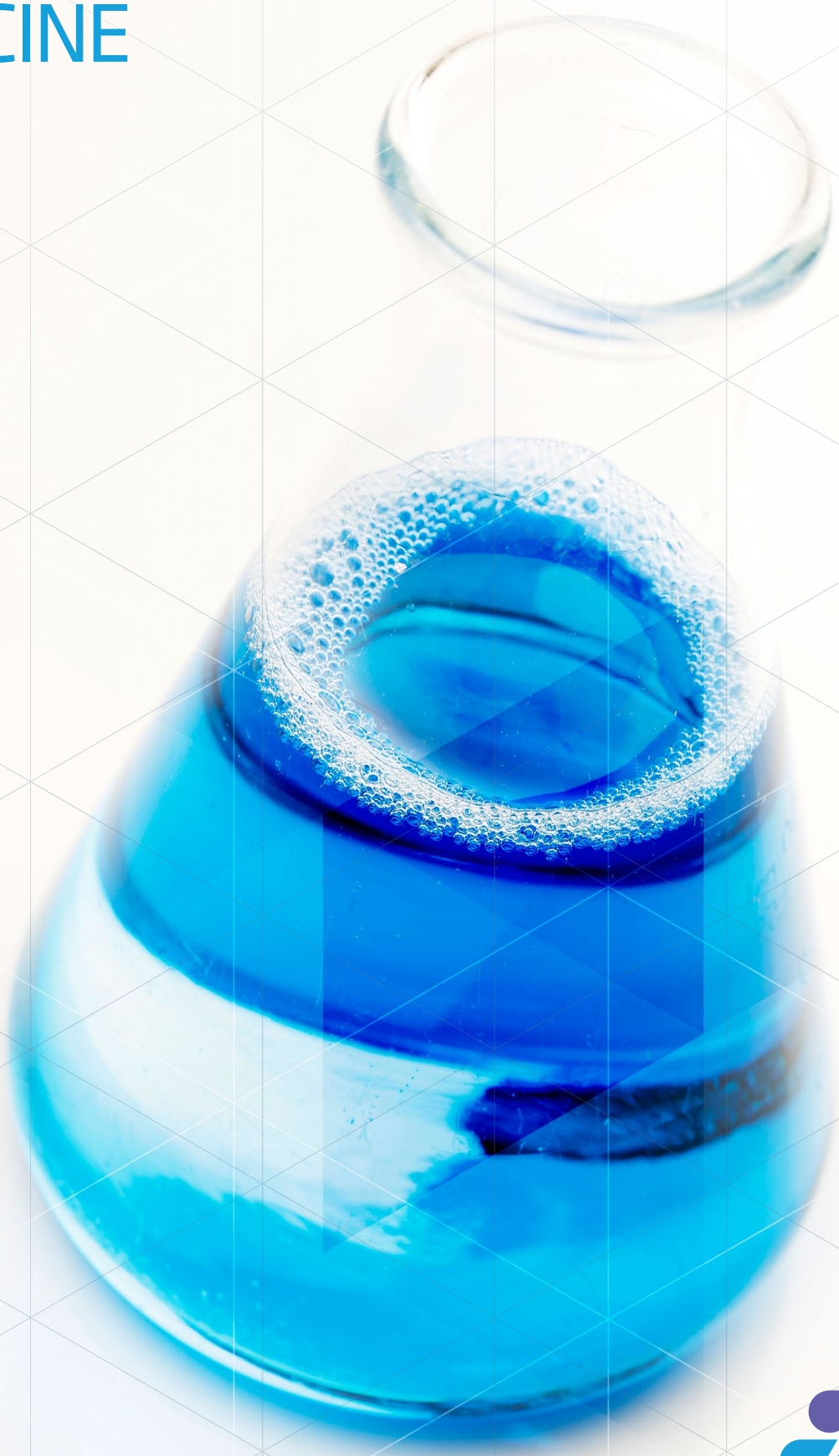
CENTRE FOR CANCER BIOMEDICINE ANNUAL REPORT 2016



CONTENTS

Co-Director Ragnhild A. Lothe and Director Harald Stenmark.

Finishing in great style

2016 represents the final full year of CCB's 10-year appointment as a Norwegian Centre of Excellence. CCB has indeed made major discoveries during these 10 years, which will be highlighted in the centre's 10-year report, and the present report will only focus on 2016.

During this year, CCB's interdisciplinary research strategy has continued to yield discoveries that will benefit the future cancer patient. PhD student Liliane Christ in Harald Stenmark´s group (in collaboration with CCB PI Knut Liestøl) has characterized proteins that mediate abscission between two cells during cell division and has identified a novel component of the abscission checkpoint which stops abscission if DNA aberrations are detected. CCB project leader June Myklebust, has uncovered important differences between different subtypes of lymphomas in terms of signal transduction downstream of the B-cell receptor, and these differences may have consequences for choice of therapy. Researcher Anita Sveen in Ragnhild A. Lothe's group has demonstrated that genetic differences between metastases within the same colorectal cancer patient who has undergone liver surgery are key determinants for survival. The patients with the largest genetic heterogeneity have the worst prognosis. PhD student Andreas Hoff in Rolf I. Skotheim's group has identified 8 new fusion genes in testicular cancer that can potentially be used as biomarkers for diagnosing this disease. CCB's biostatisticians, headed by Knut Liestøl and Ole Chr. Lingjærde, have been important collaboration partners for several of the abovementioned projects, and cross-disciplinary cooperations con-

"CCB's interdisciplinary research strategy has continued to yield discoveries that will benefit the future cancer patient."

tinue to be a key to success in CCB. CCB congratulates Ragnhild A. Lothe with the "Toppforsk" grant from the Research Council with the project "Modeling tumor heterogeneity in colorectal cancer management" and Håvard E. Danielsen with the "Lighthouse" project under the Research Council, entitled "DoMore!". For the second year in a row, H.M. the King's gold medal for best PhD thesis was awarded to a PhD student from CCB, namely Marina Vietri in Harald Stenmark's group. CCB graduated 5 PhD candidates in 2016 and published 64 articles, several of these in leading journals.

With respect to clinical translation, Clinical associate Harald Holte was the senior author of a recent national population-based study of non-Hodgkin lymphoma (NHL) patients treated with autologous stem-cell transplantation (HDT-ASCT) in Norway between 1987 and 2008 (n = 578). NHL patients treated with HDT-ASCT were at increased risk of second cancer and premature death. The mortality was still elevated at 5 years, but after 10 years mortality equalled that of the general population. Another clinical associate, Arild Nesbakken, was the senior author of a 10-year retrospective study reporting high clinical success rate in both the palliative and bridge to surgery setting for the controversial stent treatment of large bowel obstruction. Furthermore, Nesbakken and colleagues reported that frailty and old age is not a contraindication for CRC surgery but rather a significant quality of life score was present after surgery. In two clinicopathological studies of prostate cancer our clinical associate Karol Axcrona and colleagues showed the relevance of tumor stroma markers with prostate cancer specific death including lymphovascular invasion or perineural invasion combined with reactive stroma.

