Annual Report NCMM 2020

From disease mechanisms to clinical practice

NCMM

NORDIC **EMBL** PARTNERSHIP FOR MOLECULAR MEDICINE

NCMM
Co-Funders:

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Contents

Welcome
Chapter
1

The overall vision for NCMM's next five-year period is to continue strengthening our position as a leading national centre for molecular medicine, with a translational mindset.

Introduction from the Director

Dear colleagues, friends, and supporters, it is my great pleasure to welcome you to the 2020 NCMM Annual Report. The past 12 months have certainly been challenging in many respects. However, I am extremely proud of our researchers and staff for adapting to the situation posed by both the ongoing COVID-19 pandemic and the move out of half of our office and lab space in the Oslo Science Park. Many of us spent most of 2020, and this first quarter of 2021, either working from home or in rather different conditions from what we are used to. I am pleased that, despite all the challenges posed, NCMM continued to do great science. For this I wish to extend my thanks to all our supporters in addition to our motivated researchers and staff.

2020 also marked the start of our third five-year period (2020–2024). These next five years will be critical for NCMM's growth and development. The report from our most recent SAB (Scientific Advisory Board) visit in March 2021 deemed NCMM to have a strong scientific research environment and commended us on our scientific strategy and plans for the future. I warmly congratulate our group leaders, Anthony Mathelier, Nikolina Sekulic, and Irep Gözen on their successful evaluations and the subsequent extension of their groups for a further four years.

The SAB made several recommendations that we will now work to implement. This includes refining our operational vision to integrate NCMM fully into the multidisciplinary UiO:Life Science cluster; thus helping to bridge the medical and natural and life sciences. Our planned move into the UiO:Life Science building will support this objective by bringing together medical sciences, chemistry, and pharmacology with shared research infrastructures. Some Oslo University Hospital environments will also move into the building which will present us with additional opportunities for collaboration and interaction with Oslo's hospital-based research environments.

NCMM will seek to continue building critical mass in computational biology, genome medicine and clinical translation. This focus has already been strengthened by our most recent group leader hire in computational biology last spring (Sebastian Waszak). Our plan to hire additional group leaders in precision medicine, with expertise in artificial intelligence/machine learning and cell biology, will further build on this strategy. An emphasis here, along with the existing strengths provided by our current group leaders, present an opportunity for NCMM to play a leading role in these fields in Norway.

Photo: Oda Hveem

To help meet these goals, NCMM will work to nurture the right environment for translating our basic research findings into clinical practice. We will actively seek opportunities to work more closely with clinician-scientists and we are planning a number of initiatives to help fully integrate them into our research. We also want to better support our group leaders to successfully rotate out of NCMM. The current links offered through our group leaders' adjunct positions with other UiO departments have a lot of potential here, and we are looking for novel opportunities also in other organizations. We will work to fully capitalize on the EMBL model to introduce and integrate new scientific talent to enrich the Norwegian biomedical research community.

One of the future opportunities we look forward to is bridging our research to other national research environments – other health regions and universities with medical faculties. I'm expecting great success from our recently renewed associated investigator network and novel collaboration initiatives planned with the other regions of Norway. We, as others, are impatiently waiting for the post-pandemic era to further enforce these new interactions.

Finally, before our planned move into the new UiO Life Science Building in 2026, we will lay the groundwork required to ensure our young researchers can fully benefit from the opportunities offered by the move. This will involve, in addition to NCMM graduate students' enrollment in PhD programs of the Faculty of Medicine and the Faculty of Mathematics and Natural Sciences, the provision of joint training and career guidance for early-stage researchers in collaboration with the postdoctoral programmes of both the Faculties.

NCMM's next five years will certainly mark an exciting and industrious phase for the Centre. I look forward to seeing our groups and staff continue to develop and produce great science, thus cementing NCMM's standing as a key player in Norway's molecular and translational research environment.

April 2021

Professor Janna Saarela
Director, NCMM

NCMM Research

Chapter 2

Camila Esguerra

Chemical Neuroscience Group

We hope not only to contribute new insights with regards to our overall understanding of health and disease, but also to identify novel entry points for therapeutic development.

Could you describe your research in a nutshell?
Our research primarily focuses on understanding the causes of brain disorders such as epilepsy, schizophrenia, and autism. We achieve this by studying genetic models of these human neurological diseases using zebrafish, a tropical freshwater fish originating from the rivers and estuaries of South Asia and Southeast Asia. By studying how these genetic mutations affect brain function in very young fish (normally during the first week of development), we can pinpoint the earliest changes in the brain that transform it into a diseased state over time.

What do you hope to discover with your research?
By uncovering new mechanisms that lead to brain dysfunction, we hope not only to contribute new insights regarding our overall understanding of health and disease, but also to identify novel entry points for therapeutic development.

What were your highlights of 2020?
In total, we published nine papers, several describing new genetic models of epilepsy and schizophrenia. We also generated and characterized additional genetic models in zebrafish for severe infant and childhood epilepsies, this time mimicking specific human patient mutations as part of our increasing focus on personalized medicine approaches. In addition to studying "loss of function" mutants, we also modelled a "gain-of-function" genetic risk variant – i.e., where the mutation results in overproduction of a specific protein – that was originally identified in patients with temporal lobe epilepsy.

What are your goals for 2021?
We are looking forward to carrying out a large-scale drug screen for one selected epilepsy model and one schizophrenia model in 2021. Moreover, we were also awarded EU funding to investigate host-tumour interactions in zebrafish engrafted with human glioblastoma cells. In this study, we aim to elucidate the mechanisms by which tumours alter brain plasticity and, ultimately, trigger seizures. Conversely, we will also examine how neuronal activity influences tumour growth, differentiation and survival.

Irep Gözen

Bionanotechnology and Membrane Systems Group

We have interdisciplinary research interests, concentrating our efforts on integrative bionanoscience, with a special focus on bio-membranes.

Could you describe your research in a nutshell?
Our research programmes aim to understand the biophysical and materials-science aspects of complex biological problems involving lipid membranes. Through our research, we bring together biomembranes with solid interfaces with micro and nanotechnology to observe the unique membrane interactions with high-resolution microscopy. A key focus for all of our research lines is the membranes positioned on nanoengineered solid surfaces.

What do you hope to discover with your research?
We would like to understand:
- What is the exact role of surfaces in the emergence of life on the early Earth.
- How cells perceive interfaces and physically migrate on them.
- How certain organelles (e.g. the ER) form and remodel themselves.

Furthermore, we would like to develop membrane-based robust point of care assays, leading to the development of unique technology for rapid non-invasive testing.

What were your highlights of 2020?
- An art exhibition 'NanoCosmos', consisting of microscopy images from the Gözen Lab and two collaborating partners took place in February 2020 at the contemporary art gallery 'Kunstplass' in central Oslo. The UiO rector Svein Stølen and the head of UiO:Life Sciences, Carl Henrik Gørbitz, attended the opening ceremony and gave brief speeches about the exhibition. Hundreds of visitors from the public viewed the images during the exhibition period.
- Group member PhD candidate Elif Köksal received the Student Research Achievement Award and the Travel Award from the Biophysical Society for their 64th Annual Meeting, which took place in San Diego, U.S.A., in February 2020.
- Advanced Science News published a news article about our publication by Köksal et al. entitled "Heating up the debate: New findings in protocell evolution".

What are your goals for 2021?
- I was selected as the Ambassador of the Biophysical Society in Norway 2021–2023. I am looking forward to working towards strengthening the connections between the biophysics communities in the U.S. and in the Nordic region. I plan to organize a series of workshops, with a particular focus on encouraging female scientists into STEM. I will also focus on evaluating and commenting on research trends, publishing regularly for audiences from various backgrounds, and work to establish links to administrative and funding bodies in Norway.
- We have established strong new collaborations with the Natural History Museum in Oslo and the Natural History Museum of Denmark, as well as the Biosciences Department at the UiO. We are looking forward to the synergy and the interdisciplinary research work between our groups!

Emma Haapaniemi

Precision Pediatrics and Gene Editing Group

Our particular interest is in rare immune diseases, such as diseases caused by genetics and rare acquired autoimmune diseases.

Could you describe your research in a nutshell?
We work on optimizing CRISPR for monogenic immune disease treatments. Our particular interest is in rare immune diseases, for example, diseases caused by genetics and rare acquired autoimmune diseases.

What do you hope to discover with your research?
We hope to find therapies for rare monogenic diseases that are commercially uninteresting and outside the standard drug development pipelines. The therapies don't need to be curative – often incremental advances can have a significant effect on the quality of life for the patients and their families.

What were your highlights of 2020?
Our group is growing in size, just last year we recruited four new lab members; one postdoc, one PhD student and two MSc students. We have also purchased new High Throughput equipment that will facilitate and speed up our lab work.

Despite corona-related restrictions and moving to a new lab space, we have been able to keep our research going and maintain momentum with our projects.

What are your goals for 2021?
We have initiated collaborations with clinicians, and we are looking forward to further developing our translational projects. We are also in the last stage of preparing an exciting article which we are looking forward to publishing later in 2021.

Photo: Oda Hveem

Marieke Kuijjer

Computational Biology and Systems Medicine Group

We develop computational tools that can help us to better understand what drives the development and progression of cancer and other complex diseases.

Could you describe your research in a nutshell?
Our goal is to map the genome-wide landscape of transcriptional and post-transcriptional regulation for individual patients. We will then use this information to explain disease heterogeneity and identify new, and potentially targetable, regulatory alterations in complex disease. To model these landscapes, we develop computational tools that represent regulation in so-called genome-wide regulatory networks, as well as new methodologies that allow us to analyze and compare these large-scale networks across groups of individuals.

What do you hope to discover with your research?
We believe that the clinical phenotypes we observe in complex diseases cannot be adequately defined by individual genes, but that we instead should consider the underlying network of regulatory interactions between multiple different biological components. By modeling and analyzing genome-wide networks for individual patients, we hope to identify new, clinically relevant, regulatory subtypes, as well as biomarkers and potential new therapeutic targets for the treatment of cancer and other complex diseases.

What were your highlights of 2020?

- Our group has grown very nicely. Annikka (Polster) joined us in February as a Marie Curie Scientia Fellow II postdoc, Giulia (Schito) joined in September as a Master's thesis Erasmus student, Romana (Pop) and Debora (Meijer) then joined in November as a PhD student and co-supervised PhD student, respectively. During the summer we were joined by Caroline (Lunder Jensen) and Genís (Calderer), who worked with us as a UiO:Life Science summer student and Research Assistant, respectively.
- I received a Young Research Talent grant from the Norwegian Research Council, which will support a 4-year project to model the pan-cancer landscape of gene regulation.
- The group received funding for a 3-year project as part of the Pink Ribbon (Rosa sløfe) campaign from the Norwegian Cancer Society to analyze large-scale data with the aim to detect new regulatory subtypes in breast cancer.
- Tatiana (Belova) received funding from the Familien Blix Fond to identify and characterize regulatory subtypes in leiomyosarcoma.
- I joined Leiden University Medical Center, the Netherlands, on a 20% Assistant Professor position, where I am co-supervising PhD student Debora on a project in sarcoma genomics.
- Ping-Han (Hsieh) received a scholarship from the Ministry of Education, Taiwan.
- I participated in an "Ideas Lab" organized by the National Cancer Institute, Department of Energy (NCI/DoE) on digital twin modeling, which led to a new collaboration with multiple research groups across the US.
- We presented our tool PUMA at ISMB, and I gave an invited talk at the NetBioMed sattelite of NetSci.
- Together with Kimberly Glass and Maud Fagny, I edited the Research Topic "Applications and Methods in Genomic Networks" in Frontiers in Genetics.
- Members of the Kuijjer and Matheliger group set up the Regional Student Group Norway, the regional node of the International Society for Computational Biology (ISCB) Student Council.

What are your goals for 2021?

- We are looking forward to starting our newly-funded projects. Giulia has already initiated the network analyses in breast cancer and we hope to hire a postdoctoral fellow to continue this work later this year. Romana has started to integrate networks with other omics data (RCN).
- We'll be joined by summer student Shanna (Schneidewind), who will be working together with Ping-Han and Tatiana to identify coordinated expression in cancer subtypes.
- We hope to see more of our work published in 2021. Genís wrote a mini review on community detection in large-scale bipartite biological networks, which was accepted into Frontiers in Genetics. In addition, we recently posted two manuscripts to the BioRxiv—a project where we found that PD1 regulation is associated with brain cancer survival, and Ping-Han's new algorithm CAIMAN that corrects for false-positives in co-expression networks. In addition, Tatiana developed a novel comparative network analysis tool, PORCUPINE, which we hope to post on the BioRxiv in 2021.
- With Daniel (Osorio) joining us in April as a Marie Curie Scientia Fellow II postdoc, we'll be expanding our toolbox and analyses to single-cell data. In addition, Ping-Han will be focusing a bit more on using approaches from Deep Learning in network biology.
- Together with Camila Lopes-Ramos from Harvard Chan School of Public Health, I'll be editing a Special Issue on "Gene Regulatory Networks in Cancers" in the journal Cancers.
- I'l be joining the Editorial Board of the new ISCB/Oxford University Press journal *Bioinformatics Advances*.

