ANNUAL REPORT 2019

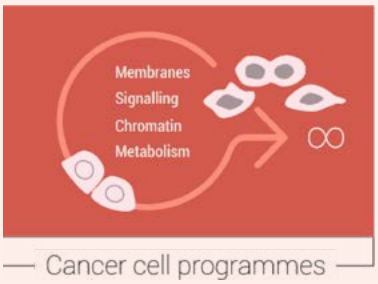
CanCell

UiO : CanCell – Centre for Cancer Cell Reprogramming
University of Oslo

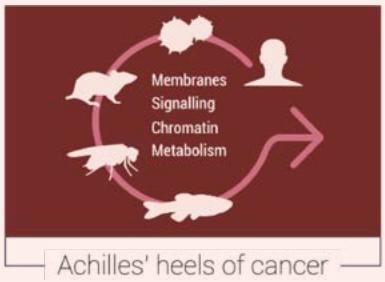
REPROGRAMMING CANCER
OMPROGRAMMERING AV KREFT

Cover: A cell leaves vesicles known as migrasomes behind when it moves. Confocal micrograph by Yan Zhen

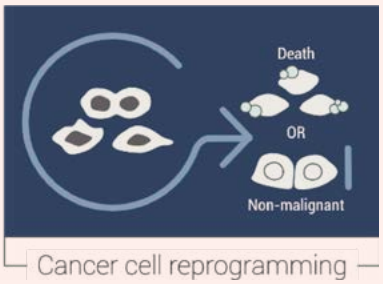
Contents



Cancer cell programmes



Achilles' heels of cancer



Cancer cell reprogramming

Gaining momentum in cancer research

2019 was the second year for CanCell as a Norwegian Centre of Excellence, and we are happy to see that our joint cancer research is fully gaining momentum. The weekly meetings in CanCell's leadership group have been characterized by enthusiasm and excellent team spirit, and we are already beginning to see the fruits of projects initiated as CanCell collaborations. These will, hopefully, bring us closer towards our joint vision of reprogramming cancer cells into harmless cells.

In particular, 2019 was a very successful year for CanCell's research on autophagy, the cellular self-eating process that is so important in cancer biology. Three high-quality articles in this field were published as collaborative efforts from CanCell scientists, in addition to several other great papers on projects related to autophagy in its many forms. The importance of autophagy research in cancer was highlighted by the award of the prestigious King Olav V's Prize to Anne Simonsen for her contributions to research on autophagy and cancer.

Cancer cell biology research on other topics was also well covered, including research on cell signalling, stress control and invasiveness. In total, CanCell published 39 papers in peer-reviewed international journals in 2019, 14 of these have first and/or senior authors from CanCell members. Many of these papers were published in high-quality open-access journals such as Nature Communications, PLoS Biology, Elife or Cell Reports.

