



Centre for Molecular Medicine Norway
Nordic EMBL partnership for Molecular Medicine

A large, stylized circular graphic composed of two concentric rings. The rings are filled with numerous small, rectangular segments in various shades of blue, ranging from light to dark. The segments are arranged in a way that creates a sense of depth and movement, resembling a molecular structure or a complex data visualization. A horizontal white bar with a thin grey border cuts across the middle of the rings, containing the text 'ANNUAL REPORTS 2009 & 2010'.

ANNUAL REPORTS 2009 & 2010



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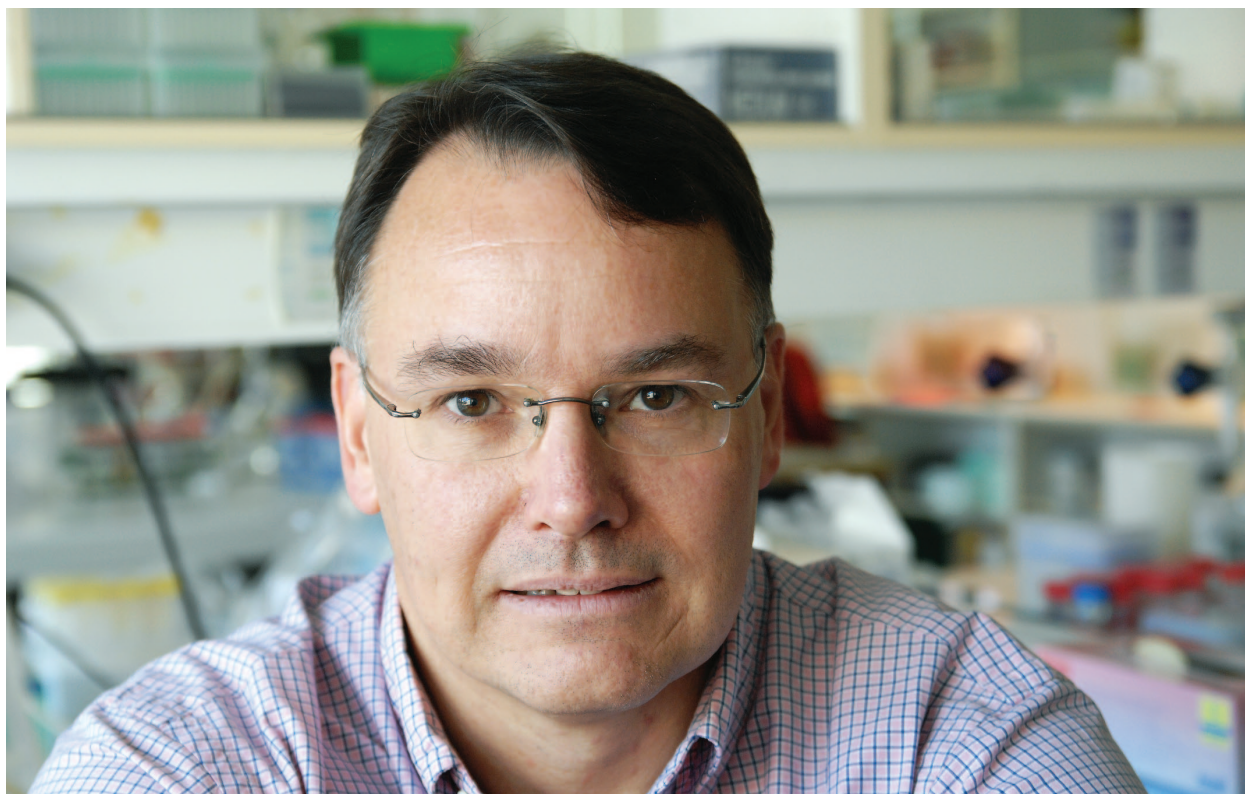
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Photo: Ola Sæther

1 Review by the Director



Professor Kjetil Taskén, Director of NCMM

Photo: Ola Sæther

“Dear friends, colleagues, and supporters of NCMM,

It is a great pleasure to look back on the last two years and write the first commentary from the Director for the NCMM Annual Reports 2009 & 2010. Although NCMM was formally established in 2008 (please see section 2 “NCMM - a Brief Overview”), the Centre had its first operational year in 2009 when Elin Kaurstad joined NCMM as Chief Administrative Officer and established a core administrative unit. Their enthusiastic efforts have been key in getting NCMM operative and functioning.

A main task in NCMM during 2009 and 2010 was hiring staff to build the centre, and by the end of 2010 there were more than 40 NCMM staff. Most importantly, NCMM hired its first three new group leaders; Dr. Ian G. Mills, Dr. Erlend A. Nagelhus and Dr. J. Preben Morth started in 2009 and 2010. Furthermore, the last two group leaders, Dr. Toni Hurtado and Dr. Judith Staerk, have been hired and will start in August 2011 and January 2012, respectively. Our new group leaders quickly

embarked on the task of building and establishing their groups, and starting vibrant new research programs that are rapidly gaining visibility (see section 5 “Research Areas and Group Leaders” for details). By November 2010, the time had come for an official inauguration of NCMM, when we presented the developing centre and received much appreciated greetings from all our partners and collaborators.

The overall objective of NCMM is to establish molecular medicine research, particularly focused on disease mechanisms where Norway has clear strengths, including immune disorders, cancer, and cardiovascular and CNS-related disease. Disease mechanisms will be studied with the long term goals of developing and adapting technologies for personalised medical applications as well as unraveling new diagnostic methods and drug targets. In order to achieve these goals, NCMM will capitalise on synergies within the Nordic region



Photo: Francesco Saggio

through its collaborations with the EMBL and the Finnish and Swedish sister centers through the Nordic EMBL partnership for molecular medicine.

As a national centre in molecular medicine, NCMM is aided by its National Reference Group and has a mission to form national networks for molecular medicine as well as to facilitate translation of discoveries in basic medical research into clinical practice. NCMM has established a national network of 12 outstanding and established Norwegian scientists affiliated with NCMM as Associate Investigators. Furthermore, with its mandate to facilitate translational research in Norway, NCMM partnered with 11 other European molecular medicine institutes in EATRIS (EU-ESFRI project European Advanced Translational Infrastructure). EATRIS is a preparatory phase infrastructure project that planned the future of translational research in Europe from 2008 to 2010 and led to a plan to organise translational research in Europe. NCMM has hosted and organised Norway's participation in the project, and now

an EATRIS Steering Committee with two members from each region in Norway works to establish EATRIS.

In order to facilitate translation of its research, NCMM has also developed strong links to its partner South-Eastern Norway Regional Health Authority and its subsidiary Oslo University Hospital. The NCMM Consortium Agreement promotes the exchange of personnel and NCMM-hosting hospital staff, an option that has already been actively pursued by several postdocs and PhD fellows/clinicians that are co-supervised in NCMM groups. Furthermore, adjunct appointments in clinical or preclinical departments in Oslo University Hospital have been established for all NCMM group leaders in order to facilitate translational research.

NCMM is still in the developing phase, with the first group leaders recruited in late 2009, most staff in the groups hired in 2010, and the first publications and extramural grants from the new groups coming in from 2011. However, with the excellent set of brilliant young group leaders recruited from an international arena, I am sure NCMM is at the start of a very interesting endeavor with great potential for excellence originating from its own research. Furthermore, the Nordic EMBL Partnership in Molecular Medicine holds great promise for collaboration and joining forces by drawing on one another's strengths. Lastly, as a national centre for molecular medicine with the responsibility of building networks and facilitating translational research, and with its National Reference Group and Network of Associate Investigators, NCMM is a tool that can be used to foster collaboration and excellence in research and in which partners across Norway are invited to take ownership and utilise."

June, 2011

Kjetil Taskén

Director NCMM

2 NCMM - a Brief Overview

The Centre for Molecular Medicine Norway (NCMM) is an international biomedical research institute with the overall objective of translating basic medical research into clinical practice. NCMM is particularly focused on disease mechanisms where Norway has clear strengths, including non-communicable diseases such as cancer, cardiovascular disease, CNS-related disease and immune disorders. By establishing new diagnostic methods and identifying potential drug targets, as well as adapting medical technologies for more patient-specific applications, the NCMM is developing new therapeutic strategies

for commercial exploitation.

The NCMM was established in October of 2008 and, together with the Finnish Institute for Molecular Medicine (FIMM, University of Helsinki) and the Laboratory for Molecular Infection Medicine Sweden (MIMS, Umeå University), composes the Nordic EMBL Partnership for Molecular Medicine. The purpose of this partnership is to facilitate scientific collaboration, and thereby capitalise on both intellectual and material resources within the Nordic region in order to exploit emerging technologies and to develop molecular and personalised medicine.

NORDIC EMBL PARTNERSHIP FOR MOLECULAR MEDICINE

In parallel with the establishment of NCMM, the Nordic EMBL Partnership for Molecular Medicine was planned and inaugurated in 2007 as a joint venture between the European Molecular Biology Laboratory (EMBL) and the University of Helsinki, Finland; the University of Oslo, Norway; and Umeå University, Sweden, and involved the building of national sister centers in each of the three countries.

The partnership between EMBL, the Institute for Molecular Medicine Finland (FIMM), the Laboratory for Molecular Infection Medicine Sweden (MIMS) and the Centre for Molecular Medicine Norway (NCMM) is dedicated to the growing field of life sciences that investigates the molecular basis of disease and explores molecular and genetically based treatments. Aiming to combine complementary strengths in the Nordic EMBL Partnership, each partner contributes a unique set of expertise, skills and facilities that encompass EMBL's recognised research strengths in the areas of molecular, cellular and developmental biology, bioinformatics and structural biology. These areas are complemented by Norway's expertise in molecular mechanisms of disease, Sweden's focus on microbial pathogenicity and molecular infection medicine, and Finland's strengths in human genomics and medical systems biology, thereby equipping the partners to tackle some of the most challenging questions in biomedicine.