Sandra Lopez-Aviles

Cell Cycle Regulations Group

By fully understanding the biological functions of protein phosphatases, we believe we can understand the implications of their inactivation and how to exploit their regulation in the treatment of cancer.

Could you describe your research in a nutshell?
We use a genetic model organism, fission yeast, to investigate basic mechanisms regulating cell division, gene expression, and cell differentiation. Due to the high degree of conservation of the key components controlling these events, our results can shed light onto the underlying causes leading to cancer development.

What do you hope to discover with your research?
Our main focus lies on the role of protein phosphatases regulating events during cell cycle progression and in response to nutrient starvation. In our group, we hope to show that the regulated activity of protein phosphatases belonging to the PP2A family play instrumental roles in the ordering of cell cycle events, the control of transcriptional programs, and the regulation of Cyclin-dependent kinase (CDK) activity. PP2A activity is often lost during cancer progression but the impact of this loss on cancer cells is not completely understood. By fully understanding the biological functions of these enzymes, we believe we can then understand the implications of their inactivation and how to exploit their regulation in the treatment of cancer.

What were your highlights of 2020?
Our PhD student Vilte Stonyte successfully defended her thesis: *Different aspects of the response to environmental challenges in S. pombe: roles of PP2A-B56 and a novel 4E-BP.*

The group also had two publications; one in the *International Journal of Molecular Sciences* and another in *iScience*.

What are your goals for 2021?
In 2021 we aim to finalize our ongoing projects on the role of PP2A phosphatases during mitotic exit and in the regulation of gene expression during differentiation. The latter is a continuation of our previous work on the importance of PP2A-B55 as a mediator of TORC1 functions during nutritional sensing. Now, we have shown that PP2A-B55 conveys nutritional cues to the transcriptional machinery that dictates cell fate, that is, the decision to proliferate, to enter quiescence or differentiate. Moreover, we are currently extending our findings to mammalian systems, in particular breast cancer cell lines. While this is still in an early stage, we have been able to show that some of the aspects regarding the functions of PP2A-B55 that we unveiled with our work in yeast, are conserved across evolution.

Finally we are very excited about a new project initiated in 2020 that has led to the discovery of a novel eIF4E-binding protein (4E-BP) in fission yeast. While 4E-BPs are present in higher eukaryotes and play instrumental roles in the control of protein translation, they had not been described in S. pombe. We have now identified a 4E-BP whose function is required during the response to a variety of stress conditions and that is required for the formation of stress granules. This protein is conserved in a number of yeast species belonging to the Ascomycota phylum, including human pathogens such as *Aspergillus fumigatus* and *Histoplasma capsulatum*. Hence, our findings have the potential to provide a new therapeutic target for the treatment of infections caused by these fungi.

Hartmut Luecke

Structural Biology and Drug Discovery Group

The Luecke Group aims to better understand the structure and function of integral membrane proteins. We also aim to identify and develop drugs that inhibit or re-activate our targets.

Could you describe your research in a nutshell?
Though most genomes contain 20–30% of membrane proteins, to date we only know the atomic structures of about 5,000 membrane proteins (vs. over 170,000 for soluble proteins). Our approach has been to employ and refine a host of specialized crystallization methods, and more recently we have begun cryo electron microscopy studies of the complex of a membrane protein with a large soluble enzyme.

What do you hope to discover with your research?
Central to more than half of all human cancers is the tumor suppressor protein p53. A subset of five single-site mutations in the DNA-binding domain of p53 is found in the vast majority of these cancers (top three are ovarian, lung and colorectal). The research group aims to identify compounds that restore the function of mutant p53, using structural studies.

Infection of the gastric mucosa by *Helicobacter pylori* affects about half the world's population and is the primary cause of gastritis, peptic ulcer disease and gastric cancer. Gastric colonization by *H. pylori* depends on the expression of a proton-gated urea channel and a cytoplasmic urease unique to this pathogen. We have determined the structure of this channel which is essential for *H. pylori* survival in the low-pH medium of the stomach and is thus an attractive cancer target.

The second general area of our research interest is structure-based drug discovery. Structural knowledge is fundamental for understanding the underlying mechanisms involved in cancer onset and proliferation. This therefore aids in the identification and the development of new and more effective drugs. We use a multidisciplinary approach that involves crystallography, nuclear magnetic resonance, cryo electron microscopy and computational techniques to obtain structural and mechanistic insights on numerous systems.

What were your highlights of 2020?
We determined the structure of 1.1 MDa urease by cryo EM to 2.0 Å resolution. These findings, 'Cryo-EM structure of Helicobacter pylori urease with an inhibitor in the active site at 2.0Å resolution' were published in the journal *Nature Communications*. We also generated a 1.68 Å cryoEM structure of *H. pylori* urease with a novel inhibitor.

What are your goals for 2021?
We are working on various other projects, but our lab has unfortunately been shut down for 3 months (as of April 2021) due to an eviction followed by asbestos contamination. We hope operations can re-start as soon as possible so that we can continue with our projects as planned.

Photo: Oda Hveem

Anthony Mathelier

Computational Biology and Gene Regulation Group

The group develops and applies computational approaches to analyse multi-omics data to study the non-coding portion of the genome and better understand gene expression dysregulation in cancers.

Could you describe your research in a nutshell?
Our group's research program aims to improve our understanding of the non-coding portion of genomes by deciphering the cis-regulatory code controlling gene expression. The derived knowledge benefits our capacity to study the mechanisms by which gene expression can be disrupted in cancers. To achieve this goal, our group develops and uses computational approaches and resources to analyze in-house and public multi-omics data.

What do you hope to discover with your research?
We aim to develop computational resources and software tools to assist in understanding and prioritising personal genomic modifications in the DNA fragments that regulate when and where genes are expressed. The ultimate goal is to conduct basic research that will fuse experimental approaches with the parallel development of computational methods to cancer patient samples. This approach has the potential to shed light on the molecular mechanisms underlying transcriptional dysregulation in cancers and deliver new knowledge in cancer research that will benefit cancer patients in the future.

What were your highlights of 2020?
We published several manuscripts as preprints and in peer-reviewed journals, which investigated the impact of different types of somatic cancer alterations (DNA copy number, DNA methylation, non-coding mutations) on carcinogenesis. Furthermore, we expanded our UniBind database providing maps of high-confidence direct transcription factor-DNA interactions now across nine species.

Our group was awarded two competitive grants: a Marie Skłodowska-Curie Scientia Fellowship and a grant from the Norwegian Cancer Society (Kreftforeningen) as part of the Pink Ribbon (Rosa sløfe) campaign. We were also lucky to have three new recruits joining the lab in 2020: Ieva Rauluseviciute, PhD, Vipin Kumar, postdoctoral fellow, and Paul Boddie, software engineer. Finally, the group saw Solveig Klokkerud, Master student, and our first PhD student, Marius Gheorghe, successfully defend their theses.

What are your goals for 2021?
Our awarded funding will allow us to launch new projects to (1) study cancer non-coding mutations in the 3D chromatin context and (2) characterize critical DNA regulatory regions active in patients for breast cancer subtypes.

Janna Saarela

Human Immune Disorders Group

The group operates in two EMBL Partnership institutes (NCMM and FIMM) and focuses on improving the understanding of biological pathways and pathogenic mechanisms behind rare and common immune diseases. At the same time the group is developing innovative tools allowing sharing and analysis of sensitive health data.

Could you describe your research in a nutshell?
The aim of my group's research is to further our knowledge of the disease pathogenesis and mechanisms of human immune disorders, and at the same time learn more about normal immune functions and their regulation. This enables developing better diagnostics and treatment for patients suffering from immune diseases. We also work to develop innovative tools for sharing and analysis of sensitive human health data, which is a prerequisite for strong genome medicine research.

What do you hope to discover with your research?
The group's research focuses on inborn errors of immunity (IEI) and multiple sclerosis (MS) as models for rare and more common immune disorders. To further the understanding of immune deficiencies and dysregulation that underlie rare immune diseases, our objective is to identify novel gene defects causing IEI and to study the functional consequences of the identified mutations to prove the causality and provide understanding on the normal function of the protein in immune defence. We have shown that dysregulation of the two key immunological pathways, the STAT3 and NFKB1 pathways, cause severe human diseases presenting with immune dysregulation and immunodeficiency, and more recently identified novel PID genes with roles in the function of the cytoskeleton.

In our long-term scientific collaboration with the international MS Genetics Consortium and the Nordic MS Genetics network, we have built a comprehensive picture of the genetic landscape of one common autoimmune disease, Multiple Sclerosis. Our ongoing EU project, MultipleMS, aims at developing novel personalised medicine approaches for MS patients by combining the genetic data with multi-omics, clinical, imaging, lifestyle, and DMT response data. We are utilizing the publicly available large-scale multi-omics data, in particular high-resolution maps of immune cells, in combination with multi-omics data from MS patients to identify the biological pathways underlying stratified patient populations.

For the needs of the clinical and multinational research collaborations processing and sharing sensitive data, we are developing innovative tools for anonymizing and synthesizing data. In our recent Novo Nordisk Foundation-funded collaboration project with the University of Copenhagen and Turku University Hospital, we are developing new methods for generating artificial datasets that keep the statistical characteristics of the original data but that do not withhold any of the identifiable characteristics of the original data subjects. Such synthetic data provides an interesting opportunity for working with health data across multiple domains and borders within the existing European GDPR framework.

What were your highlights of 2020?
In 2020 we described two novel IEIs caused by defects in proteins with roles in the function of the cytoskeleton. We identified DIAPH1 deficiency as a novel cause for combined immunodeficiency and mitochondrial dysfunction. We showed that poor T cells activation, proliferation, and impaired adhesion observed in the patients' lymphocytes are likely due to a defect in the reorganization of the cytoskeleton, particularly repositioning the microtubule-organizing centre to the immunological synapse.

In collaboration with research groups from Austria and Sweden, we identified and described a new subtype of familial hemophagocytic lymphohistiocytosis (HLH), caused by inherited mutations in a novel disease-causing gene RhoG. We showed that RhoG mediates docking of cytotoxic granules through interaction with Munc13-4 to the plasma membrane. Thus, RhoG deficiency impairs the process of exocytosis and abrogates the cytotoxic function of cytotoxic T lymphocytes and NK cells.

What are your goals for 2021?
In 2021, we aim to shed light on the function of the ADA2 protein using novel CRISPR-edited cell models. We have previously identified ADA2 as a cause for cytopenias and lymphoproliferation, but very little is currently known about the role of ADA2 in human immunity. We also aim to identify novel causes for a common variable immune deficiency, which is globally the most common form of IEIs and enriched in Finland, and for which only a few causative genes are known. The patient recruitment in our EU-funded MS project has been severely delayed by the Covid-19 pandemic but we expect to finally get into multi-omics data analysis during 2021.

Nikolina Sekulic

Structural Biology and Chromatin Group

Our lab is trying to understand the molecular determinants that ensure chromosomes are equally distributed in daughter cells during cell division.

Could you describe your research in a nutshell?
In any living organism, cells will divide constantly throughout their whole lifetime. Preserving genetic information in each newly made cell is essential for the life and functioning of an organism. Our lab is trying to understand the molecular determinants that ensure chromosomes are equally distributed in daughter cells each time cells divide.

What do you hope to discover with your research?
We hope to reveal the molecular organisation of the centromere. This is a part of the chromosome that plays an essential role during cell division by enabling chromosome attachment to microtubule fibres that in turn pull them into new daughter cells. We hope to better understand how specialized nucleosomes (containing the histone H_3 variant, CENP-A) epigenetically define and organise centromeric locus. Next, we want to understand how the centromere is able to recruit the key mitotic enzyme Aurora B to regulate chromosome attachment to microtubule fibres. Finally, we want to understand how the enzymatic activity of Aurora B is modulated at the molecular level. This knowledge is essential for understanding the basic principles of genetic stability through cell division; a process that is usually altered in cancerous cells.

What were your highlights of 2020?
Progress in 2020 was slower than expected due to the COVID-19 pandemic. However, we still managed to advance many of our projects. We published a review in the journal *Essays in Biochemistry*, where we put our structural work on CENP-A nucleosome in a wider context, summarize existing knowledge in the field and providing our perspectives on the structural organization of the centromere. We were also happy to contribute our biochemical expertise to a study led by the Lopez-Aviles lab. Another highlight was the experimental and computational analysis of mitotic kinase Aurora B. This work was led by Dr. Segura-Peña, a researcher in our lab, in collaboration with Prof. Michele Cascella (Dept. of Chemistry, UiO) and master student Oda Hovet. The study, which will be published later in 2021, has revealed the molecular determinants governing the autoactivation mechanism of Aurora B. This provides new avenues for the design of cancer drugs that target the enzyme. Despite the pandemic, our postdoc, Ahmad Ali Ahmad was able to spend four months at the Cryo-EM facility at Umeå University, working in the group of Linda Sandblad. This has helped both him and the group become more knowledgeable about cryo-EM and how we can use it for our projects.

What are your goals for 2021?
We are very happy that following an evaluation by the NCMM Scientific Advisory Group, (SAB) our group has been extended for the next four years. We are looking forward to continuing to work in this stimulating environment and to keep advancing our projects through local and international collaborations.