We are proud to conclude that 2016 has been a very successful year for CCB, and we would like to thank our host institutions, the University of Oslo and Oslo University Hospital, for excellent support. Thanks are also due to our Board, our Scientific Advisory Board, our visiting professors, and our sponsors. In particular, we would like to thank the Norwegian Cancer Society for its continued and substantial support to CCB and its scientists. We are entering 2017 with great optimism for continued success for CCB and its research during the centre´s final months and beyond. ●

Harald Stenmark, Director
Ragnhild A. Lothe, Co-Director

RESEARCH GROUPS

CONTENTS

HARALD STENMARK GROUP

Cellular membrane dynamics

Cancer is a disease characterized by uncontrolled proliferation and migration of specific cell types of the body. Stenmark's research group therefore studies cellular pathways that either prevent or promote conversion of normal cells into cancer cells. Of special interest are pathways that control cellular membrane dynamics such as intracellular traffic, autophagy (cellular self-consumption) and cell division.

The group consists of more than 20 members with research backgrounds in medicine, biology, biochemistry and biotechnology. Researchers in the group are specialists in microscopy, and the group hosts regional core facilities in confocal microscopy, electron and super-resolution microscopy. Most of the research is done with normal and cancerous cells that are grown in tissue culture flasks, but some group members also use the fruit flies as model organisms for studies of tumour suppression and carcinogenesis. The group collaborates extensively with CCB groups that specialize in analyses of human tumour samples. ●

RAGNHILD A. LOTHE GROUP

Cancer genetics

The group has 23 members, including 7 post docs/scientists, 7 PhD students and 7 research assistants/ engineers with formal education and research experience in genetics, cell biology, bioinformatics and medicine.

We study the aetiology of selected solid tumors arising in cells that originate from different germ layers, to gain novel knowledge of molecular paths across malignancies. We combine patient-oriented and biological studies using human specimens and in vitro models applying amongst others multilevel genomics. Our current main projects: 1) genomic tumor heterogeneity in colorectal cancer 2) high throughput drug sensitivity and resistance screens of CRC cells and malignant peripheral nerve sheath tumour cells 3) ubiquitin system in intercellular communication.

Our goal is to transfer novel biomedical knowledge into improved patient stratification and treatment. Lothe is a partner in the Norwegian cancer genomics consortium (www.cancergenomics.no), a national collaboration towards improved personalized cancer medicine. Group members have ongoing collaborative projects with the CCB groups, clinical associates and with the Finnish Inst for Molecular Medicine, University of Oxford, University of Porto, MD Anderson, Vall d'Hebron Institute, SAGE Bionetwork. ●

ERLEND SMELAND/JUNE MYKLEBUST GROUP

Lymphoma biology

The group consists of 13 members with research background in medicine, biology, biochemistry and biotechnology. Our research is focused on B-cell lymphoma, a heterogeneous group of malignancies originating from B cells of the immune system. Although new therapeutic approaches have highly improved overall survival, some types are still considered incurable. We aim to develop novel therapeutic strategies including immunotherapy, and to identify predictive biomarkers for therapy response.

The lab has a strong translational focus, with 2 ongoing exome sequencing projects to identify recurrent mutations associated with therapy relapse. We use advanced flow cytometry and cutting edge mass cytometry (CyTOF) to characterize tumor microenvironment composition as well as tumor cell heterogeneity in patient samples. We also utilize these techniques to test efficacy of small molecule drugs, and have established lymphoma xenograft mouse models for testing of new drugs *in vivo*. The molecular biology expertise has been strengthened with establishment of CRISPR/Cas9 genome editing to create gene knockout models. The lab has extensive collaboration with the lymphoma program at the hospital, other groups in CCB and milieus at NCI, Stanford, and Vanderbilt.

KIRSTEN SANDVIG GROUP

RESEARCH GROUPS

Intracellular transport

Sandvig's group, counting 17 members plus master students, works on mechanisms of endocytosis, intracellular transport and secretion. Uptake of receptors and ligands and correct intracellular sorting are crucial for maintenance of a normal differentiated phenotype. In some of our studies we use protein toxins such as ricin and Shiga toxin, which are well established as markers for studies of membrane traffic, and which can be used as agents in cancer diagnosis and therapy.

Our expertise is also applied to investigate uptake of nanoparticles, and in 2013 we obtained a five year grant from the Norwegian Research Council to build national competence in nanomedicine. This project, "Biodegradable nanoparticles in cancer diagnosis and therapy", headed by Sandvig, involves collaboration with ten other Norwegian groups working in academia, research institutes, hospitals and industry. We also characterize exosomes from prostate cancer cells and patients with the goal of detecting lipid and protein biomarkers.

Our research spans all the way from basic to translational medicine, including innovation, and the projects aim at increasing our knowledge about intracellular transport and biomarkers in order to provide a rational basis for diagnosis, treatment and prevention of disease. The group has extensive national and international collaboration.

HÅVARD DANIELSEN GROUP

Large scale genomic instability

Cancer is a disease characterized by heterogeneity and genomic instability. Danielsen's research group is therefore developing high throughput methods for detection and characterization of large-scale genomic instability (chromatin structure and DNA ploidy), based on high-resolution digital microscopy and advanced image analysis.

The group consists of 15 members with background in medicine, biology, mathematics, and computer science. They are studying archival material at the time of diagnosis from cancer patients with proper clinical follow-up and known prognosis. Several methods; such as IHC, FISH, DNA Ploidy, Tissue Micro Array, as well as original methods developed in the group (Nucleotyping, 3D-reconstruction, ImmunoPath and MicroTracker) are used in an attempt to reveal and understand the 3-dimensional organisation of chromatin, and how this organisation controls gene expression. They are engaged in the search for new diagnostic and prognostic markers among these methods and results, and are running clinical validation studies on large series of colorectal, breast, prostate and gynaecological cancers with a minimum of 5, and up to 20, years of clinical follow-up, with emphasis on disease-free survival.

The aim is to improve cancer treatment by the identification of better prediction and prognosis of the outcome among these patients.

KNUT LIESTØL GROUP

The statistical analysis unit

The complexity of the data sets produced by modern high throughput technologies makes extraction of information a true challenge. Our research unit therefore aims at supporting the activity of CCB groups by providing data analysis, with a focus on high throughput data. The unit has worked and published together with all CCB groups.

The statistical analysis unit at CCB is part of Biomedical Research Group at the Department of Informatics at the University of Oslo, with competence focused on statistical genomics and bioinformatics. Our philosophy is to work in close interaction with biomedical research groups and also to obtain own competence in the application areas. Typically, projects initially focus on a concrete biomedical problem, we then try to solve the statistical challenges in a broader context and finally to develop easy-to-use software tools. Examples of tools include software for copy number estimation, including allele-specific analysis, and for estimating the number of clusters in a data set.

GURO E. LIND GROUP

Epigenetics group

Cancer is the result of an accumulation of genetic as well as epigenetic changes. In the group of Epigenetics we are focusing our research on DNA methylation alterations in various cancer types, and colorectal cancer in particular. Our aim is to identify epigenetic biomarkers with clinical impact, including markers for early detection and monitoring of cancer. Simultaneously we aim at analyzing and understanding the underlying biology of these aberrations and how they affect the cancer development.

In the group we are integrating large-scale analyses, including methylome sequencing, with detailed analyses of candidate genes using various quantitative and qualitative methods. We are primarily working with patient material, in close collaboration with clinical partners. Relevant cancer cell lines are also studied, representing in vitro models for particular cancer types, which allows for a modification of the epigenome.