Each partner provides access to scientific infrastructure, including databases, facilities and instrumentation, as well as to clinical materials, networks and training activities, and adopts the EMBL model for international recruitment, staff turnover and scientific reviews. The partnership now also receives support from NordForsk as a Nordic Network of National Centers of Excellence. Collaborations and joint efforts among the centers have increased considerably during 2009 and 2010.



MOLECULAR LIFE SCIENCES AT THE UNIVERSITY OF OSLO (MLS^{UiO})

MLS^{UiO}

Molecular Life Science
- an multifaculty priority research area at UoO



Professor Odd
Stokke Gabrielsen,
MLS^{UiO} chair since
2002

MLS^{UiO} is a strategic body that promotes high quality and innovative research in molecular life sciences and facilitates interdisciplinary and interfaculty collaboration. MLS^{UiO} is particularly important as research in the molecular life science field commonly crosses the boundaries of traditionally defined disciplines and there has been significant need for strategic development and coordination.

MLS^{UiO} reports to the Rector of the University of Oslo and represents one of the university's seven inter-faculty initiatives. The activities that fall under the umbrella of MLS^{UiO} include research institutes in the Faculty of Science, the Faculty of Medicine, and the Faculty of Dentistry, as well as the Biotechnology Centre and the Norwegian Centre for Molecular Medicine; the latter two report to MLS^{UiO} as governing body. By ensuring the optimal use of resources, strategic equipment investments, excellent researchers and inter-faculty research and teaching, MLS^{UiO} contributes to the best possible framework for inter-disciplinary research.

The NCMM is a joint venture among the University of Oslo (hosting institution), the Research Council of Norway (Forskningsrådet) and South-Eastern Norway Regional Health Authority (Helse Sør-Øst). The centre's location in the Oslo Research Park results in overlap and co-localisation with the Biotechnology Centre of Oslo and the Centre for Molecular Biology and Neuroscience, thereby providing extensive access to infrastructure, instrumentation and core facilities, as well as theoretical and technical expertise. Furthermore, with its mandate to facilitate translational research in Norway, NCMM partnered with 11 other European molecular medicine institutes in EATRIS (EU-ESFRI project European Advanced Translational Infrastructure; for more information see section 7 - "National and International Infrastructure Collaborations").

As a partner institution of EMBL, the leading European institution in molecular life sciences, NCMM conforms to the EMBL model in terms of its organisation, administration and quality assessment, as well as the global recruitment of researchers. The specific combination of internationally recognised co-operation partners, state-of-the-art facilities, ac-

cess to Nordic resources and EMBL structure, and outstanding internationally recruited scientific staff provides NCMM with tools needed to achieve excellence in translational medical research.

The research conducted by the centre is linked to both biotechnology and bio-pharmaceutical industries, which is important in terms of technological development and health-related infrastructure. This co-operation, in combination with access to EMBL partners, will facilitate the translation of molecular medicine research into medical treatment, thus bridging the gap between scientific discovery and patient care.

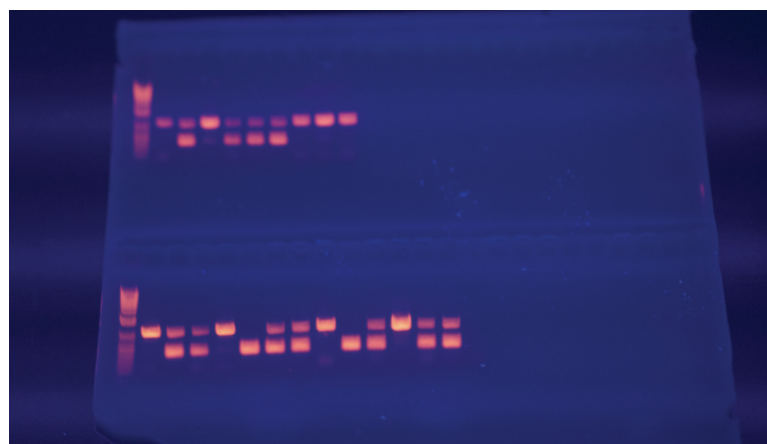


Photo: Francesco Saggio

NCMM TIMELINE - FROM CONCEPT TO REALISATION

2001 - 2002

Discussions began

EMBL and Nordic delegates to EMBL Council discussed a joint endeavor in molecular medicine.

2003 - 2004

Planning began

A white paper was drafted on the possibility of a partnership and received positive feedback from the Department of Research and Education in Norway and was similarly received in Sweden and Finland. The Research Council of Norway (RCN) invited the University of Oslo (UiO) to plan and host a national centre to participate in the partnership and identified founding partners.

2005 - 2007

Financing

A plan was drafted for the establishment and organisation of NCMM and was well received by the RCN. UiO made a financial allocation for its host contribution. Department of Research and Education allocated funds for NCMM from the national budget (starting 2007), forming the basis for the later agreements to establish NCMM as a national centre for molecular medicine.

2008

NCMM formally established

Agreements were signed by the three partners: University of Oslo, South-Eastern Norway Regional Health Authority and the Research Council of Norway. The Board was appointed. Professor Kjetil Taskén was selected as an interim director for 2009 & 2010.

2009

First operational year

Elin Kaurstad joined NCMM as Chief Administrative Officer. NCMM staff was hired to build the centre. The first three new group leaders were hired: Dr. Ian G. Mills, Dr. Erlend A. Nagelhus and Dr. J. Preben Morth.

2010

Scientific activity

2010 represents the first real year of scientific activity in the new research groups in NCMM beyond that in the groups of the founding partners. The hiring of staff continued, and by the end of 2010 more than 40 people were employed at NCMM. The official inauguration of NCMM was held in November, 2010.

2011 - 2012

Coming up...

Professor Kjetil Taskén was appointed director in January, 2011. As of 2011, Taskén's group now constitutes one of the six groups in NCMM. The final two group leaders have been hired; Dr. Toni Hurtado and Dr. Judith Staerk will start in August 2011 and January 2012, respectively. The new research groups are receiving their first extramural grants and NCMM-affiliated publications.

3 Addresses to NCMM

GREETING FROM PROFESSOR IAIN MATTAJ

Director General of EMBL (European Molecular Biology Laboratory)



Professor Iain Mattaj
EMBL Director General

Photo: EMBL

“Molecular medicine is a fast growing field, growing not only in terms of the research efforts dedicated to it, but also in terms of importance for our society. Rapidly improving sequencing technologies will revolutionise medicine as we know it; soon medical doctors will routinely sequence patients’ genomes for diagnosis and with time will be able to tailor an increasing number of personalised treatments to their needs. With its recognised strength in deciphering molecular mechanisms of disease, NCMM will undoubtedly make valuable contributions to this development. It is an important player in the European biomedical research community and, together with its partners in the Nordic EMBL Partnership for Molecular Medicine, it will help to advance molecu-

lar medicine to a stage where it can be introduced into hospitals.

The Nordic EMBL Partnership for Molecular Medicine is a strong alliance between EMBL, NCMM, the Institute for Molecular Medicine Finland (FIMM) and the Laboratory for Molecular Infection Medicine Sweden (MIMS). It builds on complementary strengths of the partners, integrates basic and medical research and establishes strong links to the clinical community.

The collaboration between EMBL and its Norwegian partners – although still in its early phase – is progressing rapidly. Over the course of the past year EMBL actively participated in the selection of young international group leaders for NCMM. The recruitment process followed stringent principles of scientific excellence and raised the node’s visibility nationally and internationally. At the same time it gave EMBL the chance to help in the task of shaping Norway’s Molecular Medicine research cluster. In this way the ambitious partnership not only reflects Norway’s commitment to state-of-the-art biomedical research but also EMBL’s dedication to building up excellence in life science research in its member states.

I am very pleased with the recent appointment of Kjetil Taskén as NCMM director, and I am convinced that under his excellent leadership the institute, and its partnership with EMBL, is in very capable hands and can look confidently to the future.”



GREETING FROM PROFESSOR RAGNHILD A. LOTHE

Chair of the Board, NCMM

“Following the initiative for an EMBL Nordic partnership in Molecular Medicine, the three leading institutions of medical research in Norway, University of Oslo, the Research Council and the Health Region South-East agreed to finance a Norwegian Centre. NCMM was established in 2008 and its inauguration was held in November, 2010. Their representatives to the board were appointed in 2008 and consisted of Professors Heidi Kiil Blomhoff, Sigbjørn Fossum, Ole Sejersted, Vidar Steen, Jon Torgils Vaage and myself. Our main task was to lead the process and employ the best qualified director for the Centre. After an international announcement and based on the united recommendation of the scientific committee, Professor Kjetil Taskén was appointed Director of NCMM. His documented exceptional scientific merits and strong leadership are necessary to lead a National Centre with high ambitions in molecular medicine. He is a pleasure to work with and has, in a relative short period of time, made sure that the necessary laboratories, offices and infrastructure are available for all new research groups.

We have also recruited outstanding new group leaders in various fields of interest. Some of them are already strongly integrated, with top research units in the Oslo area, not at least due to the fact that the centre prioritises the financing of side-positions in clinical or preclinical departments. Furthermore, the interest of top scientists to become associated investigators of NCMM has given the Centre a firm national foundation.