Judith Staerk

Stem Cell Group

We hope to discover the key molecular events that underly cell fate decisions in the hematopoietic and neural lineage.

Could you describe your research in a nutshell?
Our research revolves around deciphering the molecular processes that govern human pluripotent stem cell renewal and differentiation, as well as physiologic and malignant hematopoietic and neural development. More recently, based on results obtained from our research, we became interested in the interplay of mitochondrial biogenesis and epigenetics and its impact on cell fate decisions.

What do you hope to discover with your research?
We hope to discover key molecular events that underlie cell fate decisions in the hematopoietic and neural lineage. In addition, we have now started a project using Induced pluripotent stem (iPS) cells from patients suffering from autosomal dominant optic atrophy. We hope to further elucidate the underlying molecular pathways contributing to this disease.

What were your highlights of 2020?
We published two of our major findings and research projects in the journals *Stem Cells* and *iScience*.

What are your goals for 2021?
In 2021, we are aiming to finalize several follow ups from the 2020 publications. Since my time as a group leader at NCMM will come to an end in 2022, I will start looking for a new position to continue my research.

Sebastian Waszak

Computational Oncology Group

We use computational and data-driven approaches to analyze clinical cancer genomes and to better understand the molecular mechanisms that drive development and progression of brain tumors in children and young adults.

Could you describe your research in a nutshell?
My research group uses computational and data-driven approaches to analyze clinical cancer genomes and to improve our understanding of molecular mechanisms that drive development and progression of brain tumors in children and young adults.

Current projects in our group are focused on:

- Precision medicine for patients with diffuse midline glioma
- Origin and spatiotemporal evolution of pediatric brain tumors
- Genetic brain tumor predisposition syndromes

What do you hope to discover with your research?
We hope to improve the diagnosis and therapeutic recommendations for patients with brain tumors, such as diffuse midline glioma. We want to achieve this based on novel computational methods that integrate clinical, molecular, and imaging phenotypes that can be acquired during routine clinical practice.

What were your highlights of 2020?
During the past year, I have initiated my research group, hired my first group members, and developed a new research line that focuses on precision medicine for patients with diffuse midline glioma. We joined the international PNOC DMG-ACT working group which aims to understand drug mechanisms, find new combination therapies, and identify predictive biomarkers of therapy response. We published our first manuscripts and described the genomic landscape of children with diffuse midline glioma that were treated with ONC201, a first-in-class imipridone that is currently in clinical trials for treatment of several cancer types.

What are your goals for 2021?
Together with colleagues from the Children's Hospital Zurich and the ETH Zurich, we have received a Sinergia Consortium Grant from the Swiss National Science Foundation that will help us to harness novel technologies for precision medicine in diffuse midline glioma. Less than ten percent of children diagnosed with these tumours will live for more than two years after their diagnosis, making diffuse midline gliomas the leading cause of death among pediatric brain tumour patients. A child diagnosed with this disease today faces the same dismal prognosis as a child diagnosed decades ago. Our combined team of molecular biologists, genome scientists, and bioengineers will use a genomics-guided pre-clinical approach to identify effective drugs and combinations of drugs that work against this devastating disease.

Servicing a Research Centre:

NCMM's IT, Administration and Core Facilities

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

Information Technology (IT)

NCMM has an in-house IT team of four. The team 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.

Administration

NCMM has a dedicated in-house administration team of eleven. This includes HR, financial, strategic, communications, and research administration support. Also included under administration are an in-house media kitchen, a washing and autoclaving service, a general laboratory manager, and a health, safety, and environment (HSE) coordinator. Some research groups also have their own dedicated laboratory technicians. All these staff provide a vital service that allows the research groups to operate effectively and efficiently.

Core Facilities

NCMM is home to two core facilities; the Chemical Biology Platform and the Zebrafish Facility.

The High-Throughput Chemical Biology Screening Platform
The High-Throughput Chemical Biology Screening Platform offers a range of services to researchers who wish to discover small molecules to probe, explore, and modulate biological systems.

The platform offers all kinds of high-throughput Chemical Biology screening services to academic groups and industry. Chemical Biology High-Throughput Screening (HTS) is the 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 therefore be anything from blocking a specific enzymatic activity, to inducing distinct phenotypes in certain cells. Screening is therefore a standard first step in drug development campaigns.

For further information, contact:
Head of Facility
Johannes Landskron
+47 22 84 05 09
johannes.landskron@ncmm.uio.no

The Zebrafish Core Facility
The Zebrafish core facility offers access to fish housing, breeding and the use of several instruments specific for research on zebrafish.

The zebrafish core facility team can help other researchers without the necessary expertise to perform experiments using zebrafish. The team has experience within aqua culture, fish health, screening and characterization of new lines, GMO, 360° live-imaging of larvae, chemical screening, behavioural 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:
Principal Engineer
Ana Carolina Sulen Tavara
+47 22840542
ana.tavara@ncmm.uio.no

NCMM Alumni

NCMM acts as a greenhouse for young, talented researchers. 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 2020 and 2021, we caught up with some of our former researchers to find out more about what they are working on now.

Group Leader Alumni

Professor Ian Mills

Ian Mills was one of the first group leaders recruited to NCMM. He joined the Centre as head of the Prostate Cancer Research Group in 2010. Ian rotated out of NCMM in 2016 after accepting a permanent position at Queens University, Belfast. Despite leaving Norway, Ian continues to collaborate with many of his previous group members and colleagues. He comments:

"For me, the time and space I was given as a new NCMM group leader was extremely important. I was able to assess my data and make measure decisions about the direction I wanted to take things in. In terms of building my group, I tried to work out what each person wanted to do and did my best to make sure they were given the right opportunities to meet these goals. I have been lucky that everyone I hired in my first years has now ended up working in the field that they wanted to."

Professor Preben Morth

Professor J Preben Morth was one of the first group leaders recruited to NCMM. He joined the Centre from Aarhus University, Denmark, in October 2010. Today he is a Professor at the Technical University of Denmark (DTU) in Copenhagen. He has long-standing collaborations with NCMM, and in 2020 published a paper with one of NCMM's co-founders, Dr. Stefan Krauss. He comments:

"When I joined, NCMM had only recently been established. It was a fantastic opportunity to play a part in building something completely from scratch. I also liked the fact that the role could be extended after the first five years. I and the other new recruits certainly felt very supported by NCMM's SAB (Scientific Advisory Board) at the time, they gave us a lot of leverage to do what we wanted. Ian (Mills) and I were the first group leaders to be recruited, and we started collaborating very early on. It was very helpful to have someone in the same boat as me and who shared some of my research interests. We had different leadership styles but we complemented one another well. It took a while to publish something together, but from the start, we were thinking about how we might work together."

PhD Fellow Alumnus

Dr. Simer Bains

Dr Simer Bains joined the Taskén group at NCMM in 2008 as a researcher. She went on to defend her PhD thesis in 2016. She now works as a clinical oncologist at Oslo University Hospital and Akershus University Hospital, combined with a part-time postdoctoral position in the group of Anne Hansen Ree at Akershus.

She comments: "My research experience from NCMM has been invaluable as a clinician in a fast-moving field such as oncology. A molecular background and an understanding of basic science are crucial to be at the forefront of recent advances in oncology, especially now that next-generation sequencing has become increasing available for cancer patients and is used to direct available treatment options.

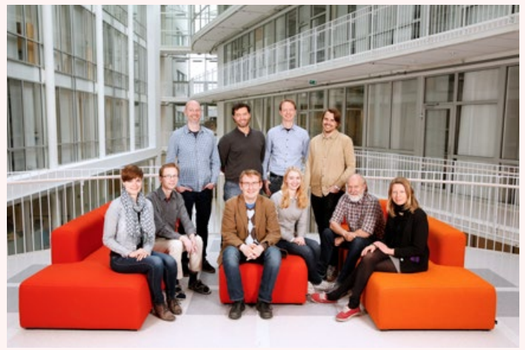
"I was affiliated with Kjetil (Taskén)'s group for almost 8 years, and feel that I almost grew up there. I have made life-long friendships that I hold dearly, and I continue my research collaboration with my supervisor and other collaborators from my time as a PhD-student."

Postdoc Alumnus

Dr. Alfonso Urbanucci

Dr. Alfonso Urbanucci joined the Mills group as a postdoc in 2011. Since leaving NCMM he has started his own group at Oslo University Hospital (OUH).

He comments: "NCMM was an interesting time to be a postdoc because I felt able to steer projects and take advantage of things that might not have been possible in a larger and more established group. Thanks to Ian (Mill)'s guidance and support I was able to start my own project and follow this up relatively independently. Ian (Mills) saw that I wanted to pursue my own project, he gave me the freedom (and support) that I needed to develop in the direction that I wanted. I felt he was extremely good at reading people and their skills and pushing them in the right direction. Having this freedom from the start helped me to be where I am today."



The Mills Group in 2015. Front row L-R: Paula Lindner, Harri Itkonen, Ian Mills, Ingrid Guldvik, Per Seglen, Verena Zuber. Back row L-R: Frank Sætre, Alfonso Urbanucci, Nikolai Engedal, Morten Luhr. Photo: Terje Heiestad

The Morth Group in 2016. (LR) Preben Morth, Carolina Alvadia, Bojana Sredic, Saranya Subramani, Stephanie Ruhland and Johannes Bauer. Photo: Terje Heiestad/NCMM

> For me, the time and space I was given as a new NCMM group leader was extremely important.
>
> Ian Mills

> I have made life-long friendships that I hold dearly, and I continue my research collaboration with my supervisor and other collaborators from my time as a PhD-student.
>
> Simer Bains.

Group Leader Evaluations 2021

Three NCMM research groups extended for a further four years

Following a successful evaluation by NCMM's Scientific Advisory Board (SAB) in March 2021, the NCMM Board decided to extend the groups of Irep Gözen, Nikolina Sekulic, and Anthony Mathelier.

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 three groups' evaluations were based on written dossiers prepared by the group leaders, letters of assessment from external scientific experts within their respective research fields, alongside presentations delivered to the SAB. Due to the ongoing restrictions imposed by coronavirus, the 2021 SAB meeting took place online.

Commenting on the successful evaluations, Professor Janna Saarela, Director of NCMM said:

> I would like to warmly congratulate all three group leaders for a well-deserved extension of their groups at NCMM. They, and their scientific contributions, will be a strong asset to the Centre for the years to come.

NCMM congratulates Drs Gözen, Sekulic, and Mathelier. The Centre looks forward to celebrating more of their future successes as they continue to develop their research programmes at NCMM.

NCMM congratulates group leaders Irep Gözen, Anthony Mathelier and Nikolina Sekulic on their successful evaluations Photo: Oda Hveem

Research Collaborations

Chapter 3

Photo: Nadia Frantsen

From Disease Mechanisms to Precision Medicine

NCMM's overall vision is to improve our molecular understanding of health and disease to facilitate improved medical practice. As a world-class international molecular medicine centre with a translational mind-set, NCMM brings 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 contact 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.

Furthermore, NCMM is the Norwegian node in the Nordic EMBL Partnership for Molecular Medicine. The Partnership includes approximately 60 research groups and teams, with a staff of 600 employees and students across the four national nodes in Oslo, Helsinki, Umeå, and Århus. 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. The Nordic EMBL Partnership was awarded a NordForsk Nordic Hub mobility grant in 2020. This funding will help to further facilitate the sharing of expertise and access to core facilities and infrastructures through lab visits and training courses.

NCMM's ambition is to build nationwide network(s) for translational research to grow expertise in our clinical focus areas, and to ensure access to patient cohorts' data and samples, as well as the sharing of knowledge. We are actively seeking matching hospital environments with whom we can establish strong collaborative teams with core competences in translating basic science algorithms, concepts, and findings to improved clinical practises. Crossing this bridge is a two-way street and requires commitment and effort from both sides.

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.

NCMM Director Professor Janna Saarela

Research Collaborations with Oslo University Hospital

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 the South-Eastern Norway Regional Health Authority (HSØ) and its subsidiary Oslo University Hospital (OUH).

All NCMM translational research group leaders have adjunct positions in clinical or para-clinical departments at OUH. These affiliations help to facilitate clinical collaborations, giving group geaders better access to patient materials, biobanks, and clinical trials. They are also crucial for facilitating translational research. These research collaborations have resulted in a number of joint publications. NCMM group leaders also report on several joint applications for the funding of new collaborative projects.

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

Department of Medical Genetics (OUH)
–
NCMM PIs: J Saarela and A. Mathelier

Department of Haematology (OUH)
–
NCMM PI: J. Staerk

Department of Medical Biochemistry (OUH)
–
NCMM PI: H. Luecke

Department of Pediatric Research, Division of Pediatric and Adolescent Medicine (OUH)
NCMM PIs: E. Haapaniemi and S. Waszak

Research Collaborations with University of Oslo

School of Pharmacy
NCMM PI: C. V. Esguerra

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

Department of Biosciences
NCMM PI: S. Lopez-Aviles

Anthony Mathelier with Vessela Kristensen. Photo: NCMM

> NCMM is a unique centre for Oslo's research environment. The group leaders are selected purely on their excellence and not so much because they work in a particular field
>
> Prof. Kristensen

Case study:

Translating basic research into clinical practice

NCMM group leaders Anthony Mathelier, Marieke Kuijjer, and Sebastian Waszak collaborate on various projects with Vessela Kristensen, head of the Cancer Genome Variation group at Oslo University Hospital (OUS) and Professor at the Department of Medical Genetics.