The group is actively working with innovation and has several established collaborations within CCB and the Institute for Cancer Research.

Genome biology

HEADED BY **ROLF SKOTHEIM**

The Genome biology group studies how genomes and transcriptomes are altered in cancer cells by using both computational biology and wet-lab based approaches. The research aim is to identify and characterise genes that are critical for development of cancer. Such genes may serve as diagnostic or prognostic biomarkers and also as targets for molecularly tailored therapy. The projects are mainly focused on prostate, testicular, and colorectal cancers.

Mutation analyses in cancer clearly benefit from knowing which genes and variants that are actually being expressed, and whether they are present in any particular isoform at the RNA or protein level. In this line, the group has particularly specialized in RNA-level analyses. Recent publications from the group have provided evidence of several novel transcripts, including fusion transcripts. An interdisciplinary set of competences is required to perform meaningful genome-scale cancer research. As such, personnel in the group have their basic education across the disciplines of biology, informatics, and medicine.

Cytogenetics group

HEADED BY **FRANCESCA MICCI**

Micci's research group studies the chromosomal aberrations of cancer cells. The research is done in parallel with diagnostic analyses of leukemias and solid tumors. Of the 16 people involved in research, only seven (five PhD-students, one student, and one technician) do so full-time. The remainder do diagnostic work half of the time.

The research begins by finding specific cytogenetic aberrations in various cancers. Then we take the investigation to the molecular level searching for the corresponding changes of genes and DNA primary structure. We have succeeded in all our three main research areas: 1) Gynecologic tumors; 2) Brain tumors; and 3) Analyses of rare tumor-specific translocations.

Our unique area of expertise is the culturing and chromosome analysis of neoplastic cells. We also have extensive experience with fluorescence in situ-based analyses and the search by molecular means for fusion genes brought about by chromosomal translocations. Our approach by combining the two screening techniques G-band karyotyping and next generation sequencing to this end is novel and has led to the discovery of several cancer-specific fusion genes during the past year.

Protein internalization and signaling group

HEADED BY **ANTONI WIEDLOCHA**

The fibroblast growth factors (FGFs) and FGF receptors (FGFRs) constitute a fundamental system for cell-to-cell communication, the so-called FGF-signaling system and exert a powerful combination of biological effects. Therefore, imbalances in FGF/FGFR signaling homeostasis contribute to the essential hallmarks of cancer.

The growth factors are frequently and abundantly expressed in various tumors and are recognized as key mediators of the epithelial-mesenchymal communication/transition, tumor cell survival, migration/metastasing and neoangiogenesis as well as stress-induced agents causing rescue of tumor tissues during/after therapy. On the other hand in some circumstances the FGF regulated signaling network contributes to tumor suppression.

The interest of FGF-induced signaling as a promising target for cancer therapy has systematically been increasing. We have been focusing on (i) how FGFs/FGFRs signaling can contribute to development of the malignant phenotype of different types of cancer when it is deregulated. (ii) Role of FGF-signaling in tumor cell migration and metastasis formation, and (iii) finding new potential molecular targets in FGF-regulated malignant processes that would be beneficial in cancer therapy.

Leaders of the clinical research programmes

COLORECTAL CANCER

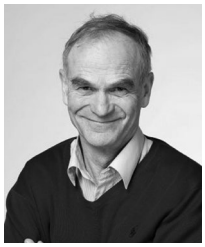
ARILD NESBAKKEN

Professor, MD, Senior Consultant, Department of Gastrointestinal Surgery, Oslo University Hospital

We study the development of this common cancer from genetic disposition, precursor lesions to metastatic disease. Diagnostic, prognostic, predictive and monitoring biomarkers are studied in both the primary bowel cancer and in metastases to the liver. The colorectal and liver surgeons are engaged in consecutive inclusion of all new patients, registration of comprehensive clinical datasets and high quality biobanking.

The contributions of dedicated and competent colorectal and liver surgeons, pathologists, radiologists and oncologists are essential. Clinical and molecular data must be integrated and joint efforts from clinicians and molecular biologists are necessary in the interpretation and presentation of the results. We have managed to create a true translational team who share knowledge and ideas in ongoing and new projects.

The cooperation with CCB and all the members of this multidisciplinary team is excellent.



LYMPHOMA

HARALD HOLTE

MD, PhD, Senior Consultant, Department of Medical Oncology and Radiotherapy, Oslo University Hospital, Head of Lymphoma Treatment Programme and Lymphoma Research Group

My connection to CCB as the head of The Lymphoma Research Group is mainly through the fruitful collaboration with researchers at Department of Immunology. We have joint projects studying tumor microenvironment and tumor genetic aberrations with impact on patient outcome. We have access to tumor material from researcher initiated prospective clinical studies, and the idea is to improve future protocols through our findings.

Lymphoma is one of the prioritized tumors of the National Cancer Genomics Consortium and we are presently performing exome sequencing on lymphomas. These studies will hopefully lead to better treatment of the heterogenous T-cell lymphoma entity and better understanding of why some B-lymphomas – and not others - become therapy resistant.

I appreciate the opportunity given to me to be a clinical associate with the CCB and hope that my clinical background and interest in translational research can further strengthen - beyond the lymphomas - the excellent research performed by CCB.

PROSTATE CANCER

KAROL AXCRONA

MD, PhD, Head of Department of Urology, Akershus University Hospital, Lørenskog

Prostate cancer is the most diagnosed cancer in Norway accounting for approximately 5,000 new cases yearly. Every fifth cancer death amongst men is prostate cancer and many patients' quality of life is affected by side effects from treatments for this cancer. However, the tools used today to diagnose and treatment stratify patients suitable for radical treatment are still quite limited.

We believe that molecular biological approaches will be necessary to deepen understanding of biological behavior and development of prostate cancer to tailor prostate cancer treatment and to choose the right treatment for the right patient.

The CCB has the crucial tools for bringing molecular biology and molecular biological thinking into the clinics. Urologists also do believe that much of the future treatment of our patients will be dependent on prevention and optimal treatment stratification of patients, i.e. based on gained knowledge from the lab.

Highlights

FUNDING

Håvard Danielsen's project DoMore! receives Lighthouse project grant from the Norwegian Research Council

Prof. Håvard Danielsen. Photo: Erling Sten Sætre-Hansen

We congratulate CCB's PI Håvard Danielsen, director of the Institute for Cancer Genetics and Informatics, Oslo University Hospital, with the prestigious Lighthouse Project grant for the DoMore! project focusing on heterogeneity in cancer. The funding is 60 million NOK over a five-year period.

About the DoMore! project

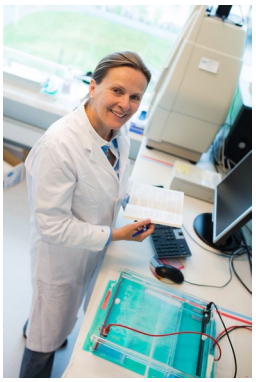
The Norwegian Research Council IKTPLUSS has selected the DoMore! project application as one of the 3 winners of the prestigious Lighthouse Project grant.

By largely digitalizing and automating diagnostics and prognostication of cancer, we can literally DoMore! and analyze a greater number of samples from the same tumor, leading to a more precise diagnosis for each patient. Safe storage, analysis and prosessing of the Big Data produced by the project, will also be handled by the project partners.

