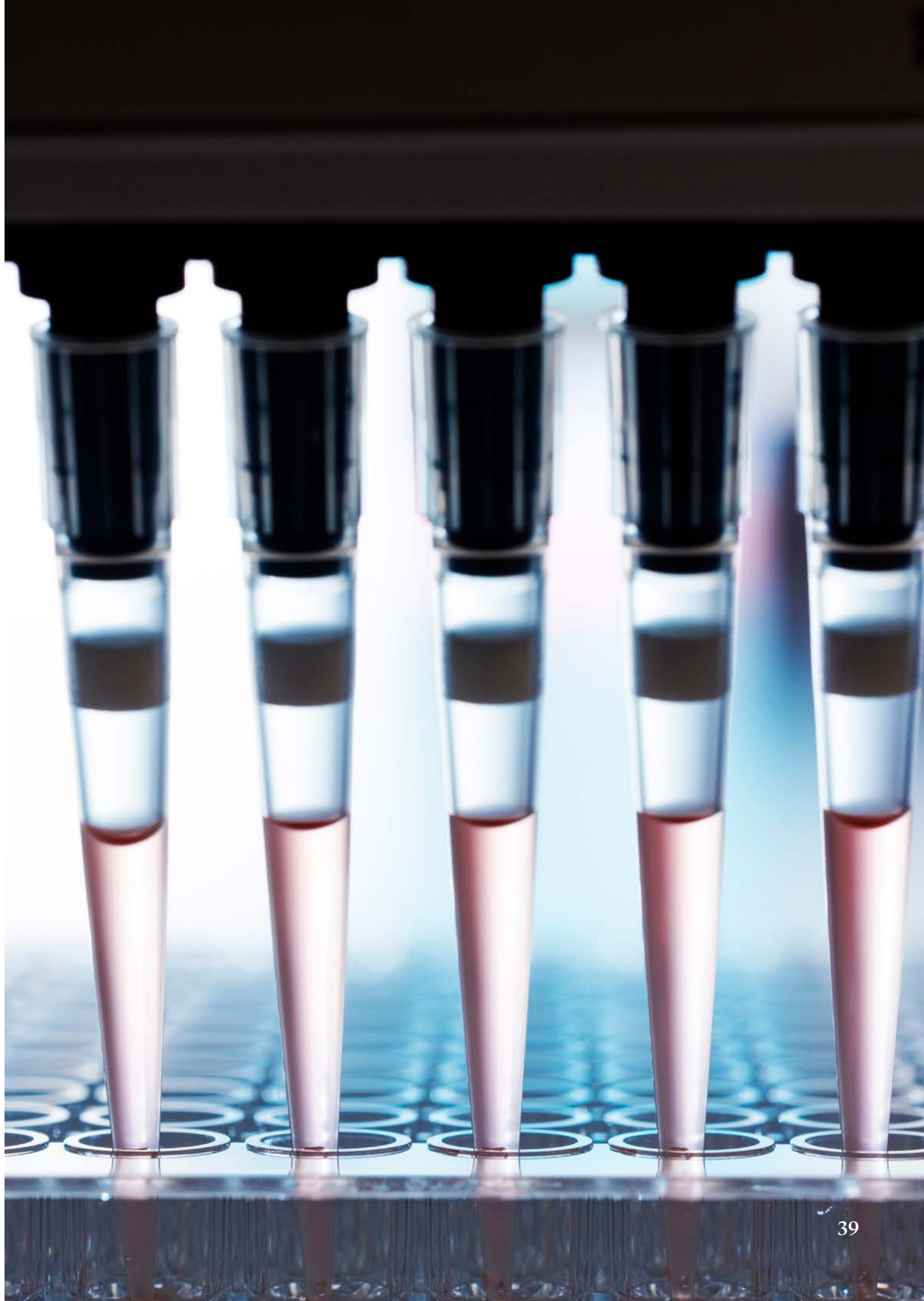


Chapter 3

Research collaborations

From disease mechanisms to precision medicine

"NCMM's ambition is to build a nationwide network for interdisciplinary translational research to grow expertise in our focus areas, and to ensure access to patient cohorts' data and samples, as well as the sharing of knowledge. We will continue to enrich clinical expertise in NCMM and to build bridges to matching hospital environments to help establish strong collaborative teams with core competences in translating scientific findings on basic biological questions to improved clinical practice. NCMM continues to hone its research focus to concentrate on a few thematic areas. Our targeted recruitment of group leaders supports this. With each new group leader appointed, we acquire further novel and complementary expertise and technologies that can help us take our research from bench to bedside, and back."

Janna Saarela

NCMM's overall vision is to improve our molecular understanding of health and disease to facilitate improved medical practice. As an international molecular medicine centre with a translational mind-set, NCMM is bringing together multidisciplinary teams to combine basic and translational research approaches to clinically relevant problems. NCMM works to provide the basis for development of improved diagnostics and more efficient and targeted therapies.

Translational research depends on close interactions between basic research and hospital environments, and NCMM has established strong links to Oslo University Hospital (OUH). The Centre is also actively exploring the possibilities to build closer links to Ahus and other university hospitals around the country.

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.

Research collaborations

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

The majority of the NCMM group leaders have adjunct positions in 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

Department of Pharmacy
NCMM PI: C.V. Esguerra

UIO

Department of Chemistry
NCMM PIs: N. Sekulic and I.Gözen

UIO

Institute of Basic Medical Sciences
NCMM PI: C. Boccara

OUH

Dept. of Medical Genetics
NCMM PIs: J. Saarela and A. Mathelier

OUH

Dept. of Haematology
NCMM PI: J. Staerk

OUH

Dept. of Pediatric Research
NCMM PIs: E. Haapaniemi and S. Waszak

OUH

Institute for Cancer Research
NCMM Ps: Biswajyoti Sahu

Research collaborations with international universities:

UCSF

University of California, San Fransisco, US, Dept. of Neurology
NCMM PI: S. Waszak

