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NCMM - Centre for Molecular Medicine Norway

Annual Report NCMM 2021







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Introduction from the Director

Dear colleagues, friends and supporters, it is my great pleasure to welcome you to the 2021 NCMM Annual Report. 2021 was proven again to be an unusual year, with most of society still experiencing disruption due to the COVID-19 pandemic and NCMM needing to move out of half of our office and lab space due to a building project in the Oslo Science Park. Despite the repeated disruptions, NCMM continued to do great scientific research and the past year brought with it many achievements to be proud of. With the challenges behind us and Norway opening up again in the first quarter of 2022, there is an air of optimism about the year ahead. I wish to extend my sincere gratitude to our staff and supporters for their continued determination towards our shared scientific goals.

We are now halfway through our third five-year period (2020-2024) and many developments are underway as NCMM continues to grow in strength. Three NCMM group leaders were evaluated in 2021 and renewed for a second 4-year period (Dr Nikolina Sekulic, Dr Anthony Mathelier and Dr Irep Gözen). Furthermore, Dr Sandra Lopez-Aviles rotated out to an Associate Professor appointment in the Department of Biosciences, UiO after ten years at NCMM.

NCMM has continued to implement the recommendations of the SAB (Strategic Advisory Board) 2021 report. In line with this, NCMM recruited two new group leaders in early 2022. Dr Charlotte Boccara brings with her extensive experience in neurobiology and sleep research, and Dr Biswajyoti Sahu will join NCMM with wide-ranging expertise in cancer research and gene regulation. I'm sure you will join me in giving them both a very warm welcome to NCMM! NCMM has also continued to strengthen its translational links through the recruitment of more clinician scientists, and we have a call open for group leaders with expertise in Artificial Intelligence and Machine Learning. NCMM has been in the process of developing our strategy and vision for the next strategic period. A key aspect of this will involve further strengthening the precision medicine thematic platform to enable interdisciplinary collaboration across NCMM and its national and international partners.

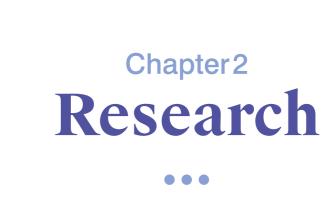
Early 2022 EMBL launched their next five-year strategic programme 'molecules to ecosystems'. It is an ambitious and thought-leading programme, which aims to push the boundaries of molecular life science through studying life in the context of our rapidly changing environment. In addition to this, the Nordic EMBL Partnership for Molecular Medicine agreement will be renewed for another 10 years in 2022. NCMM is thrilled to play a role in this journey of innovative scientific discovery and looks forward to the interdisciplinary collaboration that this will allow. This will create many training, education and work opportunities to life science researchers based in Norway. NCMM is aiming to hold more outreach activities over the coming years to raise awareness of the opportunities EMBL offers.

Our strategic activities are driven by our determination to push our understanding of molecular mechanisms of health and disease further and to translate our scientific findings into improved patient outcomes. Our groups have worked hard to produce great science and we look forward to continuing to work together to affirm NCMM's position as a leader in molecular medicine research.

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Professor Janna Saarela Director, NCMM





Welcome to:

Dr Charlotte Boccara, **Group Leader for Precision Medicine**

Dr Charlotte Boccara joined NCMM as a group leader in April 2022 and is heading the Systems Neuroscience & Sleep group.



Photo: Oda Hveem







The Boccara group. L-R: Solomiia Boccara, Ela Babursah and Lina Okinina. Photo: Oda Hveem

Dr Boccara is a neuroscientist by training. She completed her PhD in the Moser lab at the Norwegian University of Science and Technology (NTNU), after which she became a Postdoctoral Researcher at the Institute of Science and Technology in Austria, followed by a Research Associate position at King's College London. Funded by a Young Research Talent grant from the Research Council of Norway in 2019, she has led the project "Sleep, Cognition and Development" at the Institute of Basic Medical Sciences (IMB, UiO).

Dr Boccara's current research program consists of three main projects. The first one is centred on the role of sleep in healthy cognitive development. The second is the development of new wireless brain probes.

Finally, the third received support from a RCN synergy grant shared between IMB (Phillipe Collas, Nolwenn Briand, Charlotte Boccara) and the Department of Physics at UiO (Ørjan Martinsen) to investigate the links between poor sleep during adolescence and the likelihood of developing metabolic disorders, such as diabetes or obesity. The translational potential of these three lines of research is a key motivation for Dr Boccara:

"Our goal is not only to demonstrate which mechanisms occurring during sleep are necessary for our health but also to identify physiological markers that could help us to diagnose early signs of abnormal sleep function, and thus open new avenues for therapeutics."

In her first 5-year period at NCMM, Dr Boccara hopes to put her lab on the map of sleep research, developing tools to monitor and manipulate brain activity. She also plans to strengthen the translational aspect of her team, establishing collaboration with Oslo University Hospital.

Dr Boccara was attracted to NCMM by the aura of excellence, the framework to boost her team's potential and the opportunity for translational projects through NCMM's hospital collaborations. She also looks forward to collaborating scientifically with other groups at NCMM, as well as training young scientists to develop their skills.

"It is an exciting time to do research in neuroscience. Technological innovations

"Our goal is not only to demonstrate which mechanisms occurring during sleep are necessary for our health but also to identify physiological markers that could help us to diagnose early signs of abnormal sleep function, and thus open new avenues for therapeutics"

are constantly pushing the envelope of what we can do. Actually, an important part of my work is technical development. As such, we were just awarded a grant from the Research Council to design new wireless brain probes, together with SINTEF and IMB (Torkel Hafting)."

Commenting on the appointment, Professor Saarela says:

"We are extremely happy to welcome Dr Boccara as a new member of the NCMM team. Her impressive expertise in neuroscience will perfectly complement NCMM's focus on tackling fundamental biological questions with potential for applications to precision medicine. The translational impact of her research is a significant attraction for us"

Welcome to:

Dr Biswajyoti Sahu, Group Leader for Precision Medicine

Dr Biswajyoti Sahu will join NCMM as a group leader in September 2022 and will be joining us from the University of Helsinki, Finland.



Photo: University of Helsink

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Dr Sahu is a molecular biologist by training with expertise in functional cancer epigenomics, using genomewide multi-omics approaches to study transcription factors in malignant gene regulation. Dr Sahu received his PhD from the University of Helsinki on androgen-receptor signalling in prostate cancer, followed by a postdoctoral training with Professor Jussi Taipale at the University of Helsinki and University of Cambridge, taking a systems biology approach to study cellular transformation and human gene regulatory elements. Since 2019, Dr Sahu has led his independent Enhancer Biology group as a Principal Investigator in the Applied Tumor Genomics program of the Faculty of Medicine at the University of Helsinki, studying transcription factors and reprogramming of the non-coding

regulatory genome in human cancers.

At NCMM, his group will focus on the molecular mechanisms of our regulatory genome. Commenting on his hopes for the first five years of his appointment, Dr Sahu says, "I hope that within the first five years, I am able to make new discoveries with translational impact about the role transcription factors have in human cancers, using my integrative functional genomics approach from *in vivo* cellular models to patient materials. The goal is also to develop new methods and tools that can be useful for the wider research community."

Commenting on his appointment as a group leader at NCMM, Dr Sahu says: "Being a group leader allows me to expand and propagate my ideas in understanding the molecular mechanisms of our regulatory genome. It also gives me

the opportunity to take the tradition of teaching and learning forward by training young researchers in high-quality research for continuation of science."

Commenting on the appointment, Professor Saarela says: "We are delighted to welcome Dr Sahu as a new member of the NCMM team. His deep expertise in functional cancer epigenomics and high throughput biological assays will generate results that have a direct impact on NCMM's priority to strengthen our position as a national centre for molecular medicine with a translational focus."



Group photo

NCMM Group Leaders

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



Chemical Neuroscience Group



Photo: Oda Hveem

Irep Gözen

Bionanotechnology and Membrane Systems Group



Photo: Oda Hveem

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Could you describe your research?

We use the zebrafish to model neuro-developmental disorders (NDD), to understand the early mechanisms underlying nervous system diseases and to determine how and when to target these best with therapeutics.

What do you hope to discover?

Our overarching aim is to uncover how various brain insults, whether caused by genetic mutations, tumours, or environmental toxicants, alter the developing brain and how this leads to disease.

What potential impact could your research have on society?

We have established several zebrafish lines carrying patient-specific mutations. So far, the models that we are studying recapitulate aspects of the human disorder quite well and we are excited to use these models for larger scale drug screens soon, as part of a personalized medicine approach. We have also come to the realization that the zebrafish model is well-suited for identifying drugs (both FDA/EMA approved and drug candidates), with disease modifying activity.

What were your highlights of 2021? Our paper describing the early mechanisms underlying Dravet syndrome, landed in the top ten most cited papers published in the journal Epilepsia for 2020-2021! Since Epilepsia is regarded as the top journal in the field of epilepsy research, we are very happy that our paper was so well received.

My PhD student, Nancy Banono successfully defended her doctoral thesis. We were happy and grateful that the public lecture and thesis defence could be done in person (not digitally) and that we could celebrate Nancy's career milestone properly!

We performed a pilot screen using gut microbial and brain-derived metabolites isolated by a collaborator based in Sweden and found quite a few of them to be bioactive in our zebrafish seizure and behavioural assays.

We identified a unique neuronal phenotype in a new NDD model that we established and have been characterizing. It is surprisingly different from what we had observed and reported previously in our zebrafish model of Dravet syndrome. This indicates a possible novel mechanism underlying the epilepsy syndromes associated with this genetic model.

What are your goals for 2022?

Our top priority is to finally get various manuscripts published! Currently, we

have 6 manuscripts in revision, and we are hoping that we can continue now with our research at the same level of productivity we had prior to the COVID pandemic.

Our newly funded EU project, "ROBO-FISH" is underway, and we aim to successfully establish brain tumour cell xenografting and imaging in zebrafish, both manually and robotically.

We will also continue our drug screens on newly established and validated genetic epilepsy models, with a specific focus on disease modification – i.e., altering the course or onset of the disease, not just acute seizure inhibition

Finally, we are excited to start a new collaboration on developing zebrafish "avatars" for pediatric brain cancers, in collaboration with Sebastian Waszak and his team.

"Our overarching aim is to uncover how various brain insults alter the developing brain and how this leads to disease."

Could you describe your research?

Our research programs aim to understand the biophysical and materials science aspects of complex biological problems, which involve lipid membranes. We bring together biomembranes with solid interfaces as well as with micro- and nanotechnology, and observe the unique membrane interactions with high resolution microscopy. In all of our research lines, the common key structure is the membranes positioned on nano-engineered solid surfaces.

What do you hope to discover?

We would like to understand (1) the exact role of surfaces in emergence of life on the early Earth, (2) how cells perceive interfaces and physically migrate on them, (3) how certain organelles, e.g. the ER, form and remodel themselves. (4) We also would like to develop membrane-based robust point of care assays, leading to unique technology for rapid non-invasive testing.

What potential impact could your research have on society?

We are trying to answer universal questions such as how life began. This is considered as one of the 10 big pending questions in science today. It is a fundamental question which most individuals, even those without specialized knowledge, most likely have previously thought about. Another project focuses on biosensor development for rapid non-invasive testing to eliminate specimen-based tests that are transferred to and performed in a medical laboratory.

What were your highlights of 2021?

2021 was a productive year; we published six papers reporting on very interesting research results, one making it to the journal's front cover.

Two PhD students from my laboratory, Elif Köksal and Karolina Spustova, graduated successfully in 2021 and in 3 years sharp. They published great papers and got very positive reviews on their thesis by international experts, followed by excellent disputations.

Our master's student Ingrid Jin Schanke successfully defended her thesis and passed with the highest grade. She is the leading author of a paper stemming from her master's thesis work which is currently under review.

I received two major grants from the Research Council of Norway, one individual and one collaborative award in which I am the project leader. Total raised funding in 2021 was 37 million NOK.

"Our research programs aim to understand the biophysical and materials science aspects of complex biological problems, which involve lipid membranes."

We attended our first physical meetings after a long break due to the pandemic, first the European Biophysical Society Meeting in Vienna, Austria in July, and the International Biomechanics Workshop in Tøyen Hovedgård in Oslo where I was among the organizers.

What are your goals for 2022?

Our primary goal is to continue performing research and report our findings in high-impact publications. We are in the process of expanding our team right now and have several positions available in 2022. I have a PhD student and a master's student graduating this year from my group. It has been a great journey to be their main advisor, observing them to become gradually independent; I look forward to their graduations in 2022!

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Precision Pediatrics and Gene Editing Group



Photo: Oda Hveem

Marieke Kuijjer

Computational Biology and Systems Medicine Group



Photo: Oda Hveem

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Could you describe your research?

We work on developing new therapies for monogenic immunological diseases. 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?

We aim to develop efficient and safe ways to edit genomes of T cells and hematopoietic stem cells and are open to developing efficient editing tools to other primary cell types as well.

What potential impact could your research have on society?

We hope that the new gene editing approaches will make cell therapies substantially easier and cheaper to develop and manufacture. This would make them available to larger patient groups in wider geographic regions.

What were your highlights of 2021?

We published a research article "Rapid genome editing by CRISPR-Cas9-POLD3 fusion" in eLife journal. Furthermore, we received substantial funding from both the Research Council of Norway and the Norwegian Cancer Society. One of our master students, Frida Haugen, also completed her master thesis and received a perfect grade.

What are your goals for 2022?

We are currently recruiting new master students, PhD students and a senior scientist. Thanks to the funding secured, our group is going to expand substantially, and we are looking forward to meeting new colleagues and expanding our research projects. We are also looking forward to Ganna Reint's PhD defence, which will be the first one in our group!

"We aim to develop efficient and safe ways to edit genomes of T cells and hematopoietic stem cells, and are open to developing efficient editing tools to other primary cell types as well."

Could you describe your research?

We believe that the clinical phenotypes we observe in cancer cannot be adequately defined by individual genes, but that we instead should consider the underlying network of regulatory interactions between multiple different biological components. Our research focuses on developing computational tools that help us map and analyse such interactions in so-called genome-wide gene regulatory networks for individual cancer patients.

What do you hope to discover?