The DoMore! team is composed of experts within several fields, including digital imaging, processing, robotics, pathology, cell biology, surgery and oncology, both in Norway and abroad. Together, we will create solutions that will allow us to DoMore!, resulting in objective cancer diagnostics that can be made available to all patients.

www.forskningsradet.no | Har utropt tre IKT-fyrtårn innen helse
www.tu.no | 5 patologer kan gi 5 ulike svar når de ser en svulst. Det skal norsk forskning gjøre noe med.

Ragnhild A. Lothe substantially supported by FRIPRO



Prof. Ragnhild A. Lothe. Photo: Beate Willumsen

We congratulate CCB co-director Ragnhild A. Lothe with achieving the substantial NFR TOPPFORSK funding grant for the project "Modeling tumor heterogeneity in colorectal cancer management".

An open competitive arena - a tough competition

The Research Council of Norway and Norway's research institutions are providing a total of 1 billion NOK to 46 FRIPRO Toppforsk projects. Each project will receive 15–25 MNOK over a four-to-five-year period.

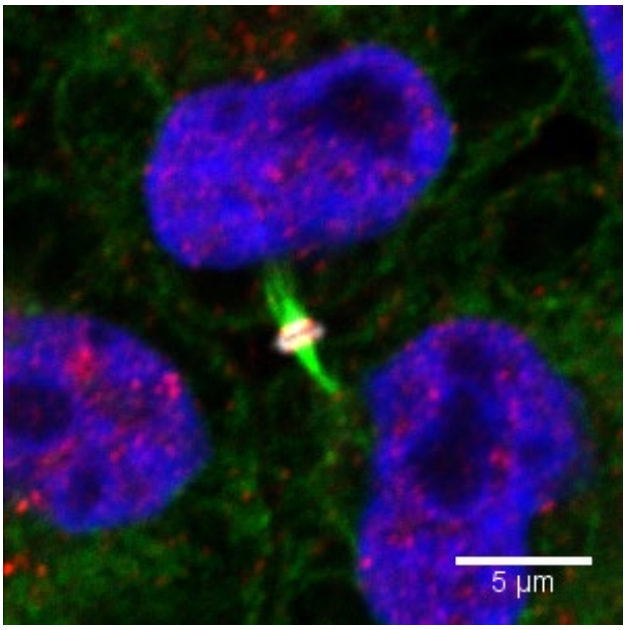
FRIPRO is an open competitive arena for all research areas and disciplines, where there are no thematic guidelines and no requirements relating to the applicability or immediate utility of the research. The competition in FRIPRO is tough, and only the best researchers with particularly good projects and very well-written proposals have a chance at succeeding.

www.forskningsradet.no | NOK 1 billion to top-notch researchers/En milliard til sterke forskningsmiljøer
www.ous-research.no | Ragnhild A. Lothe and Michael Bretthauer substantially supported by FRIPRO

PUBLICATIONS

Liliane Christ identifies mechanism for regulation of daughter cell separation

In a February issue of Journal of Cell Biology, PhD student Liliane Christ from Harald Stenmark's group provides new insight into how daughter cells are separated during the end of cell division. In the same issue, a "Biobytes" podcast with group leader Harald Stenmark and co-corresponding author Coen Campsteijn explains the importance of this work, as does a commentary article by two external experts in the field, Frankel and Audhya: Burning cellular bridges - Two pathways to the big breakup.



The image shows two daughter cells (nuclei stained blue) depleted of ESCRT-I, joined by an intercellular bridge that contains microtubules (green). ESCRT-III is shown in red. Note the recruitment of ESCRT-III to the midbody (white) in the middle of the intercellular bridge, which is mediated by ALIX.

At the end of cell division, the two daughter cells are separated by the process known as cytokinesis, which culminates in the physical severing of the thin membrane bridge that joins the two cells. This scission is mediated by the so-called ESCRTs, a machinery of protein complexes originally identified for their role in endosomal protein sorting. A filamentous protein complex called ESCRT-III is thought to execute the scission step, but its recruitment to the intercellular membrane bridge has not been clarified.

Now, Christ and co-workers show that ESCRT-III is recruited to the intercellular bridge by two parallel "arms". One arm consists of the ESCRT-I and -II complexes, similar to what has been observed previously in endosomal sorting. The other arm consists of an ESCRT-binding protein called ALIX. Importantly, the authors also uncovered an additional function for ALIX, namely in recruitment of a component of the abscission checkpoint that delays abscission in the event of any lagging chromatin in the intercellular bridge. Depletion of ALIX leads to cytokinetic furrow regression in cells with chromatin bridges, resulting in cells with two nuclei, a known risk factor in carcinogenesis. These findings thus provide a novel link between the cytokinetic abscission machinery and the abscission checkpoint, with implications for our understanding of how ESCRT proteins may function as tumour suppressors.

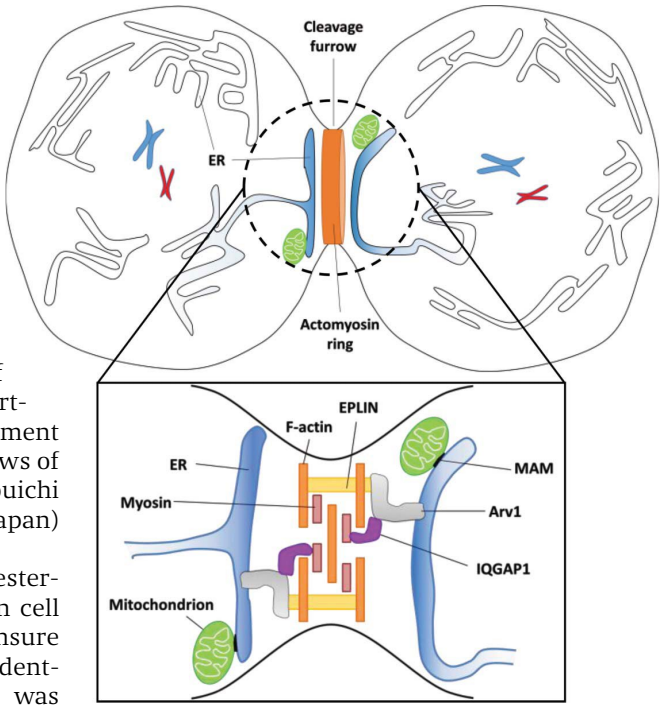
Christ L, Wenzel EM, Liestøl K, Raiborg C, Campsteijn C, Stenmark H.
ALIX and ESCRT-I/II function as parallel ESCRT-III recruiters in cytokinetic abscission
J Cell Biol, 212 (5), 499-513

PUBLICATIONS

CCB's Lene Malerød with a cover story in Cell Cycle

Scientist Lene Malerød and senior scientist Kaisa Haglund from Harald Stenmark's group published a cover story in the March-issue of Cell Cycle. The work has been performed in collaboration with scientists at the Department of Medical Genetics (Oslo University Hospital), Department of Anatomy (University of Oslo) and Department of Chemistry (University of Oslo). A News and Views of the paper was written by Associate Professor Kouichi Funato and coworkers (Hiroshima University, Japan) and published in Cell Cycle online the 22nd April.