There exists a true international atmosphere in the Centre and they add competence and initiatives



Professor Ragnhild A. Lothe

to the Oslo medical research community. We are grateful for the personal interest and advice from the EMBL director general, which have been essential in the period leading up to the inauguration of NCMM. I feel confident that the Centre will experience success and demonstrate internationally competitive research results in molecular medicine. Hopefully, the research leaders and clinical collaborators will be able to translate such findings into clinical utility and innovations that improve the hospital efficacy of patient diagnostics and treatment as well as new product developments.”



Centre for Molecular Medicine Norway
Nordic EMBL partnership for Molecular Medicine



Photo: Ola Sæther

GREETING FROM PROFESSOR OLLI KALLIONIEMI

Director of FIMM (Institute for Molecular Medicine Finland)



Photo: FIMM

Professor Olli Kallioniemi
Director of FIMM

chemical biology, drug discovery and diagnostic development. We hope to achieve concrete translational benefits to the clinic, such as by facilitating adaptation of personalised medicine.

The year 2010 at FIMM was characterised by rapid growth, exciting research progress, and the setup of major national and international research infrastructures as well as biobanking. The number of employees at FIMM grew to 125, and the personnel now represent 20 nationalities. There are altogether 13 group leaders at FIMM, six of whom are EMBL-style principal investigators: Sergey Kuznetsov, Emmy Verschuren, Denis Kainov, Krister Wennerberg, Samuli Ripatti and as of 2011 Tero Aittokallio. We have been highly excited about the prospects and the ongoing close collaboration within the Nordic EMBL Partnership."

"2010 marked the third year in the build-up of the Institute for Molecular Medicine Finland (FIMM, www.fimm.fi) as a Finnish node for the Nordic EMBL Partnership for Molecular Medicine, operated by the University of Helsinki, in collaboration with three other institutions (HUS, THL and VTT). The mission of FIMM is to build a bridge from discovery to medicine. Research at FIMM is focused on human genomics and medical systems biology. In addition, FIMM operates a biobank and develops molecular medicine infrastructures and research services for genomics, bioinformatics, metabolomics, RNAi,

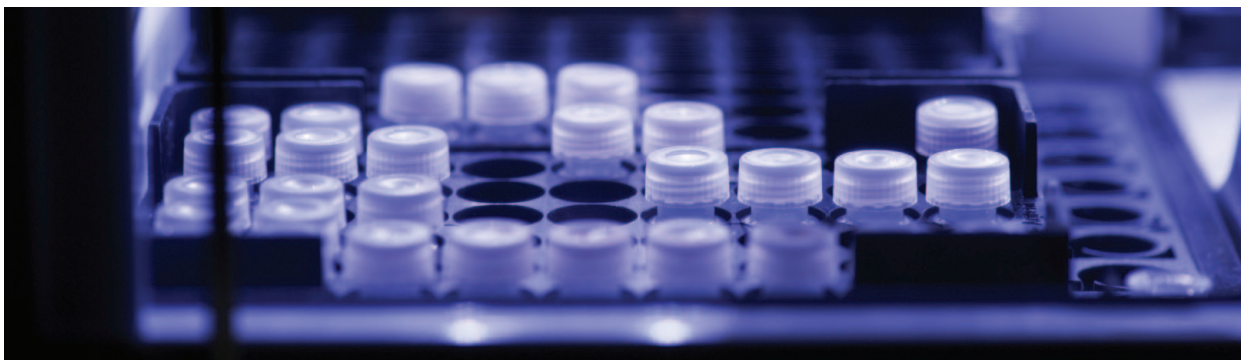


Photo: Francesco Saggio

GREETING FROM PROFESSOR BERNT ERIC UHLIN

Director of MIMS (Laboratory for Infection Medicine Sweden)

“The Laboratory for Molecular Infection Medicine Sweden (MIMS, www.mims.umu.se) is hosted by Umeå University within the Umeå Centre for Microbial Research (UCMR), which is an interdisciplinary research consortium devoted to molecular research and novel applications in relevant fields to infectious diseases. MIMS has been established with main support from the Swedish Research Council and with the aim to form a national laboratory for research in molecular infection medicine and by promoting career opportunities for young scientists. During the period 2008 to 2010, several new group leaders have been establishing their groups: Emmanuelle Charpentier, Constantin Urban, Jörgen Johansson, and Nelson Gekara have been recruited with support to build new groups; Niklas Arnberg and Andrei Chabes are provided support as affiliated group leaders. In addition, during 2010 a new initiative with recruitment of MIMS Clinical Research Fellows was launched and, starting in January 2011, two new young group leaders, Anna Överby and Rickard Lundmark, are joining MIMS. Together with the founding groups of Anders Sjöstedt, Bernt Eric Uhlin, Hans Wolf-Watz, Sven Bergström, Thomas Borén, and Åke Forsberg, the MIMS groups represent several different areas of infectious disease research and include investigations of many bacterial pathogens, viruses, and pathogenic fungi.

The establishment of the Nordic EMBL Partnership for Molecular Medicine and the joint efforts among



Photo: MIMS

Professor Bernt Eric Uhlin
Director of MIMS

FIMM, NCMM, MIMS and EMBL in the recruitment and build-up phase of the three Nordic nodes has been a very positive development. It will be a very good basis for us to expand our collaborative efforts and promote further synergistic scientific interactions. My MIMS colleagues and I are looking forward with great enthusiasm to the continued partnership activities and interactions among the research groups.”

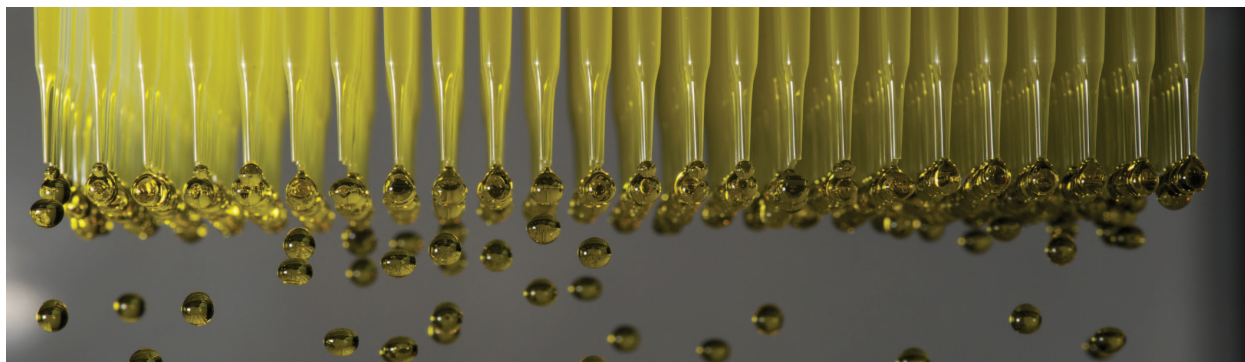


Photo: Francesco Saggio

4 NCMM Launch Event

The NCMM Opening Ceremony took place on the 11th of November, 2010 and included addresses from both national and international speakers. Professor Ragnhild Lothe (Chair of the Board of NCMM), Professor Ole Petter Ottersen (Rector, University of Oslo), Kyrre Lekve (State Secretary for Minister of Higher Education and Research), Are Helseth (Member of the Committee on Health and Care Services, Norwegian Parliament), Hilde Jerkø (Deputy Director, Division for Science Research Council of Norway), Professor John Torgils Vaage (Director for Research, South-Eastern Norway Regional Health Authority, and Erlend Smeland (Director for Research, Education and Innovation, Oslo University Hospital) each expressed their support for the NCMM while foreseeing great opportunity for international recruitment and scientific collaboration.

Dr. Silke Schumacher (Director International Relations, EMBL) outlined the core operating principles and strengths of EMBL, while Professor Olli Kallioniemi (Director of FIMM), Professor Bernt Eric Uhlin (Director of MIMS) and Professor Kjetil Taskén (Director of NCMM) introduced their respective institutions and emphasised the mutual benefits of the Nordic EMBL Partnership for Molecular Medicine. Finally, Odd Stokke Gabrielsen (Chair of the Steering Board, Molecular Life Science, UiO) discussed the advantages of the NCMM in both the local and global context of molecular medicine.

Following the opening ceremonies, a reception dinner was hosted by Professor Ole Petter Ottersen (Rector, University of Oslo), at Tøyen Hovedgård.



Photos: Jean Lorentzen



Photo: Vidar Iversen

5 NCMM Research Areas and Group Leaders

AN INTRODUCTION FROM THE DIRECTOR KJETIL TASKEN

NCMM's overall objective is to translate basic medical research into clinical practice. This is achieved through a co-operative approach between the research and clinical departments, allowing investigators to take advantage of Norwegian areas of strength in molecular medicine. By exploiting Nordic biobanks, patient materials, clinical trials and health registries, and employing state-of-the-art techniques, the NCMM researchers investigate disease mechanisms and strive towards developing more personalised medicine.

Three founding partners were chosen by the Research Council of Norway and affiliated with NCMM in order to provide "scientific mass" from the start; Professors Ole Petter Ottersen, Stefan Krauss and myself (Kjetil Taskén). As Ottersen currently serves at the Rector of the University of Oslo, his group is now represented by acting group leader Dr. Mahmood Amiry-Moghaddam.

NCMM group leaders are hired to non-tenured positions for five years with sufficient funding to establish a group. Given satisfactory performance, NCMM group leader contracts can be renewed once, allowing each group leader to stay at BiO / NCMM for up to 10 years. Group leaders are internationally recruited based on excellence criteria, are relatively young and have the potential to develop into fully qualified senior faculty. Five new group leaders have been hired, and have quickly embarked on the task of building and establishing their groups. Since my appointment as Director in January of 2011, my group also now constitutes one of the six research groups in NCMM.