We hope that the novel approaches we develop can help identify drivers of cancer development, progression, and heterogeneity in several cancer types and potentially pan-cancer. Through this, we aim to find new, clinically relevant ways of stratifying disease, as well as potentially targetable alterations in cancer.

What potential impact could your research have on society?

Our research could have an impact on the way we classify disease and suggest potential new targets for cancer treatment. Some of our tools can be used to analyse other types of networks and have, for example, been applied to study microbiota co-occurrences. Applications outside of biology are also possible, and thus, our approaches could have a wide range of impact.

What were your highlights of 2021?

One of our core applications of network analysis in cancer was published in Cancer Research. This was a large collaborative project involving multiple group members and collaborators, which gave us the opportunity to make new connections and combine our strengths to produce great science. The group also expanded - we were joined by Daniel Osorio (postdoctoral fellow), Genís Calderer (research assistant), and Shanna Schneidewind (summer student). Romana Pop started as a PhD student in April. Giulia finished her Master's project and will be joining us as PhD student in 2022. Finally, we got multiple projects awarded, including a Marie Skłodowska-Curie Scientia Fellowship, funding through the Joint Design of Advanced Computing Solutions for Cancer program (US DoE and NCI/NIH), a Familien Blix Fond grant, four collaborative projects with NCMM Associate Investigators and with young researchers from the Arctic University of Norway.

"We hope that the novel approaches we develop can help identify drivers of cancer development, progression, and heterogeneity in several cancer types and potentially pan-cancer."

What are your goals for 2022?

More Network Zoo animals are under development—we hope to release these in 2022. We also started several wetlab collaborations to validate results from our analyses and hope to get new results to combine with and strengthen our computational work. Through our newly funded projects, we will focus on expanding our tools to single-cell and spatial transcriptomics data, with a new postdoc joining the group. Giulia will start her PhD in 2022 and will help strengthen our breast cancer focus.

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Cell Cycle Regulations Group



Photo: Oda Hveem

Hartmut Luecke

Structural Biology and Drug Discovery



Photo: Oda Hveem

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Could you describe your research?

We use a genetic model organism, fission yeast, to investigate the 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?

Our main focus lies on the role of protein phosphatases regulating vents 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 2021?

I started as an Associate Professor at IBV (Department of Biosciences) at the University of Oslo on the 1st of December 2021. I am continuing with the research that I have built up over the last nine years. Moreover, I'll continue to concentrate on cell signalling and cell cycle progression, as well as gene programmes and transcription. In terms of my group, Marina Portantier will come with me, and we will also hire a PhD student and, eventually, I hope to recruit several Master students.

"I started as an Associate Professor at IBV (Department of Biosciences) at the University of Oslo on the 1st of December 2021. I am continuing with the research that I have built up over the last nine years"

Could you describe your research?

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?

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 lowpH 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.

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Computational Biology and Gene Regulation Group



Photo: Oda Hveem



Could you describe your research?

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 analyse in-house and public multi-omics data.

Specifically, our focus lies within the following main lines of research: (i) develop computational tools and resources to model and map genome-wide transcription factor (TF)-DNA interactions; (ii) characterize somatic cis-regulatory alterations that alter gene regulatory networks in cancer cells; (iii) decipher patient-specific cis-regulatory activity to provide cisregulatory signatures and onco-enhancers in breast cancer subtypes.

What do you hope to discover?

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 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 potential impact could your research have on society?

We observe different clinical behaviours between breast cancer patients in response to the same treatment regime. Hence, it is critical to stratify patients to provide them with optimal personalized clinical treatment options. Current strategies rely on the expression of gene panels for patient stratification. Nevertheless, studies recurrently showed the importance of cancer alterations occurring outside of genes, specifically in regulatory regions that act as gradual regulatory switches to express genes at the correct time, in the correct tissue, and at the correct intensity. Unfortunately, these regulatory regions have been relatively understudied, particularly in the context of cancer patients. Our goal is to better characterize these regulatory regions to identify regulatory signatures specific to breast cancer subtypes with the goal to improve breast cancer patient stratification and highlight new biomarkers and therapeutic targets. Such a new classification could be crucial for clinical management and clinical trials and will provide means for a more effective approach targeting the molecular drivers of patients individuals' cancer.

What were your highlights of 2021?

One of the main highlights of 2021 was the renewal of our Computational Biology & Gene Regulation group for a final four years after evaluation by international scientific experts and the NCMM Scientific Advisory Board. I would like to acknowledge here the fantastic contributions from the people in the group over the years. They bring together diverse scientific backgrounds and cultures and their dedication and excitement for science has made our past successes possible and will allow for more to come.

Moreover, our group published 6 manuscripts in 2021. Finally, we are happy that

Katalin Ferenc, PhD student, and Dina Aronsen, lab researcher, joined the group on our new project to characterize critical DNA regulatory regions active in patients for breast cancer subtypes.

What are your goals for 2022?

Our continued main goal is to provide an optimal working environment for the trainees to develop their skills, in line with their career goals. This will result in delivering on our ongoing scientific projects. Moreover, we will continue to develop the wet-lab part of our group with the implementation of a new experimental assay in Oslo.

"The ultimate goal is to conduct basic research that will fuse experimental approaches with the parallel development of computational methods to patient samples."

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Human Immune Disorders Group



Photo: Oda Hveem



Could you describe your research?

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?

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 the mechanisms 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 nor-

mal function of the protein in immune defence. By analysing whole-exome and RNA sequencing data of undiagnosed IEI patients, we have recently identified *DIAPH1*, *RHOG* and *IKZF2* as novel causes of severe human diseases presenting with immune dysregulation and immunodeficiency. Analysis of the gene defects provided new knowledge of their roles in the function of the cytoskeleton, release of cytotoxic granules by lymphocytes, and T cell activation and differentiation, respectively.

In our long-term scientific collaboration with the International MS Genetics Consortium (IMSGC), we have built a comprehensive map of the genetic landscape of Multiple Sclerosis. Currently, 236 variants have been confirmed to increase susceptibility to MS. Our ongoing EU project, MultipleMS, aims at developing novel personalised medicine approaches for MS patients by combining the genetic data with multiomics, 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 multiomics 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 in Finland, 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 2021?

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 to the plasma membrane. Thus, RhoG deficiency impairs the process of exocytosis and abrogates the cytotoxic function of cytotoxic T lymphocytes and NK cells.

We also identified *IKZF2* as a novel cause for a combined immunodeficiency and immune overactivation. In collaboration with research groups from the University of Helsinki, we showed that loss-of-function mutation in IKZF2 led to reduced expression of the encoded protein Helios and was associated with chronic T cell activation and increased production of pro-inflammatory cytokines. The patients also presented with severely reduced numbers of circulating MAIT cells.

What are your goals for 2022?

In 2022, 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. With partners of the Multiple MS EU project, we also aim to identify novel omics based profiles enabling subgrouping MS patiens for improving prediction of disease prognosis and allowing more targeted treatment selection. We also expect to report the first genetic variants associated with disease progression in our ongoing collaboration with IMSGC.

"Our objective is to identify novel gene defects causing inborn errors of immunity 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."

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Structural Biology and Chromatin Group



Photo: Oda Hvee

Judith Staerk

Stem Cell Group



Photo: Oda Hveem

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Could you describe your research?

In any living organism, cells divide constantly throughout their whole lifetime. Preserving genetic information during each cell division is essential for functioning and identity of the organism. Our lab is trying to understand the molecular determinants that ensure chromosomes, carriers of genetic information, are equally distributed in daughter cells each time the cells divide.

What do you hope to discover?

We want to understand how the centromeric chromatin, which is a constitutive part of the chromosome, differs from the rest of the chromatin. We are working towards elucidating the complete structural architecture of the centromeric chromatin, including all known centromeric proteins and underlining DNA sequences. Next, we want to understand how the centromere is recruiting the key mitotic enzyme, Aurora B, to regulate chromosome attachment to microtuble fibers, and finally how enzymatic activity of Aurora B is modulated at a molecular level. The acquired knowledge is essential to understand the basic principles of genetic stability through cell division, a process that is usually altered in cancerous cells.

What potential impact could your research have on society?

We expect the knowledge from our basic research to help in engineering centromeres for gene therapies and to contribute to a better understanding of diseases connected to cell aneuploidy (cancers and congenital disorders, like Down syndrome).

What were your highlights of 2021, and what are you looking forward to for 2022?

First of all, I am extremely happy that my appointment with NCMM has been extended for another four years after the Scientifc Advisory Board evaluation in March 2021. I am very grateful to all present and past members of the group who have contributed to the success of the lab. Another big prize for our team efforts has been a 12 million NOK grant from the Research Conucil of Norway for our project CENTROchromatin. Together with NCMM funding, this will really help us propel our research for the next four years. Also, a lot of our work is now maturing into publications. A project led by Dario Segura-Peña, revealing a multi-step autoactivation mechanism of Aurora B kinase, is already published in

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

the form of a preprint (currently undergoing peer-review), while results from a project led by Ahmad Ali-Ahmad on the structure of centromeric chromatin are in preparation for publication. Last year was also fruitful for starting several national collaborations involving the use of the hydrogen-deuterium exchange technique that we run as part of the Structural Biology Core Facility. In 2022, we are looking forward to continuing with good work and productive collaborations, and we hope to return to a Covid-free world.

Could you describe your research?

In developmental biology a major interest is to identify the molecular mechanisms that direct cell fate decisions, including how stem cells renew and differentiate into more specialized cell types. Pluripotent stem cells are characterized by their ability to self-renew indefinitely, while retaining the ability to differentiate into any cell type found in the body. Pluripotency and differentiation are tightly regulated through transcription factors as well as epigenetics and metabolism. My groups' research uses human pluripotent stem cells to understand the interplay between mitochondria, the cells' metabolism and gene regulation during stem cell renewal as well as early blood and neuronal cell specification.

What do you hope to discover?

We aim to discover key molecular events that drive stem cell renewal and cell fate decisions in the hematopoietic and neural lineage, both in the physiologic and pathologic setting. We are in particular interested to determine how the availability of metabolites influences mesoderm and ectoderm differentiation, and how mitochondrial fusion and fission defects affect transcriptional regulation and nuclear DNA methylation.

What potential impact could your research have on society?

Understanding the molecular events needed to direct cell fate decisions is crucial to improve current hESC to somatic cell differentiation protocols and to derive functional cell types that could be used for transplantations / regenerative medicine. To date, these protocols are often inefficient or result in cell types that are not fully functional. One ultimate goal in the stem cell field is to derive functional long-term repopulating CD34+ hematopoietic stem cells, which could not only be used for transplantation but also advance studies using mouse xenograft models.

What are your goals for 2022?

I am looking forward to new challenges outside of NCMM since I am finishing my second and final group leader period at the institute in the fall 2022.

"We aim to discover key molecular events that drive stem cell renewal and cell fate decisions in the hematopoietic and neural lineage, both in the physiologic and pathologic setting."

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Computational Oncology Group



Photo: Oda Hveer

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Could you describe your research?

Our group develops computational and experimental approaches to study child-hood brain tumours. Our group's vision is to understand the development of pediatric brain tumours, improve molecular diagnostics using novel technologies, and utilise knowledge gained from cancer genomes in clinical decision making.

What do you hope to discover?

We hope to identify the cellular origin of childhood brain tumours at single-cell resolution, develop novel computational approaches for rapid brain tumour diagnostics, and study clinical cancer genomes within clinical studies for children and young adults with malignant brain tumours.

What potential impact could your research have on society?

Our lab is co-affiliated with the Department of Neurology at the University of California San Francisco (UCSF), and we are now contributing to multidisciplinary pediatric brain tumour boards. Moreover, the Pacific Pediatric Neuro-Oncology Consortium (PNOC) is an international consortium with centres within the United States, Europe, Asia, and Australia, and we and NCMM have recently become

PNOC members. The PNOC network is dedicated to advancing preclinical research and bringing new therapeutics for children with brain tumours into the clinic. In 2021 we finalised a precision medicine trial for children with newly diagnosed diffuse intrinsic pontine gliomas (DIPGs). Comprehensive molecular profiling was performed to assign a therapy plan with up to four FDA-approved drugs based on genomic findings. Such an extensive interventional clinical trial for children with DIPG has not been done previously.

What were your highlights of 2021?

We were able to contribute, along with 200 other authors and editors, to the 5th edition of the World Health Organisation (WHO) Classification of Tumors of the Central Nervous System. The WHO book is the international standard for oncologists and pathologists and serves as a guide for use in the design of studies monitoring response to therapy and clinical outcome. The 5th edition presents a fundamental change in how pediatric central nervous system tumours are classified. For example, pediatric brain tumours are now described separately from adult ones; integrated diagnosis is based on histology and molecular diagnostics, and many new brain entities are included. I

"Our group's vision is to understand the development of pediatric brain tumours, improve molecular diagnostics using novel technologies, and utilise knowledge gained from cancer genomes in clinical decision making."

am excited that our research has contributed to updated sections, diagnoses, and pathogenesis mechanisms on embryonal tumours. We also wrote a new section and introduced ELP1-medulloblastoma as a new genetic tumour predisposition syndrome.

What are your goals for 2022?

We have recently received funding from the US DoD Congressionally Directed Medical Research Program, the Ian's Friends Foundation, and Enterprise Estonia. I am very much looking forward to starting these projects and developing new lines of research that range from digital pathology to studying genomic biomarkers of drug sensitivity.



NCMM Alumni

NCMM operates under the EMBL model and serves as a greenhouse for young, talented researchers within the fields of molecular medicine, biotechnology and translational research. The Centre prides itself on providing an environment that allows all of our staff to develop and grow so that, when they are ready for their next challenge, they are equipped with the experience and skills needed to succeed. Over 2021 and 2022, we caught up with some of our former researchers to find out more about what they are working on now.



The Taskén Group at NCMM in 2015.

Photo: John Hughes

Group Leader alumna

. . .

"NCMM offered me a great start. The generous startup package meant that I could have a lot of freedom to develop my research programme and grow my group as I wished"

Associate Professor Sandra Lopez-Aviles

Dr Sandra Lopez-Aviles has been Head of the Cell Cycle Regulations group at NCMM since 2011. At the end of 2021 she rotated out of NCMM to an Associate Professor position at the Department of Biosciences (IBV), University of Oslo.