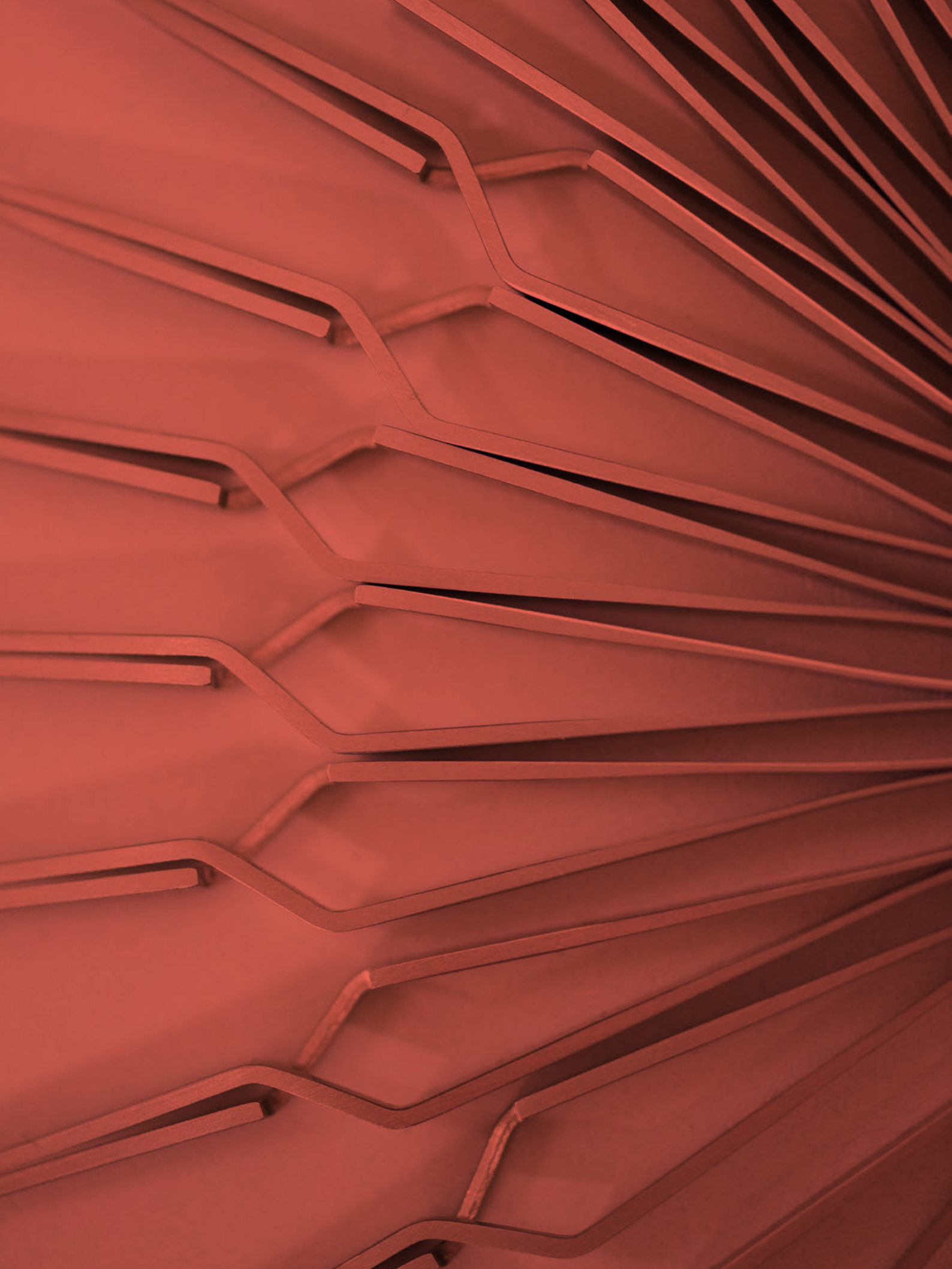
One of the main ambitions of CanCell is to train tomorrow's leading cancer researchers, and we are happy that two of our PhD students, Marte Sneeggen and Ignacio Cuervo, successfully defended their theses in 2019. Likewise, we are delighted that four CanCell junior scientists, Helene Knævelsrud, Kay O. Schink, Swarupa Panda, and Viola Nähse, obtained major research grants in 2019. Together with other centres of excellence in the Oslo area, CanCell is involved in a programme aimed at career development of young scientists, and one of the outcomes of this programme has been the establishment of CanCell Young Scientists (CYS), a forum for career development, networking, and social and scientific activities. Representatives of CYS participate in CanCell's leadership meetings on a regular basis and in this way have their hands on the steering wheel for CanCell's future. We believe that diversity promotes creativity, and CanCell has recently launched its Equality Forum, chaired by Ragnhild Eskeland, with the aim of promoting gender equality as well as minority and youth leadership.

International cooperations are essential in cutting-edge biomedical research, and CanCell´s scientists have collaborations all over the world as indicated elsewhere in this report. Several major international projects were launched in 2019, including an EU-funded Initial Training Network on autophagy with Anne Simonsen as partner, an INT-PART project on cancer cell biology with two leading Chinese laboratories, coordinated by Harald Stenmark and Anne Simonsen, and a new collaboration on cancer cell invasion with the Institut Curie in Paris, coordinated by Harald Stenmark. The latter project is generously sponsored by Trond Paulsen, and we are grateful for the active involvement of a private citizen in CanCell´s research programme.

We are also grateful to the Research Council of Norway for the CoE support and for supporting some of our individual projects. Likewise, we thank the Norwegian Cancer Society and the South-Eastern Norway Regional Health Authority for funding several of our projects. Thanks are also due to our host institutions, the University of Oslo (Faculty of Medicine) and Oslo University Hospital, which provide excellent administrative support and infrastructures. Special thanks to our committee of user patient representatives, who provide valuable advice from the patient's perspective and motivate our researchers with their own stories. In the years to come, we hope to pay back the trust from our hosts, sponsors and patient representatives in the form of discoveries that can benefit the future cancer patient.

Harald Stenmark
director

Anne Simonsen
co-director



Research groups presentations

The group has 34 members
from 12 nations.