Dr. Ian G. Mills was recruited from Cambridge Research Institute, Cancer Research UK, University of Cambridge, UK and formally started at the NCMM at the end 2009. Dr. Mills is interested in transcriptional and regulatory networks in prostate cancer and aims to better define the interplay between mem-

brane trafficking, metabolism and transcription in prostate cancer, as proteins in regulatory hubs for these processes that have potential value as cancer biomarkers and therapeutic targets. He is now actively building networks in the biomedical community and organizing clinical collaborations. The first research paper from Dr. Mills with NCMM affiliation came out in EMBO Journal in May, 2011 and received significant media attention. He has also established himself as a clear voice in the international molecular medicine community with a commentary article in Science Translational Medicine, 2010, and as senior author on a Nature Genetics, 2011 Perspectives article on the use of data from genome-wide association studies.



Photo: Ola Sæther

Dr. Erlend A. Nagelhus returned to NCMM in October, 2009 from a Research Assistant Professor position at Rochester University, NY. Dr. Nagelhus is a trained neurologist, and was formerly affiliated with Centre for Molecular Biology and Neuroscience, a Norwegian CoE embedded in the Institute for Basic Medical Sciences. Dr. Nagelhus performs molecular and functional analysis of glial cells and is focused on aquaporins

and associated molecules at the brain-blood and brain-liquor interfaces. He has implemented a new set of techniques for *in vivo* multiphoton imaging to study cerebral blood flow regulation and synaptic function. Dr. Nagelhus is also the head of the Letten Centre for Neuroimaging; a technology platform for imaging funded by a private donation. His first research paper with NCMM affiliation was published in PNAS 2011.

Dr. J. Preben Morth trained in structural biology at the EMBL Outstation in Hamburg and was recruited from Aarhus University to NCMM, where he started in October 2010. His research is in the area of structure and function of membrane transporters, particularly membrane pumps or P-type ATPases such as the sodium and calcium ATPases. In NCMM, Morth has started a new program on pH regulation and structure-function studies on bicarbonate trans-

porters, which has now been short-listed for ERC Starting Grant funding. His research has relevance to cardiology, neurobiology and kidney diseases, and he also jointly runs a drug targeting project with Lundbeck Pharma in Denmark. Morth has published a review in Nature Reviews Molecular Cell Biology with NCMM affiliation.

Dr. Toni Hurtado and **Dr. Judith Staerk** will join NCMM in the coming 6 months and will initiate research programs on transcriptional networks in breast cancer and stem cell therapy for hematological diseases.

The NCMM research groups are presented in more detail in the following pages.

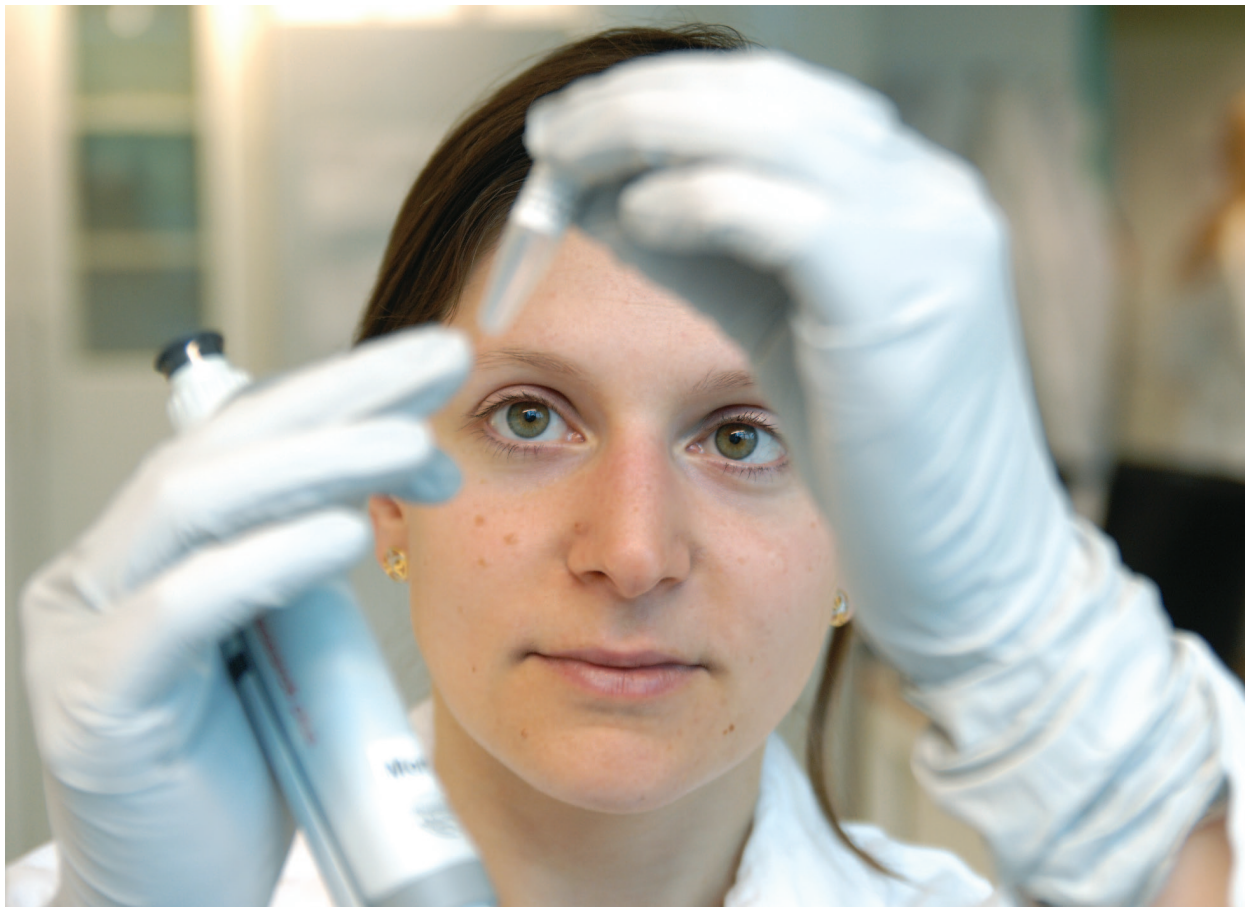


Photo: Ola Sæther

GROUP TASKEN - SIGNALLING NETWORKS IN HEALTH AND DISEASE



Photo: Ola Sæther

NCMM Director and Group Leader Kjetil Taskén

A major goal of the Taskén group is to understand the role of the cAMP second messenger system in the regulation of T cell function and its involvement in disease mechanisms, as well as to translate this understanding into therapeutic strategies and clinical practice.

One main focus is complex intracellular signalling networks, how such networks require anchoring and localisation, and how they mediate hormonally regulated physiological and pathophysiological processes. A second main focus is on cAMP-mediated immune-modulation with application in immune diseases and inflammation. In pursuit of this understanding, the group maps signalling pathways, identifies drug targets, develops small molecular compounds and provides “proof-of-principle” experiments using specific disease models.

Taskén's group employs a variety of techniques in bioinformatics, proteomics, high-throughput screening assays and genetic tools in order to screen new targets for *in vitro* and *in vivo* function. In order to isolate signalling complexes from a variety of targets, including T cells, placenta, and mitochondria, a chemical genomics approach is used and then combined with phosphoproteomics

GROUP MEMBERS

Research Scientists:

Torunn Berge
Elisa Bjørge
Torkel Vang
Einar Martin Aandahl

Postdoctoral fellows:

Birgitte Lygren
Isabelle Cortez
Arnaud David
Guro Mørk Johnsen
Johannes Landskron
Marie Rogne
Susanne Weedon-Fekjær

PhD Fellows:

Kristoffer Watten Brudvik
Morten Hagness
Karen Henjum
Maria Kalland
Kristine Moltu

MD/PhD & MSc students:

Simer Jit Bains
Anders Egeland
Trine Lise Larsen
Grunde Wibetoe
Ellen Østensen

Administrative Officer:

Berit Barkley

Scientific Officers:

Jorun Solheim, Engineer
Gladys Tjørhom

Chemical Biology Platform:

Anne Jorunn Stokka
Niko Sahlberg

External Funding

In addition to NCMM funding, the Taskén group receives support from a variety of sources, including the Norwegian Functional Genomics Program, Research Council of Norway, Norwegian Cancer Society, European Union and Molecular Life Sciences, University of Oslo

to understand spatiotemporal dynamics of phosphorylation in anchored complexes. Bioinformatics, peptide array and high-throughput screening assays are used to identify and characterise anchoring proteins for signal components of the cAMP pathway in addition to engineering anchoring disruptors to inhibit signalling in defined localisations. Transgenic mouse models and disease models have also been developed for *in vivo* proof-of-principle experiments and are currently used to study cAMP signalling in tumour models as well as in the heart and adipocytes, in regard to cardiovascular and metabolic diseases.

By combining flow cytometry with a panel of phospho-specific antibodies against signal molecules it is possible to obtain a global understanding of the signal transduction dynamics at a single cell level. The group had adapted this technology and combined it with fluorescent cell bar coding (FCB) for high-throughput to reveal intracellular signalling events that take place during T cell activation. This technique makes it possible to pursue studies of signalling responses in mixed cell populations and is used to map signalling by prostaglandins, cytokines and other inflammatory mediators, as well as regulatory T cell pathways involved in immune suppression, cancer and control of inflammation. This method is also used to investigate how these networks can be perturbed by small molecules and inhibitory signals. The improved understanding of signalling networks can be applied to many disease states, including immune-deficiencies, inflammatory disorders and cancers and will promote the development of highly specific pharmaceuticals that maximise their therapeutic value, while minimizing unwanted side-effects.