Commenting on her successful appointment she said: "NCMM offered me a great start. The generous start-up package meant that I could have a lot of freedom to develop my research programme and grow my group as I wished. It was certainly overwhelming at the start as coming straight from a postdoc to being a group leader is a big change. It's certainly been a steep learning curve. However, it's been a wonderful opportunity, and I've been able to get to know many great researchers through my time at NCMM. It was also very positive to be in the same position as other new group leaders who started at the same time as me. We were all in the same position and so naturally supported one another. Finally, I am also grateful to the NCMM

administration team who always made things run very smoothly; I always felt very supported."



Sandra Lopez-Aviles. Photo: Oda Hveem

Postdoc Alumni

Dr Sigrid Skånland

Dr Sigrid Skånland joined the Taskén group in 2011. She is now Project Group Leader, Lab Leader and Researcher at the Institute for Cancer Research, Oslo University Hospital.

She comments: "At the end of my post-doc period with Kjetil Taskén, in 2014, I was awarded a career fellowship from the Norwegian Cancer Society. This was on a project where the aim was to develop drug sensitivity testing of hematological malignancies to guide precision medicine. This project became the start to what my research is focusing on now, and I am very thankful to Kjetil, who introduced me to this exciting field. During my time at NCMM, I also initiated collaborations that are still central in my ongoing work."

Dr Andrea Cremaschi

Dr Andrea Cremaschi joined the Taskén group at NCMM and the Institute of Cancer Research from 2016 until July 2019. He is currently a Senior Research Fellow at the Singapore Institute for Clinical Sciences (SICS), A* STAR, Singapore.

He comments: "My postdoc allowed me to expand my knowledge of biostatistics and biomedical applications. I benefitted from being able to contribute to the research environment by providing useful analytic insights into data. At NCMM, I was able to focus on the analysis of dose-response data derived from cancer patients."

"This time was pivotal in helping me to build my research interests, as I was able to provide useful statistical insights into data collected as part of our group's research projects. My time at NCMM was valuable and certainly helped guide me to where I am today."

Dr Aziz Khan

Dr Aziz Khan joined the Mathelier group in 2016. Since leaving he has become a staff scientist at the Curtis Lab at the Stanford Cancer Institute, US.

He comments: "No doubt, my stay at NCMM has been very transformative in shaping my career path. Being the

first postdoc in the lab allowed me to see and learn things first hand while the Mathelier lab was growing and research evolving. It provided opportunities to engage with the local and international bioinformatics and gene regulation community. I had the privilege to participate in several international conferences to network and present our work through talks and poster presentations. That helped to enhance my research and commutation skills and broaden my academic network. During these three years, Anthony, his team, and I accomplished great things together, and I am very proud of it."



The Mathelier Group at NCMM in 2019. Photo: Anthony Mathelier

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Servicing a Research Centre:

NCMM's Administration, IT team and Core Facilities

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

• • •



Administration

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

Information Technology (IT)

NCMM has an in-house IT team 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.

Core Facilities

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

Here, Alexandra Gade, Senior Engineer of the High-Throughput Chemical Biology Screening Platform and Dr Camila Esguerra, Facility Manager of the Zebrafish Core Facility and Group Leader, share some insight into the services on offer at NCMM's core facilities.

The High-Throughput Chemical Biology Screening Platform

Excerpts from an interview with Senior Engineer, Alexandra Gade The facility provides services for highthroughput screening in chemical biology, which is the rapid testing of thousands of small molecules to identify compounds that show a desired effect in biological systems. Our users have employed this technology to develop research tools for understanding biological processes, find lead molecules for drug discovery, and develop methods for personalized medicine. We provide access to our collection of ~80,000 small molecules as well as the EU-Openscreen collection of 100,000 compounds. We have advanced robotics that we use to run high throughput screens and we give users access to specialized instrumentation for liquid handling and assay readout.

In 2021, we began our first project implementing the 100,000-member library from EU-Openscreen. We successfully screened and validated hit compounds in a pilot screen to identify molecules that inhibit tankyrase activity. Tankyrases are proteins that help regulate cellular processes such as proliferation, differentiation, and death and thus are interesting targets for cancer therapeutics. We identified six selectively active compounds in this pilot screen that the user will take for further development. We also continued screening the 100k collection, gathering data for ~42,000 compounds with validation results pending in 2022.

For further information contact:

Senior Engineer
Alexandra Gade
+47 22844130
alexandra.gade@ncmm.uio.no

The Zebrafish Core Facility

Excerpts from a Nordic EMBL Partnership interview with Facility Manager, Camila Esguerra

Our facility hosts the beautiful zebrafish, a powerful model system for biomedical research. Zebrafish are used to study a wide variety of research questions in molecular, cell, developmental and neurobiology, genetics, and drug discovery research.

Zebrafish are a time and cost-effective model organism. They have a compressed developmental time – zebrafish lay about 300 eggs at a time and within 24 hours, there is a beating heart, circulating blood, and the brain is developing. In addition, the fish maintain their optical transparency for up to two weeks after fertilization, which marks the start of the juvenile stage, facilitating studies of more complex behaviour. They also have relatively low maintenance costs and offer easy genome manipulation.

Our facility offers access to expertise, facilities and instrumentation specific for housing, breeding and research with zebrafish for researchers and industry working with drug discovery, pharmacology, toxicology, and any type of genetic model. 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.

Working with living organisms such as zebrafish, requires a dedicated team to keep them healthy and in stable conditions, so that researchers can perform their experiments. This work needed to be performed also during pandemic restrictions and lockdown periods. I would like to recognize the efforts of our team in continuing to run the Zebrafish Core Facility at a high standard.

For further information contact:

Research Technician **Alejandro Pastor Remiro** +47 22840542 a.p.remiro@ncmm.uio.no



Above: NCMM's administration, IT and core facilities team. L-R from the bottom: Edna Xian Hu, Nuru Saadi, Gang Cheng, Ingrid Kjelsvik, Larissa Lily, Rasma Gutsmite, Alexandra Gade, Harold Gutch, Luis Alberto Quintero Linares, Mette Kvernland, Carlos Romeo Rodríguez, Melaku Tadesse, Gladys Marie Tjørhom, Karen-Marie Heintz, Torfinn Nome, Eirin Solberg, Anita Elisabeth Skolem, Nina Modahl and Elisa Bjørgo. Photo: Lysebu Complex staff

Annual Report 2021 Chapter 2 Chapter 2

Chapter3
Research
collaborations

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 an international molecular medicine centre with a translational mind-set, NCMM is bringing together multidisciplinary teams to combine basic and translational research approaches to clinically relevant problems. NCMM works to provide the basis for development of improved diagnostics and more efficient and targeted therapies.

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

NCMM is the Norwegian node in the Nordic EMBL Partnership for Molecular Medicine. The Partnership includes around 60 research groups and teams,

with a staff of 600 employees and stu-translational research, with shared access dents across the four national nodes in to scientific infrastructures, including Oslo, Helsinki, Umeå, and Århus, The Partnership has created a joint Nordic as well as clinical materials and networks powerhouse for molecular medicine and across the Nordic countries.

databases, facilities, and instrumentation



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

Janna Saarela

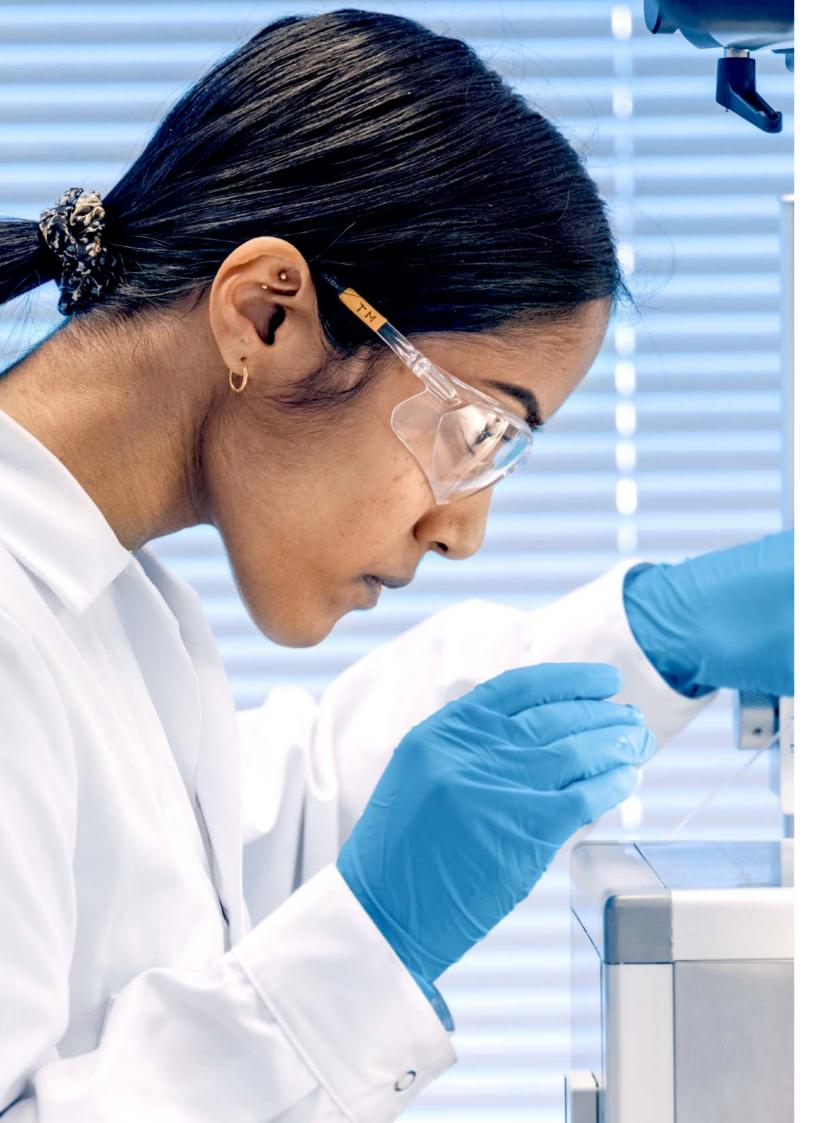
Case study in translational research: Contribution to WHO international standards

"NCMM group leader Sebastian Waszak was invited to contribute, along with 200 other authors and editors, to the 5th edition of the World Health Organisation (WHO) Classification of Tumors of the Central Nervous System"

NCMM group leader Sebastian Waszak was invited to contribute, along with 200 other authors and editors, to the 5th edition of the World Health Organisation (WHO) Classification of Tumors of the Central Nervous System. This WHO book is the international standard for oncologists and pathologists and serves as a guide for use in the design of studies monitoring response to therapy and clinical outcome. Reflecting on the significant publication he commented:

"The new 2021 edition presents a fundamental change in the way pediatric central nervous system tumors are classified. For example, pediatric tumors are now described separately from adult tumors; integrated diagnosis is based on histology with molecular diagnostics; and many new pediatric brain tumor entities are included. I am really excited that our research has contributed to updated sections, diagnoses, and pathogenesis mechanisms on embryonal tumors, and that, together with Prof. Stefan Pfister at DKFZ, I was able to write a new section to introduce ELP1-medulloblastoma as a new genetic tumor predisposition syndrome."





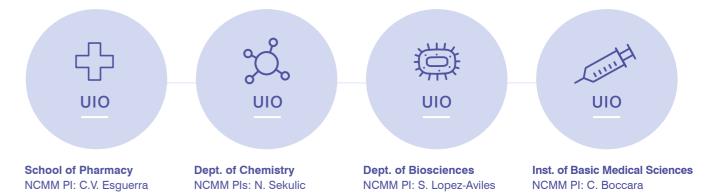
Research Collaborations

NCMM group leaders in 2021 held adjunct appointments at the following departments:



Dept. of Medical Genetics NCMM Pls: J Saarela and A. Mathelier **Dept. of Haematology** NCMM PI: J. Staerk Dept. of Pediatric Research, Div. of Pediatric and Adolescent Medicine. NCMM Pls: E. Haapaniemi and S. Waszak **Dept. of Medical Biochemistry** NCMM Pls: H. Luecke

Research Collaborations with University of Oslo. NCMM group leaders also hold adjunct positions at the following university departments:



Research collaborations with international universities:



Dept. of Neurology, University of California, San Fransisco, US NCMM PI: S. Waszak Dept. of Pathology, Leiden University Medical Center NL NCMM PI: M. Kuijjer Six NCMM group leaders have adjunct positions at OUH and our two incoming group leaders, Dr Charlotte Boccara and Dr Biswajyoti Sahu, are in the process of identifying matching hospital affiliations. These affiliations help to facilitate clinical collaborations, giving Group Leaders better access to patient materials, biobanks, and clinical trials. They are also crucial for facilitating translational research. These research collaborations have already resulted in a number of joint publications. NCMM group leaders also hold adjunct positions at national and international university departments, resulting in fruitful collaboration

Case study:

Meet Anne-Martina Kraus and Sophie Mottl - clinician scientists at NCMM



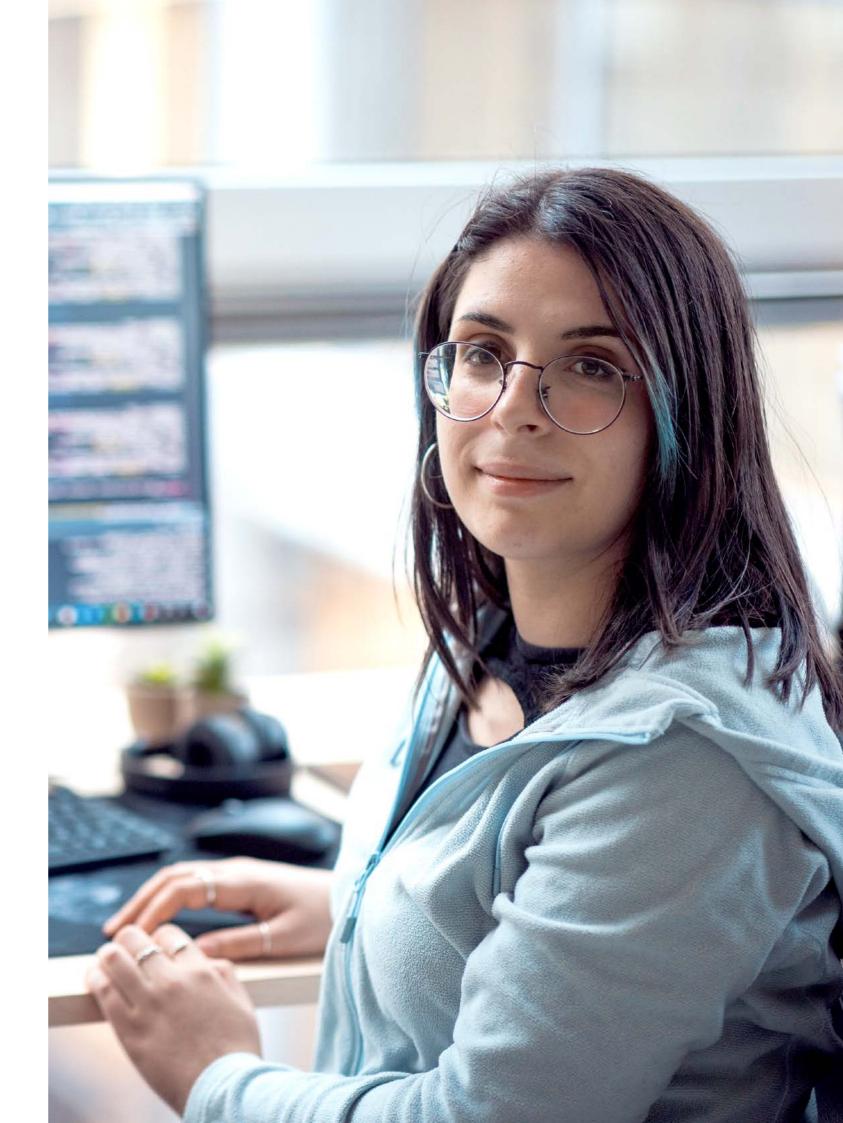
Anne-Martina Kraus and Sophie Mottl. Photo: Birgit Kriener

Anne Martina Kraus is a physician and currently enrolled in the MD program at the University of Zurich and Sophie Mottl is a medical student at the Technical University of Munich and enrolled within the MD program at the University of Heidelberg.