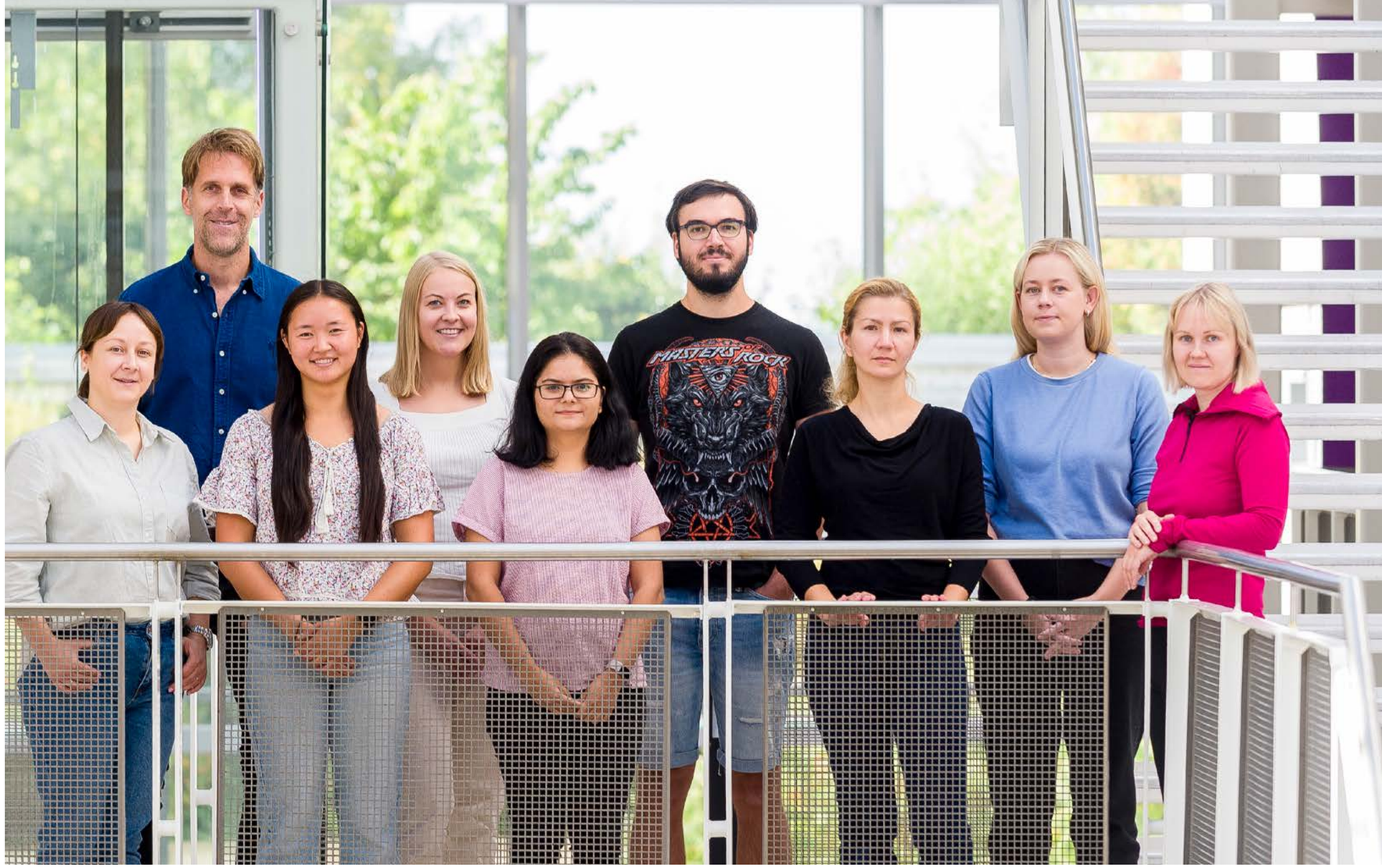
LUMC

Leiden University Medical Center NL, Dept. of Pathology
NCMM PI: M. Kuijjer

Case study:

Translating CRISPR from the lab to the clinic

Meet Hans Christian Erichsen Landsverk, the pediatrician working with the Haapaniemi lab to develop a future cure for rare immune disorders.



The Haapaniemi group, from left to right: Monika Szymanska, Hans Christian Erichsen Landsverk, Sigrid Fu Skjelbostad, Britt Olaug Lindestad, Shiva Dahal-Koirala, Pavel Kopcil, Anna Komisarczuk, Oline Rio, Emma Haapaniemi. Photo: Øystein Horgmo, UiO

Hans Christian Erichsen Landsverk works as a pediatric immunologist at the Division of Paediatric and Adolescent medicine at Oslo University Hospital. Here, he is responsible for investigating, treating and following up young patients with immune deficiencies from all over Norway. He is now also working 50% as a consulting pediatrician in the group of Emma Haapaniemi at NCMM, with a shared goal of developing CRISPR-based gene editing tools to treat his future patients.

Several of the patients that Hans Christian meets suffer from primary immunodeficiencies, a rare group of genetic immune disorders. The underlying cause of these diseases are monogenic mutations in genes that are critical for the immune system to function. The goal of the Haapaniemi group is to develop treatments based on the gene editing tool CRISPR to correct the underlying mutations. This could then restore the immune system's ability to fight infections.

Using patient samples to optimize CRISPR for tailored therapies

"Emma and I were discussing one of my young patients that we were struggling to treat, because he had a severe infection that his defective immune system couldn't control. We speculated that if we were able to take out his immune cells, correct them with CRISPR, and put them back, his body might be able to fight off the infection", says Hans Christian about how the idea for the project came to be.

Currently, the Haapaniemi group is working on developing optimized CRISPR protocols to effectively create and test patient tailored treatments that are safe and reliable. As consulting clinician, Hans Christian's role in the project is to identify patients that can contribute blood samples.

"We have now collected blood samples from 50 patients with different types of immunodeficiencies. Emma's lab is working to see if they can develop an experimental workflow that will allow them to create tailored gene editing tools to each individual patient sample in a fast and cost-effective way", says Hans Christian.

Translational collaborations will likely bring CRISPR to the clinic

In the long term, Hans Christian will also be responsible for setting up potential clinical trials. He is optimistic about the future of using CRISPR gene editing as a treatment strategy, not only for primary immunodeficiencies, but for a wide range of diseases caused by genetic defects.

"Many people are working on this, and there is a lot of expertise and collaborations across Oslo University Hospital and Oslo Science Park working to implement CRISPR in the clinic. I strongly believe that we will make this work in the future", says Hans Christian.

Being part of a team aiming to translate basic research to the clinic has so far been a rewarding experience for Hans Christian.

"I think it is fantastic to get to work together with such talented experts in molecular biology. It is a great experience to be part of a team working towards a common goal, and I feel privileged to work here at NCMM and contribute with what I can."

National Activities

NCMM Associate Investigators

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

NCMM's Associate Investigators are drawn from a group of outstanding scientists who are based in Norway, with expertise compatible with NCMM's research areas and who 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 Investigator	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
Dr. Lorena Arranz	Department of Medical Biology, University of Tromsø and Department of Hematology, University Hospital of Northern Norway
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, Faculty of Mathematics and Natural Sciences, 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
Dr. 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, University of Tromsø, and University Hospital of Northern Norway
Associate 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
Dr. Helene Knævelsrud	Institute for Cancer Research, Oslo University Hospital and CanCell, 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
Associate Professor Reidar Lund	Section for Chemical Life Sciences, Department of Chemistry, University of Oslo
Dr. 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
Dr. Lynn Butler Odeberg	University of Tromsø and the Karolinska Institute
Professor Jacob Odeberg	Institute for Clinical Medicine, University of Tromsø 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, University of Tromsø and University Hospital North Norway
Dr. 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 Oslo University Hospital
Associate Professor Axel Sandvig	Integrative Neuroscience Group, Department of Neuromedicine and Movement Science, NTNU
Professor Anne Simonsen	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	Deptartment of Tumor Biology, Institute for Cancer Research, Oslo University Hospital
Associate Professor Eivind Valen	Computational Biology Unit, Department of Informatics, University of Bergen
Dr. 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)

Sharing knowledge:

PhD courses in precision medicine

In 2022, 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.