Through his adjunct position, Dr. Mathelier is embedded within Professor Kristensen's group at OUS, attending her weekly group meetings at Ullevål Hospital when possible. The two groups are currently working together on several projects. These include looking at the non-coding portion of the human genome containing regulatory regions that control when and where genes are specifically activated. The two groups have also recently started to work on a new project, where they will combine the application of state-of-the-art experimental technologies with computational approaches to identify regulatory signatures to improve breast cancer patient stratification. Through this work, they will be able to highlight a specific set of regulatory regions essential for breast cancer cell survival. The hope is that the knowledge derived from this basic research project will help to build better understanding of breast cancer, with the mid-term objective of better stratifying patients and discovering new biomarkers and therapeutic targets.

Discussing her work with NCMM's group leaders, Prof. Kristensen comments:

"NCMM is a unique centre for Oslo's research environment. The group leaders are selected purely on their excellence and not so much because they work in a particular field. This is a huge investment for Norway; these star scientists come from all over the world to work here in Oslo and I think this is wonderful for our research as a whole. Translational medicine needs to be backed up by science and research if it is to be useful. The work of researchers at NCMM, like Anthony (Mathelier), Marieke (Kuijjer) and Sebastian (Waszak), is at the interface of the very latest knowledge and technology available when it comes to computational biology."

Anthony Mathelier adds: "We partner from the very beginning of the projects to maximize the input using each group's specific expertise throughout the progress of the research. This multidisciplinary aspect is key for the future of biology."

NCMM Associate Investigators

NCMM aims to continue and develop its scientific community and knowledge capabilities, through establishing 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. Associate Investigators contribute their expertise in molecular and translational medicine, and support newly recruited young NCMM Group Leaders and earlier-career Associate Investigators through mentoring activities. 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.

Renewal and evaluation of the Associate Investigator network

In 2020, NCMM entered its third five-year period (2020–2024). This resulted in an evaluation of the Associate Investigator network. All existing NCMM Associate Investigators were invited to apply for renewal and a new call was opened in June 2020. Based on applications for renewal, 21 Associate Investigators were re-appointed in the Spring of 2020 and 26 new Associate Investigators were appointed in December 2020. The network now consists of 47 scientists from all over Norway.

As of spring 2021, the NCMM Associate Investigator network consists of the following scientists:

Professor Tero Aittokallio, Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital (newly appointed Fall 2020)

Professor Ole A. Andreassen, Division of Mental Health and Addiction, Oslo University Hospital and Institute of Clinical Medicine, University of Oslo (re-appointed)

Dr. Thomas Arnesen, Department of Molecular Biology, University of Bergen and Department of Surgery, Haukeland University Hospital (re-appointed)

Dr. Magnus Aronsen, Division of Physiology, Institute of Basic Medical Sciences, University of Oslo and Oslo University Hospital (newly appointed Fall 2020)

Dr. Lorena Arranz, Department of Medical Biology, University of Tromsø and Department of Hematology, University Hospital of Northern Norway (re-appointed)

Dr. Charlotte Boccara, Institute of Basic Medical Sciences, University of Oslo (newly appointed Fall 2020)

Professor Yvonne Böttcher, Department of Clinical Molecular Biology, Akershus University Hospital and Institute of Clinical Medicine, University of Oslo (newly appointed Fall 2020)

Associate Professor Simona Chera, Department of Clinical Science, University of Bergen (re-appointed)

Professor Rafal Ciosk, Section for Biochemistry and Molecular Biology, Department of Biosciences, Faculty of Mathematics and Natural Sciences, University of Oslo (newly appointed Fall 2020)

Associate Professor Rune Enger, Institute of Basic Medical Sciences, University of Oslo (newly appointed Fall 2020)

Professor Marianne Fyhn, Section for Physiology and Cell Biology, Department of Biosciences, University of Oslo (newly appointed Fall 2020)

Professor Joel Glover, Institute of Basic Medical Sciences, University of Oslo (newly appointed Fall 2020)

Associate Professor Victor Greiff, Institute of Clinical Medicine, University of Oslo (newly appointed Fall 2020)

Dr. Gunnveig Grødeland, Institute of Clinical Medicine, University of Oslo and Oslo University Hospital (newly appointed Fall 2020)

Associate Professor Nils Halberg, The Department of Biomedicine, University of Bergen (re-appointed)

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 (re-appointed)

Professor Guttorm Haraldsen, Institute of Clinical Medicine, University of Oslo and Department of Pathology, Oslo University Hospital (newly appointed Fall 2020)

Professor Arne Klungland, Department of Microbiology, Division of Diagnostics and Intervention, Oslo University Hospital and University of Oslo (re-appointed)

Dr. Helene Knævelsrud, Institute for Cancer Research, Oslo University Hospital and CanCell, University of Oslo (newly appointed Fall 2020)

Professor Vessela Kristensen, Department of Medical Genetics, Oslo University Hospital and Institute of Clinical Medicine, University of Oslo (newly appointed Fall 2020)

Professor Dirk Linke, Section for Genetics and Evolutionary Biology, University of Oslo (re-appointed)

Dr Alicia Llorente, Institute for Cancer Research, Oslo University Hospital (newly appointed Fall 2020)

Professor Ragnhild A. Lothe, Department of Cancer Prevention, Institute for Cancer Research, Oslo University Hospital and University of Oslo (re-appointed)

Associate Professor Reidar Lund, Section for Chemical Life Sciences, Department of Chemistry, University of Oslo (re-appointed)

Professor Karl-Johan Malmberg, Department of Cancer Immunology, Institute for Cancer Research, Oslo University Hospital and University of Oslo (re-appointed)

Professor Hans-Peter Marti, Department of Medicine, Haukeland University Hospital, University of Bergen (newly appointed Fall 2020)

Professor Emmet McCormack, Department of Clinical Science, University of Bergen (newly appointed Fall 2020)

Dr. Espen Melum, Research Institute for Internal Medicine, Oslo University Hospital and University of Oslo (re-appointed)

Associate Professor June Myklebust, Institute for Cancer Research, Oslo University Hospital and Institute for Clinical Medicine, University of Oslo (newly appointed Fall 2020)

Professor Hilde L. Nilsen, Department of Clinical Molecular Biology, Akershus University Hospital and University of Oslo (re-appointed)

Professor Pål R. Njølstad, KG Jebsen Center for Diabetes Research, University of Bergen and Haukeland University Hospital (re-appointed)

Dr. Lynn Butler Odeberg, University of Tromsø and the Karolinska Institute (re-appointed

Professor Jacob Odeberg, Institute for Clinical Medicine, University of Tromsø and University Hospital of North Norway (newly appointed Fall 2020)

Professor Johanna Olweus, KG Jebsen Center for Cancer Immunotherapy, Department of Cancer Immunology, Institute for Cancer Research, University of Oslo and Oslo University Hospital (re-appointed)

Professor Cinzia Progida, Section for Physiology and Cell Biology, Department of Biosciences, University of Oslo (newly appointed Fall 2020)

Professor Christine Hanssen Rinaldo, Department of Clinical Medicine, University of Tromsø and University Hospital North Norway, (newly appointed Fall 2020)

Dr. Hege Russnes, Department of Pathology and Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital and University of Oslo (re-appointed)

Dr. Even Holth Rustad, Akershus University Hospital and Oslo University Hospital (newly appointed Fall 2020)

Associate Professor Axel Sandvig, Integrative Neuroscience Group, Department of Neuromedicine and Movement Science, NTNU (newly appointed Fall 2020)

Professor Anne Simonsen, Institute of Basic Medical Sciences, University of Oslo (re-appointed)

Professor Rolf Skotheim, Department of Molecular Oncology, Institute for Cancer Research, Oslo University Hospital and University of Oslo (re-appointed)

Dr. Asbjørg Stray Pedersen, Norwegian National Unit for Newborn Screening, Oslo University Hospital and Institute for Clinical Medicine, University of Oslo (newly appointed Fall 2020)

Professor Kjetil Taskén, Institute for Cancer Research, Oslo University Hospital and University of Oslo (re-appointed)

Dr Alfonso Urbanucci, Dept. of Tumor Biology, Institute for Cancer Research, Oslo University Hospital (newly appointed Fall 2020)

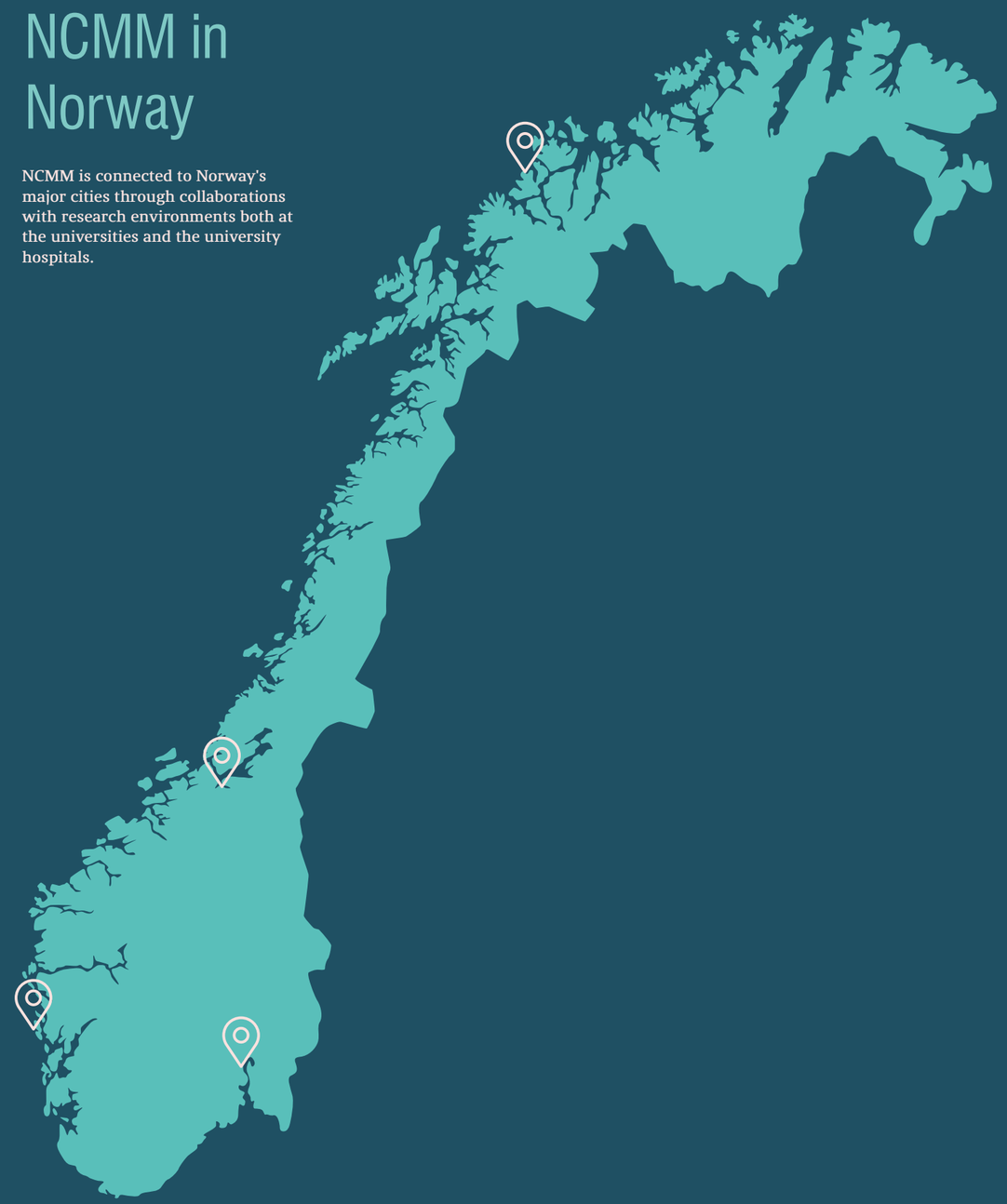
Associate Professor Eivind Valen, Computational Biology Unit, Department of Informatics, University of Bergen (newly appointed Fall 2020)

Dr. Marc Vaudel, Department of Clinical Science, University of Bergen (newly appointed Fall 2020)

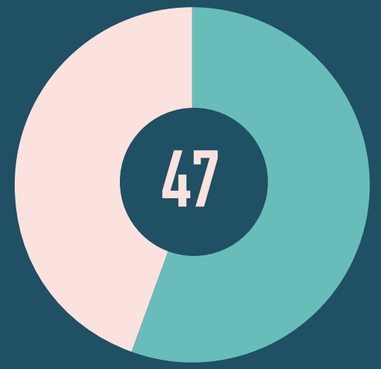
Professor Emre Yaksi, Kavli Institute for Systems Neuroscience/Centre for Neural Computation, Norwegian University of Science and Technology (NTNU) (re-appointed).

NCMM in Norway

NCMM is connected to Norway's major cities through collaborations with research environments both at the universities and the university hospitals.