Anne and Sophie are undertaking their research projects within the Waszak group at NCMM to understand the genetics of childhood brain cancers. Their projects aim to understand the pathway through which specific mutations can cause the development of a brain tumor. The team uses bioinformatic methods to build a thorough profile of what mutations cause depending on the patient's genetic background. This could result in faster screening and diagnosis, more precise medicines, and ultimately increase life expectancy and quality of life.

Discussing the translational impact of their projects, Anne commented: "Sebastian is cooperating both with clinical trials and with other preclinical labs, and what is great about diffuse midline glioma is that there are cooperation between different laboratories and clinics to really make the treatment better. We want the results to improve patient outcomes, for example through informing the physicians in the clinical trials we might already be able to define the treatment or make the treatment different for a selection of the patients that show a profile that we found in our analysis"

Sophie adds: "It's very important to study childhood tumors. Every little step is one step further to giving children and their parents some more years together, which already makes a big difference. Moreover, the aim here is that maybe in a few years, we will be talking about a more prolonged survival in general and an everyday life."



National Activities

NCMM Associate Investigators

community and knowledge capabilities, through strong collaborative links with in collaborating with NCMM. NCMM key scientists and research groups across Associate Investigators continue to work Norway. These links and collaborations at their host institutions, but are credited

NCMM continues to develop its scientific with expertise compatible with NCMM's research areas and who are interested greatly support translational networking. an affiliation to NCMM and the Nordrawn from a group of outstanding Medicine. They are eligible to apply for scientists who are based in Norway, seed-funding grants for collaborative

projects with NCMM group leaders. As of Spring 2022, NCMM has 47 Associate Investigators.

In 2021, NCMM made 6.7 million NOK available for new collaborative projects between Associate Investigators and NCMM's Associate Investigators are dic EMBL Partnership for Molecular NCMM group leaders. In total, 11 new projects received seed funding:

Associate Investigators	Collaborating NCMM group	Project title
Rune Enger	Camila Esguerra	Identifying astroglial molecular contributors to epileptogenesis
Rafal Ciosk / Marianne Fyhn	Marieke Kuijjer	Cold-induced neuronal degeneration: dissecting the mechanism, inducing resistance
Joel Glover	Anthony Mathelier	Molecular networks defining vestibulospinal neuron diversity and function
Joel Glover	Judith Staerk	Interfacing brain organoids and high throughput optical recording approaches for 3D functional assessment of human neural circuits
Victor Greiff	Nikolina Sekulic	Towards uncovering the structural rules of antibody specificity
Vessela Kristensen	Anthony Mathelier	Single-cell regulatory atlas of normal breast epithelium
Vessela Kristensen	Sebastian Waszak	Haplotype-resolved cancer genomes and epigenomes with single-molecule optical genome mapping (Bionano Genomics)
Nils Halberg / Kalle Malmberg & June Myklebust	Marieke Kuijjer	Spatial Tumor Biology
Cinzia Progida	Irep Gözen	Molecular and biophysical mechanisms driving endoplasmic reticulum dynamics
Asbjørg Stray-Pedersen	Janna Saarela	Gene dosage differences causing primary immune deficiencies
Eivind Valen	Emma Haapaniemi	PegRNA screening platform for primary immunodeficiency mutation correction





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



As of spring 2022 NCMM had **47** Associate Investigators



6,7 mnok were made available for colaborative projects



11 new projects received seed funding

1.2 million NOK granted as seed funding to collaborative projects between NCMM and UiT

researchers at the Faculty of Health inflammation progression.

In 2021, NCMM, in collaboration with Sciences, UiT. Altogether, 1.2 million UiT (The Arctic University of Norway, NOK was awarded as seed funding to co-funded a pilot collaboration program. four projects investigating lung cancer The aim is to spark innovative research treatment, pathogenic bacterial cells, between NCMM group leaders and young breast cancer metastasis and kidney

UiT researchers	Collaborating NCMM group	Project title
Jonathan Hira	Irep Gözen	BacPac (Bacteria Capturing Programmable Artificial Cell System)
Simin Jamaly	Janna Saarela	Kidney Inflammation Signature (KIS): Validation of KIS as a Potential Disease Progression Biomarker in Autoimmune Diseases
Erik Knutsen	Marieke Kuijjer	Development of an epithelial-mesenchymal transition score for prognostic evaluation of breast cancer
Ilona Urbarova	Marieke Kuijjer	Towards precision treatment for lung cancer patients from serum cfRNA – a pilot study

PhD course in Molecular Medicine

NCMM hosted the annual national PhD course on Molecular Medicine in November 2021. The aim of the course is to provide a good overview of selected topics in molecular medicine that are relevant to understanding disease mechanisms and development, aspects of translational medicine and the future of diagnostics and targeted therapies integrated to stratified,

tailored and personalized medicine.

Topics covered included: Disease mechanisms and development, animal models of disease, imaging disease, biobanks, health registries and biomarker discovery, structure-based drug discovery, tailored and personalized medicine, computational biology, advanced cellbased therapies as well as SARS-CoV-2

detection, vaccination and drug targeting. The course was well-received, with 38 registered participants.

The course is among the joint Nord-Forsk supported courses offered across the Nordic EMBL Partnership. Travel grants funded by NordForsk are available for PhD students taking courses at the other Nordic nodes.

Case study:

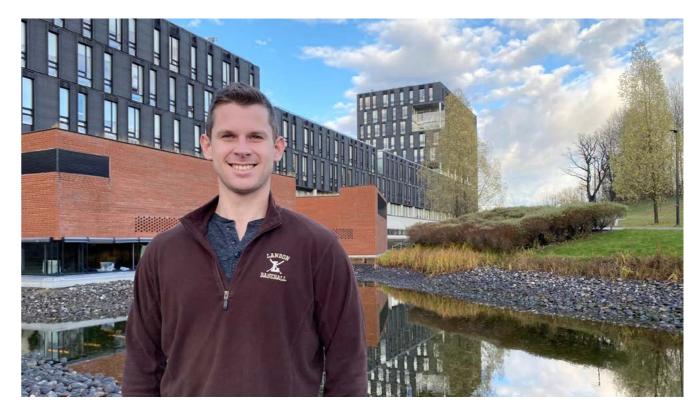
Knowledge sharing across the Nordics - NCMM hosts national PhD course in Molecular Medicine

With the support of the Partnership's joint NordForsk grant, Alex Harvey, a PhD student from DANDRITE. NCMM's sister Center in Aarhus, Denmark, attended the PhD course in Molecular Medicine in Oslo during 2021. Joining the course at NCMM in Oslo provided Alex with

an opportunity to meet new people and experience a different environment. He saw science from new angles while still focusing on developing his scientific education in neuroscience. He commented:

Just looking at my notes so far, there are so many different ideas and such a wide overview that I feel I've gotten a good spread of molecular medicine. These insights are not only helpful to my current project but also to other future research ideas that I may potentially have.

> Alex Harvey Photo: Larissa Lilv



The Nordic EMBL Partnership







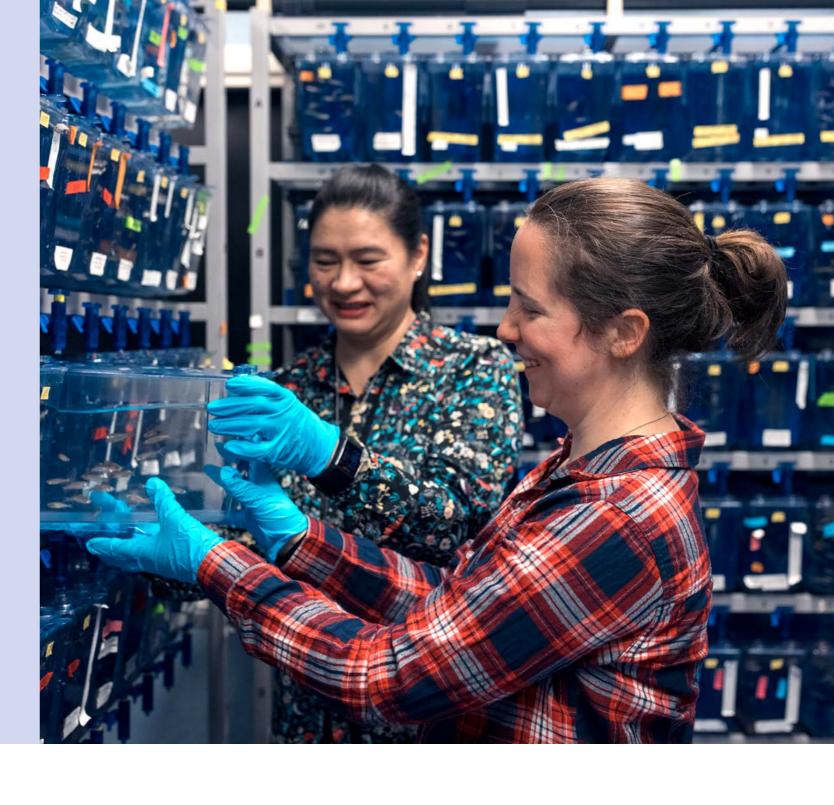


The Nordic EMBL Partnership for Molecular Medicine is a major strategic player in Europe's molecular understanding of disease mechanisms, thanks to its complementary research expertise, outstanding research infrastructures and industry collaborations.

The Partnership was founded in 2008 and constitutes a collaboration between the EMBL (European Molecular Biology Laboratory) and FIMM (Institute between the Nordic nodes, each of the of Molecular Medicine Finland) at the research centres collaborates locally and University of Helsinki, MIMS (Laboratory for Molecular Infection Medicine public health institutes, hospitals, and Sweden) at Umeå University, NCMM (Centre for Molecular Medicine Norway) at the University of Oslo and DAN-

DRITE (Danish Research Institute of Translational Neuroscience) at Aarhus University. In addition to the Partnership nationally with their host universities, research councils. This has resulted in a strong and far-reaching Nordic network for molecular medicine.

The extension of the Nordic EMBL Partnership Agreement is in progress during 2022 and will be renewed for an additional 10 years (2023-2032).





Annual Report 2021

Highlights from 2021 and Q1 2022

Fostering excellence, diversity, and mobility in the Nordic EMBL Partnership



Mark Daly. Photo: Veikko Somerpuro

Mark Daly is the FIMM director and the Speaker of the Nordic EMBL Partnership for Molecular Medicine since September 2021. Ahead of the 11th annual meeting in 2022, Mark Daly explained his vision for the partnership.

Excerpts from the originally published article on the EMBL website.

What do you see as the future directions for the Nordic EMBL Partnership?

By design, the Partnership has very diverse focus areas, which provides unique opportunities for interdisciplinary approaches and challenges us to find the natural axes of collaboration. But I think we can do a lot to bring them forward. Our plans, whether it's training or joint scientific activities, require support from partners. And so, we will most likely have to turn to our respective governments and funding agencies to help us fully deliver on new ideas.

I think there's great potential in the excellence at all four Nordic nodes of the Partnership, together with the global reach and connectivity of EMBL. I think we can achieve great things together, as well as individually.

How do you see the future of the collaboration between the Nordic partners and EMBL in the context of the new EMBL Programme 'Molecules to Ecosystems'?

In the Nordic nodes, we have broad expertise in molecular medicine. In

particular, I see the Nordic network as well-positioned to become a hub for translational activities for EMBL. The four Nordic nodes bring strong expertise in molecular medicine and bring many strengths that uniquely complement the EMBL network in a way that synergises with the new EMBL programme. I would particularly emphasise the efforts in infection biology and the interplay between human host and pathogen, as well as innovative research in neuroscience, cancer, and genome biology, in which the Nordic nodes' expertise and proximity to translational medicine perfectly complements the basic and structural biology expertise of other networks. With our efforts in molecular medicine, we are deeply committed to "research that bridges to some of society's biggest challenges". Of course, we additionally eagerly look forward to continuing our long-standing efforts in data sciences and computational biology in concert with EMBL as well.

What's the value of the EMBL model in the Partnership?

There is great value in how the institutes in the Partnership are run based on the EMBL model. Thanks to it, the Partnership attracts excellent international talent that feeds the scientific strengths of the Nordic and wider EU regions. The model entails the turnover of group leaders, which brings diversity to the local research environment. Diversity is not simply diversity and inclusion

among our staff. We also pay attention to diversity and inclusion in our research subjects, as well as in how research is conducted and how research institutes are administered. The EMBL model not only supports all these types of diversity, but also facilitates large, innovative projects and infrastructures as an important component of a diverse and successful research environment.