In this paper a novel role for the putative cholesterol-transporting protein Arv1 was characterized in cell division. Here Arv1 was found to regulate and ensure correct cleavage of the two daughter cells independently of its cholesterol-modulating capacity. Arv1 was found to act as an adaptor protein, binding IQGAP1 which in turn facilitates efficient recruitment of myosin to the cleavage furrow. Myosin, together with actin, builds the actomyosin ring, which upon constriction promotes the physical separation of the two daughter cells. Mechanistically, depletion of Arv1 interrupted normal cell division resulting in multinuclear cells both in human cells lines and in follicle epithelial cells of egg chambers of Drosophila melanogaster in vivo. Thus Arv1-dependent regulation of the actomyosin ring-formation represents a novel regulatory mechanism operating in parallel with alternative pathways that recruit myosin to the cleavage furrow such as actin, Anillin and Rho. Together, these parallel pathways provide robustness to this crucial step of cell division.



During cell division, EPLIN recruits Arv1 to the cleavage furrow. Here Arv1 promotes formation of the contractile actomyosin ring (orange) by stabilizing the essential component Myosin, which together with F-actin facilitates the physical separation of the two daughter cells. Importantly, Arv1 stabilizes Myosin indirectly by interacting with the scaffolding protein IQGAP1. Illustration by Ass Prof Kouichi Funato

Scientist Lene Malerød. Photo: Terje Heiestad

Sundvold H, Sundvold-Gjerstad V, Malerød-Fjeld H, Haglund K, Stenmark H, Malerød L.
Arv1 promotes cell division by recruiting IQGAP1 and myosin to the cleavage furrow
Cell Cycle, 15 (5), 628-43

PRIZES

OUS award to CCB's Jarle Bruun for outstanding scientific article

On the 17th of June six research prizes were awarded to scientists from Oslo University Hospital. CCBs Jarle Bruun was among the prize winners. Jarle Bruun is a member of Ragnhild A. Lothe's group.

Postdoc Jarle Bruun. Photo: Private

Prize for excellent research article

The prizes were presented at a ceremony at Rikshospitalet taking place in the month of June. We congratulate Postdoc Jarle Bruun with the Excellent Original Article Award of 50.000 NOK.

Bruun J, Kolberg M, Ahlquist TC, Røyrvik EC, Nome T, Leithe E, Lind GE, Merok MA, Rognum TO, Bjørkøy G, Johansen T, Lindblom A, Sun XF, Svindland A, Liestøl K, Nesbakken A, Skotheim RI, Lothe RA.
Regulator of Chromosome Condensation 2 Identifies High-Risk Patients within Both Major Phenotypes of Colorectal Cancer
Clin Cancer Res, 21 (16), 3759-70

www.ous-research.no | Oslo University Hospital has awarded 6 excellent articles for the second half-year of 2015

H.M. the King's Gold Medal to Marina Vietri

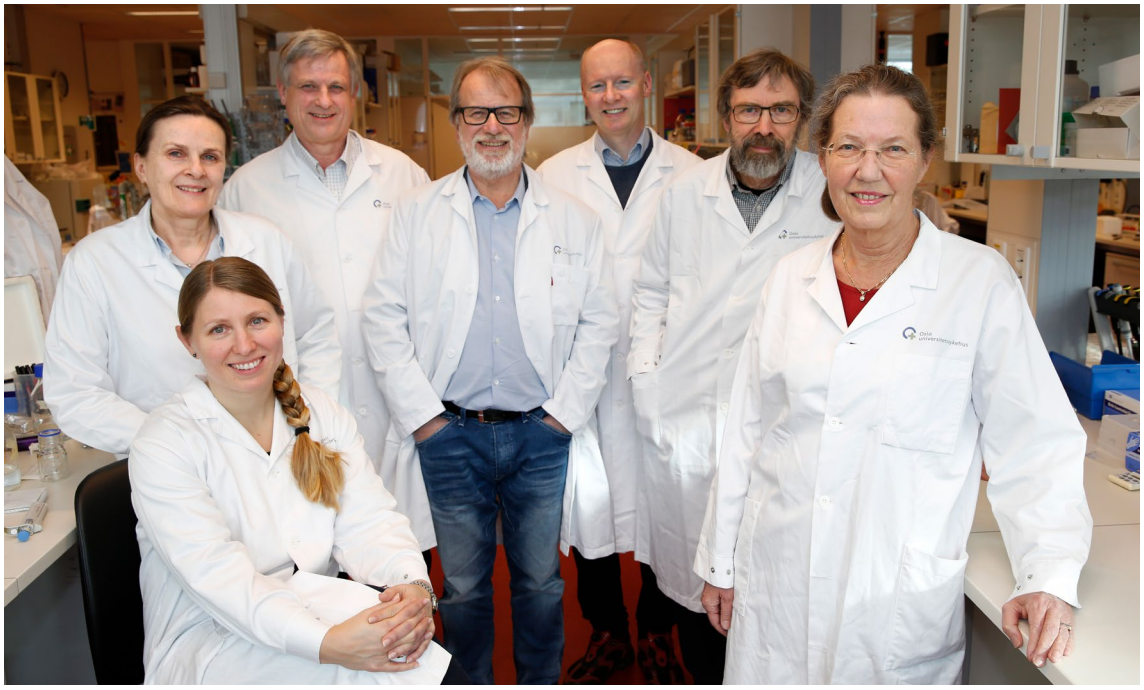
Marina Vietri from Institute for Cancer Research and Centre for Cancer Biomedicine was awarded H.M. the King's Gold Medal for best thesis of the Faculty of Medicine. She received the medal at the annual celebration of the University of Oslo in the University Aula on the 2nd of September.

Marina Vietri, PhD

Marina defended her PhD thesis "Closing the gap - ESCRT-III orchestrates nuclear envelope sealing" on 6th November 2015. It is interesting to note that this thesis, contrary to current practice, only contained a single published article. This article was published in the world-leading journal Nature with Marina as first author and gained worldwide attention as illustrated by the fact that it was dedicated commentary articles in both Nature and Science. The reason for this attention was that the article solved an enigma in cancer cell biology, namely how the newly formed nuclear envelope is sealed at the end of cell division. Marina showed that nuclear envelope sealing is mediated by a protein complex known as ESCRT, and that this is coordinated with disassembly of the mitotic spindle by the microtubule-severing enzyme Spastin. She found that cells with impaired ESCRT function have leaky nuclei and acquire DNA damage typical of cancer cells. Thus, this discovery provides new potential targets in cancer medicine.

Congratulations!

HIGHLIGHTS



The CCB PI group 2016-2017. Photo: Terje Heiestad

Group leader Guro E. Lind awarded two-year PI position in CCB for 2016-2017

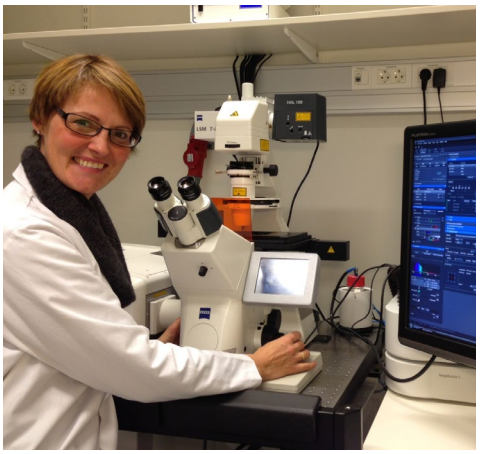
As part of CCBs strategy for supporting the career development of young scientists, the PI group decided in 2012 to announce an internal call for a PI position in CCB for a young CCB scientist every year from 2013 to 2017.