NCMM Associate Investigators



- 21 NCMM Associate Investigators re-appointed in Spring 2020
- 26 new NCMM Associate Investigators appointed in Fall 2020

Examples of some of the expertise offered by the Associate Investigator network

Omics
Precision Medicine
Drug Delivery
Diabetes
Immunology
T cells
Epilepsy
Bioinformatics
Sleep
RNA Sequencing
Membrane Trafficking
CRISPR-Cas9
Migraine
Thrombosis
Obesity
Computational Biology
Structural Biology
Neurodegenerative Disease
Artificial Intelligence
Epigenetics
Autophagy
Transcriptomics
Virology
Machine Learning
DNA Repair
Cell Biology
Genetics
Neuroscience
Cancer
Gene Expression
Psychiatry
Behavior
Stem Cells

The Nordic EMBL Partnership

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 as well as DANDRITE (Danish Research Institute of Translational Neuroscience) at Aarhus University.

In addition to the Partnership between the Nordic nodes, each of the research centres collaborates 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.

From left: Prof. Inge Jonassen. Photo: Eivind Senneset/UiB, Dr. Line M Grønning-Wang. Photo: RCN, Dr. Jacob Wang. Photo: RCN, Prof. Oddmund Bakke. Photo: UiO

With the next phase of Norway's EMBL membership, I would like to see more interest from early career Norwegian researchers to work at EMBL.

Dr Jacob Wang

Highlights from 2020

Representing Norway at EMBL:
The roles and importance of Norway and its EMBL delegates past and present

The EMBL (European Molecular Biology Laboratory) is regarded as one of the world's leading research institutions. It is also Europe's flagship laboratory for the life sciences.

EMBL is inter-governmental, relying on public research money from its 27 member states. These member states are represented in the EMBL Council; the highest decision-making body of EMBL. The EMBL Council has several responsibilities, including setting the financial framework for the organization and agreeing on its scientific direction. Each decisions requires agreement across all member states. As a member of EMBL since 1985, Norway has traditionally had two EMBL delegates; one administrative and one scientific.

Dr Jacob Wang, a Special Advisor at the Research Council of Norway, was appointed as the EMBL administrative delegate for Norway in 2009 and served in this role until 2020. Dr Wang also served as the Chairman of the EMBL Finance Committee for some years. Dr. Wang worked alongside Norway's scientific delegate, Professor Oddmund Bakke. Professor Bakke served as the scientific delegate from 2012 until 2020. He has first-hand experience of EMBL, having spent two periods there, first as a postdoc in 1988 and then for a sabbatical in 2003. Professor Bakke also served on the EMBL Alumni Council for six years. As Norway does not appoint EMBL delegates directly from the Norwegian government, close collaboration with the Norwegian Ministry of Education and Research is required.

EMBL is world-leading when it comes to molecular biology. Norway has access to all of its outstanding facilities, technologies, and courses. The new EMBL Programme, 'Molecules to Ecosystems' and its focus on oceans, with the TARA Oceans Project, will be very important for Norway given that we are an ocean-nation with important fisheries and a varied ecosystem.

Prof Oddmund Bakke

Norway's membership has helped to establish two important partnerships with EMBL; the Centre for Molecular Medicine Norway (NCMM), and the Sars Centre for Marine Molecular Biology. Both of these centres have adopted the 'EMBL model' for recruitment, and nurture a collaborative and international research environment.

Dr Jacob Wang

EMBL's membership is extremely important for Norway. As Prof. Bakke explains: "EMBL is world-leading when it comes to molecular biology. Norway has access to all of its outstanding facilities, technologies, and courses. The new EMBL Programme, 'Molecules to Ecosystems' and its focus on oceans, with the TARA Oceans Project, will be very important for Norway given that we are an ocean-nation with important fisheries and a varied ecosystem. It will be important for us to be part of this exploration, both for improving sustainability and for understanding how we can best support and exploit our oceans for future generations. It will be exciting to see the new EMBL programme in action and to also see EMBL's achievements under the leadership of the new Director General Edith Heard."

Dr Wang adds: "Norway's membership has helped to establish two important partnerships with EMBL; the Centre for Molecular Medicine Norway (NCMM), and the Sars Centre for Marine Molecular Biology. Both of these centres have adopted the 'EMBL model' for recruitment, and nurture a collaborative and international research environment."

As the role of a delegate is finite, with a maximum of two four-year terms, two new EMBL delegates for Norway were appointed in late 2020. Dr Line Mariann Grønning-Wang, Senior Adviser for Health Research and Innovation at the Research Council of Norway, will now represent Norway as the administrative delegate. The scientific delegate role has been succeeded by Professor Inge Jonassen, a professor at the Department of Informatics at the University of Bergen (UiB), and Director of the Computational Biology Unit, an inter-disciplinary centre including research groups from five different departments at UiB.

Dr. Wang concludes, "With the next phase of Norway's EMBL membership, I would like to see more interest from early career Norwegian researchers to work at EMBL. We have had a few PhD students over the past years, but a Norwegian EMBL group leader would be fantastic!"

NCMM looks forward to working with Dr Grønning-Wang and Professor Jonassen in the future, and wishes to thank Prof. Bakke and Dr. Wang for their great collaboration.

Plamena Markova. Photo: EMBL

International relations and their role in research at EMBL:

Excerpts from an interview with Plamena Markova

The Nordic EMBL Partnership has proven that it can take the concept of EMBL and implement it nationally with great success, and also that you can do life science research at a fast pace.

Plamena Markova joined EMBL in 2011. In November 2020, she was appointed as the organisation's Head of International Relations.

Could you give a brief outline of the new EMBL Scientific Programme 2022–2026, and how the Nordic EMBL Partnership can support EMBL here?

The new programme is called 'Molecules to Ecosystems'. It was conceived by our Director General and was unanimously endorsed by our member states in November 2020. The programme aims to go beyond the lab and understand life in its natural context. EMBL will offer the mechanistic understanding of molecular biology and will build as many bridges as possible to other disciplines and other member states to bring all this knowledge together. The partnerships will be critical to this process and we want to use the programme to work together in a more intense and more collaborative and thematically relevant way. This year are working to get the approvals needed for the financial framework.

The Nordic EMBL Partnership has proven that it can take the concept of EMBL and implement it nationally with great success, and also that you can do life science research at a fast pace.

Usually, it takes years to see concrete applications of discovery-driven research but in the case of the Nordic EMBL Partnership, and our other partnerships, we see something developing so fast. The partnerships have this incredible ability to empower young talent, as EMBL does, and then multiply it. Emmanuelle Charpentier and her research and achievements are of course a great example of this.

The Nordic EMBL Partnership Agreement is due to be renewed in 2023, what do you hope for the Nordic EMBL Partnership in the next Agreement period?

Going forward, I would like to see more connections between the nodes and with EMBL in terms of exchanges, shared projects and themes. I think it's time that we capitalise more on the potential for collaboration and, in doing so, help to attract and train even more excellent people.

The clinical and translational side of the Nordic EMBL Partnership is positive for EMBL; it reaches other disciplines and brings more complementary expertise for the whole EMBL ecosystem. I would also like to see the Partnership propagating EMBL more in the national system and helping more people to connect to EMBL. I think we also have a lot of potential when it comes to attracting competitive funding.

We want to see EMBL opening a new era for life science research – one that is highly collaborative, ambitious, societally relevant and can deliver impact for both human and planetary health. We can only do this hand in hand with our partners and Member States, and I am convinced that the Nordic EMBL Partnership will play an important role in helping build bridges and delivering groundbreaking scientific discoveries.

The clinical and translational side of the Nordic EMBL Partnership is positive for EMBL; it reaches other disciplines and brings more complementary expertise for the whole EMBL ecosystem.

Nordic EMBL Partnership annual meeting 2020:

Connecting with colleagues to increase future interactions

The Nordic EMBL Partnership for Molecular Medicine held its 10th annual conference in slightly different circumstances to previous years. MIMS (Laboratory for Infection Medicine Sweden) hosted the conference from their home in Umeå. With travel restrictions in place due to COVID-19, the conference moved online in its entirety for the first time. Thanks to some excellent technical organisation from the MIMS team, NCMM researchers were able to join the conference from Oslo. The ease of being able to present and participate online opened up access for both speakers and attendees, with a record 344 people registering for the event; the highest number in the meeting's 10-year history.

The online format also created new opportunities in terms of the meeting's programme, with six keynote talks from leading international scientists and an introduction from EMBL Director General, Edith Heard, where she gave insight into EMBL's future plans. The programme also featured a panel discussion on Open Science, over 40 research presentations from scientists from the four Nordic nodes and EMBL, four online poster sessions where over 50 posters were presented, a YIM (Young Investigators Meeting), and plenty of opportunities to interact with peers and colleagues thanks to breakout sessions and a 'Meet the Speakers' Slack channel.

Professor Oliver Billker opening the Nordic EMBL Partnership Conference 2020 in Umeå. Photo: Nora Lehotai/MIMS

News and Events

Chapter 4

NCMM PhD Defences 2020

Paula Lindner

Paula defended her thesis titled, “Role of endoplasmic reticulum Ca2+ depletion, the unfolded protein response, and autophagy in thapsigargin-induced cell death” at the Faculty of Medicine, University of Oslo, in May 2020. Paula’s PhD was a joint project between NCMM, UiO, and DANDRITE (the Danish Research Institute of Translational Neuroscience), Aarhus University which is also the Danish node of the Nordic EMBL Partnership. The main goal of the project was to understand the cellular pathways connected to thapsigargin, especially in terms of cell death. The project also examined autophagy as a parallel pathway to this cell death. Paula is now a product manager at Gentian Diagnostics in Moss, Norway.

Marius Gheorghe

Marius defended his thesis titled, “Integrative approaches to study TF-DNA interactions” at the Faculty of Medicine, UiO, in June 2020. Marius’ work was carried out in the group of Anthony Mathelier at NCMM. Marius’ thesis presented the development of new computational methods and resources that are derived from in-depth analyses of experimentally generated data to study gene expression regulation and how it can be disrupted in diseases such as cancer. Marius is now a senior bioinformatician at the Oslo-based bioinformatics company NEC OncoImmunity AS.

Vilte Stonyte

Vilte defended her thesis titled, “Different aspects of the response to environmental challenges in fission yeast: roles of PP2A-B56 and a novel 4E-BP” at the Department of Biosciences, UiO, in October 2020. Vilte carried out her PhD project in the group of Sandra Lopez-Aviles at NCMM. Vilte’s thesis addressed different aspects of cellular stress, with a particular focus on the role of protein phosphatase PP2A-B56. The thesis also identified and characterised a novel fission yeast eukaryotic initiation factor 4E (eIF4E)-binding protein. Vilte is now a postdoctoral researcher in the group of Beata Grallert at the Institute for Cancer Research, Oslo University Hospital.

Julia Weikum

Julia defended her thesis, “Bacterial protein systems at the membrane interface: Structural and biophysical studies of the E.coli adhesion receptor intimin and the magnesium transporter MgtA" at the Department of Pharmacy, UiO, in November 2020. Julia’s PhD project was carried out under the supervision of former NCMM group leader, J. Preben Morth. The project was initiated at NCMM and completed at the Technical University of Denmark. Julia’s project investigated two E. coli proteins, which are involved with the bacterial infection and drug resistance process. Julia is now a development scientist at Gentian Diagnostics.

NCMM News Highlights

1. L-R: Harald Stenmark, Gry Oftedal, Svein Stølen, Andreas Carlson and Irep Gözen. Photo: Lin Xue
2.Some of the artwork on display. Photo: Lin Xue
3. Visitors to the NanoCosmos Exhibition's opening night. Photo: Lin Xue

Gözen Group participates in NanoCosmos contemporary art exhibition

As part of the Oslo Life Science Conference in February 2020, the Gözen group at NCMM exhibited a range of their engaging microscopy images at Oslo's Kunstplass Contemporary Art Exhibition Space. The event was established by the Programmable Cell-like Compartments interdisciplinary research environment at the University of Oslo, which features NCMM's Irep Gözen along with researchers from the fields of Mathematics, Philosophy and Medical Science. The event was opened by UiO Rector, Svein Stølen and also featured speeches from UiO: Life Science director, Carl Henrik Gørbitz, and Irep Gözen.

Linda Sandblad with Ahmad Ali Ahmad at the Umeå Core Facility for Electron Microscopy (UCEM). Photo: Nora Lehotai

NCMM visits Umeå to learn the A-Z of cryo-EM

Ahmad Ali Ahmad is a postdoctoral researcher in the Sekulic group at NCMM. He spent four months with the group of Dr. Linda Sandblad, director of the Umeå Core Facility for Electron Microscopy (UCEM), and MIMS team leader, based at Umeå University, Sweden. Norway currently does not have a cryo-EM facility, however, researchers at NCMM and within the Nordic EMBL Partnership can travel to use facilities at the other Partnership nodes. The Umeå Core Facility for Electron Microscopy (UCEM) is supported by MIMS, which is the Swedish node of the Nordic EMBL Partnership. The visit was funded by a mobility grant from the Research Council of Norway.

The visit was invaluable for Ahmad and the Sekulic group's research, and he is now equipped with the knowledge to take on projects involving cryo-EM from start to finish. The visit was also hugely beneficial for Ahmad's learning. He comments, "Aside from the benefits to my project and the group's research, the time in Umeå was a fantastic opportunity for me and for my career."