How does science in the Nordics compare to research elsewhere?

In the Nordics, there are substantial opportunities for biomedical research, especially on the translational side. The nationalised health care and systematic data registries on all citizens across our participating countries stretch back many decades. For example, at FIMM, we've leveraged that to build the FinnGen project - one of the world's foremost biobanking genetics research programs. And the Nordic systems allow molecular medicine research to be translated faster than anywhere else in the world. In addition, Nordic citizens understand that their data is a research resource. There is a comfort with participation in research and a sense of responsibility for each generation to help the next to have better health care. I found that this mindset is much more pervasive in the Nordics than anywhere else, creating a great environment for innovative researchers to see a path forward, legally, ethically, and responsibly, and to realise ideas in years rather than decades.

Nordic EMBL Partnership 11th annual meeting 2022

The 11th annual Nordic EMBL Partnership meeting focused on multidisciplinarity, access to cutting-edge technologies, and future research directions.

Excerpts from the originally published article on the Nordic EMBL Partnership website.

Between 31 January and 2 February 2022, the Nordic EMBL Partnership for Molecular Medicine came together for its 11th annual meeting. DANDRITE, the Danish node of the Partnership, located at Aarhus University, hosted the meeting in a virtual format.

The meeting included a day of research presentations and updates from each Partnership node, as well as discussions about expanding opportunities for new collaborations, knowledge exchange, and access to cutting-edge technologies. Several speakers highlighted the importance of multidisciplinary collaboration and diversity across the nodes, access to services and new technologies, tool development, as well as theoretical models and data sciences in the partnership.

Keynote speakers from EMBL and all four Nordic nodes presented their latest work in the areas of functional proteomics, immune sensing in infection, stem cell replacement therapy for Parkinson's Disease, new approaches to leukemia therapies, drug metabolism in multiple myeloma, and developments in imaging technologies.

One of the highlights was the presentation by Virginijus Šikšnys from Vilnius University in Lithuania. Lithuania became an EMBL member state in 2019, and relations were intensified a year later through a Partnership with

the Vilnius University Life Sciences Centre. Participation in the meeting introduced this new Partnership to the existing Nordic network with a view to establish additional cross-partnership and cross-regional collaborations. The institute's long-standing expertise in genome editing can be an important contribution to the research conducted in the Nordic network.

The Nordic Partnership also welcomed three new group/team leaders at the Nordic nodes, who presented their research plans in the areas of molecular mechanisms of neuroplasticity, bidirectional communication in the gut-brain axis, and proteomics approaches to protein function in gut microbiome species.

Summing up the meeting, DANDRITE Director Poul Nissen said: "It really was a great meeting this year. Over the last two years, people have spent a little more time on studying new, advanced approaches and how they can be integrated into their research programmes and projects. We saw numerous examples of emerging technologies, such as AI-based data analysis, gene editing in model organisms and cells, and the integration of genetics, proteomics, and imaging to unveil complex pathways and networks. It was an inspiration to step up the exchange of know-how and facilities in the partnership."



Aarhus university. Photo: Jasper Rais/AU-foto

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Chapter 3

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Chapter 3

New EMBL programme offers opportunities for researchers in Norway

The Norwegian research environment stands to benefit from the launch of the new European Molecular Biology Laboratory programme 'Molecules to Ecosystems'.

From Molecules to Ecosystems

EMBL has recently launched their next five-year strategic programme 'Molecules to Ecosystems'. It is an ambitious and thought-leading programme, which aims to push the boundaries of molecular life science through studying life in the context of our rapidly changing environment. The programme sets out a strategic plan and vision, which will guide all activities at EMBL, and enable innovative research that addresses the human and planetary health challenges we face, thus aiming to bridge the gap between molecular biology and other disciplines.

What Norway-based researchers can get out of the new programme

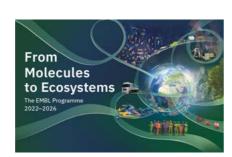
The launch of the new programme offers many training, education and work opportunities to life science researchers based in Norway. Researchers have the career boosting opportunity to go to EMBL as a PhD student or a postdoc. They can also apply for EMBL fellowships at all career levels. Norway-based researchers can also benefit from training, lab visits and conferences hosted at EMBL and across the nodes.

Plamena Markova, Head of International Relations at EMBL, shared her vision for how the Nordic EMBL partnership, and Norway in particular, can contribute to the new EMBL program.

"With the new Program EMBL kickstarts a new era of life sciences that will not only address new and unexplored research questions, but will also connect talent, disciplines, services and technologies like never before. It will create a unique collaborative ecosystem to deliver for science and society. The EMBL partnerships are an important conduit of this new way of doing science. They have the ability to translate EMBL's vision and operational model into the national system, while at the same time they help channel unique national strengths, expertise and networks into EMBL's work. This two-stream model ensures that we can continuously learn from each other and create research, services and training programs that are of mutual benefit but also of benefit for the society."

"Norway's strengths in health and environmental research, both of which are

represented also in the two partnerships we have, will feed into EMBL's ambition to understand life in the context of its changing environment. In addition, Norway is one of the most innovative countries in Europe, which makes it an exceptionally well positioned partner to benefit from EMBL's long-standing expertise in invention, innovation and technology diffusion."



Creative Team/EMR

With the new Program EMBL kickstarts a new era of life sciences that will not only address new and unexplored research questions, but will also connect talent, disciplines, services and technologies like never before. It will create a unique collaborative ecosystem to deliver for science and society.

New Nordic EMBL Partnership Communications Director

As of September 2021, Gretchen Repasky joined the Nordic EMBL Partnership in the role of Communications Director. Gretchen has a background in cancer biology research, research training and teaching. She previously held Chief Operating Officer positions at the Novo Nordisk Foundation Center for Stem Cell Biology in Copenhagen, Denmark and Elevate Scientific Academy in Malmö, Sweden. Prior to these roles she was a senior researcher and research training coordinator at our sister institute, Institute for Molecular Medicine Finland (FIMM) for eight years, following a

research and undergraduate teaching career in the United States.

As Communications Director, Gretchen will work to increase the visibility of the vibrant Nordic research environment, showcasing research and technology advances. She will also engage with scientists and staff within the Partnership to build collaborations, raise awareness of opportunities among the Nordic EMBL nodes, and promote knowledge exchange and mobility. She will also support EMBL with its wider communications objectives with particular focus on the Nordics.



Gretchen Repasky. Photo: Kalle Kallio



2021 Nordic EMBL Science & Art Competition

Dr Andrea Moreno, Assistant Professor at DANDRITE, won the 2021 Nordic EMBL Science & Art Competition with her painting titled 'A Walk to Remember'. Reflecting on her inspiration for the artwork she said: "The painting represents the spontaneous release of neurotransmitters that might be one of the causes of memory decay by synaptic depotentiation. In an allegory, by preventing the 'neurotransmitter rain' to reach certain spots, the figure saves some memory traces from weakening."

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Poul Nissen, Director of DANDRITE, awarded the Anders Jahre Medical Prize 2021

Excerpts from the originally published article on the Nordic EMBL Partnership website.

The Anders Jahre Medical Prize was awarded to Prof. Nissen, Director of the Danish Research Institute of Translational Neuroscience, DANDRITE, in recognition for his ground-breaking research on the structure and function of membrane proteins. We caught up with Prof. Nissen after the award ceremony in Oslo, Norway to hear what impact he expects the recognition will have on his

career and future approach to science.

Commenting on the achievement he said "This should encourage us to aim for new interdisciplinary approaches in molecular medicine where one both tries to nail very difficult questions and mechanisms in cell biology and molecular physiology, and at the same time tries to use that information to drive discovery and biotechnology forward."



Prof. Poul Nissen. Photo: UiO/Jarli&Jordan.



Prof. Poul Nissen and Prof. Janna Saarela. Photo: Larissa Lily

EATRIS

Infrastructure Consortium (ERIC) that offers a unique one-stop shop access to academic expertise and high-end technologies required to advance new products through the translational process from target validation to early clinical trials. The infrastructure is open to both academic researchers and companies in need of support for advancing biomedical innovations. NCMM coordinates the Norwegian participation in EATRIS and NCMM's Director, Professor Janna Saarela, is also the EAT-RIS National Scientific Director of Norway. EATRIS has five scientific platforms: Advanced Therapy Medicinal Products, Biomarkers, Imaging and Tracing, Small Molecules, and Vaccine, Inflammation and Immune Monitoring.

EATRIS offers a range of services which directly benefit Norway-based researchers. A main aspect of this is support for funding applications, which includes help forming a consortium, participating in research funding proposals as a full partner providing various centralised services, a letter of support for research proposals, and taking a leading role in supporting the development and management of proposals coming from EATRIS member institutes.

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

Discussing the opportunities presented by EATRIS, NCMM Director and EATRIS National Scientific Director of Norway, Professor Janna Saarela commented

"EATRIS offers a great opportunity for Norway-based researchers to drive

EATRIS is a non-profit European Research Infrastructure Consortium (ERIC) that offers a unique one-stop shop access to academic expertise and high-end technologies required to advance new products through the translational process from target validation to early clinical trials. forward the translation of research discoveries into benefits for patients. The access to critical research infrastructure and the network of academic and industry actors, as well as funding agencies, charities and policy makers is a significant advantage to the Norwegian research community"



News and events

News and Events

NCMM PhD Defences 2021

Highlights









Elif Senem Köksal

Elif defended her thesis entitled "Surface-assisted formation and development of model protocells" at the Dept. of Chemistry, Faculty of Mathematics and Natural Sciences, University of Oslo, in June 2021. Elif's PhD was carried out in the group of Irep Gözen at NCMM. The thesis investigated the possible involvement of solid surfaces in the formation and development of primitive cells on the early Earth. Elif is now a postdoctoral researcher at the University Hospital of Zürich, Switzerland.

Nancy Saana Banono

Nancy defended her thesis entitled "Functional analysis of psychiatric risk genes in zebrafish (Danio rerio): a focus on the L-type voltage-gated calcium channel subtypes Cav 1.2 and Cav 1.3" at the School of Pharmacy, Faculty of Mathematics and Natural Sciences, University of Oslo, in October 2021. Nancy's PhD was carried out in the group of Camila V. Esguerra at NCMM. The goal of the thesis was to characterise the effects of mutations in CACNA1C and CACNA1D voltage-gated calcium channel genes on early brain function, using three zebrafish mutant lines. Nancy is now a joint postdoctoral researcher in the groups of Sebastian Waszak and Camila Esguerra at NCMM.

Karolina Spustova

Karolina defended her thesis entitled "Membranous Protocell Superstructures" at the Dept. of Chemistry, Faculty of Mathematics and Natural Sciences, University of Oslo. Karolina's PhD was carried out in the group of Irep Gözen at NCMM. The thesis tested the theory of how life originated on the early Earth by investigating the formation and development of colony-like primitive cell structures and populations using water, fat molecules and solid surfaces.



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Group Leader Evaluations 2021

Three NCMM research groups extended for a further four years

Following a successful evaluation by international scientific experts and NCMM's Scientific Advisory Board (SAB) in March 2021, the NCMM Board decided to extend the research 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, allow-

ing 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. 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 group leaders Irep Gözen, Nikolina Sekulic and Anthony Mathelier on their successful evaluations. Photo: Oda Hyeem

Annual Report 2021 Chapter 4



NCMM group leader Sandra Lopez-Aviles appointed as an **Associate Professor at** the University of Oslo

Dr Sandra Lopez-Aviles has been head greenhouse for young talented researchers period, she was externally evaluated and renewed for a second and final period meaning they must rotate out of NCMM as a whole. Thus, NCMM serves as a and transcription."

of the Cell Cycle Regulations group at that after their group leader period at the NCMM since 2011. After her first 5-year Centre, should be attractive candidates for permanent positions around Norway

We are delighted to announce that Dr from 2017. Like other nodes in the Nordic Lopez-Aviles successfully rotated out EMBL Partnership, NCMM follows the to an Associate Professor position at EMBL model for recruitment, where the
the Department of Biosciences at the Centre's group leaders are recruited for University of Oslo on 1 December 2021. 5+4 year contracts with mid-term review, Commenting on her successful appointment, Dr Lopez-Aviles said: We've worked upon completing the second stage of their hard as a group over the last nine years group leader role. The NCMM model aims and so I'll now aim to continue what we to attract the brightest and the best young started at NCMM. I'll continue to conresearchers to Norway, thereby benefitting centrate on cell signalling and cell cycle both NCMM and UiO and the Nordics progression, as well as gene programmes

NCMM visits EMBL Headquarters in Heidelberg

Fellow in the Mathelier group at NCMM. database of transcription factor binding profiles. Recently, Ieva spent one month with the groups of Dr Judith Zaugg and Dr in Heidelberg, Germany.

Krebs' group to learn about the new data Hubs' initiative. they generate from single molecule footprinting experiments to assess TF-DNA interactions at the molecular level. These very important for a researcher. Due particular experimental data and methods to the global pandemic, I did not have of analysis are relevant for one of her opportunities to go to conferences and PhD projects, where she is working on interact with researchers besides online identifying cooperative binding of TFs talks and seminars, so this was a really to the DNA. Single molecule footprinting amazing chance to connect and work allows a deeper dive into TF cooperativity at single-molecule resolution.

related to the analysis of transcription reasons - others will remember you regulation through TF cooperativity. She more after such a visit rather than from collaborated with Dr Zaugg's group to an email that you sent! In addition, you investigate TF cooperativity in human immune cells using the computational method she is developing at NCMM. The goal of the project is to reveal TFs visits also help you to exercise critical acting as collaborative partners to add thinking and science communication a layer of knowledge onto immune cells skills because you need to describe and gene regulatory networks derived by explain your research. Moreover, you researchers in Dr Zaugg's group.

development of Ieva's PhD project. She scientific discussions."

Ieva Raulusevicuite is a Doctoral Research was able to get interesting preliminary results using the data from the Krebs In her PhD, she studies how transcription group. In addition, Ieva presented her factors (TF) bind to DNA. For instance, she research on multiple occasions and was was one of the main drivers of the recent able to get helpful feedback on her work update of JASPAR, a popular open-access from researchers in both visited groups. Ieva will continue to collaborate on further analyses with the groups in the future.