We congratulate Guro E. Lind with being awarded a two-year PI stipend for the period 2016-2017 including financial research support of 1 MNOK.

Filming live cancer cells - Camilla Raiborg's ongoing scientific activities presented in popularised form

The ongoing work of CCB's Camilla Raiborg has been presented on the Norwegian popular science website forskning.no, as well as on the Norwegian Cancer Society web page. Raiborg is heading the project group "Protein dynamics in tumor suppressor pathways" in Harald Stenmark's group.

www.forskning.no | Undersøker hvordan kreftcellene sprer seg (Investigating how cancer cells spread)
www.kreftforeningen.no | Filmer levende kreftceller (Filming live cancer cells) ●



Camilla Raiborg at the confocal microscope, her most important working tool. Photo: Private

PhD- and master degrees

PhD DEGREES

Hege Marie Vedeld - Epigenetic biomarkers for early detection and prognosis of colorectal cancer
Faculty of Medicine, University of Oslo, Desember 2016

Tor Espen Thorvaldsen - Dissecting the β-catenin destruction complex: Novel implications of tankyrase inhibitors
Faculty of Medicine, University of Oslo, November 2016

Simona Kavaliauskiene - Membrane dynamics in cancer cells
Faculty of Mathematics and Natural Sciences, University of Oslo, September 2016

Bjarne Johannessen - Identification of novel DNA and RNA changes in solid tumors by high-throughput methodologies
Faculty of Medicine, University of Oslo, August 2016

Thale Kristin Olsen - The enigma of ependymal tumors: A journey in their genomic and transcriptomic landscapes
Faculty of Medicine, University of Oslo, May 2016

MASTER DEGREES

Hélène Spangenberg, M.Sc. in Biochemistry - PI(3)P-binding proteins in macropinocytosis
Faculty of Biology, Chemistry and Pharmacy, Freie Universität Berlin, November 2016

Stian Lågstad, M.Sc. in Informatics - Visualizing chimeric RNA
Faculty of Mathematics and Natural Sciences, University of Oslo, June 2016

Jonas Meier Strømme, M.Sc. in Informatics - Computational analyses of transcriptome instability in cancer
Faculty of Mathematics and Natural Sciences, University of Oslo, June 2016

Trym Vogt, M.Sc. in Pharmacy – Toxicology of cytostatic drug-loaded nanoparticles: The role of endocytosis
Faculty of Medicine, Norwegian University of Science and Technology, June 2016

Nikoline Rasmussen, M.Sc. in Molecular Biosciences - The role of tumor necrosis factor α (TNFα) in regulation of connexin43 ubiquitination, endocytosis and degradation
Faculty of Mathematics and Natural Sciences, University of Oslo, June 2016

Dhaksshaginy Rajalingam, M.Sc. in Molecular Biosciences - Regulation of exosome release by 2-hydroxyoleic acid and oleic acid
Faculty of Mathematics and Natural Sciences, University of Oslo, June 2016

Publications

- TOTAL NUMBER OF CCB PUBLICATIONS IN 2016: **64 PUBLICATIONS**
- NUMBER OF PUBLICATIONS IN HIGH IMPACT JOURNALS (IMPACT FACTOR > 9): **8 PUBLICATIONS (13 %)**
- NUMBER OF PUBLICATIONS WITH CCB SCIENTISTS AS CORRESPONDING AUTHOR: **44 PUBLICATIONS (69 %)**
- NUMBER OF COLLABORATION PUBLICATIONS WITH CLINICIANS AND PATHOLOGISTS: **29 PUBLICATIONS (45 %)**
- NUMBER OF PUBLICATIONS WITH INTERNATIONAL PARTNERS: **24 PUBLICATIONS (38 %)**

PUBLICATIONS 2016:

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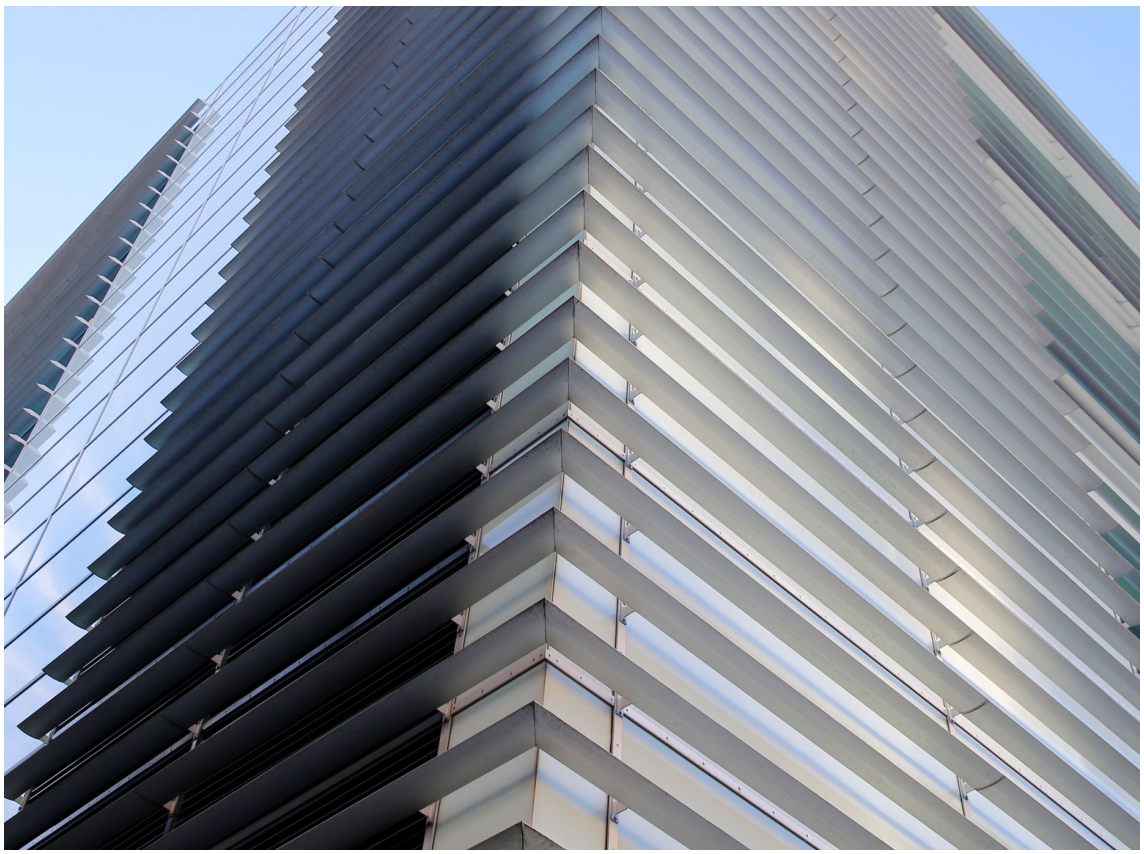


About CCB

Centre for Cancer Biomedicine was established in September 2007 as a Centre of Excellence appointed by the Research Council of Norway with the University of Oslo as host institution. Our Centre is located at the Norwegian Radium Hospital, Oslo University Hospital. A consortium agreement regulates cooperation between the University of Oslo and Oslo University Hospital with the intention to make conditions favourable for fulfilling the scientific aims and strategic plans of CCB.