Stenmark Group

Cellular Membrane Dynamics

We aim to establish how changes in the dynamics of cellular membranes contribute to cancer development.

@harald_stenmark

Current projects

- Endosomal control of metastasis (Harald Stenmark)
- Coincidence detection of proteins and lipids in regulation of cellular membrane dynamics (Harald Stenmark)
- Autophagy and lipid droplets in regulation of cell metabolism (Harald Stenmark)
- Autophagy of large protein assemblies (Andreas Brech)
- Mechanisms and functions of lysosome repair (Harald Stenmark)
- Lysosome dynamics and their involvement in cancer invasion (Camilla Raiborg)
- Nuclear envelope dynamics in maintenance of genome stability (Marina Vietri)
- Macropinocytosis in cancer cell feeding (Kay O. Schink)
- Regulation of Wnt signalling (Eva M. Wenzel)
- Regulation of cytokinetic abscission *in vivo*, and its relevance to cancer (Kaisa Haglund)

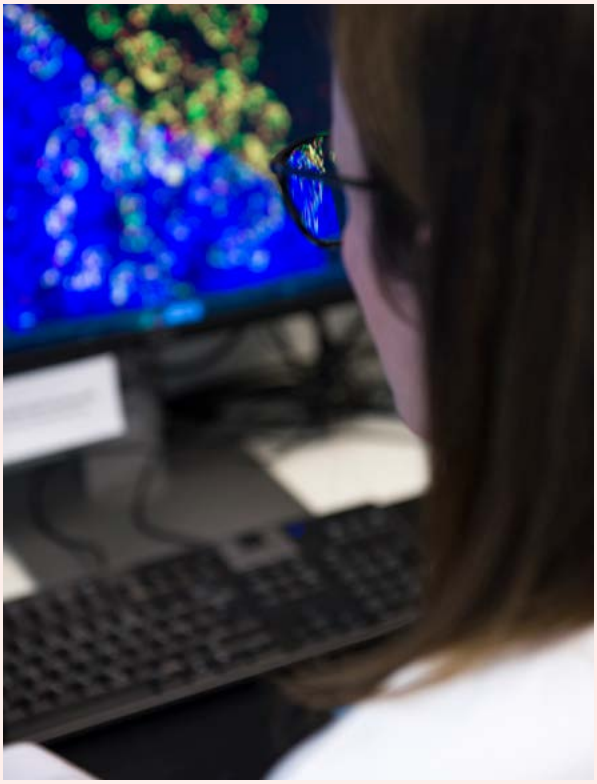
Recent achievements

- New mechanism of tumor suppression – intracellular retention of matrix metalloproteinases (Sneeggen et al., Nature Communications 2019). Awarded publication prize from Oslo University Hospital.
- ESCRT proteins promote autophagy by mediating sealing of newly formed autophagosomes (Zhen et al., Autophagy, 2019).
- Novel mechanism for recruitment of the abscission machinery to the midbody during cytokinesis – (Lie-Jensen et al., Current Biology, 2019). Dedicated a commentary article in Current Biology.
- Comprehensive review on ESCRT proteins in sealing and scission of cellular membranes (Vietri et al., Nature Reviews Molecular Cell Biology, 2019).
- Major grants in 2019 to Kay O. Schink, Harald Stenmark, and Viola Nähse.
- Members of the group published 13 original papers and 3 reviews in 2019.

Life in the group

Because the group is large, five project leaders (Camilla Raiborg, Andreas Brech, Kay Schink, Kaisa Haglund, Antoni Wiedlocha) help the group leader with grant acquisition and research supervision. In spite of the group size, we have a non-hierarchical and friendly working environment. We combine molecular biology methods such as transgenesis and genome editing with advanced light and electron microscopy to understand the molecular biology that controls cellular membrane dynamics. Models include cell cultures, simple organoid models, invasion assays, and fruit flies.

Watch Kay Shink's project on macropinocytosis through this QR code



The group currently has 15 members from 10 nations. We are localized at the Institute of Basic Medical Sciences, UiO.

Simonsen Group

Autophagy

We aim to characterize the mechanisms involved in recognition and targeting of cancer-promoting cargo, including damaged mitochondria and aggregate-prone proteins, for degradation by autophagy.