Ieva's visit was funded by NordForsk Arnaud Krebs at the EMBL headquarters through funding awarded to the Nordic EMBL Partnership by NordForsk as part At EMBL, Ieva collaborated with Dr of their 'Nordic Research Infrastructure

Commenting on the visit, Ieva said:

"These kinds of opportunities are with great researchers at EMBL for a full month. Beside the scientific relevance, The second part of her visit was also such visits are important for networking get to see how other labs work, what research areas they are focusing on and what methods they are using. These can get input on your work from other The visit has been invaluable for the people and participate in important





Celebration of UiO:Life Sciences' first generation convergence environments

NCMM group leader Irep Gözen's project 'Programmable Cell-like Compartments' was one of UiO:Life Science's first convergence environment joint projects. The concept of "convergence" refers to integrated interdisciplinary research collaboration. Wednesday 30th of March 2022 was the closing event of UiO:Life Sciences' first generation convergence environments. The leaders of the convergence environments, including Dr Irep Gözen, presented results and shared experiences of interdisciplinary research collaboration.

Irep Gözen. Photo: Fartein Rudjord/UiO



Leaders of the first generation convergence environments. L-R: Stefan Krauss, Kjetill Jakobsen, Arnoldo Frigessi, Irep Gözen, Katrine Borgå, Arne Klungland. Photo: Fartein Rudjord/UiO

Highlights Highlights

NCMM social away days for PhD students and Postdoctoral Researchers



The trip to Grefsenkollen for postdocs. From the far left: Wietske van der Ent, Artur Grzegorz Cieslar-Pobuda, Inga Poldsalu, Jaime Castro-Mondragon, Adnan Hashim, Marina Portantier

In August 2021 NCMM organised social outings for PhD students and postdocs. A group of postdocs enjoyed a trip to Oslo's rooftop Grefsenkollen for food and drinks overlooking the city and Oslo fjord. Meanwhile, a group of PhD students enjoyed a trip to Oslo's summer climbing park at Tryvann.



The away day for PhD students at Tryvann climbing park. L-R: Marianna Lehtonen, Elham Shojaeinia, Nancy Saana Banono, Sandra Kunz, Flore Kersten, Rafael Ruidavets-Puig, Ieva Raulusevicuite

2021 Biomechanics workshop at Tøyen Hovedgård

by NCMM group leader Irep Gözen as together researchers from different fields and different corners of the world, all with an interest in mechanical processes of biology. The event ran 29-30 Octo-

The Biomechanics workshop organized ber and was attended by 40 researchers. Commenting on the workshop Irep well as Professor Andreas Carlson and Gözen said: "As the ambassador of the Professor Kent-Andre Mardal from the American Biophysical Society in Nor-Department of Mathematics, brought way I am very happy to see researchers coming together from different parts of Scandinavia and from Germany, to share their ideas and research in biomechanics which is a subfield of biophysics."



The Biomechanics workshop was attended by 40 researchers. Photo: Larissa Lilv

Sebastian Waszak joins the Department of Neurology at the University of California, San Francisco

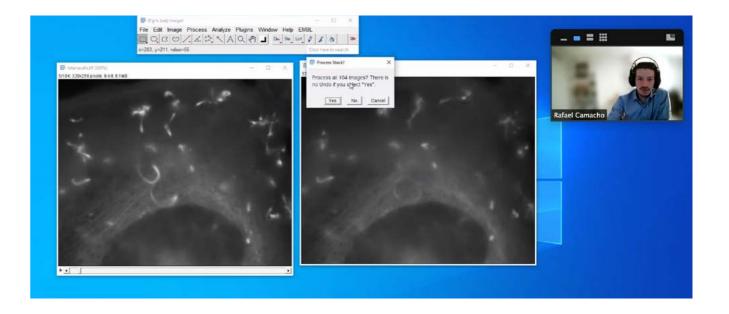
In October 2021, Dr Sebastian Waszak was appointed Associate Adjunct Professor at the University of California, San Franscisco (UCSF). This affiliation allows his group to become more involved in the preclinical Pacific Pediatric Neuro-Oncology Consortium (PNOC) working groups and trials, and in multidisciplinary neuro-oncology tumor boards at UCSF.

6th and 7th NorMIC Imaging Workshops bring together young researchers with world-leading microscopy experts

NCMM and the Department of Biosciences at the University of Oslo in 2021 hosted both the 6th and 7th NorMIC Imaging Workshop, focusing on imaging processing, methods in optical microscopy and 3D printing for microscopes. The workshops, organised by Xian Edna Hu from NCMM and Oddmund Bakke from the Department of Life Sciences

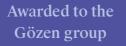
at the University of Oslo, took place online in May and November 2021 and provided teaching from world-leading researchers in the field, as well as from local experts. Participants learned about the basics of optical microscope image formation, common artifacts, image data management with regards to the FAIR data principle and many popular

state of the art imaging techniques. The organisers received extensive technical support from USIT, University of Oslo's Centre for Information Technology and received financial support from Digital Life Norway, UiO:Life Sciences and BNMI (NordForsk Research Infrastructure Hubs).



NCMM Funding Successes







Awarded to the Haapaniemi group



Awarded to the Awarded to the Sekulic Haapaniemi group and Gözen groups

25 million NOK for Gözen group and collaborators to help answer basic scientific questions about autophagy

her project 'Biophysics of double bilayer the Research Council's call for large, pioneering interdisciplinary research projects in December 2021. The project aims will help researchers to further understand the role autophagy plays in diseases such as cancer, inflammatory autophagy pathway has the potential

Dr Gözen was awarded 25m NOK for to revolutionize the way such diseases are treated. Commenting on the grant, membrane compartments', as part of Dr Irep Gözen said: "First of all, an inter-disciplinary effort enables that this research problem is approached from different angles. This is very useful for complex problems such as the one we focus on in this project. The project will help us continue our group's tradition to disease, infection, and neurodegenerative collaborate with researchers from other disease. The possibility to disrupt the disciplines and will strengthen my experience as a project manager."



Irep Gözen. Photo: Oda Hveem

Dr Gözen was awarded 25m NOK for her project 'Biophysics of double bilayer membrane compartments', as part of the Research Council's call for large, pioneering interdisciplinary research projects in December 2021





Haapaniemi group receives 20 million NOK to research personalized gene editing

for her project 'CRISPR-Cas9 corrected T cells for personalized therapy', as part of the Research Council's call for radical innovative technology projects in March 2022. The project proposes to use a gene editing tool called CRISPR to correct T cells from patients with diverse T cell immunodeficiencies. After the researchers correct the T cells, they will be infused back into the patient's body. The correction of the T cells will enable

that protects their body from disease and infection properly. Commenting on the grant, Dr Haapaniemi said: "There are many different mutations. Individually they are rare, but collectively they become quite common. That's why we want to develop one platform that can treat a large spectrum of mutations."



24 million

Emma Haapaniemi. Photo: Oda Hveem

Dr Haapaniemi was awarded 20m NOK for her project 'CRISPR-Cas9 corrected T cells for personalized therapy', as part of the Research Council's call for radical innovative technology projects in March 2022



NCMM Funding Successes





Nikolina Sekulic. Photo: Oda Hveem

Irep Gözen. Photo: Oda Hveem

Haapaniemi group receives nearly 8m NOK from the Norwegian Cancer Society

Dr Haapaniemi was awarded 8m NOK for developing CRISPR-Cas9 gene therapy for blood cancer predisposition syndromes from the Norwegian Cancer Society. The study proposes to develop CRISPR-based gene-editing therapies for two model cancer predisposition syndromes: ADA2 deficiency and Nijmegen Breakage Syndrome. These are rare childhood diseases caused by hereditary gene mutations that make the patients susceptible to developing cancer. Commenting on the grant, Dr Haapaniemi said: "Pavel Kopcil, Monika Szymanska, Ganna Reint and Jacob Conradi have all put in an enormous effort for setting up the mouse stem cell xenotransplant protocols that are necessary for conducting the proposed studies."



Haapaniemi group. L-R: Oda Almåsbak Dønåsen, Emma Haapaniemi, Pavel Kopcil, Frida Høsøien Haugen Zhuokun Li, Monika Szymanska. Photo: Ganna Reint.

KREFTFORENINGEN

Dr Haapaniemi was awarded 8m NOK for developing CRISPR-Cas9 gene therapy for blood cancer predisposition syndromes from the Norwegian Cancer Society.

24m NOK awarded to Sekulic group and Gözen group by the Research Council of Norway

Nikolina Sekulic and Irep Gözen were each awarded a 'FRIPRO' grant of 12m NOK for their projects titled 'Determining the Molecular Architecture of Centromeric Chromatin' and 'Did surfaces enable the origins of life? The role of interfaces in the emergence of primitive cells on the early Earth' respectively.

Commenting on her award, Dr Sekulic said: "I am thrilled that RCN has recognised the importance and potential long-term impact of our basic research. The support from RCN will enable a talented young researcher, Ahmad Ali-Ahmad, who generated a wealth of preliminary data for the project, to continue his efforts

in the lab. The funding will also allow us to further expand local expertise in cryo-electron microscopy, a revolutionary structural biology technique, that is only starting to develop in Norway. Finally, I believe that funded basic research will generate a fertile ground for the design and development of future therapies."

I would also like to thank all members of our group, our local and international collaborators and staff at NCMM for constant support in our research.

Commenting on her award, Dr Gözen said: "I am very happy to receive the grant, which will allow me to obtain

proposed for this RCN project in the Ground-Breaking Research scheme. Enabled by the latest interdisciplinary bionanotechnological and methodological developments, to which my team contributed significantly, the proposed hypothesis is ready to be tested. The subject of the development of life on Earth is of exceptionally broad interest, which puts this project at the forefront of research on a competitive international scale."



Nikolina Sekulic and Irep Gözen were each awarded a 'FRIPRO' grant of 12m NOK for their projects titled 'Determining the Molecular Architecture of Centromeric Chromatin' and 'Did surfaces enable the origins of life? The role of interfaces in the emergence of primitive cells on the early Earth' respectively.

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NCMM Research Highlights

How lethal hyperinflammation emerges from a novel gene defect

An international team of researchers in Finland, Norway, Sweden and Austria have discovered the origins of a disease characterized by immune dysregulation called 'familial hemophagocytic lymphohistiocytosis' (HLH). Published in the high-ranked scientific journal Blood, the study provides a basis for both a deeper understanding of the biology of HLH and the exploration of new therapeutic approaches. Commenting on the publication, Professor Janna Saarela, co-senior author of the study, said: "Tight connections between clinical diagnostics and research helps defining molecular diagnosis for rare disease patients suffering from yet unidentified disorders. It also provides opportunity for discovery of novel disease genes and understanding their pathomechanisms, which may impact disease management and prognosis."



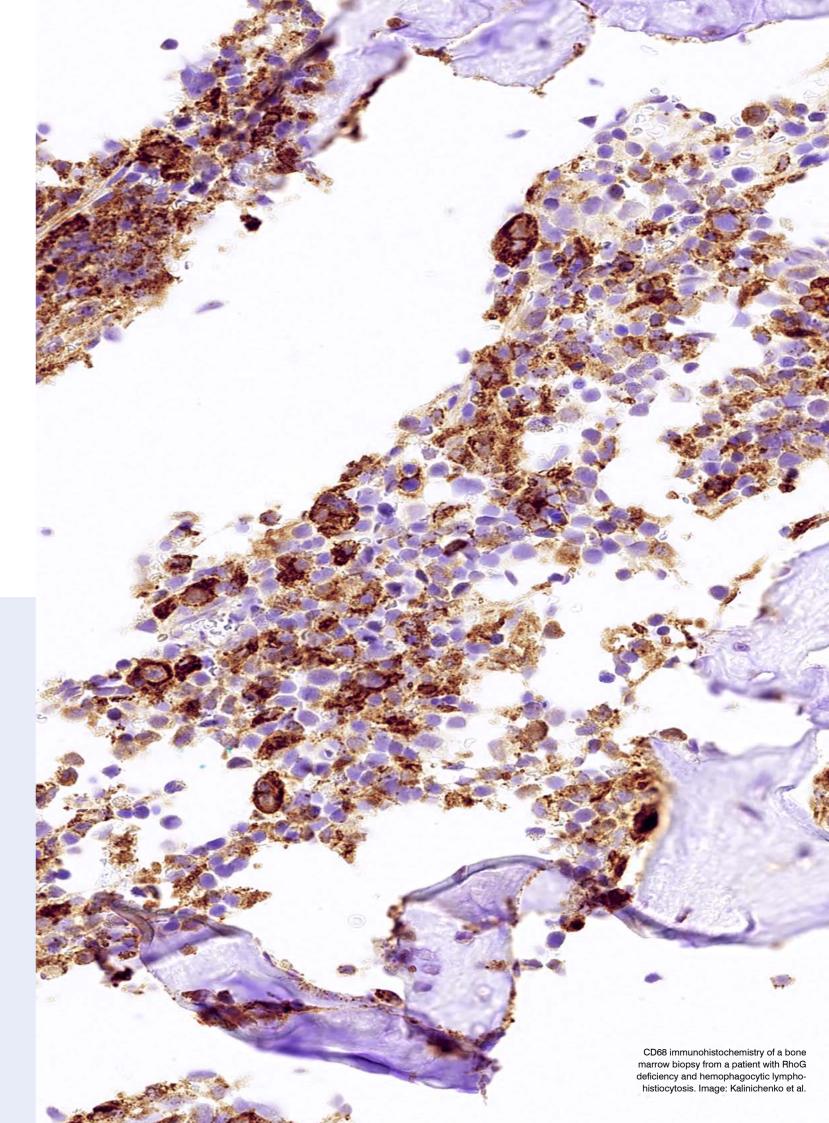
RhoG deficiency abrogates cytotoxicity of human lymphocytes and causes hemophagocytic lymphohistiocytosis. Kalinichenko et al., Blood (2021). DOI: https://doi.org/10.1182/blood.2020008738

Rapid genome editing by CRISPR-Cas9-POLD3 fusion

The Haapaniemi group's study, published in the journal eLife, aimed to improve the precision of the CRISPR-Cas9 gene editing instrument. They tested fusions of Cas9 nuclease with more than 450 proteins/protein domains which take part in the cellular DNA repair processes and determined their effect on the gene editing outcomes. A panel of the best-performing Cas9 fusions detected in the screens include some previously reported variants, as well a handful of novel ones, with the leading candidate - Cas9-POLD3. Commenting on the study, co-first author Ganna Reint said "Cas9-POLD3 enriches the toolkit for precise genome editing. Combined with advancements in this direction from other groups, we expand the panel of available instruments that could be used for genome editing both in basic biological research and in clinically oriented science." The authors thank Dr Judith Staerk and Dr Artur Cieslar-Pobuda for their help related to the stem cell work, and Dr Xian (Edna) Hu for her help with image analysis.