Selected Key Publications from PI:

Mosenden R, Singh P, Cornez I, Heglund M, Ruppelt A, Moutschen M, Enerback S, Rahmouni S, and Tasken K. (2011) Mice with disrupted type I protein kinase anchoring in T cells resist retrovirus-induced immunodeficiency. *J. Immunol.* 186(9): 5119-5130.

Bjorgo E, Solheim SA, Abrahamsen H, Baillie GS, Brown KM, Berge T, Okkenhaug K, Houslay MD, and Tasken K. (2010) Cross talk between phosphatidylinositol 3-kinase and cyclic AMP (cAMP)-protein kinase pathways at the level of a protein kinase B/beta-arrestin/cAMP phosphodiesterase 4 complex. *Mol. Cell Biol.* 30(7): 1660-1672.

Oberprieler NG, Lemeer S, Kalland ME, Torgersen KM, Heck AJ, and Tasken K. (2010) High-resolution mapping of prostaglandin E2-dependent networks identifies a constitutively active PKA node in CD8+CD45RO+ T cells. *Blood.* 116(13): 2253-2265.

Yaqub S, Henjum K, Mahic M, Jahnsen FL, Aandahl EM, Bjornbeth BA, and Tasken K. (2008) Regulatory T cells in colorectal cancer patients suppress anti-tumor immune activity in a COX-2 dependent manner. *Cancer Immunol. Immunother.* 57(6): 813-821.

Lygren B, Carlson CR, Santamaria K, Lissandron V, McSorley T, Litzenberg J, Lorenz D, Wiesner B, Rosenthal W, Zaccolo M, Tasken K, and Klussmann E. (2007) AKAP complex regulates Ca²⁺ re-uptake into heart sarcoplasmic reticulum. *EMBO Rep.* 8(11): 1061-1067.



Photo: Francesco Saggio

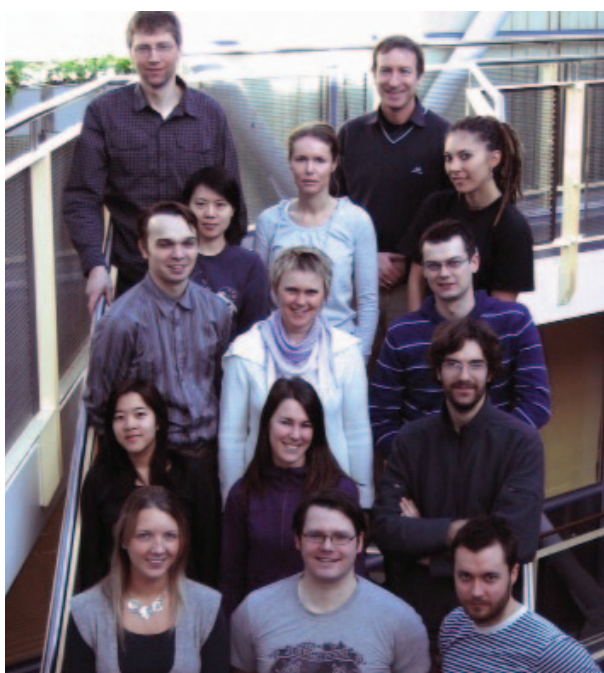
GROUP KRAUSS - STEM CELL SIGNALLING

Group Leader - Stefan Krauss

Stefan Krauss is one of the founding partners of NCMM. The NCMM-affiliated laboratory for cell signalling is located at the Cancer Stem Cell Innovation Centre (CAST) and is focused on Shh and canonical Wnt signalling in development, stem cells, and tumors. Currently, the group is investigating pathways that feed into Hh and Wnt signalling, as these pathways play important roles in various tumors and in stem cells. The knowledge of how these signalling pathways control tumour and stem cell populations is also being used to develop signalling antagonists, which may in turn be developed into pharmaceuticals, and therefore have an important influence on cancer treatment.

Using pancreas adenocarcinoma and colon cancer as models, Krauss' group has found that slow cycling cells (SSCs) have an increased potential to survive chemotherapeutic treatment and are able to recreate the initial heterogeneous tumour cell population. In addition, SSCs show an increased invasive and tumourigenic potential. Based on this knowledge, the group has identified novel small molecules that specifically inhibit beta-catenin, an integral component of Wnt-signalling, from entering the nucleus and therefore interfere with the Wnt-signalling pathway. The molecules are currently being tested in various *in vitro* and *in vivo* models with the aim of reaching clinical candidate status.

The Krauss group is also focused on the mechanisms that lead to cancer heterogeneity. Of particular interest is the understanding of the interplay between stem cell signalling (Wnt/Hh) and chromatin morphology. This knowledge should facilitate the development of further strategies to interfere with stem cell-ness in cancer. A central aim of this research is to identify and characterise druggable targets in stem cell pathways.



GROUP MEMBERS

Photo: CAST

Senior Scientist:
Ondrej Machon

Postdoctoral fellows:
Petter A. Olsen
Jennifer Dembinski

Visiting scientist:
Andrey Voronkov

PhD fellows:
Martin Strand
Jo Waaler
Nina Solberg
Jing Ying

Technicians:
Olga Machonova
Monika Gelazauskaite
Line Mygland
Huyen Mong Thi Dinh

MSc students:
Stine Bråtesveen (thesis completed)
Eline Buchman (thesis completed)

Secretary:
Bie Ekblad

Selected Key Publications from PI:

Waalder J, Machon O, von Kries JP, Wilson SR, Lundenes E, Wedlich D, Gradl D, Paulsen JE, Machonova O, Dembinski JL, Dinh H, and Krauss S. (2011) Novel synthetic antagonists of canonical Wnt inhibit colorectal cancer cell growth. *Cancer Res.* 71(1): 197-205.

Olsen PA, Gelazauskaite M, Randol M, and Krauss S. (2010) Analysis of illegitimate genomic integration mediated by zinc-finger nucleases: implications for specificity of targeted gene correction. *BMC. Mol. Biol.* 11:35.: 35.

Wilson SR, Strand MF, Krapp A, Rise F, Petersen D, and Krauss S. (2010) Hedgehog antagonist cyclopamine isomerizes to less potent forms when acidified. *J. Pharm. Biomed. Anal.* 52(5): 707-713.

Dembinski JL, and Krauss S. (2009) Characterization and functional analysis of a slow cycling stem cell-like subpopulation in pancreas adenocarcinoma. *Clin. Exp. Metastasis.* 26(7): 611-623.

Solberg N, Machon O, and Krauss S. (2008) Effect of canonical Wnt inhibition in the neurogenic cortex, hippocampus, and premigratory dentate gyrus progenitor pool. *Dev. Dyn.* 237(7): 1799-1811.

GROUP AMIRY-MOGHADDAM - LABORATORY FOR MOLECULAR NEUROSCIENCE

Group Leader - Mahmood Amiry-Moghaddam



Amiry-Moghaddam is the head of the Laboratory for Molecular Neurosciences (LMN), formerly led by Ole Petter Ottersen, one of the NCMM founding partners. The NCMM-affiliated LMN investigates the molecular mechanisms involved in physiological processes such as cell volume regulation, gliovascular signalling, the maintenance of blood-brain-barrier integrity and the role of the brain extracellular matrix in normal brain function. The aim is to use this knowledge to unravel the molecular basis for cell death and edema development in stroke and other neurological conditions, and to explore the pathophysiology of temporal lobe epilepsy, Alzheimer's disease and other neurodegenerative disorders.

Several areas of interest are currently being explored by LMN members, including brain volume regulation and osmosensing, the physiopathological roles of aquaporins in the brain, and the role of the brain extracellular matrix in health and disease. LMN is also investigating glutamate as a transmitter substance in the normal brain as well as a mediator of excitotoxicity in pathological conditions and unraveling the physiological and pathophysiological roles of astrocyte endfeet. The long term goals of the LMN are to identify new mechanisms of disease and new molecular targets for the treatment of neurological diseases.

GROUP MEMBERS

Professors / Emeriti:

Finn Mogens Haug
Eric Rinvik
Kirsten Osen
Ole Petter Ottersen
Peter Agre - Guest professor

PhD fellows:

Laura Camassa
Lisa K. Lunde
Maria Mylonakou
Silje Alvestad
Øyvind Jacobsen
Eystein Hoddevik
Didrik Frydenlund
Lisa Olsson

Researchers:

Katja Stahl
Reidun Torp

Head engineers:

Bashir A. Hakim
Björg Riber
Johannes Helm
Jorunn Knutsen
Karen Marie Gujord

Undergraduate student:

Faraz H. Khan

Senior consultant:

Maria Beatriz Da Roche

Selected Key Publications from PI:

Mylonakou MN, Petersen PH, Rinvik E, Rojek A, Valdimarsdottir E, Zelenin S, Zeuthen T, Nielsen S, Ottersen OP, and Amiry-Moghaddam M. (2009) Analysis of mice with targeted deletion of AQP9 gene provides conclusive evidence for expression of AQP9 in neurons. *J. Neurosci. Res.* 87(6): 1310-1322.

Amiry-Moghaddam M, Hoddevik EH, and Ottersen OP. (2010) Aquaporins: multifarious roles in brain. *Neuroscience.* 168(4): 859-861.