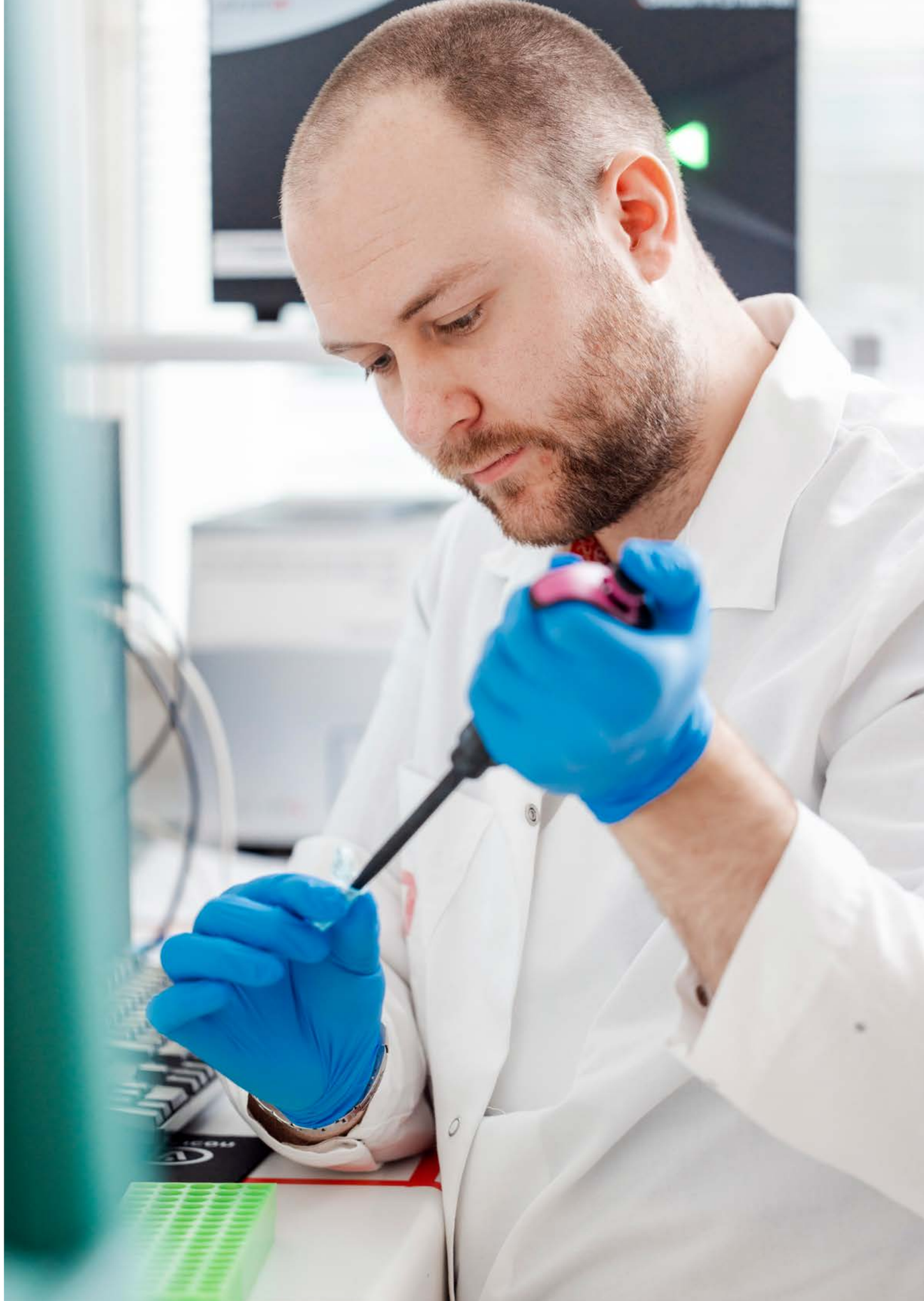
PhD course in Molecular Medicine

NCMM hosted the annual national PhD course on Molecular Medicine in November 2022. The aim of the course is to provide a comprehensive overview of selected topics in molecular medicine. The course featured talks from 46 national and international experts in the field. They covered a broad array of molecular medicine topics such as disease mechanisms and development, animal models of disease, imaging disease, computational biology, health registries and biomarker discovery, virology and immunology, tailored and personalised medicine, computational biology, advanced cell-based therapies and neuroscience.

New PhD course in multiomic data analysis and integration for precision medicine

In December 2022, NCMM hosted a new PhD course introducing approaches to multi-omic data analyses. The course presented an overview of computational methods to analyse multi-omic datasets in healthy and disease settings. International speakers presented state-of-the-art computational approaches to analyse multi-omic datasets e.g. whole genome sequencing, ChIP-sequencing, and mRNA sequencing. Besides the lectures and scientific papers, the course included practical workshops to familiarise students with good practices and hands-on experience in processing, quality control, visualising, summarising, integrating, and analysing large-scale multi-omics data sets.

Saikat Das Sajib found the practical parts of the multiomics course highly relevant for his own PhD project. Photo: Larissa Lily.



The Nordic EMBL Partnership

DANDRITE

FIMM

NCMM

MIMS

The Nordic EMBL Partnership for Molecular Medicine is a major strategic player in Europe's molecular understanding of disease mechanisms, thanks to its complementary research expertise, outstanding research infrastructures and industry collaborations.

The Partnership was founded in 2008 and constitutes 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.

The Nordic EMBL Partnership Agreement was renewed for another 10 years in the Spring of 2023 (2023-2032).

NORDIC **EMBL** PARTNERSHIP FOR MOLECULAR MEDICINE

4th EMBL Partnership Conference 2022

This year, the Nordic EMBL Partnership joined the extended EMBL network for the fourth EMBL Partnership Conference in Heidelberg, Germany.

Photo: Johanna Lehtonen

Between 21-23 September 2022, the conference brought together more than 300 participants from EMBL and EMBL's partner institutions. NCMM's Director Janna Saarela was part of the steering committee organising the conference.

Excerpts from the originally published article on the EMBL website.

The programme included a focus on three key areas – stem cells and development; genomics and disease; and neurobiology – all chosen to bring researchers together in a meaningful way. The event started with a welcome from EMBL Director General Edith Heard, and a keynote speech from Andres Metspalu, Head of the Estonian biobank. Participants were then able to choose from a diverse range of sessions across the three overarching themes, followed by flash talks, poster sessions, and networking opportunities.

The programme also included the Young Investigators Meeting, for PhD students and postdoctoral fellows from EMBL and partner institutes. The YIM ran for 1.5 days after the Conference, and gave a great opportunity for participants to exchange ideas with peers from a wide range of organisations, as well as helping to lay the foundations for long-lasting professional networks.

The Conference offered many valuable opportunities for EMBL and its partner institutes, as well as a fantastic chance to meet face-to-face after so long. As the partner institutes apply a stringent scientific turnover model, the conference was an opportunity for new groups and their leaders to meet and connect.

Photo: Johanna Lehtonen

Knowledge sharing across the Nordic EMBL Partnership

In 2020, the Nordic EMBL Partnership was awarded 2.5 million NOK by NordForsk, as part of their "Nordic Research Infrastructure Hubs" initiative. The funding is designed to help increase knowledge transfer and interactions across the Nordic EMBL Partnership. This has been achieved through the arrangement of courses, as well as the covering of travel expenses for researchers and students visiting across the nodes.

NCMM visits DANDRITE

Elham Shojaeinia, a PhD student in the Esguerra group at NCMM, visited DANDRITE to participate in a PhD course focusing on the principles of neural organization.

Elham studies rare neurodevelopmental disorders causing epileptic seizures in children using the zebrafish model organism. The Principles of Neural Organization PhD course at The Danish Research Institute of Translational Neuroscience (DANDRITE), an interdisciplinary research institute hosted by Aarhus University in Denmark, gave Elham the opportunity to learn in depth about neural design and apply that to what she observes in her zebrafish research.

FIMM visits NCMM

Liye He, a postdoctoral researcher in the group of Professor Tero Aittokallio at FIMM, visited the Mathelier group at NCMM. Liye builds machine learning models to identify synergistic and personalised drug combinations for cancer patients using different types of data, such as omics data. He visited the research group of Anthony Mathelier at NCMM to learn in-depth from their expertise with methylation data and how it could be applied to his work of predicting drug responses.

In addition, four members of Human Immune Disorders group situated at FIMM visited the Saarela group at NCMM. Meri Kaustio, Ville Almusa, Anna Sulonen and Pu Chen came to Oslo to get to know the rest of the group in person and to present and discuss projects and future plans.

From left to right: Meri Kaustio, Henrikki Almusa, Verena Strumlehner, Yasaman Pakdaman, Pu Chen, Johanna Lehtonen, Anna Maija Sulonen, Monika Szymanska, Jaana Saarela. Photo: Øystein Horgmo/UiO

Tools of the Trade Webinar Series

In the Fall of 2022, the Nordic EMBL Partnership launched a webinar series of online seminars and clinics for scientists within the Partnership and their local collaborators. The webinar covered topics in data science, informatics, and computational approaches and methods applicable in molecular medicine research. Speakers came from both within the different nodes, as well as affiliated research institutes.

The Nordic EMBL Partnership Coordination and Operations team assemble to advance joint initiatives

In early May, NCMM hosted thirteen colleagues from its three sister Nordic research centers and EMBL. The program offered a warm reception for the team after more than two years of solely remote interactions.

Strategic, engaging discussions on the first day covered a range of current and future operational topics. On the second day, the team engaged in a hands-on, interactive workshop to unfold new ideas for cross-node collaborations, held at NCMM facilities in the heart of the Oslo Science Park.

"We developed some new ideas to facilitate cross-node collaboration, and I'm looking forward to seeing these actions take hold as the nodes strengthen their partnership through cross-border collaborations with each other and EMBL", said Elisa Bjørgo, NCMM Head of Research Strategy, Communication and International Relations.