Rapid genome editing by CRISPR-Cas9-POLD3 fusion. Reint and Li et al., eLife (2021). DOI: https://doi.org/10.7554/eLife.75415



NCMM Research Highlights

Update of vital resource for the study of gene expression regulation

The Mathelier group and collaborators have published the results of the 9th release of the JASPAR database in the Nucleic Acids Research journal. It is now expanded with more than 600 new transcription factor binding profiles. Commenting on the release, co-first authors Jaime Castro-Mondragon said: "This is a free database that users can go to and download from. We are doing this because we want to help other researchers, and I think it's important to keep this kind of tools available to all. It's the data that others need for starting their projects"



JASPAR 2022: the 9th release of the open-access database of transcription factor binding profiles. Castro-Mondragon, Riudavets-Puig and Rauluseviciute et al., Nucleic Acids Research (2021). https://doi.org/10.1093/nar/gkab1113

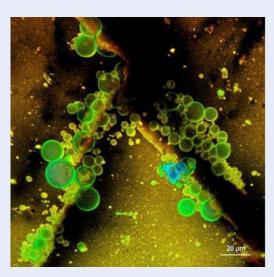
Central Nervous
System Tumours
WHO Classification
of Tumors

As a result of the past five years, Dr Sebastian Waszak was invited to contribute, along with 200 other authors and editors, to the 5th edition of the World Health Organisation (WHO) Classification of Tumors of the Central Nervous System. This WHO book is the international standard for oncologists and pathologists and serves as a guide for use in the design of studies monitoring response to therapy and clinical outcome.



WHO Classification of Tumours, 5th Edition, Volume 6. ISBN: 978-92-832-4508-7

Autonomous formation of primitive cells has been observed on ancient Earth surfaces and on a specimen from Mars



Populations of primitive cells emerging at the fracture of the mineral eclogite. Image: Dr Irep Gözen

Research from the Gözen group provides experimental evidence that populations of ancient primitive cells could have autonomously assembled on minerals under early Earth conditions, and on the ancient crust of Mars. In a study published in the journal ChemSystemsChem, the findings showed the autonomous development of prebiotic compartments on thin sections of natural surfaces, one of them obtained from the martian meteorite NWA 7533 "Black beauty".



Spontaneous Formation of Prebiotic Compartment Colonies on Hadean Earth and Pre-Noachian Mars. Köksal et al., *ChemSystemsChem* (2021). DOI: https://doi.org/10.1002/syst.202100040

Angular and linear speed cells in the parahippocampal circuits

The Boccara group and collaborators have provided evidence of a widespread parahippocampal network involved in linear and angular speed coding that could have a crucial role in the updating of the cognitive map, or perhaps be part of the map itself. Published in the Nature Communications journal, their findings offer robust experimental evidence particularly relevant for the reappraisal of theories describing navigation based on grid and head direction cells interacting in continuous attractor neural networks (CAN).



Angular and linear speed cells in the parahippocampal circuits. Spalla et al., *Nature Communications*. (2022). DOI: https://doi.org/10.1038/s41467-022-29583-z

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NCMM Publications 2021-22

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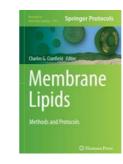
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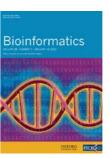
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Press items for NCMM 2021 & Q1 2022

Press items 2021

Waszak Group

- 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

- 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 Cell
- The Times Hub, February, Proof that Earth's first cells might have had specialized compartments

Press items 2021

- 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
- Haapaniemi group
- Kreftforeningen, November, Kreftforeningen gir over 170 millioner til livsviktig forskning

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

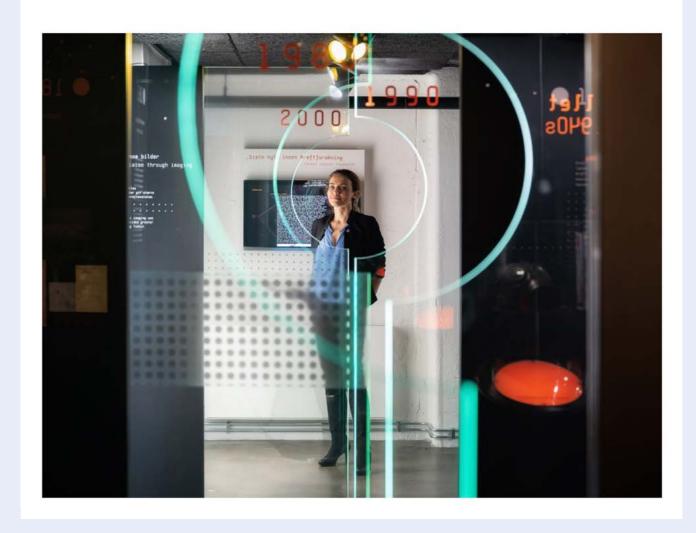
Press items 2022

Gözen Group

- Inverse.com, January, Primitive cells could help confirm Mars once hosted life
- Phys.org, February, Autonomous formation of primitive cells observed on ancient Earth surfaces and on a specimen from Mars
- Haapaniemi Group
- Khrono, January, Deler ut 195 millioner kroner til nyskapende teknologiprosjekter
- Boccara Group
- VG, April, Norske forskere: Hjernen din har superceller!

Kreftforeningen gir over 170 millioner til livsviktig forskning

– Dette vil føre til viktige gjennombrudd for kreftsaken, for aldri har kvaliteten på forskningsprosjektene i søkerbunken vært høyere, sier generalsekretær Ingrid Stenstadvold Ross.



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Norske forskere: Hjernen din har superceller!





Study sheds new light on the origins of life on Earth





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NCMM Board

The NCMM Board is, in collaboration with the Director, responsible for the Centre's overall coordination and progress. The Board steers and supervises NCMM's activities and finances as well as approves the Centre's strategic plans, objectives, and budget. The Board's decisions contribute to promoting excellence in the Centre's recruitments, research, collaborations, and translational value. The Board consists of the Chair and five members representing NCMM's host, the University of Oslo and the consortium partner Health South-Eastern Norway Regional Health Authority (HSØ), as well as a national representative.

. . .

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

I am pleased that despite the continued working restrictions during 2021 due to the COVID-19 pandemic, NCMM has persevered and conducted innovative research throughout the year. In the first quarter of 2022, normal activity has resumed, and I anticipate the relief felt by NCMM to get back to doing great science, as they have always done. The continuous efforts for scientific excellence and quality by NCMM employees plays a key role in ensuring we reach our goals, and it is greatly appreciated. The implementation of the recommendations in the Centre's SAB report for 2021 is well underway and NCMM is well-positioned to be a key scientific hub in the new UiO Life Science building.

I wish to congratulate the two new NCMM group leaders, Dr Charlotte Boccara and Dr Biswajyoti Sahu, on their appointments. Dr Boccara brings with her deep expertise in neuroscience and will establish and head the Systems Neuroscience & Sleep group at NCMM. She will develop tools to monitor and manipulate brain activity, which can create avenues for new therapeutics related to neural disorders. Dr Sahu's expertise lies within functional cancer epigenomics, using a genome-wide multi-omics approach to study transcription factors in malignant gene regulation. He will advance knowledge that can enable new discoveries with translational impact about the role transcription factors have in human cancers. Their appointments show great promise

in the direction NCMM is taking towards its goal to tackle fundamental biological questions with potential for applications to precision medicine.

I would also like to take this opportunity to congratulate the three NCMM group leaders, Dr Nikolina Sekulic, Dr Irep Gözen, and Dr Anthony Mathelier on their evaluation and extension for a further four years.

The efforts and contributions from the NCMM Board members and the scientific and administrative leadership of NCMM are highly appreciated. Finally, as Chair of the Board, I express my gratitude for the support from The Research Council of Norway, The South-Eastern Norway Regional Health Authority and the University of Oslo.





Chair



Professor Jens Petter Berg,

University of Oslo / Oslo University Hospital



Board members

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













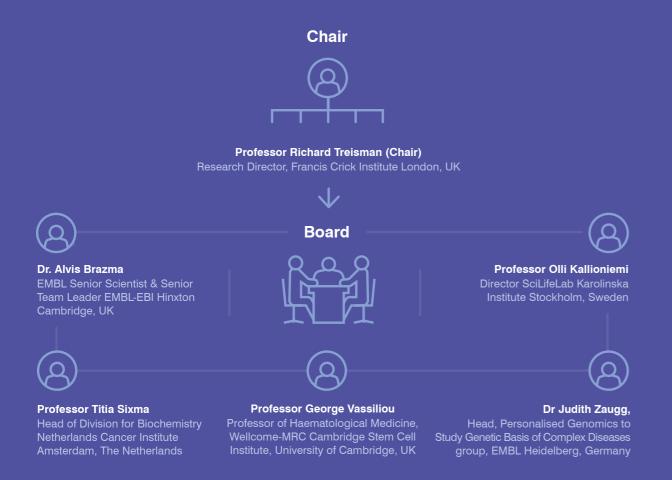


Professor Magne Børset, Norwegian Torunn Berge, Special Advisor, University of Science and Technology (NTNU) (deputy national representative)

South-Eastern Norway Regional Health Authority (HSØ)

Professor Arnoldo Frigessi, University of Oslo

Scientific Advisory Board (SAB)



The SAB's main mission is to offer academic and strategic advice, as well as benchmark the performance of NCMM's research groups and the Centre internationally. The SAB meets with NCMM core members every 18-24 months. These meetings allow for the review of recent progress and advice on future strategies. The most recent SAB visit took place in March 2021, when three NCMM group leaders were evaluated and recommended for extension. Due to the ongoing pandemic, this meeting was held online. The next SAB visit is scheduled for February 2023.



Funding

2021



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



29



29 mnok in competive funding for 2021

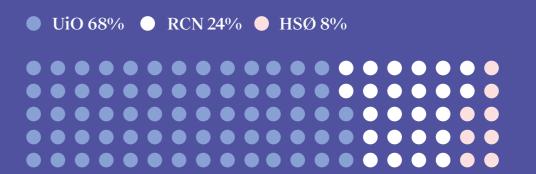
233 mnok in competitive funding for 2015-21

The core funding for NCMM in the period 2020-2024 is 54,5 mnok per year Core Funding: The core funding for NCMM in the period 2020-2024 is 54.5 million NOK per year from the three consortia partners UiO, the Research Council of Norway (RCN) and South-Eastern Norway Regional Health Authority (HSØ). Overhead income from core facilities and production-based income comes in addition.

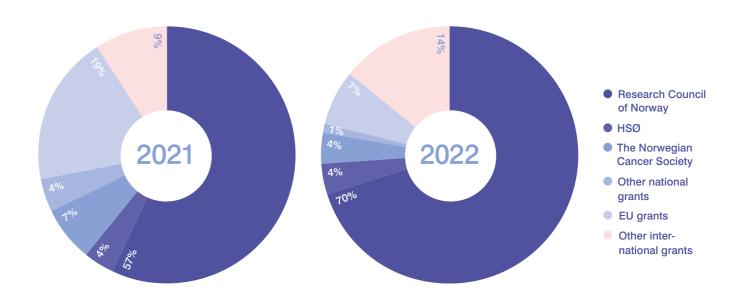
Competitive funding: NCMM competitive funding, in the form of grants to the group leaders and other competitive funding, increased steadily from 7 mNOK in 2010 to 42 mNOK in 2015. Due to rotations of research groups, the

level of competitive funding fluctuates somewhat depending on research groups rotating in and out of the Centre. For 2021, the amount of competitive funding obtained by the research groups reached 29 million NOK. This funding includes grants from the Research Council of Norway, the Norwegian Cancer Society, South-Eastern Norway Regional Health Authority, the European Commission, the Swiss National Science Foundation Sinergia and private foundations and organizations such as the World Cancer Research, Barncancerfonden and Ians Friends Pedriatric brain tumor foundation USD.