Jacobsen O, Maekawa H, Ge NH, Gorbitz CH, Rongved P, Ottersen OP, Amiry-Moghaddam M, and Klaveness J. (2011) Stapling of a 3(10)-helix with click chemistry. *J. Org. Chem.* 76(5): 1228-1238.

Benfenati V, Caprini M, Dovizio M, Mylonakou MN, Ferroni S, Ottersen OP, and Amiry-Moghaddam M. (2011) An aquaporin-4/transient receptor potential vanilloid 4 (AQP4/TRPV4) complex is essential for cell-volume control in astrocytes. *Proc. Natl. Acad. Sci. U. S. A.* 108(6): 2563-2568.

GROUP NAGELHUS - GLIO-VASCULAR IMAGING GROUP

Group Leader - Erlend A. Nagelhus

Nagelhus' research has focused on the molecular characterisation of membrane domains in glial cells, in particular glial endfoot membranes at brain-blood and brain-liquor interfaces. His research group, which joined the NCMM in 2010, is affiliated with the Centre for Molecular Biology and Neuroscience and runs its neuroimaging activity in Letten Centre at the Institute of Basic Medical Sciences, Domus Medica. Nagelhus' group explores the roles of glia in neurological disorders by *in vivo* two-photon laser scanning microscopy. This minimally invasive technique offers real-time imaging of physiological and pathophysiological processes in the brains of living animals. Through a cranial window or the thinned skull, the group is able to image the dynamics of neuronal and glial calcium signalling, cell morphology and motility, as well as cerebral blood flow.

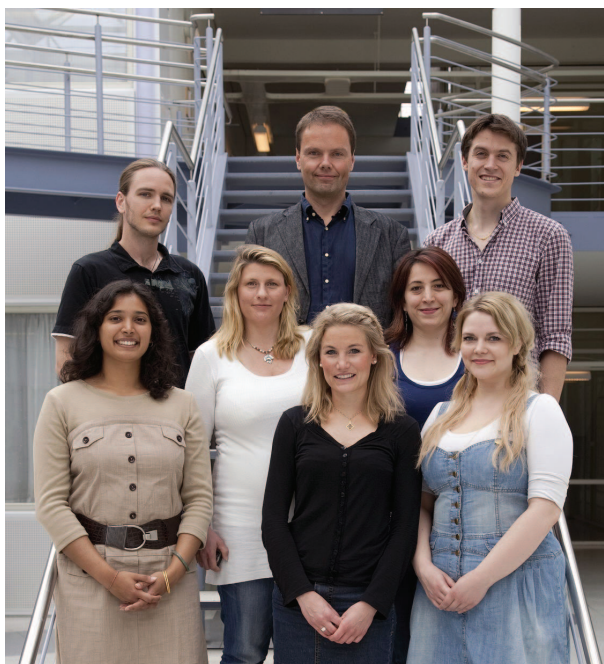
Currently, the group is using gene knockout strategies to study the roles of glial aquaporins and associated molecules in extracellular volume dynamics, synaptic transmission and at the brain-blood interface. The overall aim is to gain insight into mechanisms underlying glial control of neurons and the vasculature. Understanding neuronal-glial-vascular interactions may provide new treatment strategies for brain disorders with perturbed circulation and water homeostasis.

Selected Key Publications from PI:

Thrane AS, Rappold PM, Fujita T, Torres A, Bekar LK, Takano T, Peng W, Wang F, Thrane VR, Enger R, Haj-Yasein NN, Skare O, Holen T, Klungland A, Ottersen OP, Nedergaard M, and Nagelhus EA. (2011) Critical role of aquaporin-4 (AQP4) in astrocytic Ca²⁺ events elicited by cerebral edema. *Proc. Natl. Acad. Sci. U. S. A.* 108(2): 846-851.

This article earned a comment in *Nature Reviews Neuroscience*:

Welberg L. (2011) Glia: aquaporin: not so swell? *Nat. Rev. Neurosci.* 12(2): 66.



GROUP MEMBERS

Researchers:

Anna Thoren
Vidar Jensen (associate member)

Postdoctoral fellows:

John Burkhardt
Karolina Szokol (associate member)

PhD fellows:

Alexander S. Thrane
Vinita R. Thrane
Gry F. Vindedal
Nadia N. Haj-Yasein
Kjell Heuser (associated member)

Students in the Medical Student Research Program:

Cecilie E. Bugge
Georg Andreas Gundersen

External Funding

In addition to NCMM funding, the group is supported by the Research Council of Norway.

GROUP MILLS - PROSTATE CANCER

Group Leader - Ian G. Mills

Prostate cancer accounts for one third of all male cancer cases in Norway and is the second most significant cause of cancer mortality in men in Europe. In spite of the high incidence only around 20 to 30 percent of cases progress to metastatic disease. The goal of the group is to understand the biology of prostate cancer in order to improve detection and treatment.

The basis for much of the group's work is the study of the androgen receptor, a transcription factor and a primary molecular target in prostate cancer research. Genomics and transcriptomics have been used to identify androgen receptor target genes that play a significant role in the development of prostate cancer. Based on these approaches the Mills' group is exploring several themes in prostate cancer research and uses a number of traditional and state-of-the-art techniques. The structure and function of calcium/calmodulin-dependent kinases, which play an important role in energy metabolism, are studied using a structural biology approach. Western blots and imaging are used to evaluate the calcium-dependent regulation of autophagy and stress, as well as the regulation of glycosylation by hormones and metabolic flux. Metabolic prostate cancer biomarkers are validated in clinical samples by confirming which genes are upregulated, at both mRNA and protein levels, using real-time PCR, Western blotting and immunohistochemistry. Bioinformatics and chromatin immunoprecipitation approaches are used to define gene targets in prostate cancer for other significant transcription factors.

Evidence points consistently to metabolic pathways as critical regulatory hubs reflecting changes in transcription and mediating alterations in signalling and cell growth in the early stage of prostate cancer. Some of these changes are also fundamental to cancer biology as a whole, as typified by the Warburg Effect. We believe that by detecting and more selectively controlling metabolic responses in prostate cancer we will be able to identify the disease more effectively and have an impact on progression.



Photo: Kim Langmach Hein

GROUP MEMBERS

Postdoctoral fellow:
Kim Nikolai Hartlieb Engedal

Principal engineer:
Ingrid Jenny Guldvik

PhD fellows:
Lisa Gerner,
Harri Itkonen,
Stefan Barfeld
(from July 2011)

External Funding

In addition to NCMM funding, Mills' group is supported by the Norwegian Cancer Society, Molecular Life Sciences (University of Oslo), and two EU FP7 programs: P-CUBE (Infrastructure for Protein Production Platforms) and PRO-NEST (Prostate Research Organizations-Network of Early Stage Training, an EU/Marie Curie Training Network grant).

Selected Key Publications from PI:

Massie CE, Adryan B, Barbosa-Morais NL, Lynch AG, Tran MG, Neal DE, and Mills IG. (2007) New androgen receptor genomic targets show an interaction with the ETS1 transcription factor. *EMBO Rep.* 8(9): 871-878.

Freedman ML, Monteiro AN, Gayther SA, Coetzee GA, Risch A, Plass C, Casey G, De BM, Carlson C, Duggan D, James M, Liu P, Tichelaar JW, Vikis HG, You M, and Mills IG. (2011) Principles for the post-GWAS functional characterization of cancer risk loci. *Nat. Genet.* 43(6): 513-518.

Massie CE, Lynch A, Ramos-Montoya A, Boren J, Stark R, Fazli L, Warren A, Scott H, Madhu B, Sharma N, Bon H, Zecchini V, Smith DM, Denicola GM, Mathews N, Osborne M, Hadfield J, MacArthur S, Adryan B, Lyons SK, Brindle KM, Griffiths J, Gleave ME, Rennie PS, Neal DE, and Mills IG. (2011) The androgen receptor fuels prostate cancer by regulating central metabolism and biosynthesis. *EMBO J.* (Epub ahead of print. May 20, 2011).

Massie CE, and Mills IG. (2011) Mapping protein-DNA interactions using ChIP sequencing. *Methods Mol. Biol.* Chapter for "Transcriptional Regulation: Methods and Protocols" (In Press. July 2011).

Robinson JLL, MacArthur S, Ross-Innes CS, Tilley WD, Neal DE, Mills IG, and Carroll JS. (2011) Androgen Receptor driven transcription in molecular apocrine breast cancer is mediated by FoxA1. *EMBO J.* In press.

GROUP MORTH - MEMBRANE TRANSPORT

Group Leader - Jens Preben Morth

The Morth group employs a structural systems biology approach to investigate the proteins involved in acid-base homeostasis and metal ion transport across the cellular membrane.

The kidneys are highly complex organs with the vital role of maintaining homeostasis of small organic solutes and minerals in the body. The nephron in the kidney absorbs solutes from the blood and excretes residual products in the urine, and represents the main site for extensive solute exchange in mammals. It is the solute carrier (SLC) transporters that control this exchange.

A variety of techniques are used in order to identify and characterise both soluble and membrane bound proteins involved in pH regulation. A bioinformatics approach is used to target new proteins and interaction partners of interest. Structural information is obtained by X-ray crystallography, small angle X-ray scattering (SAXS). Several biophysical and biochemical techniques are also used, including activity assays and isothermal titration calorimetry (ITC) for protein-protein binding and small molecule interactions. The group is currently developing purification and lipid vesicle reconstitution protocols for the membrane proteins to study their three-dimensional atomic structure and aims to purify and characterise members of the SLC4 and SLC26 family.