The Nordic EMBL Partnership Coordination and Operations Team in Oslo, May 2022

New Nordic EMBL Partnership Communications Director

As of January 2023, Nóra Lehotai joined the Nordic EMBL Partnership in the role of Communications Officer. Nóra has a background in plant biology research, which took her from her home country, Hungary, first to Dijon, France, and then to Umeå in Sweden. After several years of postdoc experience and getting to know the Swedish research network, she was ready to take the next step in her career and switched sides. In 2020, she joined the Swedish node of the Partnership, MIMS in Umeå, as project coordinator and communications officer. Since then, she has gained powerful experience in project management and both internal and external communications, which is equally shared between the Nordic EMBL Partnership and MIMS in her role.

As Communications Officer of the Partnership, Nóra works to increase the visibility of the dynamic Nordic research environment, highlighting advances in research and technology. Her engagement with staff members at each node of the Partnership and her communications approach, enable building collaborations, elevate opportunities for connections and promote knowledge exchange, increasing the value of the Partnership. She also supports EMBL with its wider communications objectives, with particular focus on the Nordics.

Nóra Lehotai, Photo: Niklas Mähler

eatris NORWAY

EATRIS is a non-profit European Research Infrastructure Consortium (ERIC) that offers a unique one-stop shop access to 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 for advancing biomedical innovations. NCMM coordinates the Norwegian participation in EATRIS and NCMM's Director, Professor Janna Saarela, is also the EATRIS National Scientific Director of Norway. EATRIS has five scientific platforms: Advanced Therapy Medicinal Products, Biomarkers, Imaging and Tracing, Small Molecules, and Vaccine, Inflammation and Immune Monitoring.

EATRIS offers a range of services which directly benefit Norway-based researchers. A main aspect of this is support for funding applications, which includes help forming a consortium, participating in research funding proposals as a full partner providing various centralised services, 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 rare disease researchers, a matchmaking service to facilitate academic collaborations with industry, and educational and training offers for next generation translational scientists.

Chapter 4

News and events

News and Events

Group Leader Evaluation 2022

Marieke Kuijjer's group extended for a further four years

Following a successful evaluation by NCMM's Scientific Advisory Board (SAB) in February 2023, the Computational Biology and Systems Medicine group led by Marieke Kuijjer has been extended for four years.

NCMM follows the EMBL model for group leader recruitment and review, meaning that each group is evaluated before the end of their first five-year period at the Centre. A successful evaluation means that the research group and the group leader's appointment is extended for a further four years, allowing them to continue with their research programme at NCMM for a total of nine years.

The evaluation of Marieke Kuijjer's group was based on a written dossier she prepared and letters of assessment from external scientific experts within her research fields. During the SABs visit to NCMM in February, Marieke Kuijjer also met with the board to present the progress and future plans of the Computational Biology and Systems Medicine group.

Following this meeting, the NCMM board decided on the renewal of the group for a second period according to the recommendation by the SAB.

"On behalf of NCMM, and myself, I want to congratulate Marieke Kuijjer on the well-deserved extension of her research group. We look forward to the impressive research and computational tools she and her well-established group will produce in the coming years in Oslo", says NCMM Director Janna Saarela about the successful evaluation.

NCMM PhD Defence 2022

Ganna Reint

Ganna defended her thesis entitled "Refinement strategies for CRISPR-Cas9 genome editing" at the Dept. of Biosciences, Faculty of Mathematics and Natural Sciences, University of Oslo, in May 2022. Ganna's PhD was carried out in the group of Emma Haapaniemi at NCMM. The thesis focused on methods to improve CRISPR Cas9 performance and make it more efficient in achieving precise editing. After completing her PhD thesis, Ganna moved to a postdoc position at Broad Institute, John Doench lab.

Photo: Oda Hveem

NCMM News Highlights

NCMM gathers for its first scientific retreat following the pandemic

In June 2022 NCMM organised its first scientific retreat in three years. Participants gathered at Son Spa in Akershus for two days of excellent talks from the research environment and Associate Investigator network. The retreat included sessions on cellular and molecular biology, cancer and immunity and blood disorders.

"It was an honour to welcome more than 80 participants from NCMM and its Associate Investigator network at Son to learn about the scientific research progress that has been made across the network in the past few years. Presenters received invaluable feedback and support from their peers, which I'm sure will positively impact their work going forward. We are all grateful for the hard work of the organisers, technical support and the speakers in making the retreat possible", said NCMM Director Professor Janna Saarela.

The retreat also presented the opportunity for networking, with social activities organised by the social committee. The activities successfully created a cheerful atmosphere and attendees left having created stronger connections after three years without in-person events.

Group photo of the participants at the NCMM Scientific Retreat in June 2022. Photo: Son Spa and Hotel

Emma Haapaniemi part of a new Centre of Excellence in immunotherapy research

Emma Haapaniemi is part of the core group of researchers in the new Centre of Excellence called PRIMA – Precision Immunotherapy Alliance. The centre is led by Associate Investigators Johanna Olweus and Karl-Johan Malmberg and will focus on developing personalized immunotherapies against several types of cancer that could benefit even more patients than before. The technique they are developing is not only important for cancer, but also for autoimmune diseases and rare, congenital diseases.

Oslo Bioinformatics Workshop Week brings scientists from diverse backgrounds together

The first ever Oslo Bioinformatics Workshop Week (OBiWoW) was hosted at the University of Oslo in December, with Roza Berhanu Lemma and Tatiana Belova from NCMM among the organisers. The event was aimed at reaching the bioinformatics community and anyone who wants to learn bioinformatics regardless of academic background and level. Between 200-250 participants attended the workshops, and some participants attended two or more workshops.

"The workshop week created a nice environment for interesting discussions within the topics of the workshop, it provided networking opportunities and potential collaborations. I really enjoyed witnessing these along with the continuous in person feedback we received both from workshop attendees and instructors indicating that this is an excellent event, they enjoyed the workshops, and that they really would like to see this happening again. To have all these positive feedbacks and witness the excitement and enthusiasm of everyone involved in the workshop is quite fulfilling", said Roza about the experience.

Tatiana Belova and Roza Berhanu Lemma. Photo: Larissa Lily.

NCMM Funding Successes

20 million

Haapaniemi group allocated 20m NOK to prepare a clinical trial with genome-edited T cells

Emma Haapaniemi was awarded 20m NOK in December 2022 by the national programme for clinical treatment research - known as KLINBEFORSK - for developing CRISPR-Cas9 gene therapy for STAT1 Gain-of-Function disease. The project aims to use gene editing tools to develop T-cell therapy for STAT1 Gain-of-Function disease and other immunodeficiencies, where bone marrow transplant is not an immediate treatment option. The proposal was developed together with Hans Christian Erichsen, a consultant pediatric immunologist, who wished more treatment options for his patients with STAT1 Gain-of-Function disease.

KLINBEFORSK

20 million

Haapaniemi group receives 20 million NOK to research personalized gene editing

In March 2022, Emma Haapaniemi was awarded 20m NOK for her project 'CRISPR-Cas9 corrected T cells for personalized therapy', as part of the Research Council's call for radical innovative technology projects. The project proposes to use a gene editing tool called CRISPR to correct T cells from patients with diverse T cell immunodeficiencies. After the researchers correct the T cells, they will be infused back into the patient's body. The correction of the T cells will enable the patients to have an immune system that protects their body from disease and infection properly.

Forskningsrådet

9 million

Saarela group receives 9m NOK from Helse Sør-Øst to identify underlying genetic causes of rare diseases

Janna Saarela was awarded 9m NOK from Helse Sør-Øst in December 2022 to develop a functional genomics platform that will improve diagnostics of rare inherited diseases. Determining the underlying genetic cause of such diseases is important for selecting targeted treatments for patients and genetic counselling for the families. The platform will use RNA sequencing, genome editing and functional cell-based assays to identify novel disease-causing genetic variants in patients with rare inherited immune disorders. The same platform can be extended to all rare disease areas and can improve our understanding of the mechanisms underlying more common immune diseases as well.