RESEARCH GROUPS

CCB consists of seven research groups and three associated groups embracing an average of 150 people in 2016.

As part of CCBs strategy for supporting career development of young scientists, the PI group decided in 2012 to announce an internal call for a one-year PI position in CCB for a young scientist every year from 2013 to 2017. For 2016-2017, we congratulate Guro E. Lind with being awarded the PI stipend, and we welcome her as the seventh member of the PI group.

The seven research groups are headed by Prof. Harald Stenmark, Prof. Ragnhild A. Lothe, Prof. Kirsten Sandvig, Prof. Erlend Smeland, Prof. Håvard Danielsen, Prof. Knut Liestøl, and Prof. Guro E. Lind.

Three independent groups are associated with CCB. These are the groups of Antoni Wiedlocha PhD, Ass. Prof. Rolf I. Skotheim and Prof. Francesca Micci.

MANAGEMENT

The day-to-day management of CCB is performed by Director Harald Stenmark, Co-director Ragnhild A. Lothe, and Administrative coordinator Anette Sørensen. The Centre management reports to the CCB board.

THE BOARD

The CCB board has two members from the University of Oslo as well as two members from Oslo University Hospital. The board members are:

Prof. Hilde Irene Nebb | Chairperson, Dean of Research, Faculty of Medicine, University of Oslo

Prof. Svein Stølen | Dean of Research, Faculty of Mathematics and Natural Sciences, University of Oslo

Prof. Karl-Erik Giercksky | Department of Gastrointestinal & Paediatric Surgery, Division of Cancer Medicine, Oslo University Hospital

Prof. Ole M. Sejersted | Head of Institute for Experimental Medical Research, Division of Cardiovascular and Pulmonary Diseases, Oslo University Hospital

SCIENTIFIC ADVISORY BOARD

The Scientific Advisory Board supports our Centre with valuable input on strategy and science which helps us achieve our goal of becoming one of Europe's leading centres for cancer research. The SAB members are:

Professor Manuel Sobrinho-Simões | Head of Department of Pathology, Medical Faculty of Porto & Director, Institute of Molecular Pathology and Immunology of the University of Porto (IPATIMUP), Portugal

Professor Marja Jäättelä | Head of research unit Cell Death and Metabolism, Danish Cancer Society Research Center, Copenhagen, Denmark

Professor Olli Kallioniemi | Director, Institute for Molecular Medicine Finland (FIMM), Nordic EMBL Partnership for Molecular Medicine, University of Helsinki & Director, Academy of Finland Centre of Excellence in Translational Genome-Scale Biology, Helsinki, Finland.

Professor David J. Kerr | Professor of Cancer Medicine, Nuffield Department of Clinical and Laboratory Sciences, University of Oxford, UK

VISITING PROFESSORS

CCB has three professors associated to the Centre.

Professor Manuel Teixeira | Portugese Oncology Institute, Porto, Portugal
Professor Marco Novelli | University College London Hospitals, UK
Professor Jan Delabie | University Health Network, Toronto, Canada

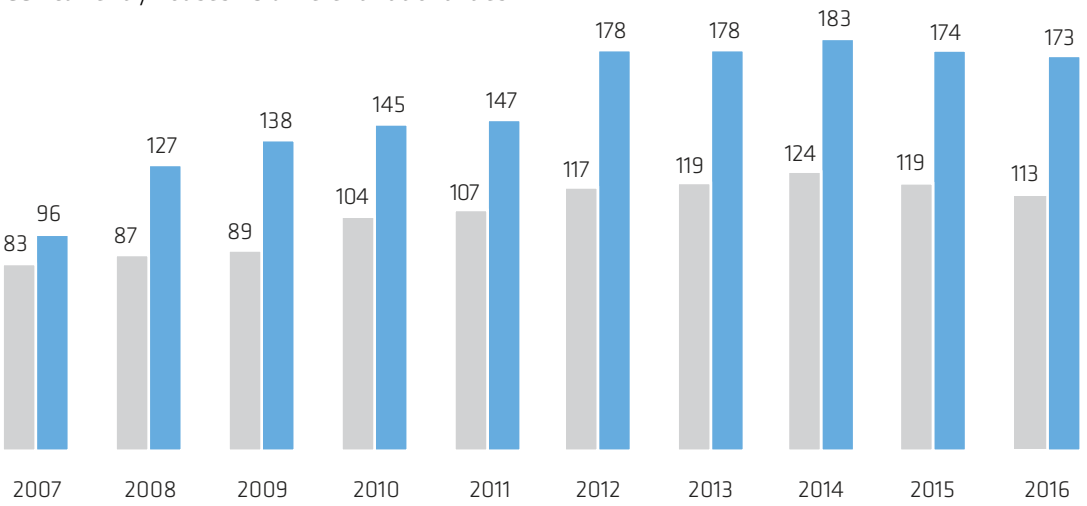
Facts and figures 2016

CCB staff – Development in man-years/headcount

The total number of people registered in the centre in 2016:

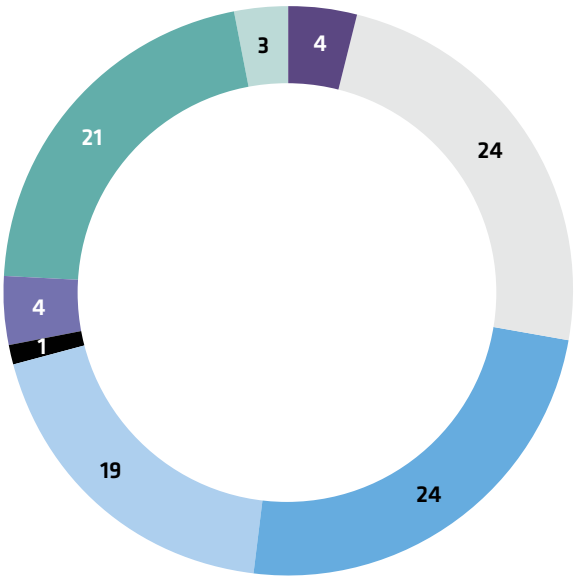
- Man-years, excluding students: 113
- Headcount, including students: 173

CCB currently houses 28 different nationalities.



CCB staff categorized by position in % of total man-years

CCB staff equals 113 man-years in 2016. The pie chart shows the categorization of our staff by position. In addition 9 master students were hosted by CCB in 2016.