A project recently started in the Morth group is focused on bicarbonate transporters from the kidney and brain and will benefit from the experience gained over the last several years of working with P-type ATPases. Bicarbonate transporters are involved in the exchange of acids and tightly control the regulation of intracellular pH across the plasma membrane. The system is strongly dependent on the ion gradients maintained by the P-type ATPases. The group aims to develop a complete structural model for anion transport and recognition. The structural analysis of P-type ATPases will continue with focus on the prokaryotic Ca^{2+} -ATPases and Mg^{2+} -ATPases, as well as Na^+/K^+ -ATPase, from both eukaryotic and prokaryotic origin.



Photo: Ola Sæther

GROUP MEMBERS

Postdoctoral fellows:
Harmonie Perdreau
Kim Langmach Hein

Principal engineer:
Hanne Guldsten

External Funding

In addition to NCMM funding, the group is supported by Lundbeck fondet.

Selected Key Publications from PI:

Morth JP, Pedersen BP, Toustrup-Jensen MS, Sorensen TL, Petersen J, Andersen JP, Vilse-n B, and Nissen P. (2007) Crystal structure of the sodium-potassium pump. *Nature*. 450(7172): 1043-1049.

Olesen C, Picard M, Winther AM, Gyrupe C, Morth JP, Oxvig C, Moller JV, and Nissen P. (2007) The structural basis of calcium transport by the calcium pump. *Nature*. 450(7172): 1036-1042.

Laursen M, Bublitz M, Moncoq K, Olesen C, Moller JV, Young HS, Nissen P, and Morth JP. (2009) Cyclopiazonic acid is complexed to a divalent metal ion when bound to the sarcoplasmic reticulum Ca^{2+} -ATPase. *J. Biol. Chem.* 284(20): 13513-13518.

Poulsen H, Khandelia H, Morth JP, Bublitz M, Moritsen OG, Egebjerg J, and Nissen P. (2010) Neurological disease mutations compromise a C-terminal ion pathway in the Na^+/K^+ -ATPase. *Nature*. 467(7311): 99-102.

Morth JP, Pedersen BP, Buch-Pedersen MJ, Andersen JP, Vilse B, Palmgren MG, and Nissen P. (2011) A structural overview of the plasma membrane Na^+/K^+ -ATPase and H^+ -ATPase ion pumps. *Nat. Rev. Mol. Cell Biol.* 12(1): 60-70.

Morth's group also has a keen interest in homology modeling, which is used to link known disease models to structural information. The structural interpretation of both homology models and experimentally determined structures has led to drug discovery and drug design.

6 NCMM Associate Investigators

In order to further develop its scientific and technological capabilities, the NCMM has established strong collaborative links with key scientists and research groups working across Norway through the appointment of Associate Investigators. These appointments, evaluated by a Selection Committee, were based on scientific excellence and translational merit, as well as added value and compatibility with NCMM mission. The first seven appointments as Associate Investigators affiliated with NCMM and the Nordic EMBL Partnership in Molecular Medicine were determined at the end of 2009 and are listed below in alphabetical order.



Professor Lars A. Akslen
Gade institute, Section for Pathology, University of Bergen

Professor Akslen is a specialist in surgical pathology, and his research group is currently engaged in translational cancer research, investigating genetic and molecular markers of aggressive tumour behavior and vascular proliferation.



Professor Anne-Lise Børresen-Dale
Department of Genetics
Institute for Cancer Research, Norwegian Radium Hospital

Professor Børresen-Dale's research group is focused on the study of ovarian and breast cancer, in particular the identification and characterisation of genotype and gene regulation profiles associated with elevated risk of cancer and lower responsiveness to treatment.



Professor Rolf Bjerkvik
NorLux Neuro-Oncology Laboratory, Department of Biomedicine, University of Bergen

Professor Bjerkvig's research group has recently focused on experimental neurooncology, in particular the mechanisms responsible for tumour angiogenesis in the brain and therapeutic interventions that could prevent such events.



Professor Geir Christensen
Institute for Experimental Medical Research, Oslo University Hospital Ullevål

Professor Christensen's research group is currently focused on the molecular mechanisms of heart failure.



Professor Per Eystein Lønning
Section of Medicine, University of Bergen, & Department of Oncology, Haukeland University Hospital

Professor Lønning's group is focused on translational research in cancer treatment, in particular the mechanisms of drug resistance to breast cancer therapy.



Professor Pål Rasmus Njølstad
Department of Pediatrics, Haukeland University Hospital

Professor Njølstad's group has a long history of translational research in diabetes, in terms of both characterizing new diabetes syndromes and establishing novel targeted treatments.



Professor Vidar M. Steen

Department of Clinical Medicine, Section for Medical Genetics and Molecular Medicine, University of Bergen

Professor Steen's group is currently investigating biological and genetic factors involved in the aetiology, pathophysiology, and treatment of schizophrenia and bipolar disorder.



Professor Arne Klungland

Centre for Molecular Biology and Neuroscience, Oslo University Hospital and University of Oslo

Professor Klungland's group is focused on the identification and characterisation of genes whose products are involved in DNA repair, with the aim elucidating the contribution of single genes to protection against mutations, genomic instability, ageing and ageing related diseases.

New NCMM Associate Investigators from 2011 (in alphabetical order):



Professor Ole A. Andreassen

Institute of Clinical Medicine, University of Oslo and Div. of Mental Health and Addiction, Oslo University Hospital

Professor Andreassen's research field is psychiatry, in particular schizophrenia and bipolar disorder, genetics and brain pathology, somatic health and psychotropic pharmaceuticals.



Professor Ole Petter Rekvig

Molecular Pathology Research Group, Institute of Medical Biology, University of Tromsø

Professor Rekvig's research group is focused on the central aspects of Systemic Lupus Erythematosus and lupus nephritis, including immunological tolerance, apoptosis and necrosis, autoimmune pathophysiology, transcriptomics/ RNA biology and the regulation of renal DNases.



Professor Bjarne Bogen

Centre for Immune Regulation, Institute of Clinical Medicine, University of Oslo; Department of Immunology, Div. of Diagnostics & Intervention, Oslo University Hospital

A major focus for Professor Bogen's group is the role of T cell subsets in immune regulation and autoimmunity, as well as protection and vaccination against B cell lymphomas and multiple myeloma. Another interest is the development of recombinant antibodies as vaccines.



Professor Helga B. Salvesen

Department of Clinical Medicine, University of Bergen and Department of Obstetrics and Gynecology, Haukeland University Hospital

Professor Salvesen's research is focused on the molecular mechanisms of cancer, and makes use of a large biobank of cancer specimens in order to define reliable molecular markers for aggressive disease.

7 National and International Infrastructure Collaborations

NCMM is involved in a number of institutional level collaborations and infrastructure initiatives, with the objective of scientific integration and facilitating translational research. Both the breadth of internationally recognised co-operation partners and the access to Norwegian, Nordic and European resources provide the NCMM with the infrastructure tools to achieve excellence in translational medical research. The national and international infrastructure collaborations in which NCMM is involved are outlined below.

NATIONAL

NCMM is a joint venture among the University of Oslo (hosting institution), the Research Council of Norway (Forskningrådet) and South-Eastern Norway Regional Health Authority (Helse Sør-Øst). Its location in the Oslo Research Park provides overlap and co-localisation with the Biotechnology Centre of Oslo and the nearby Centre for Molecular Biology and Neuroscience, thereby providing extensive access to infrastructure and instrumentation in addition to both theoretical and technical expertise.

The Biotechnology Centre of Oslo also hosts the

Chemical Biology Platform, a high throughput screening facility that offers competence and technologies that enable researchers to study the effect of chemical compounds on biological function. The platform is part of a larger Norwegian network (ChemBioNet Norway / NOR-OPENSOURCE), which brings together leading chemists, biologists and informaticians from complementing units located in Tromsø, Trondheim, Bergen and Oslo, and thereby provides access to a host of national infrastructure tools. The Norwegian platform is a full partner of the European ChemBioNet and thereby has access to their chemical libraries.

EUROPEAN

The European Strategy Forum on Research Infrastructures (ESFRI) was designed to develop the scientific integration of Europe and to strengthen its international outreach. The competitive and open access to high quality research infrastructures both supports and benchmarks the quality of the activities of European scientists, and attracts the best researchers from around the world. The challenge of ESFRI was to identify and address the needs for



EU FP7 RESEARCH PROJECT

PROSTATE RESEARCH ORGANIZATION-NETWORK OF EARLY STAGE TRAINING (PRO-NEST)

PRO-NEST is an FP7 Marie Curie Initial Training Network investigating the initiation and progression of prostate cancer on a molecular level, and ultimately aims to improve diagnosis, treatment and prevention by identifying new biomarkers and therapeutic targets. As a training program, PRO-NEST provides young scientists with the tools they need to become independent and versatile prostate cancer researchers, with both a broad knowledge base and specific expertise in basic, clinical and applied research. PRO-NEST is an integrated European training program involving respected scientists from more than 16 institutions in 9 different European countries, and the multi-disciplinary approach trains skills in specific technical areas as well as in project management and the communication of science.

EU FP7 RESEARCH PROJECT

NATURAL PRODUCTS FROM MARINE FUNGI FOR THE TREATMENT OF CANCER (MARINE FUNGI)

MARINE FUNGI is an FP7 project that aims to explore the potential anti-cancer properties of compounds naturally produced by various strains of marine fungi collected off the coasts of Elba, Chile, and Indonesia. Eleven partner institutions from seven countries have joined the MARINE FUNGI project. Each partner was specifically chosen for their expertise in the various fields needed, such as the collection, isolation and fermentation of marine fungi strains, identification and characterisation of active secondary metabolites, screening of these compounds for biological activity against a panel of human cancer cell lines, and the eventual large scale production of these products.

large research infrastructures in Europe for the next 10 to 20 years, covering all scientific areas. ESFRI published its first “European Roadmap for Research Infrastructures” in 2006, including EATRIS (ESFRI project European Advanced Translational Infrastructure) as one of six prioritised life science infrastructures.