Sebastian Waszak appointed as group leader in precision medicine

Dr. Waszak joined NCMM in March 2020 from the EMBL in Heidelberg, Germany as head of the Computational Oncology group. Dr. Waszak's research group focuses on large patient populations, multi-modal data integration, and computational methods to study rare cancers. Commenting on his recruitment, Dr. Waszak said: "NCMM provides a fantastic environment to establish a research program in computational oncology. The dual affiliation with Oslo University Hospital will facilitate translation and clinical collaborations."

NCMM group leader, Irep Gözen, appointed as Biophysical Society Ambassador

In January 2021, it was announced that Dr. Gözen had been selected as an ambassador as part of the Biophysical Society's (BPS) inaugural Ambassador Programme. Dr. Gözen became the first ambassador from the Nordic countries for the prestigious international scientific society. Dr. Gözen comments, "Aside from being great recognition for me and my group, the role is also great recognition for the standard of research taking place at NCMM and the Faculty of Medicine, UiO. Being an ambassador will help to build on Norway's status within the biophysics community and provide the Biophysical Society with great opportunities for networking and collaboration in the region. Being an ambassador will also mean that I am involved in outreach activities, such as organising meetings and events in the Nordic region and regularly contributing to the BPS' blog – all things that I'm really looking forward to doing."

BPS Ambassadors are selected from amongst the Society's members. They come from all over the globe and represent biophysics, scientific research, and information in their home countries for a three-year term. Dr Gözen was selected alongside scientists from Turkey, Argentina, the UK, Canada, Portugal, India, and Malaysia.

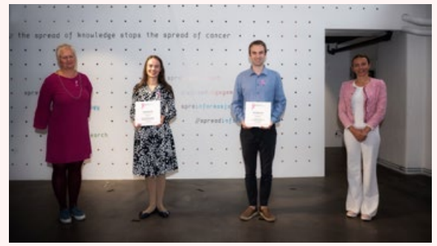
NCMM Funding Successes

Kreftforeningen funding awarded to NCMM group leaders

Marieke Kuijjer and Anthony Mathelier were both awarded funding in August 2020 as part of the Rosa sløyfe ('Pink Ribbon') campaign by the Norwegian Cancer Society (Kreftforeningen). With NCMM's focus on growing its precision and systems medicine research, and building research groups that can interact and complement one another, it is very positive for the Centre to have received two of the Rosa sløfe grants in the same call. The funding further demonstrates the importance of this area of research to wider society.

Anthony Mathelier was awarded funding for his project 'Cis-regulatory signatures for improved identification and stratification of breast cancer subtypes.

Marieke Kuijjer was awarded funding for her project 'Personalised large-scale omics networks to identify new regulatory subtypes and targeted therapies in breast cancer.



(L-R) Ellen Harris Utne (Chair of the Norwegian Breast Cancer Society), Marieke Kuijjer, Anthony Mathelier, and Ingrid Stenstadvold Ross (Secretary General, Kreftforeningen). Photo: Kreftforeningen

Young Research Talent award for Marieke Kuijjer from the Research Council of Norway (Forskningsrådet)

Forskningsrådet

Dr. Kuijjer was awarded 7.9m NOK for her project, 'Large-scale personalized omics networks to model the disruption of gene regulation in cancer' as part of the Research Council of Norway's annual call for 'Free project support' (FRIPRO) in December 2020. Describing the project aims, Dr Kuijjer comments:

"In the past decade, new technologies like next-generation sequencing have been widely applied to study cancer. This research has led to a greater understanding in terms of gene expression, mutations, and methylation profiles in a wide variety of cancer types. However, these approaches have not had a major impact on patient outcomes. We know that to understand what drives cancer and to identify new biomarkers and therapeutic targets, we need to better integrate multiple 'omics data types."

The project ultimately aims to advance the field of precision network medicine, improve the understanding of gene regulation in cancer, and identify the underlying biological mechanisms that drive cancer development, progression, and how the disease presents in different patients.

The Kuijjer group. Photo: Ping-Han Hsieh.

NCMM group leader part of an international consortium awarded funding from the Swiss National Science Foundation (SNSF) for precision medicine in pediatric brain tumours

FNSNF
Swiss National Science Foundation

An international and multidisciplinary team of researchers, clinicians, and data scientists was awarded a Sinergia grant from the Swiss National Science Foundation (SNSF) to improve treatment for children with aggressive brain tumours. The new Sinergia consortium involves principal investigators from the DMG/DIPG Center Zurich, at University Children's Hospital, the ETH Zurich, and the Centre for Molecular Medicine Norway (NCMM) and aims to harness novel technologies for precision medicine in pediatric diffuse midline glioma (DMG) and diffuse intrinsic pontine glioma (DIPG). NCMM group leader, Dr. Sebastian Waszak, is part of the consortium and his role will involve charactersing the genomic and epigenomic landscape of preclinical DMG models and develop a computational drug repurposing strategy for DMG/DIPGs.

Scientia Fellowships awarded for postdoc projects

Eight postdocs were awarded Scientia Fellowships to undertake research projects in six different research groups at NCMM. Scientia Fellows is a trans-national fellowship program at the Faculty of Medicine, University of Oslo that is co-funded by the EU. It allows postdocs to undertake projects within the field of health life sciences, with an aim to support innovation activities and to bring together academia, hospital and industry in cross-sectoral collaborations. Our Scientia Fellow postdocs are:

- Wietske van der Ent (Netherlands), Esguerra Group
- Nail Fatkhutdinov (Russia), Haapaniemi Group
- Javier Gutierrez (Spain), Luecke Group
- Vipin Kumar (France), Mathelier Group
- Daniel Osorio (Colombia), Kuijjer Group
- Annikka Polster (Germany), Kuijjer Group
- Inga Põldsalu (Estonia), Gözen group
- Marta Sanz-Gaitero (Spain), Luecke Group

In addition, several NCMM group leaders now have positions open as part of the third and final call for new Scientia Fellows.

NCMM Research Highlights

Review from the Sekulic group:

CENP-A nucleosome – a chromatin-embedded pedestal for the centromere: lessons learned from structural biology

The Sekulic group shared their findings and insight in an in-depth review article in the journal *Essays in Biochemistry*. The centromere is a chromosome locus that directs equal segregation of chromosomes during cell division. A nucleosome containing the histone H3 variant CENP-A epigenetically defines the centromere. The group summarized their findings from recent structural biology studies, including several CryoEM structures, that contributed to elucidate specific features of the CENP-A nucleosome and molecular determinants of its interactions with CENP-C and CENP-N. Based on their findings, the group proposes a role of the CENP-A nucleosome in the organization of centromeric chromatin beyond binding centromeric proteins.

CENP-A nucleosome—a chromatin-embedded pedestal for the centromere: lessons learned from structural biology. Ahmad Ali Ahmad and Nikolina Sekulic. *Essays Biochem* (2020) 64 (2): 205–221. https://doi.org/10.1042/EBC20190074

Research from the Esguerra group

provides novel insight into the disease mechanisms of Dravet syndrome

Dravet syndrome is a severe and devastating type of epilepsy that occurs in children and infants, and is very difficult to treat. A better understanding of the mechanisms within neuronal cells that promote disease progression could potentially improve our ability to treat this syndrome, which would have a substantial impact on patients and their families.

To address this need, the Esguerra group at NCMM have been working towards a better understanding of the earliest cellular defects driving the onset of seizures (the so-called 'epileptogenic period'). In a scientific article, published in the journal *Epilepsia*, the group analyzed brain development in a new zebrafish model of the Dravet syndrome, enabling new insight into the mechanisms associated with disease development.

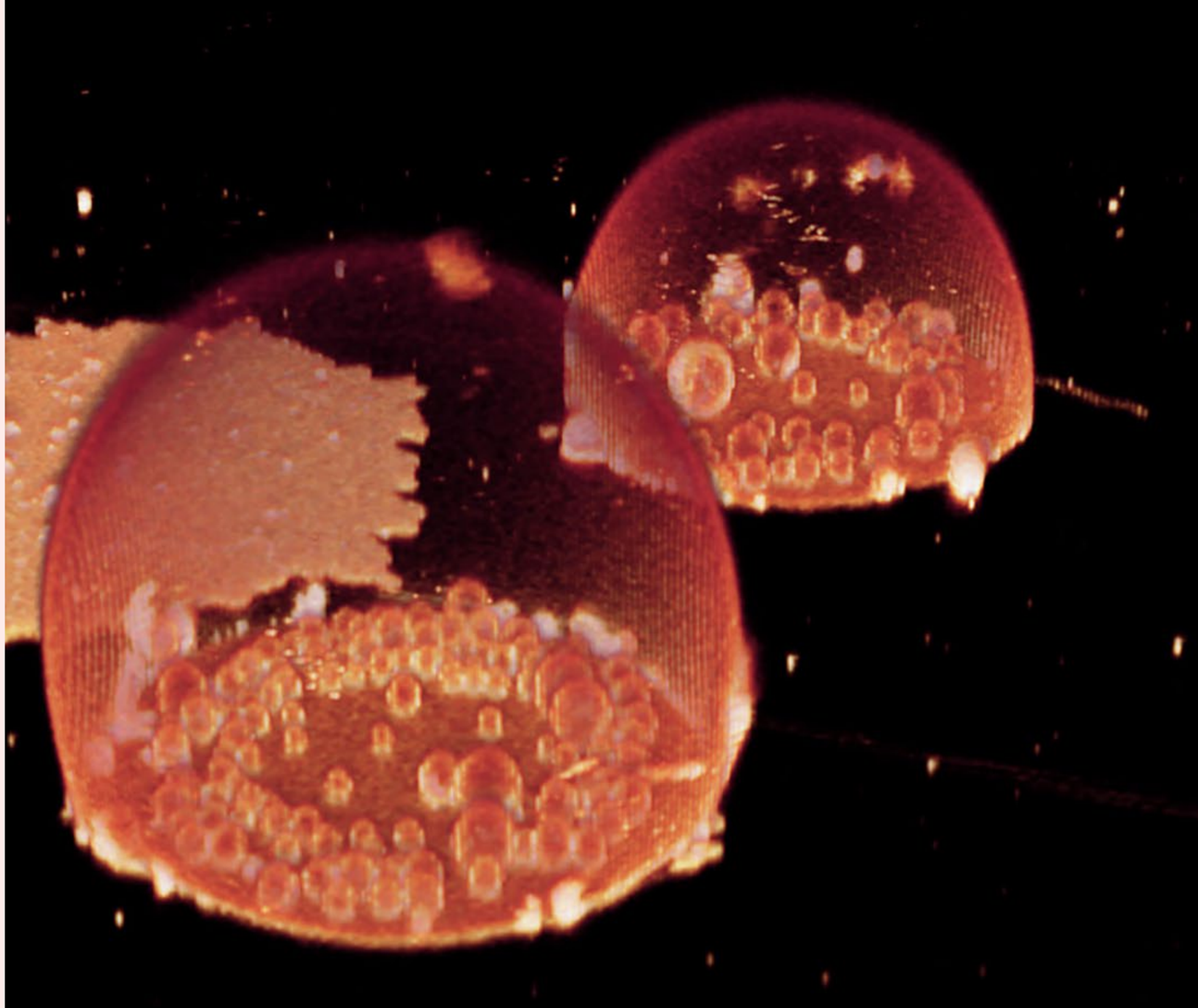
New insights into the early mechanisms of epileptogenesis in a zebrafish model of Dravet syndrome, Tiraboschi et al., *Epilepsia* 2020. doi: 10.1111/epi.16456

Earth's first cells could have made specialized compartments

New research by PhD student, Karolina Spustová, and colleagues in the Gözen Group at NCMM provides evidence that the "protocells" that formed on the earth's surface around 3.8 billion years ago, could have had specialized bubble-like compartments. The research has found that these compartments are thought to have formed spontaneously and encapsulated small molecules, forming "daughter" protocells. Protocells are simple, cell-like structures that formed from non-living elements, and are thought to have appeared before bacteria and single-celled organisms.

The research was presented by Karolina Spustová at the 65th Annual Meeting of the Biophysical Society. (Wednesday 24 February 2021). The research was originally published in January 2021 in the journal *Small:* **Subcompartmentalization and Pseudo-Division of Model Protocells.**

"Protocells" containing bubble-like compartments formed spontaneously on a mineral-like and encapsulated fluorescent dye. Image: Karolina Spustova

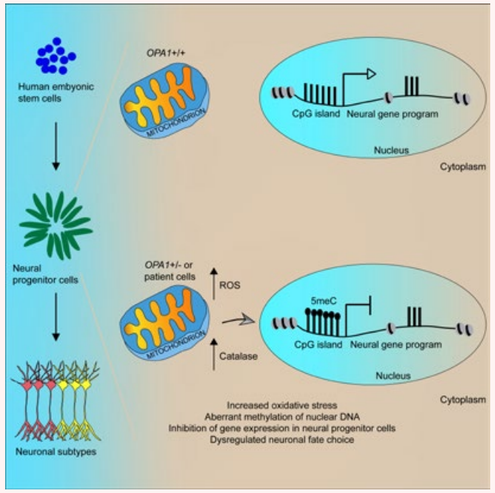


Heating up the debate: New findings in protocell evolution

A publication from the Gözen group in the journal *Small* was featured by Advanced Science News. The paper, 'Rapid Growth and Fusion of Protocells in Surface-Adhered Membrane Networks' was highlighted by the journal's editor, Valentina Lombardo, in an in-depth feature. The article discusses the findings from the Gözen group, in particular how the research has identified new pathways that could have led to the formation and development of primitive cells on early Earth.