HELSE SØR-ØST

2 million

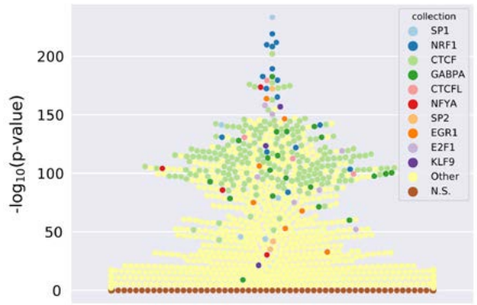
Sebastian Waszak receives 2m NOK to develop novel zebrafish models for aggressive brain tumors in children

Shortly before Christmas 2022, Sebastian Waszak was awarded 2 million NOK from the Norwegian Cancer Society for his proposed Pioneer Project. The goal of the project is to find new treatment strategies for DIPG, an aggressive type of brain tumor in children, by establishing novel zebrafish models of the disease. By funding Pioneer Projects, the Norwegian Cancer Society aims to support early-stage exploration of novel and innovative ideas: in other words, high risk-high gain research ideas. The zebrafish model to be developed at NCMM will be the first of its kind and has the potential to become an important new animal model for studying aggressive pediatric brain tumors. The project will be developed in collaboration with the zebrafish core facility at NCMM/UiO.

KREFTFORENINGEN

NCMM Research Highlights

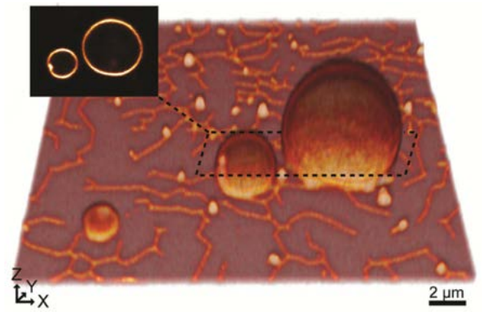
13 special genes linked to epigenetic changes in cancer samples



Abnormal DNA methylation patterns are frequently reported in cancer patients. To better understand how such abnormal patterns occur, the Mathelier group developed a computational framework to examine the relationship between DNA methylation and transcription factors that bind the DNA. Analysis of several different cancer types led to the identification of 13 transcription factors that are likely to influence the DNA methylation pattern around their binding sites. Published in Epigenetics & Chromatin, the study demonstrates how these transcription factors could potentially drive cancer development.

Pioneer transcription factors are associated with the modulation of DNA methylation patterns across cancers
Lemma et al., Epigenetics & Chromatin (2022).
DOI: https://doi.org/10.1186/s13072-022-00444-9

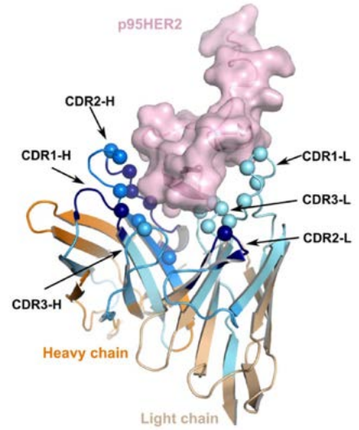
How primitive cells may have communicated on the early Earth



Cells must be able to communicate with their surroundings in order to self-replicate and grow. In a new article in the Nanoscale journal, The Gözen group demonstrate how primitive cells on the early Earth may have communicated through networks that allow the exchange of molecules like DNA and RNA. This communication could explain how non-living protocells transitioned into living matter on the early Earth, by establishing a means for self-replication. The study brings us a step closer to understanding the origin of life.

Transport among protocells via tunneling nanotubes.
Schanke et al., Nanoscale (2022).
DOI: https://doi.org/10.1039/D2NR02290G

Characterization of antibody with potential for breast cancer treatment and diagnostics



Combining their expertise, the Sekulic group at NCMM and Kyte group at Oslo University Hospital collaborated on characterizing a new antibody with therapeutic potential. The study employed HDX-MS to map the binding of the antibody, named Oslo-2, against a variant of HER2 that is seen in a group of breast cancer patients with poor prognosis. Antibodies directed against HER2 are already used in breast cancer therapy, and the new antibody developed by the collaboration has potential to be used as a diagnostic tool or future cancer treatment.

Development of a high-affinity antibody against the tumor-specific and hyperactive 611-p95HER2 isoform.
Dorraji et al., Cancers (2022).
DOI: https://doi.org/10.3390/cancers14194859

Using mutations in non-coding areas of the genome to predict cancer-associated genes

A new study by the Mathelier group and collaborators found a way to predict genes that may be associated with cancer by looking at mutations in areas of the genome that do not code for proteins. The authors designed a computational approach to predict mutations likely associated with a cascading effect altering gene regulatory networks in cancer. Published in Nucleic Acids Research, the study highlights the importance of studying mutations in non-coding areas of the genome.

Cis-regulatory mutations associate with transcriptional and post-transcriptional deregulation of gene regulatory programs in cancers.
Castro-Mondragon et al., Nucleic Acids Res (2022).
DOI: https://doi.org/10.1093/nar/gkac1143

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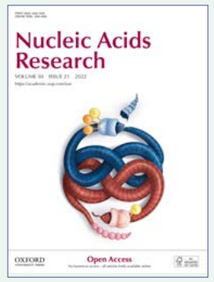
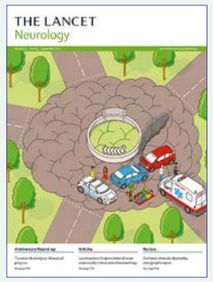
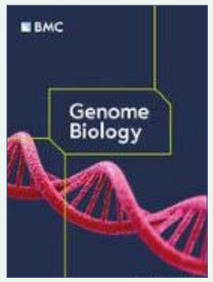
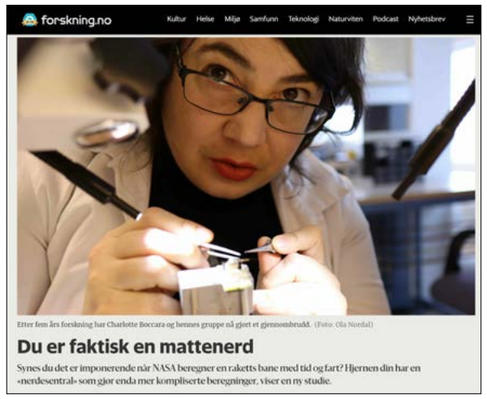






Highlighted press items for NCMM 2022 & Q1 2023



Chapter 5

NCMM Operations

NCMM Board

The NCMM Board is, in collaboration with the Director, 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.

A message from the Chair of the Board of NCMM, Jens Petter Berg:
On behalf of the Board, I am pleased to see the significant progress and impressive achievements in basic and translational research by NCMM during 2022. The center's dedication to multidisciplinary collaboration and the integration of clinical research is particularly noteworthy, as it underscores the potential for real-world impact in improving human health. I would like to commend the center's staff and the scientific leadership among group leaders for their outstanding work over the past year resulting in several prestigious publications and research grants. I would also like to take this opportunity to congratulate NCMM group leader Marieke Kuijjer on her evaluation and extension for a further four years.

I am also looking very much forward to follow Dr. Charlotte Boccara and Dr. Biswajyoti Sahu, who signed group leader contracts in 2022. Their work will play a significant role in defining NCMM's future role and position. The recruitments at NCMM showcases the center's efforts to promote diversity, equity, and inclusion in research, which is crucial for ensuring that scientific progress benefits all members of society. I am grateful for the efforts NCMM has taken to improve the work environment in connection with the ARK survey in 2022. Improving the work environment is a continuous process, and requires follow up.

The partnership agreement between EMBL and UiO for 2023-2032 was recently renewed. NCMM is currently in its third 5-year funding period and receives core funding annually from UiO, RCN, and the South-East Regional Health Authority (HSØ) until the end of 2024. The Board is grateful for the financial support provided by the consortium. An important and a challenging task for the Board in the coming year is to work together with UiO and HSØ to secure future funding for NCMM.