During the period from 2008 to 2010, NCMM acted as a national host for the Preparatory Phase of the project EATRIS, the European Advanced Translational Research Infrastructure in Medicine, with Professor Kjetil Taskén as the scientific partner representing Norway. EATRIS is an international research infrastructure initiative aimed at strengthening health research and development (R&D) in Europe in order to allow the more efficient transfer of research discoveries into new clinical applications for disease prevention, diagnosis and treatment. The infrastructure includes expertise in technology transfer, regulatory affairs and product development, training programs, and translation centers with state-of-the-art facilities for complete R&D development pipelines for different product types. Effectively, EATRIS will operate to increase the return on the investments made in publicly funded biomedical research by removing existing bottlenecks to translation, quickly bringing new discoveries closer to the clinic (‘bench-to-bedside’) and to society in general.

The EATRIS Preparatory Phase was funded with €4.2 million by the European Community’s 7th Framework Programme, supporting the formation of

a consortium consisting of ten countries: Denmark, Finland, France, Germany, Italy, the Netherlands, Norway, Spain, Sweden and the UK. NCMM was responsible for the preparation of a grant application to the Norwegian Research Council (NRC) for support to build a Norwegian EATRIS node (an EATRIS Centre), submitted in 2010, and was short listed by the NRC to submit a revised application.

The European Infrastructure of Open Screening Platforms for Chemical Biology (EU-OPENSSCREEN) consists of 20 partners from 17 European countries. EU-OPENSSCREEN aims to build an association of screening centres with the most advanced technology, to be used by European researchers for identifying new compounds and targets in a variety of fields in Life Sciences (e.g. human and veterinary medicine, systems biology, biotechnology, agriculture and nutrition). These association centres will include high-throughput screening platforms, chemical libraries, chemical resources for hit discovery and optimisation, bio- and chem-informatics support, and a publicly accessible database containing screening results, assay protocols, and chemical information. The Chemical Biology Platform at the Biotechnology Centre of Oslo is part of the Norwegian participation in the EU-OPENSSCREEN (ChemBioNet Norway/NOR-OPENSSCREEN, with Professor Kjetil Taskén as a Norwegian partner and Steering Committee member), thereby giving NCMM access to leading chemistry, biology and informatics resources.

8 Board and National Reference Group

NCMM BOARD



Chair of the Board

Professor Ragnhild A. Lothe
Norwegian Radium Hospital
Oslo University Hospital/ University of Oslo

Members of the Board



Professor
Heidi Kiil Blomhoff
Faculty of Medicine
University of Oslo



Professor
Sigbjørn Fossum
Faculty of Medicine
University of Oslo



Professor
Ole Sejersted
Oslo University Hospital
Ullevål



Professor
John Torgils Vaage
Oslo University Hospital
Rikshospitalet



Professor
Vidar Steen
National Reference
Group NCMM



Marianne Grønsløth
Research Council of
Norway
Observer to NCMM
Board proceedings

Deputy Members of the Board

Professor Frode Vartdal
Faculty of Medicine, University of Oslo

Assistant Professor Ingvild Mikkola
University of Tromsø

NATIONAL REFERENCE GROUP

Members

Professor Vidar Steen, University of Bergen

Assistant Professor Ingvild Mikkola, University of Tromsø

Professor Terje Espevik, Norwegian University of Science and Technology

Professor Anne-Brit Kolstø, University of Oslo

Mandate

The National Reference Group is responsible for national coordination and ensuring that other regions can benefit from the academic and recruitment opportunities represented by the EMBL node.

Appointment

The reference group is appointed by the Research Council of Norway for a term of two years from nominees by the Universities and the Health Regions authorities.

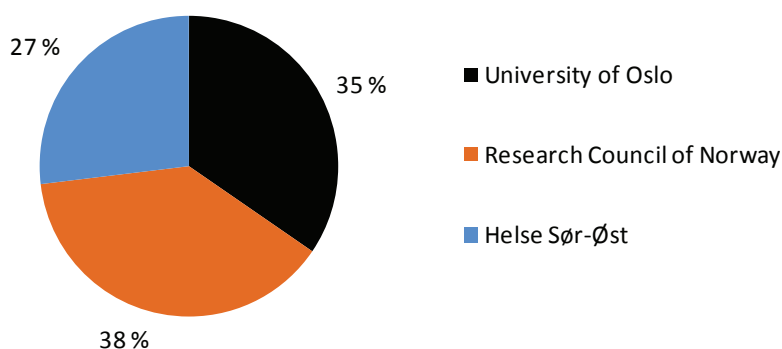


NCMM Management Team: Director Kjetil Taskén, Chief Administrative Officer Elin Kaurstad,
Chair of the Board Ragnhild Lothe

Photo:
Ola Sæther

9 NCMM Funding

The sources of funding for NCMM operations can be seen in the pie chart below. Total NCMM funding is 26 million NOK per year (approximately 3.3 million EURO per year).



An additional 2.5 million EURO is provided by external funding (not shown in pie chart).

The Nordic nodes within the EMBL Nordic partnership in Molecular Medicine are supported by Nordforsk for a Nordic Network of National Centres of Excellence (NCE). This network “Nordic Molecular

Medicine Network” (NMMN) promotes collaboration and exchange between the three NCE/Nordic nodes FIMM, NCMM, MIMS and EMBL.

10 NCMM-Affiliated Publications (2009 & 2010)

Structural insights into the high affinity binding of cardiotonic steroids to the Na(+),K(+)-ATPase.

Yatime L, Laursen M, Morth JP, Esmann M, Nissen P, and Fedosova NU. (2011) *J. Struct. Biol.* 174(2): 296-306.

Tumor necrosis factor receptor expression and in renal cell carcinoma.

Al-Lamki RS, Sadler TJ, Wang J, Reid MJ, Warren AY, Movassagh M, Lu W, Mills IG, Neal DE, Burge J, Vandenebeele P, Pober JS, and Bradley JR. (2010) *Am. J. Pathol.* 177(2): 943-954.

Novel mechanism of by CD28.

Bjorgo E, and Tasken K. (2010) *Immunol. Lett.* 129(1): 1-6.

Cross talk between phosphatidylinositol 3-kinase and cyclic AMP (cAMP)-protein kinase pathways at the level of a protein kinase B/beta-arrestin/cAMP phosphodiesterase 4 complex.

Bjorgo E, Solheim SA, Abrahamsen H, Baillie GS, Brown KM, Berge T, Okkenhaug K, Houslay MD, and Tasken K. (2010) *Mol. Cell Biol.* 30(7): 1660-1672.

Spatiotemporal control of cyclic AMP immunomodulation through the PKA-Csk inhibitory pathway is achieved by anchoring to an Ezrin-EBP50-PAG scaffold in effector T cells.

Cornez I, and Tasken K. (2010) *FEBS Lett.* 584(12): 2681-2688.

Taking risks with translational research.

Mills IG, and Sykes RB. (2010) *Sci. Transl. Med.* 2(24): 24cm10.

A novel human CD4+ T-cell inducer subset with potent immunostimulatory properties.

Ndhlovu LC, Leal FE, Eccles-James IG, Jha AR, Lanteri M, Norris PJ, Barbor JD, Wachter DJ, Andersson J, Tasken K, Torheim EA, Aandahl EM, Kallas EG, and Nixon DF. (2010) *Eur. J. Immunol.* 40(1): 134-141.

The adaptor protein EBP50 is important for localisation of the protein kinase A-Ezrin complex in T-cells and the immunomodulating effect of cAMP.

Stokka AJ, Mosenden R, Ruppelt A, Lygren B, and Tasken K. (2009) *Biochem. J.* 425(2): 381-388.

Waking up regulatory T cells.

Tasken K. (2009) *Blood*. 114(6): 1136-1137.

Interleukin-10-secreting T cells define a suppressive subset within the HIV-1-specific T-cell population.

Torheim EA, Ndhlovu LC, Pettersen FO, Larsen TL, Jha AR, Torgersen KM, Kvale D, Nixon DF, Tasken K, and Aandahl EM. (2009) *Eur. J. Immunol.* 39(5): 1280-1287.

Design of proteolytically stable RI-anchoring disruptor peptidomimetics for in vivo studies of anchored type I protein kinase A-mediated signalling.

Torheim EA, Jarnaess E, Lygren B, and Tasken K. (2009) *Biochem. J.* 424(1): 69-78.

Physiological Substrates of PKA and PKG.

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Photo: Ola Sæther

11 Personnel



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(as of January 2011)

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Toni Hurtado (ES)

(to start August 2011)

Hiring of staff initiated

Q2, 2011

Judith Staerk (DE)

(to begin January 2012)

Hiring of staff to be initiated

Q4, 2011

Note: The nationality of each employee is indicated in brackets.

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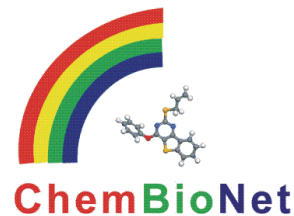
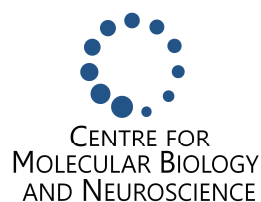
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