Rapid Growth and Fusion of Protocells in Surface-Adhered Membrane Networks, E. S. Köksal et al., *Small* (2020). (DOI: 10.1002/smll.202002529)

The FIMM NGS Sequencing Lab. Photo: FIMM



Graphical abstract, Optic Atrophy 1 Controls Human Neuronal Development by Preventing Aberrant Nuclear DNA Methylation. Caglayan et al.

Staerk group publishes in iScience

The Staerk group's research examined the role of optic atrophy 1 (OPA1), a GTPase at the inner mitochondrial membrane involved in regulating mitochondrial fusion, stability, and energy output. OPA1 is crucial for neural development, and inactivating mutations in OPA1 are linked to human neurological disorders. The group used genetically modified human embryonic and patient-derived induced pluripotent stem cells to reveal that OPA1 haploinsufficiency leads to aberrant nuclear DNA methylation and significantly alters the transcriptional circuitry in neural progenitor cells (NPCs). The group's data reveals that OPA1 controls nuclear DNA methylation and expression of key transcription factors needed for proper neural cell specification.

Optic Atrophy 1 Controls Human Neuronal Development by Preventing Aberrant Nuclear DNA Methylation. Caglayan. S et al *iScience* (23) 101154 2020.

How a single gene defect can affect both neuronal development and immune system function

Reserchers in Finland and Norway have discovered a gene defect that causes a novel inherited immune deficiency. The same gene, DIAPH1, has been previously shown to cause SCBMS syndrome, a rare genetic disease associated with severe brain development defects. The results help to gain a deeper understanding of the biology of SCBMS and will provide a basis for the exploration of new therapeutic approaches.

The novel immunodeficiency syndrome caused by pathogenic variants in the DIAPH1 gene was identified by an international collaborative study led by Professors Janna Saarela (NCMM Director) and Johanna Uusimaa, Professor of Paediatric Neurology at the University of Oulu, and a co-senior author of the study. DIAPH1 has been previously associated with a rare inherited neurodevelopmental disorder characterized by early-onset epileptic seizures, severely delayed psychomotor development, cortical blindness, and microcephaly, also referred to as SCBMS.

Loss of DIAPH1 causes SCBMS, combined immunodeficiency and mitochondrial dysfunction. Kaustio et al., *Journal of Allergy and Clinical Immunology* 2021 DOI: https://doi.org/10.1016/j.jaci.2020.12.656

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NCMM Publications 2020

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NCMM Publications 2021

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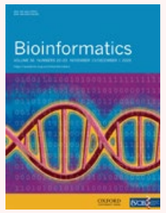


Press items for NCMM 2020 & Q1 2021

Press items 2020

Gözen Group research

- Forskning.no, February, *Viser frem kunst fra cellenes mikroverden*
- ScienceNorway, February, *From the laboratory to the gallery: Microscopic images of our cells as art*
- UngForskning.no, February, *Cellene våre blir kunst I mikroskopet*

Esguerra Group research

- ScienceNorway, January, T*he fish helping scientists to understand the human brain*
- Philippine Canadian News, January, Science: *Dr Camila Esguerra is world's leading researcher on epilepsy*
- UiO homepage, January, *Fisken som hjelper forskerne å skjønne menneskehjernen*
- Oslo University Hospital news, January, *Fisken som hjelper forskerne å skjønne menneskejernen*
- Forskning.no, February, *Fisken som hjelper forskerne å skjønne menneskehjernen*
- Dagbladet, November, *Meninger: Denne kan sikre beredskapen*

Press items 2021

Waszak Group research

- Parents Daily News, January, *International Consortium Awarded SNSF Sinergia Grant to Improve Treatment for Pediatric Brain Tumors*
- ETH Zurich, January, *International Consortium Awarded SNSF Sinergia Grant to Improve Treatment for Pediatric Brain Tumors*
- Institute of Neuroinformatics, January, *Neurotechnology Group is part of a new SNSF grant*
- Barnekreftforeningen, January, *31 millioner til forskning på barn med aggressive hjernesvulster* (and shared to group's 38,322 Facebook followers)
- Dagens Medisin, January, *Får 31 millioner til å forske på barnekreft*

Gözen Group research

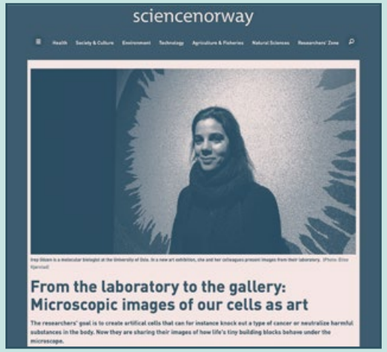
- Biophysical Society Newsroom, February, *Evidence That Earth's First Cells Could Have Made Specialized Compartments*
- Science Daily, February, *Evidence that Earth's first cells could have made specialized compartments*
- Inside Science, February, *Surface Bubbles Could Have Evolved into Earth's First Cells*

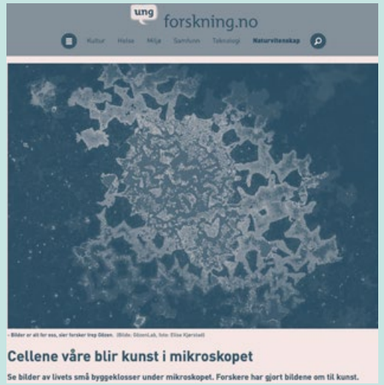
Press items 2021

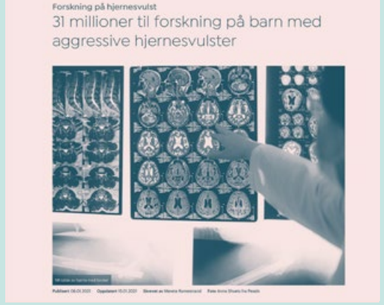
- The Times Hub, February, *Proof that Earth's first cells might have had specialized compartments*
- Earth.com, February, *Scientists find new clues in the mystery of how life began on Earth*
- ScienMag, February, *Evidence That Earth's First Cells Could Have Made Specialized Compartments*
- BioEngineer.org, February, *Evidence that Earth's first cells could have made specialized compartments*
- ScienceNewsNet, February, *Evidence That Earth's First Cells Could Have Made Specialized Compartments*
- NewsMedical, February, *New study sheds light on specialized compartments exhibited by Earth's single-celled ancestors*
- NewsBuzz18, February, *Evidence That Earth's First Cells Could Have Made Specialized Compartments*

NCMM

- Nature.com, March, *Why industry internships can be your 'golden ticket' to a prosperous career* (featuring comments from Esguerra group PhD student, Nancy Saana Banono







NCMM Press cuttings from 2020 and 2021

NCMM Operations

Chapter 5

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 and 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.

Chair:

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

NCMM Board:

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.

Members:

Professor Ola Myklebost,
UiB University of Bergen
(national representative)

Professor Bente Halvorsen,
Oslo University Hospital

Members:

Professor Arne Klungland,
Faculty of Mathematics and
Natural Sciences, UiO

Members:

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

Professor Hilde Nilsen,
Faculty of Medicine, UiO and
Akershus University Hospital

BOARD

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)

Deputy Members:

Professor Arnoldo Frigessi,
Faculty of Medicine, UiO
–

From the Chair of the NCMM Board, Jens Petter Berg:

It has been a pleasure to continue in my role as Chair of the Board of NCMM. Under the leadership of Professor Saarela, the Centre has enjoyed a busy and successful year and, as NCMM enters its third five-year period of operations, I look forward to seeing Professor Saarela's vision for the Centre in action. In particular, her focus on precision and systems medicine, and the building of a more team-orientated research culture, will ensure that NCMM continues to act as a greenhouse for young, talented scientists, attracting the brightest and best international recruits.

In support of this, I wish to welcome NCMM's most recently recruited group leader, Dr. Sebastian Waszak, who will lead the computational oncology group. Dr Waszak's research will complement the Centre's existing expertise, and his focus on large patient populations, multi-modal data integration, and computational methods to study rare cancers will also support our continued focus on translational molecular research and precision medicine. Furthermore, I would like to congratulate Dr Camila Esguerra on a successful evaluation and the subsequent renewal of her group for a further four years.

As Chair of the Board, I am very grateful for the collaboration and support from The Research Council of Norway, The South-Eastern Norway Regional Health Authority and the University of Oslo. Finally, I would also like to take this opportunity to thank the NCMM Board for their ongoing collaboration; I look forward to seeing what the next five years will bring for the Centre.

Current Chair of the NCMM Board,
Professor Jens Petter Berg
Photo: Øystein Horgmo, UiO

SAB | Scientific Advisory Board

Chair:

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

SAB (Scientific Advisory Board):

The SAB consists of six internationally-renowned scientists

Members:

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

Professor Olli Kallioniemi
Director SciLifeLab
Karolinska Institute
Stockholm, Sweden

Members:

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

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

Dr. Judith Zaugg Head of the 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 March 2021, when three NCMM group leaders were evaluated and recommended for extension. Due to the ongoing pandemic, this meeting was held online.

Nadia Frantsen

NCMM funding

2020 & Q1 2021

After an external evaluation in 2018, funding for a third five-year period (2020–2024) was secured.

Core funding

Core funding 2020

54,5 MNOK

Extramural Funding Sources

Extramural funding 2020

30 MNOK

The 2021 overview below is an estimate.

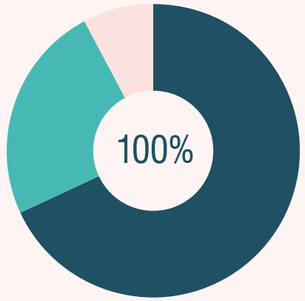
Core Funding

The core funding for NCMM in the period 2020–2024 is 54.5 mNOK 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

NCMM extramural funding, in the form of grants to the group leaders and other competitive funding, increased steadily from 7 mNOK in 2010 to 42 mNOK in 2015. Due to rotations of research groups, the level of competitive funding fluctuates somewhat depending on research groups rotating out and in. For 2020, the amount of extramural funding obtained by the research groups reached 30 mNOK. This funding includes grants from the Research Council of Norway, the Norwegian Cancer Society, South-Eastern Norway Regional Health Authority, the European Commission, competitive grants at UiO and private foundations and organizations such as the World Cancer Research and Barncancerfonden.

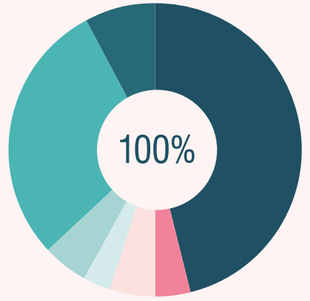
Core funding 2020



NCMM Core Funding Sources 2020 (%)

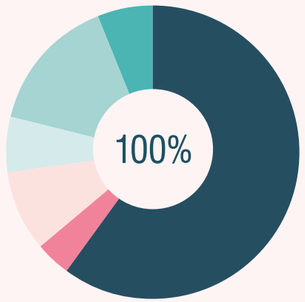
UIO 68 RCN 24 HSØ 8

Extramural Funding Sources



Extramural Funding Sources 2020 (%)

46 8 29 5 3 5 4



Est Extramural Funding Sources 2021 (%)

60 6 15 6 9 4

RCN
UIO
HSØ
The Norwegian Cancer Society
Other national grants
EU grants
Other International grants

Personnel statistics

for NCMM in 2020 and Q1 2021

Year 2015	Year 2016	Year 2017	Year 2018	Year 2019	Year 2020
68 people	73 people	103 people	109 people	107 people	103 people

NCMM Staff

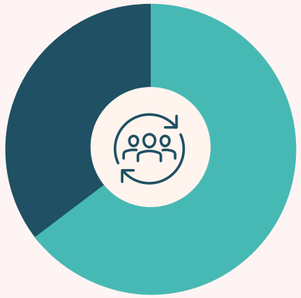
Numbers of staff since 2017 represent NCMM after the merger with the Biotechnology Centre of Oslo. For 2018, the research group of former NCMM Director Kjetil Taskén was included. This research group moved to Oslo University Hospital in November 2018. Two new research groups joined NCMM in 2019 and a third research group was recruited in March 2020. These groups will grow in size over the coming years.
–

NCMM Staff according to type of employment

02	11	09	18	20
NCMM Director / Assistant Director	Group Leaders –	Senior researchers –	Postdocs –	PhD fellows –