The efforts and contributions from the NCMM Board members and the scientific and administrative leadership of NCMM are highly appreciated. Personally, I will miss the discussions and collaboration, which I have had for several years with Board member Øystein Krüger and Board secretary Elisa Bjørgo, who left the Board in 2022. Thank you for your efforts and dedication!

Overall, NCMM demonstrates a high level of commitment to excellence and innovation in molecular medicine research. It is a pleasure to witness such exceptional progress and we look forward to continued success in the years ahead.

Oslo, 19th March 2023

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

Photo: Øystein Horgmo, UiO

Board members

The Board consists of the Chair and five members representing NCMM's host, the University of Oslo and the consortium partner Health South-East Regional Health Authority (HSØ), as well as a national representative.

Chair

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

Board

Professor Ola Myklebost,
University of Bergen
(national representative)

Professor Arne Klungland,
University of Oslo

Professor Hilde Nilsen,
University of Oslo

Head of Research Øystein Krüger,
Dept. of Research and Innovation,
South-Eastern Norway
Regional Health Authority (HSØ)

Professor Bente Halvorsen,
Oslo University Hospital

Deputy members

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

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

Professor Arnoldo Frigessi,
University of Oslo

Scientific Advisory Board (SAB)

Chair

Professor Richard Treisman (Chair)
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, Personalised Genomics to Study Genetic Basis of Complex Diseases group, EMBL Heidelberg, Germany

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. This was also the first physical SAB meeting since the pandemic.

Funding

54

54,5 mNOK per year in core funding for 2020-24

30

30 mNOK in competive funding for 2022

263

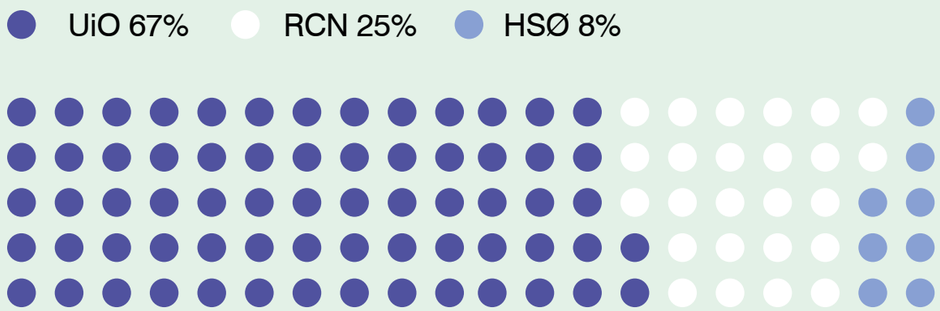
263 mNOK in competitive funding for 2015-22

The core funding for NCMM in the period 2020-2024 is 54,5 mNOK per year

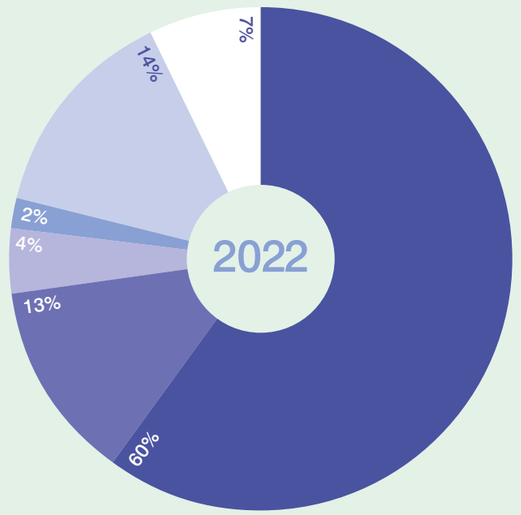
Core funding: The core funding for NCMM in the period 2020-2024 is 54.5 million NOK per year from the three consortia partners UiO, the Research Council of Norway (RCN) and South-Eastern Norway Regional Health Authority (HSØ). Overhead income from core facilities and production-based income comes in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

Extramural funding: For 2022, the amount of extramural funding obtained 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 such as the World Cancer Research, Barncancerfonden and Ians Friends Pedriatric brain tumor foundation USD.

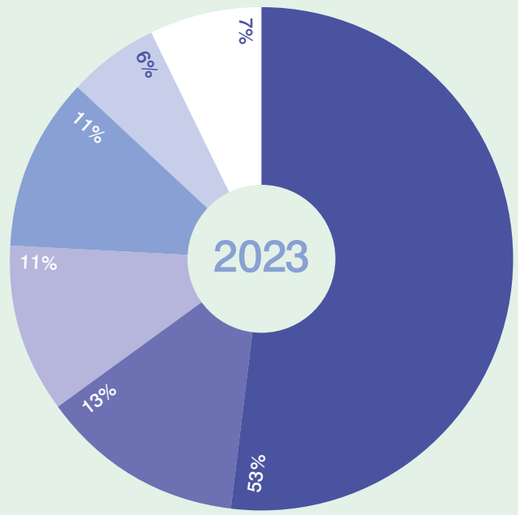
Core funding 2022

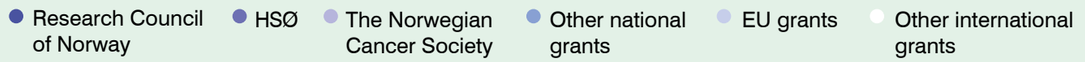


Extramural funding sources 2022



Estimated extramural funding sources 2023

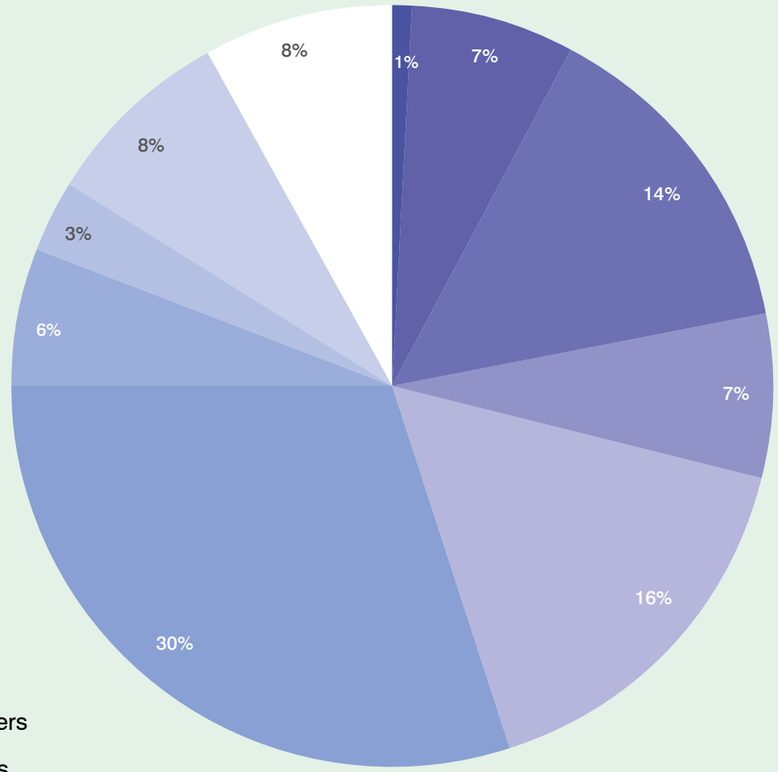




Personnel statistics

in 2022 and Q1 2023

Staff according to type of employment (%)

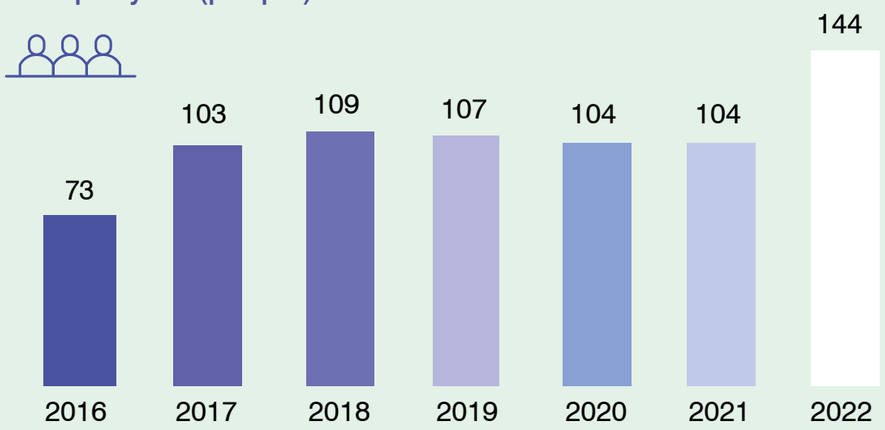


- Director
- Group leaders
- Researchers
- Postdocs
- PhD fellows
- Students
- Administration
- IT
- Engineers
- Other personnel

144

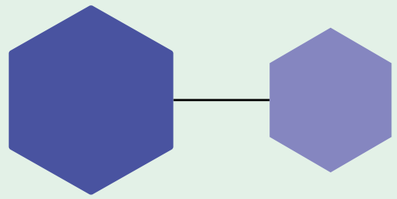
NCMM had 144 staff members and students in 2022. 44% of these are group leaders, researchers, postdocs and PhD fellows.