Core funding 2021



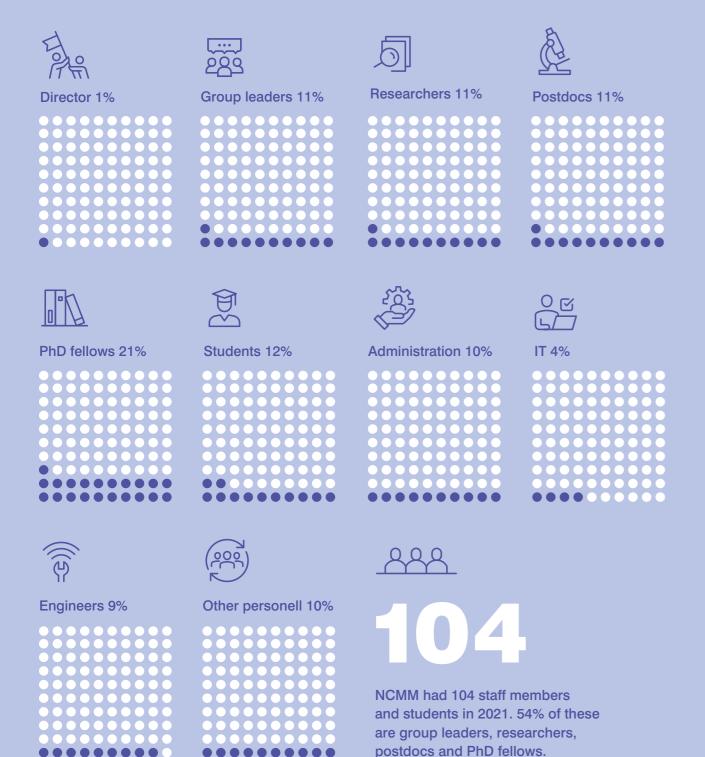
Competitive funding 2021 Est. competitive funding 2022

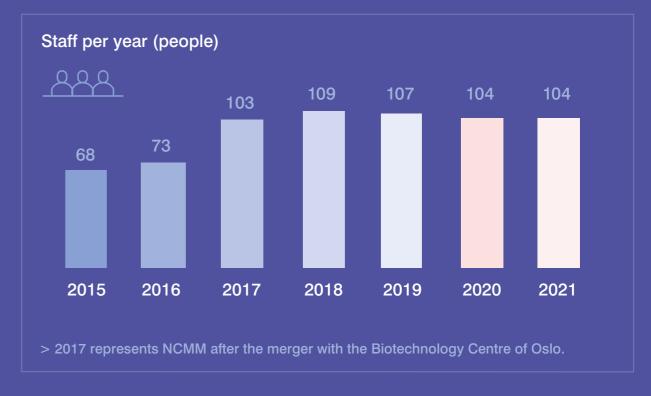


Personnel statistics

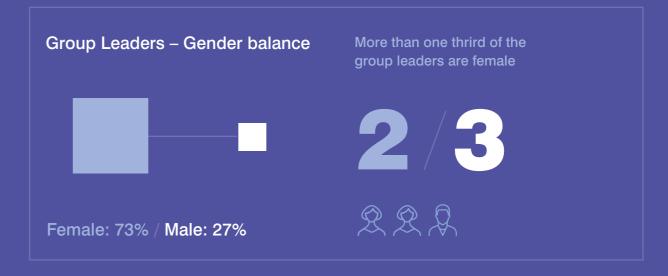
in 2020 and Q1 2021

Staff according to type of employment (%)









Distribution of staff

As of Q1 2021

37 nations in total

• 80 international staff members

O1 person

Countries represented:

Argentina, Belgium, Croatia, Cuba, El Salvador, Estonia, Ghana, India, Italy, Latvia, Lithuania, Pakistan, Romania, Serbia, Slovakia, Sweden, Taiwan, Thailand, The Czech Republic, Ukraine

02 people

Countries:

Colombia, Etiopia, Iran, Mexico, The Netherlands, Portugal, Russia, UK, USA 03 people

Countries:

Poland, Turkey

05 people

Countries:

China, Finland

06 people

Countries:

France

08 people

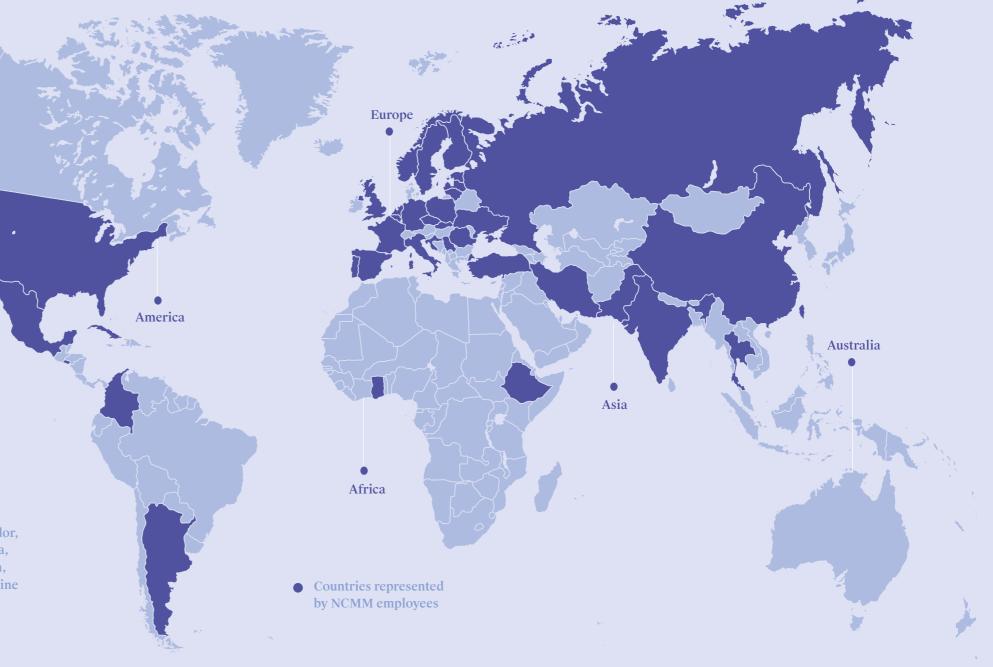
Countries:

Spain

12
people

Countries:

Germany





Personnel at NCMM 2021 & Q1 2022

Director and administration

Director

Janna Saarela

Assistant Director

Hartmut Luecke (until September 2021)

Chief Administrative Officer Ingrid Kjelsvik

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

Financial OfficersMette Kvernland
Anita Elisabeth Skolem

Human Resources Officer

Nina Modahl

Communications Officers

Annabel Darby (until September 2021) Nuru Saadi (from December 2021)

EATRIS Coordinator

Anita Kavlie

Higher Executive Officer

Carlos Romeo Rodriguez

IT Team

Harold Gutch
Gang Cheng
Melaku Tadesse
George Magklaras (until May 2021)
Torfinn Nome (from February 2022)

Administrative Officer

Larissa Lily

Laboratory Operations and Core Facilities

HSE Coordinator

Karen-Marie Heintz

General Lab Manager

Xi (Edna) Hu

Senior Engineer

Gladys Tjørhom

Research Technician

Luis Alberto Quintero Linares

Chemical Biology Core Facility

Johannes Landskron
(Platform manager)
Alexandra Gade (HTS Scientific
Officer, Screening & Chemistry)
Eirin Solberg (HTS Scientific Officer,
Screening & Robotics)
Bojana Sredic

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

NCMM Group Leader

Janna Saarela

Head Engineer / Lab manager

Monika Szymanska

PhD Fellow

Johanna M. Lehtonen

Researcher

Yasaman Padakman (from January 2022)

Stem Cell Group

NCMM Group Leader

Judith Staerk

Postdoctoral Fellows

Artur Cieslar-Pobuda João Santos *(until July 2021)*

Researcher

Adnan Hashim

Computational Biology and Gene Regulation

NCMM Group Leader

Anthony Mathelier

Researchers

Jaime Abraham Castro Mondragón Roza Berhanu Lemma

Postdoctoral Fellow

Vipin Kumar

PhD Fellows

Rafael Puig Riudavets Ieva Rauluseviciute Katalin Terézia Ferenc (from August 2021)

Lab Engineer

Dina Ruud Aronsen (from November 2021)

Software Engineer

Paul Boddie

MSc Students

Edgar Leal (from September 2021) Thomas Tubbehaugen (from January 2022) Jamal Farid Romman (from January 2022)

Miguel Angel Pérez Elena Emily Martinsen

Emily Martinsen Edgar Leal

Structural Biology and

Drug Discovery

NCMM Group Leader

Hartmut Luecke (until September 2021)

Research Scientist

Eva Cunha

Principal Engineer

Rasma Gutsmite

Postdoctoral Fellows

Javier Gutierrez Marta Sanz Gaitero

Joel Benjamin Heim (until July 2021)

PhD Fellows

Flore Kersten

Mateu Montserrat Canals

Precision pediatrics and gene editing

NCMM Group Leader

Emma Haapaniemi

Head Engineer

Monika Szymanska

Postdoctoral Fellow

Nail Fatkhutdinov (until November 2021)

PhD Fellows

Ganna Reint Zhuokun Li

Katariina Aino Inkeri Mamia

Pavel Kopcil

MSc Students

Jacob Conradi (from August 2021)

Oda Almåsbak Frida Haugen

Computational Oncology

NCMM Group Leader

Sebastian Waszak

Postdoctoral Fellows

Nancy Saana Banono (from February 2022)

Martin Burkert (from February 2021)

Researchers

Hanna Magdalena Sahlström

(from October 2021)

Ina Skaara Brorson (from March 2022) Birgit Kriener (from January 2022)

PhD student

Sandra Kunz (from August 2021)

MD Students

Sophie Mottl (from October 2021) Anne Martina Kraus (from September 2021)

Research Assistant

Frida Moi (January-December 2021)

Cell Cycle Regulations

NCMM Group Leader

Sandra Avilez-Lopes

Head Engineer

Mari Nyquist-Andersen (until March 2021)

Research Scientist

Ruth Martín Martín (until June 2021)

Marina Portantier

Chemical Neuroscience

NCMM Group Leader

Camila Vicencio Esguerra

Head Engineer

Ana C. S. Tavara

Researcher

Wietske van der Ent

PhD Fellows

Nancy Saana Banono

(until October 2021)

Elham Shojaeinia

Nastaran Moussavi (shared with School of Pharmacy)

Research Technicians

Alejandro Pastor Remiro Karolina Kirstein-Smardzewska

Hellen My Ky Lam Taradol Sutjaritvorakul

MSc Students

Daarathy Pathmanathan Sellathurai Zuhur Said (from September 2021) Frie Dewaele (from February 2022) Ana Pardo Perez (from February 2022) Geoffroy van Dessel

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Structural Biology and Chromatin

NCMM Group Leader

Nikolina Sekulic

Principal Engineer

Stine Malene Hansen Wøien

Research Scientist

Dario Segura- Peña

Postdoctoral Fellows

Ahmad Ali Ahmad Saranya Subramani *(until April 2021)*

PhD Fellow

Hermanga Gogoi (from February 2022)

MSc Students

Ole Magnus Fløgstad (from November 2021) Anna Mørch (from February 2022)

Bionanotechnology and Membrane Systems

NCMM Group Leader

Irep Gözen

Postdoctoral Fellow

Inga Põldsalu Thomas Aga Legøy

PhD Fellows

Elif Köksal *(until May 2021)* Karolina Spustova Aysu Kucukturhan Kubowicz Lin Xue Jicheng Li *(from October 2021)*

MSc Student

Ingrid J. Schanke (Until September 2021) Maivizhi Thiyagaraja (until August 2021)

Research Assistant

Ingrid J. Schanke (from September 2021)

Computational Biology and Systems Medicine

NCMM Group Leader

Marieke L. Kuijjer

Postdoctoral Fellows

Tatiana Belova Annikka Polster Daniel Osorio *(until September 2021)*

PhD Fellows

Ping-Han Hsieh Romana T. Pop Giulia Schito (from January 2022) Debora Meijer (co-supervised with Judith Bovée, Leiden University Medical Center) Saikat Das Sajib (co-supervised with Erik Knutsen, Arctic University of Norway, from January 2022)

MSc Student

Gabriel Bratseth Stav (from November 2021)

Research Assistant

Genís Calderer i Garcia (from August 2021)

BSc Student

Shanna Schneidewind (May to August 2021)

Systems Neuroscience & Sleep

NCMM Group Leader

Charlotte Boccara (from April 2022)

Research Scientist

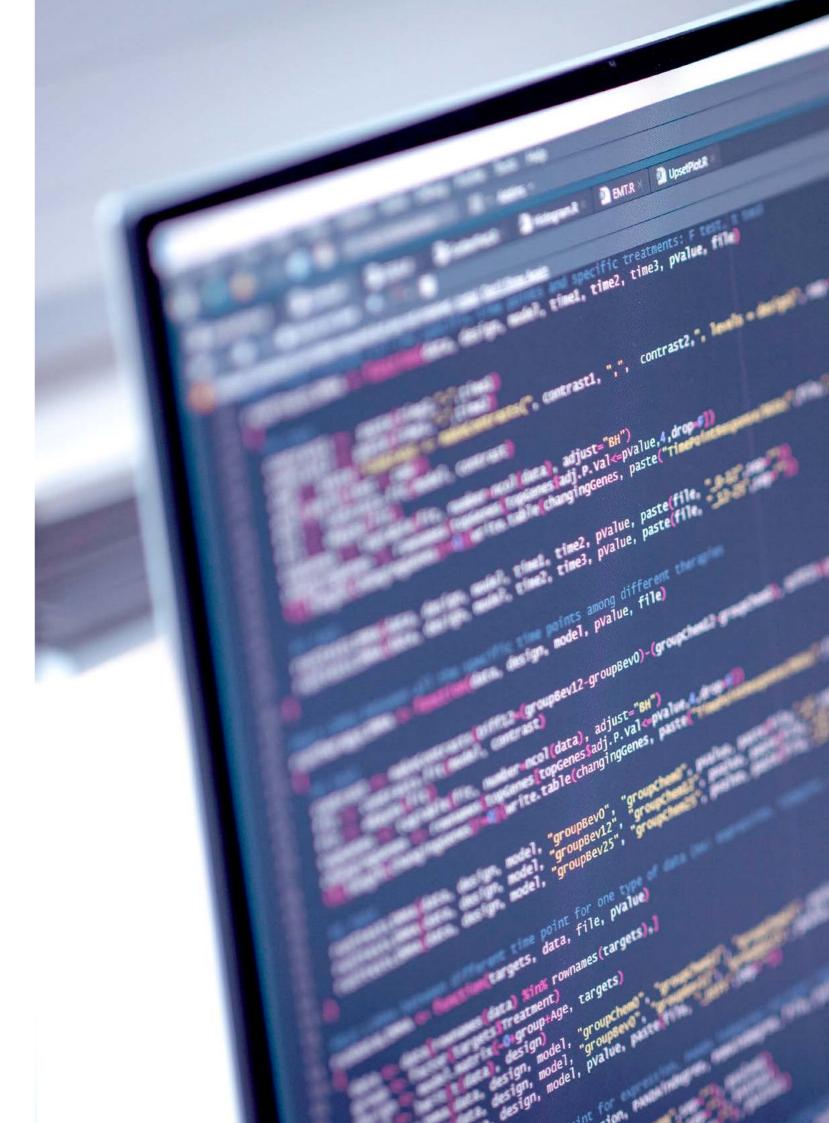
Solomiia Korchynska (from April 2022)

Postdoctoral Fellow

Eis Annavini (from April 2022)

Students

Ela Babursah (from April 2022) Elisabeth Mathisen (from April 2022)



NCMM CO-FUNDERS:







NORDIC EMBL PARTNERSHIP FOR MOLECULAR MEDICINE:











NATIONAL AND INTERNATIONAL COLLABORATORS:







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