There were 103 people employed at NCMM in 2020

NCMM Staff Gender Balance



APPROX. 2/3
of the NCMM staff are female

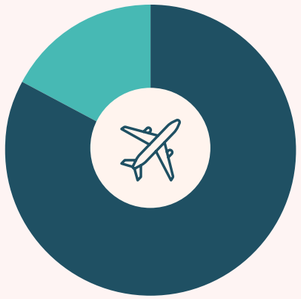
Female 68% Male 32%

NCMM Group Leader Gender Balance

8 FEMALES
amongst the 11 group leaders

Female 73% Male 27%

NCMM International staff –



83/103 STAFF
members are of international origin

International 83% Norwegian 17%

NCMM Staff according to type of employment

11	11	11	04	08
Students –	Engineers –	Administration –	IT –	Other personnel –

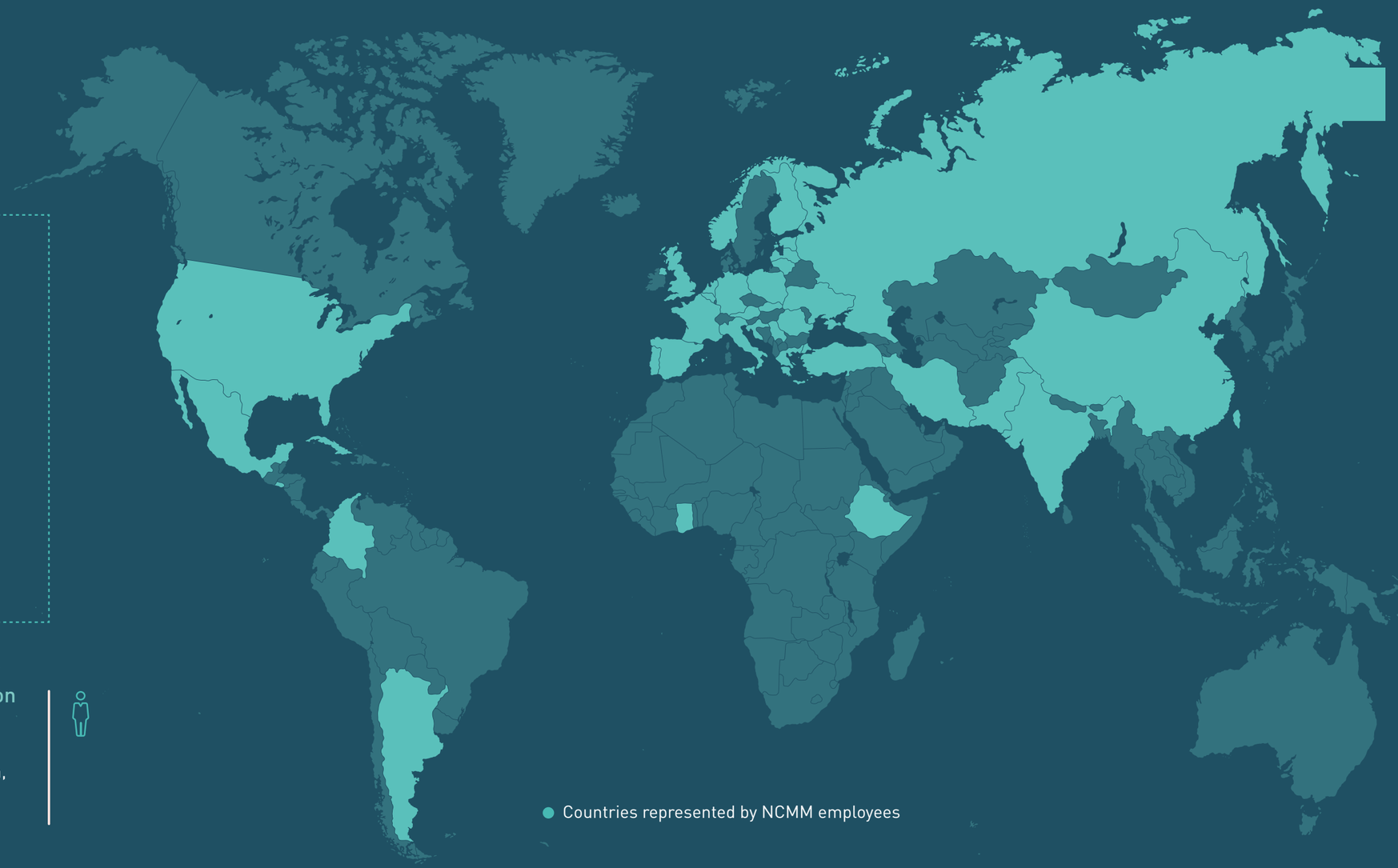
Staff distribution

As of Q1 2021, NCMM staff from

36 NATIONS ARE REPRESENTED

83 PEOPLE

in total are from outside of Norway



Countries represented by NCMM employees

01 people
Countries represented by one person
Argentina, Belgium, Cuba, El Salvador, Estonia, Ghana, Greece, India, Iran, Italy, Latvia, Mexico, Pakistan, Romania, Slovakia, Taiwan, The Czech Republic, Ukraine

02 people
Colombia, Croatia, Etiopia, Lithuania, Portgugal, Russia, Serbia, The Netherlands, UK
–

03 people
Turkey, USA

04 people
Poland
–

05 people
China, Finland
–

07 people
Spain
–

08 people
France
–

12 people
Germany
–

Personnel at NCMM 2020 & Q1 2021

NCMM's staff includes researchers of all levels, from Master students to group leaders and senior researchers. All administrative and support functions, including laboratory operations and core facilities, are provided by a dedicated in-house administration department.

Director and administration

Director
Janna Saarela

Assistant Director
Hartmut Luecke

Chief Administrative Officer
Ingrid Kjelsvik

Head of Section for Research Strategy, Communication and International Relations
Elisa Bjørgo

Financial Officers
Mette Kvernland
Anita Elisabeth Skolem

Human Resources Officer
Nina Modahl

Communications Officer
Annabel Darby

EATRIS Coordinator
Anita Kavlie

Higher Executive Officer
Carlos Romeo Rodriguez

IT Team
George Magklaras *(Head of IT)*
Gang Cheng
Melaku Tadesse
George Marselis *(until September 2020)*
Harold Gutch *(from October 2020)*

Administrative Officer
Berit Barkley *(until August 2020)*
Larissa Lily *(from December 2020)*

Laboratory Operations and Core Facilities

HSE Coordinator
Liv E. Alver Bjørland *(until September 2020)*
Karen-Marie Heintz *(from September 2020)*

General Lab Manager
Edna Xi Hu *(from September 2020)*

Moving Coordinator
Sandra Kunz *(August 2020–February 2021)*

Senior Engineer
Gladys Tjørhom

Research Technician
Luis Alberto Quintero Linares

Chemical Biology Platform
Johannes Landskron *(Platform Manager)*
Eirin Solberg *(HTS Scientific Officer, Screening & Robotics)*
Alexandra Gade *(HTS Scientific Officer, Screening & Chemistry)*
Maria À. Jimenez Sigstad *(Head Bioinformatician, from January 2021)*
Bojana Sredic *(from January 2021)*

Zebrafish Core Facility
Camila V. Esguerra *(Core Facility Leader)*
Ana C. Sulen Tavara *(Head Engineer & Fish facility manager)*
Alejandro Pastor Remiro *(Fish Facility Technician)*

Research groups

Human Immune Disorders Group

NCMM Group Leader
Janna Saarela

Head Engineer / Lab manager
Monika Szymanska

PhD Fellow
Johanna M. Lehtonen *(from November 2020)*

Group members based at FIMM
(Institute for Molecular Medicine Finland, University of Helsinki)
https://www2.helsinki.fi/en/researchgroups/human-immune-disorders/people

Stem Cell Group

NCMM Group Leader
Judith Staerk

Postdoctoral Fellows
Adnan Hashim
Artur Cieslar-Pobuda
Safak Caglayan *(until March 2020)*
João Santos

Computational Biology and Gene Regulation Group

NCMM Group Leader
Anthony Mathelier

Researchers
Jaime Abraham Castro Mondragón
Roza Berhanu Lemma

Postdoctoral Fellow
Vipin Kumar

PhD Fellows
Rafael Puig Riudavets
Ieva Rauluseviciute *(from April 2020)*

Software Engineer
Paul Boddie *(from March 2020)*

MSc Students
Solveig M. Knoph Klokkerud *(until July 2020)*
Kim Brunel *(from September 2020)*
Agathe Chabassier *(from December 2020)*

Structural Biology and Drug Discovery Group

NCMM Group Leader
Hartmut Luecke

Research Scientist
Eva Cunha

Principal Engineer
Rasma Gutsmite *(from August 2020)*

Postdoctoral Fellows
Javier Gutierrez
Marta Sanz Gaitero
Joel Benjamin Heim

PhD Fellows
Flore Kersten
Mateu Montserrat Canals *(from February 2020)*

Precision Pediatrics and Gene Editing Group

NCMM Group Leader
Emma Haapaniemi

Head Engineer
Monika Szymanska

Postdoctoral Fellow
Nail Fatkhutdinov *(from October 2020)*

PhD Fellows
Ganna Reint
Zhuokun Li
Katariina Aino Inkeri Mamia
Pavel Kopcil *(from October 2020)*

MSc Students
Frida Høsøien Haugen *(from January 2021)*
Julia Halang *(from February 2021)*

Computational Oncology Group

NCMM Group Leader
Sebastian Waszak *(from March 2020)*

Head Engineer
Sandra Kunz *(from February 2021)*

Researcher
Martin Burkert *(from February 2021)*

Research Assistant
Frida Moi *(from January 2021)*

Guest Researcher
Javad Nazarian *(from May 2021)*

Student
Maëlle Caroff *(June to September 2021)*

Cell Cycle Regulations Group

NCMM Group Leader
Sandra Lopez-Aviles

Head Engineer
Mari Nyquist-Andersen *(until March 2021)*

Research Scientists
Ruth Martîn Martîn
Marina Portantier

Postdoctoral Fellow
Shixiong Wang

PhD Fellow
Vilte Stonyte *(until November 2020)*

Chemical Neuroscience Group

NCMM Group Leader
Camila Vicencio Esguerra

Head Engineer
Ana C. S. Tavara

Postdoctoral Fellows
Kinga Aurelia Gawel
Wietske van der Ent

PhD Fellows
Nancy Saana Banono
Elham Shojaeinia
Nastaran Moussavi *(shared with School of Pharmacy, from March 2019)*

Research Technicians
Alejandro Pastor Remiro *(from March 2020)*
Karolina Kirstein-Smardzewska (from February 2020)

MSc Students
Linus De Witte *(January 2020 – June 2020)*
Hellen My Ky Lam *(from August 2020)*
Daarathy Pathmanathan Sellathurai *(from August 2020)*

Structural Biology and Chromatin Group

NCMM Group Leader
Nikolina Sekulic

Principal Engineer
Stine Malene Hansen Wøien

Research Scientist
Dario Segura-Pena

Postdoctoral Fellows
Ahmad Ali Ahmad
Saranya Subramani

Research Assistant
Mira Dombi *(until October 2020)*

MSc Student
Oda Selvåg Hovet *(until September 2020)*

Bionanotechnology and Membrane Systems Group

NCMM Group Leader
Irep Gözen

Postdoctoral Fellows
Inga Põldsalu
Thomas Aga Legøy *(October 2020 until January 2021)*

PhD Fellows
Elif Köksal
Karolina Spustova
Aysu Kucukturhan Kubowicz
Lin Xue
Annie Stephenson (NSF GROW Fellow from Harvard University) *(January – August 2020)*

MSc Students
Ingrid J. Schanke *(from January 2020)*
Maivizhi Thiyagaraja *(from August 2020)*

Computational Biology and Systems Medicine Group

NCMM Group Leader
Marieke L. Kuijjer

Postdoctoral Fellows
Tatiana Belova
Annikka Polster *(from February 2020)*
Daniel Osorio *(from April 2021)*

PhD Fellows
Ping-Han Hsieh
Romana T. Pop *(from November 2020)*
Debora Meijer *(co-supervised with the Bovée Group at Leiden University, from November 2020)*

Research Assistant
Genís Calderer *(June-August 2020)*

MSc Student
Giulia Schito *(from August 2020)*

BSc Student
Shanna Schneidewind *(From May 2021)*

Membrane Transport Group

PhD Fellow
Julia Weikum *(until November 2020)*

Autophagy Team

PhD Fellow
Paula Szalai *(until May 2020)*

Visiting Group from UiT: Stem Cell Aging and Cancer

Group Leader
Lorena Arranz
Postdoctoral Fellow
Marko Ristic

Research Assistant
Vincent Cuminetti

Photo: John Hughes

NCMM CO-FUNDERS:

UiO : University of Oslo

The Research Council of Norway

HELSE SØR-ØST

NORDIC EMBL PARTNERSHIP FOR MOLECULAR MEDICINE:

FIMM
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Nordic EMBL Partnership for Molecular Medicine

MIMS
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Nordic EMBL Partnership for Molecular Medicine

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Centre for Molecular Medicine Norway
Nordic EMBL Partnership for Molecular Medicine

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

EMBL
European Molecular Biology Laboratory

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NATIONAL AND INTERNATIONAL COLLABORATORS:

ESFRI

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European infrastructure for translational medicine

VISITING ADDRESS:
Centre for Molecular Medicine Norway,
Oslo Science Park, Gaustadalléen 21,
0349 Oslo, Norway

POSTAL ADDRESS
Centre for Molecular Medicine Norway, Nordic EMBL
Partnership for Molecular Medicine, University of Oslo,
P.O. Box 1137 Blindern, NO-0318 Oslo, Norway

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