Staff per year (people)



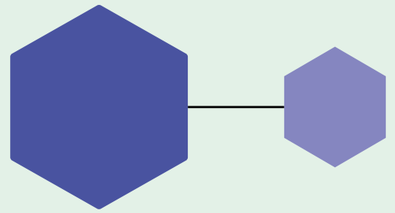
> 2017 represents NCMM after the merger with the Biotechnology Centre of Oslo.

Staff – Gender balance



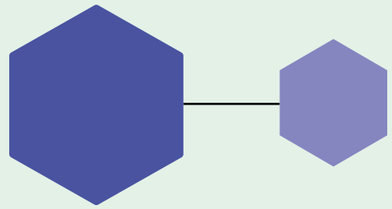
Female: 65% Male: 35%

International staff



International: 76% Norway: 24%

Group Leaders – Gender balance



8/11

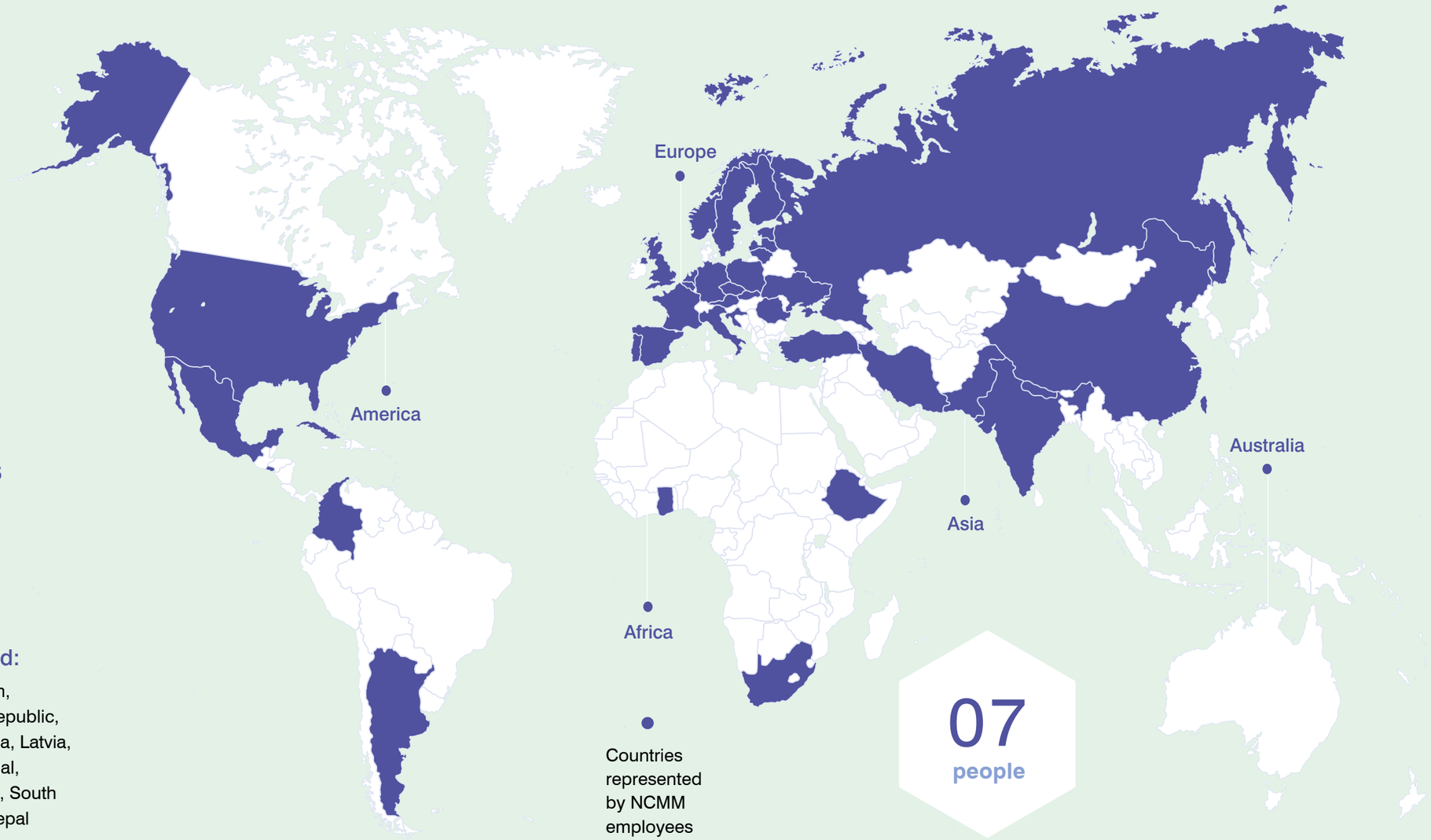
Female: 72,7% Male: 27,3%

8 out of 11 group leaders are female.

Distribution of staff

As of Q1 2023

- 38 nations in total
- 80 international staff members



Countries represented by NCMM employees

01 person

Countries represented:
Argentina, Austria, Belgium, Colombia, Cuba, Czech Republic, El Salvador, Estonia, Ghana, Latvia, Lithuania, Pakistan, Portugal, Romania, Russia, Slovakia, South Africa, Sweden, Taiwan, Nepal

02 people

Countries:
Belgia, Croatia, Etiopia, Italy, Turkey, UK, USA

03 people

Countries:
India, Iran, Mexico, Ukraine

04 people

Countries:
Poland, The Netherlands

07 people

Countries:
Finland

08 people

Countries:
China, Spain

10 people

Countries:
Germany

12 people

Countries:
France

Personnel at NCMM

2022 & Q1 2023

Director and administration

Director
Janna Saarela

Associate Director
Anthony Mathelier *(from March 2023)*

Chief Administrative Officer
Ingrid Kjelsvik

Head of Section for Research Strategy, Communication and International Relations
Elisa Bjørgo *(until August 2022)*

Financial Officers
Mette Kvernland
Anita Elisabeth Skolem

Human Resources Officer
Nina Modahl

Communications Officers
Nuru Saadi *(until September 2022)*
Nikoline L. Rasmussen
(from January 2023)

EATRIS Coordinator
Anita Kavlie

Higher Executive Officer
Carlos Romeo Rodriguez

IT Team
Harold Gutch
Gang Cheng *(until May 2022)*
Melaku Tadesse
Torfinn Nome *(from February 2022)*
Pavel Zarva *(from January 2023)*

Administrative Officer
Larissa Lily

Laboratory Operations and Core Facilities

HSE Coordinator
Karen-Marie Heintz
(until December 2022)

General Lab Manager
Xian Hu (Edna)

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)
Taradol Sutjaritvorakul

Research groups

Human immune disorders

NCMM Group Leader
Janna Saarela

Head Engineer / Lab manager
Monika Szymanska

Researcher
Yasaman Padakman

PhD Fellow
Johanna M. Lehtonen

MSc Student
Tuva Sundell *(shared supervision with Emma Haapaniemi)*

Stem Cell Group

NCMM Group Leader
Judith Staerk

Researcher
Artur Cieslar-Pobuda
Adnan Hashim

Computational Biology and Gene Regulation

NCMM Group Leader
Anthony Mathelier

Researchers
Jaime Abraham Castro Mondragón *(until April 2022)*
Roza Berhanu Lemma