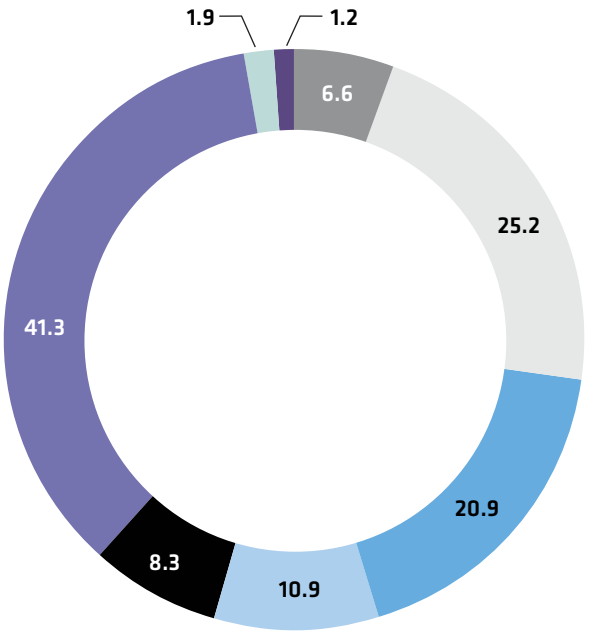


FUNDING IN MNOK

The total funding for 2016 is 116.3 MNOK excluding in-kind contributions from our two host institutions. The overall funding for CCB has increased with 5 MNOK from 2015 to 2016 and the centre has succeeded to obtain sufficient financial resources to implement all its planned activities. CCB's Centre of Excellence funding from the Research Council of Norway amounts to 10.9 MNOK, including 0.1 MNOK in Gender Equality funding.

This year funding from the Norwegian Cancer Society is showing a solid increase from 19.7 MNOK in 2015 to 25.2 MNOK in 2016.

CCB's international funding includes both a Latvian-Norwegian and a Polish-Norwegian Research Fund grant.



- The Research Council of Norway
- The Norwegian Cancer Society
- South-Eastern Norway Regional Health Authority
- Centre of Excellence
- University of Oslo
- Oslo University Hospital
- International
- Vestfold Hospital Trust

GENDER DISTRIBUTION IN % OF TOTAL HEADCOUNT

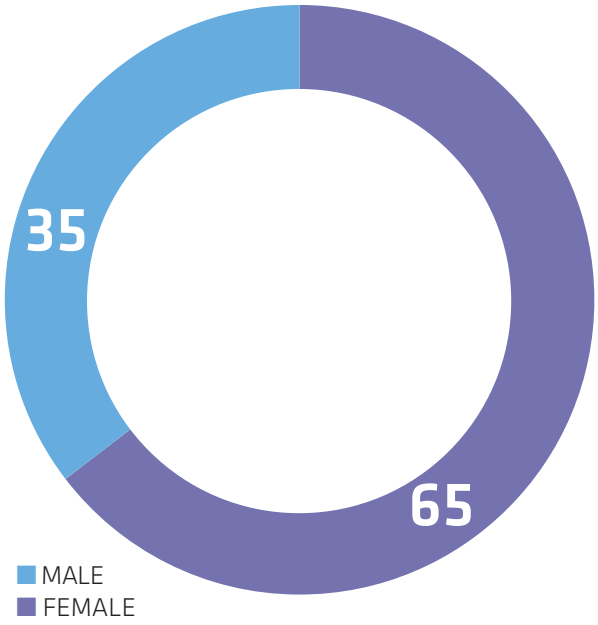
GENDER BALANCE

The gender balance in CCB is 65% women and 35% men among our total staff. Approximately the same percentages account for the postdoc category as well as for the PhD student category. However, for the highest scientific categories (principal investigators and scientists) our male colleagues constitute the majority.

GENDER EQUALITY ACTIONS

CCB actively supports the promotion of talented female scientists through various means where the overall strategy is to create predictability and continuity, and thereby motivating women to stay in their current career path.

CCB's focus on gender equality is in line with the gender equality policy of our host institution, the University of Oslo. Working with gender equality is a strategic choice for CCB. During the Centre of Excellence period CCB has obtained two grants earmarked gender equality actions from the Research Council of Norway resulting in extra funding of 5.6 MNOK for this important area of commitment.



Staff and Students 2016

NAME	POSITION	GROUP	NATIONALITY	EMPLOYER	ACADEMICTITLE
Agostini, Antonio	PhD student	Micci	Italy	Oslo University Hospital	MSc
Alagaratnam, Sharmini	Scientist	Lothe	Malaysia	Oslo University Hospital	PhD
Andersen, Hege Kilen	Technician	Micci	Norway	Oslo University Hospital	
Andresen, Kim	Technician	Lind	Norway	Oslo University Hospital	PhD
Askautrud, Hanne	Section leader, Postdoc	Danielsen	Norway	Oslo University Hospital	PhD
Bai, Baoyan	Postdoc	Smeland	China	University of Oslo	PhD
Bakken, Anne Cathrine	Technician	Skotheim	Norway	Oslo University Hospital	MSc
Bassols, Jose Maria	Computer specialist	Stenmark	Spain	Oslo University Hospital	
Berg, Kaja Christine Graue	PhD student	Lothe	Norway	Oslo University Hospital	MSc
Bergersen, Anne Gro	Technician	Stenmark	Norway	Oslo University Hospital	
Bergsland, Christian Holst	Research fellow/PhD student	Lothe	Norway	Oslo University Hospital	MSc
Bjørnslett, Merete	Technician	Lothe	Norway	Oslo University Hospital	PhD
Blaker, Yngvild Nuvin	PhD student	Smeland	Norway	Oslo University Hospital	MD
Bogaard, Mari	Master student	Wiedlocha	Norway	University of Oslo	
Bollum, Lise Kristin	PhD student	Smeland	Norway	Oslo University Hospital	MSc
Brandal, Petter	Scientist	Micci	Norway	Oslo University Hospital	PhD
Brech, Andreas	Project leader, Senior scientist	Stenmark	Norway	Oslo University Hospital	PhD
Brunetti, Marta	PhD student	Micci	Italy	Oslo University Hospital	MSc
Brunsell, Tuva Høst	PhD student	Lothe	Norway	Oslo Univ. Hosp./University of Oslo	MD
Bruun, Jarle	Postdoc	Lothe	Norway	Oslo University Hospital	PhD
Campsteijn, Coen	Postdoc/Scientist	Stenmark	Holland	Oslo University Hospital	PhD
Carm, Kristina	Master student	Skotheim	Norway	University of Oslo	
Cekaite, Lina	Scientist	Lothe	Lithuania	Oslo University Hospital	PhD
Christ, Liliane Florence	PhD student	Stenmark	Switzerland	Oslo University Hospital	MSc
Cyll, Karolina	PhD student	Danielsen	Poland	Oslo University Hospital	MSc
Danielsen, Håvard	P.I., professor	Danielsen	Norway	Oslo University Hospital	Dr. Philos
Danielsen, Stine Aske	Scientist	Lothe	Norway	Oslo University Hospital	PhD
Dostal, Vojtech	Guest PhD student	Stenmark	Czechrepublic	Charles University, Prague	MSc
Eibak, Anne Mette	Technician	Micci	Norway	Oslo University Hospital	
Eide, Peter Andreas Wold	PhD student	Lothe	Norway	Oslo University Hospital	MSc
Eilertsen, Ina Andrassy	PhD student	Lothe	Norway	Oslo University Hospital	MSc
Eknæs, Mette	Technician	Lothe	Norway	Oslo University Hospital	
Engen, Anne	Technician	Stenmark	Norway	Oslo University Hospital	
Ersvær, Elin	PhD student	Danielsen	Norway	Oslo University Hospital	MSc
Fiorito, Elisa	Postdoc	Wiedlocha	Italy	Oslo University Hospital	PhD
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NAME	POSITION	GROUP	NATIONALITY	EMPLOYER	ACADEMICTITLE
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