Postdoctoral Fellow
Vipin Kumar

PhD Fellows
Rafael Puig Riudavets
Ieva Rauluseviciute
Katalin Terézia Ferenc
Hallvard Wæhler *(main supervisor: Ragnhild Eskeland)*

Lab Engineer
Dina Ruud Aronsen

Software Engineer
Paul Boddie *(until January 2022)*

MSc Students
Sebastian Mørch
Miguel Angel Pérez Elena
Emily Martinsen

BSc Students
Joel Rodriguez Herrera
(co-supervised with Marieke Kuijjer)
Edgar Leal
Thomas Tubbehaugen
Jamal Farid Romman

Interns
Chloé Vogel
Fabrizio Guidotti

Structural Biology and Drug Discovery group

Principal Engineer
Rasma Gutsmite

Postdoctoral Fellows
Javier Gutierrez
Marta Sanz Gaitero

Precision pediatrics and gene editing

NCMM Group Leader
Emma Haapaniemi

Head Engineer
Monika Szymanska

Lab technician
Britt Olaug Lindestad

Senior Scientists
Anna Zofia Komisarczuk
Shiva Dahal-Koirala

MD consultant
Hans Christian Erichsen

PhD Fellows
Ganna Reint *(until May 2022)*
Zhuokun Li
Katariina Aino Inkeri Mamia
Pavel Kopcil
Oline Rio
Carolina Ervik

Research Assistant
Jacob Conradi

MSc Students
Oda Almåsbak
Sigrid Fu Skjelbostad
Nelson Thapelo Mathabela
Tuva Sundell *(shared supervision with Janna Saarela)*
Henriette Myrland *(shared supervision with Charlotte Boccara)*
Ruchi Saigal *(shared supervision with Charlotte Boccara)*

Computational Oncology

NCMM Group Leader
Sebastian Waszak

Postdoctoral Fellows
Nancy Saana Banono
Martin Burkert

Researchers
Ina Skaara Brorson
Birgit Kriener

PhD Fellows
Sandra Kunz
Sophie Mottl *(until October 2022)*
Anne Martina Kraus
(until September 2022)

Chemical Neuroscience

NCMM Group Leader
Camila Vicencio Esguerra

Head Engineer
Ana C. S. Tavara

Researcher
Wietske van der Ent

PhD Fellows
Elham Shojaeinia

Research Technicians
Alejandro Pastor Remiro
Karolina Kirstein-Smardzewska

MSc Students
Daarathy Pathmanathan Sellathurai
Zuhur Said
Frie Dewaele
Ana Pardo Perez
Geoffroy van Dessel
Ola Lødøen Vethe
Hawo Hassan Isaq

MD student
Maren Fjelstad Holt

Structural Biology and Chromatin

NCMM Group Leader
Nikolina Sekulic

Principal Engineer
Stine Malene Hansen Wøien

Research Scientist
Dario Segura- Peña
Ahmad Ali Ahmad

PhD Fellow
Hemanga Gogoi

MSc Students
Ole Magnus Fløgstad
Anna Mørch

Bionanotechnology and Membrane Systems

NCMM Group Leader
Irep Gözen

Postdoctoral Fellow
Inga Põldsalu *(until April 2022)*

PhD Fellows
Aysu Kucukturhan Kubowicz
Lin Xue
Jicheng Li
Maivizhi Thiyagaraja

Research Assistant
Ingrid J. Schanke

Computational Biology and Systems Medicine

NCMM Group Leader
Marieke L. Kuijjer
Researcher
Tatiana Belova

Postdoctoral Fellows
Ladislav Hovan
Annikka Polster *(until February 2022)*

PhD Fellows
Ping-Han Hsieh
Romana T. Pop
Giulia Schito
Debora Meijer
(co-supervised with Judith Bovée, Leiden University Medical Center)
Saikat Das Sajib
(co-supervised with Erik Knutsen, Arctic University of Norway)

MSc Student
Gabriel Bratseth Stav

Research Assistant
Genís Calderer i Garcia
(until September 2022)

BSc Students
Bror Johannes Tidemand Ruud
Joel Rodriguez Herrera
(co-supervised with Anthony Mathelier)

Summer students
Ismael Manzanares García
Theodor Midtbø Alstad
Kristine Lippestad

Systems Neuroscience & Sleep

NCMM Group Leader
Charlotte Boccara

Researcher
Solomiia Korchynska

Postdoctoral Fellow
Brijesh Modi *(from October 2022)*
Damien Dufour
(from January 2023, co-supervised with Nolwen Briand, IMB, UiO)

PhD Fellows
Florian Dapsance *(from September 2022, co-supervised with Ørjan Martinsen, Dept. of Physics, UiO)*

Engineer/Data Scientist
Eis Annavini *(from April 2022, in collaboration with IMB, UiO)*

Lab technician
Lina Okinina *(from June 2022)*

Lab manager
Ryo Iwai *(from January 2023)*

MSc Students
Ela Babursah
Ruchi Saigal *(shared supervision with Emma Haapaniemi)*
Adrian Engberg *(from January 2023)*
Henriette Myrland *(shared supervision with Emma Haapaniemi)*
Laure Gosse *(from February 2023)*

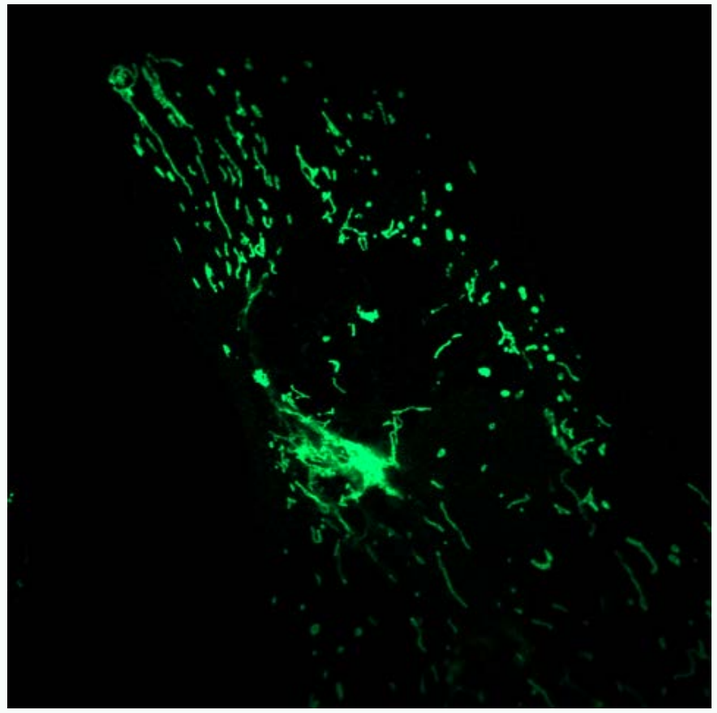
MD student
Mats Helmersen

Precision Cancer Epigenomics group

NCMM Group Leader
Biswajyoti Sahu
(from September 2022)

Postdoctoral Fellow
Liangru Fei *(from January 2023)*

PhD Fellow
Celina Wiik *(from January 2023)*



Confocal images showing mitochondria (in green, mito-GFP) in wild-type (top) and DNMT3B knockout (bottom) WA#22 human emryonic stem cells, showing a significant increase of branched mitochondria in DNMT3B knockout cells. Credit: Staerk group

NCMM CO-FUNDERS:

UNIVERSITY OF OSLO

The Research Council of Norway

HELSE SØR-ØST

NORDIC EMBL PARTNERSHIP FOR MOLECULAR MEDICINE:

FIMM
Institute for Molecular Medicine Finland
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

NATIONAL AND INTERNATIONAL COLLABORATORS:

ESFRI

eu-openscreen

eatris

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0349 Oslo, Norway

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