@simonsen_lab

Current projects

- The role of selective autophagy in tumor development (funded by the Norwegian Cancer Society)
- The role of lipid-binding proteins in health and disease ("Toppforsk" project funded by the Research Council of Norway)
- Driving next generation autophagy researcher towards translation (DRIVE) (H2020-MSCA-ITN-2017 765912)
- Secretion and Autophagy and their role in Neurodegeneration (SAND) (H2020-MSCA-ITN-2018 860035

Recent achievements

- Identification of NIPSNAP proteins as "Eat Me" Signals for Mitophagy (Abudu et al, ***Dev Cell***. 2019). Dedicated a commentary article and cover of the same issue of Dev Cell.
- Showing that different ATG16L1 isoforms have distinct functions in membrane binding and LC3B lipidation in autophagy-related processes (Lystad et al, ***Nat Cell Biol***. 2019)
- Extensive review about Lipids and Lipid-Binding Proteins in Selective Autophagy (de la Ballina, Munson and Simonsen, ***J Mol Biol***. 2019).
- Comprehensive review on Mechanisms and Pathophysiological Roles of the ATG8 Conjugation Machinery (Lystad and Simonsen A, ***Cells*** 2019)
- Members of the group published 10 original papers and 4 reviews in 2019.
- Kong Olav Vs Kreftforskningspris 2019 to Anne Simonsen

Life in the group

The group includes a good mix of early stage researchers and more senior postdocs and researchers that together create a scientifically stimulating, fun and friendly working environment. Everyone in the lab are involved in projects focusing on unravelling the mechanisms of autophagy. We use cutting-edge genome editing technology and advanced microscopy to study such mechanisms in human cell lines and zebrafish, but also collaborate with clinicians and patients to investigate the role of cellular waste recycling in tumorigenesis.

The annual lab retreat was this year a joint retreat with the Farhan Lab to Evje where we enjoyed great science and team building activities, including rafting.

Here you can find an explanation of the central theme in their research on autophagy

The Enserink group presently consists of two project group leaders, seven post-docs, three PhD students, four MSc students, in addition to a clinician in a 20% affiliated position. In addition, there are four vacant post-doc positions that will be filled during 2020.

Enserink Group

Cancer Molecular Medicine

Most projects in the group employ high-throughput screening methods to gain insight into three main research problems:

i. Development of novel therapeutic strategies that bypass development of drug resistance in leukemia and other forms of cancer.
ii. Understanding how cells respond to sudden changes in nutrient levels, particularly at the 'systems' level
iii. Development of treatment for antibiotic-resistant fungal infections.

@enserinklab

To reach first goal, we have developed a high-throughput platform to systematically screen large numbers of drug combinations using cell lines and primary cancer cells obtained from cancer patients. This part of our research is also an important element of the "PINpOINT node of the Centre for Digital Life Norway, which is jointly led by Dr. Enserink and Dr. K. Taskén (ICR, OUH), and which involves biostatisticians from the group of Dr. A. Frigessi (UiO). In addition, we generate data for the Horizon2020 project 'RESCUER', which is a large international research network led by Dr. V. Kristensen (OUH) with the aim of developing personalized medicine strategies for breast cancer.

To reach the second goal, we are using high-content microscopy to systematically screen dynamic responses of cells to a sudden loss followed by re-gaining of access to nutrients. We are primarily using the model organism budding yeast, using autophagy as a read-out for these responses, with the aim of describing the effect of each and every gene on regulation of this process.

In parallel, project group leader Dr. H. Knævelsrud is using the model organism *D. melanogaster* to model leukemia and to study dynamic nutrient responses from the perspective of a developing multicellular organism (supported by a grant from HSØ and a young researcher talent grant from the Norwegian Research Council). We aim to develop a dynamic and synergistic research environment in which hypotheses generated in one research model can be quickly tested in other models.

Project group leader Dr. I. Garçia is focused on developing novel treatment for drug-resistant fungal infections in leukemia patients. Drug-resistant fungal infections in cancer patients are sharply increasing, but no new antibiotics have been developed in the past decades. As a starting point, Dr. Garçia has already identified several lead compounds that selectively kill fungal cells but not human cell lines.

Finally, we are developing new bioinformatics tools to analyse the large datasets generated in the group, using neural networks and machine learning strategies.

Projects

- Identification of the upstream pathways that switch on and switch off autophagy.
- Unraveling genetic networks that determine the response of cancer cells to anticancer drugs using genome-wide CRISPR/Cas9 screens.
- Identification of synergistic drug combinations to overcome drug resistance of cancer cells.
- Development of antibiotics to treat drug-resistant fungal infections.
- Development of bioinformatics tools for analysis of large and heterogeneous datasets.

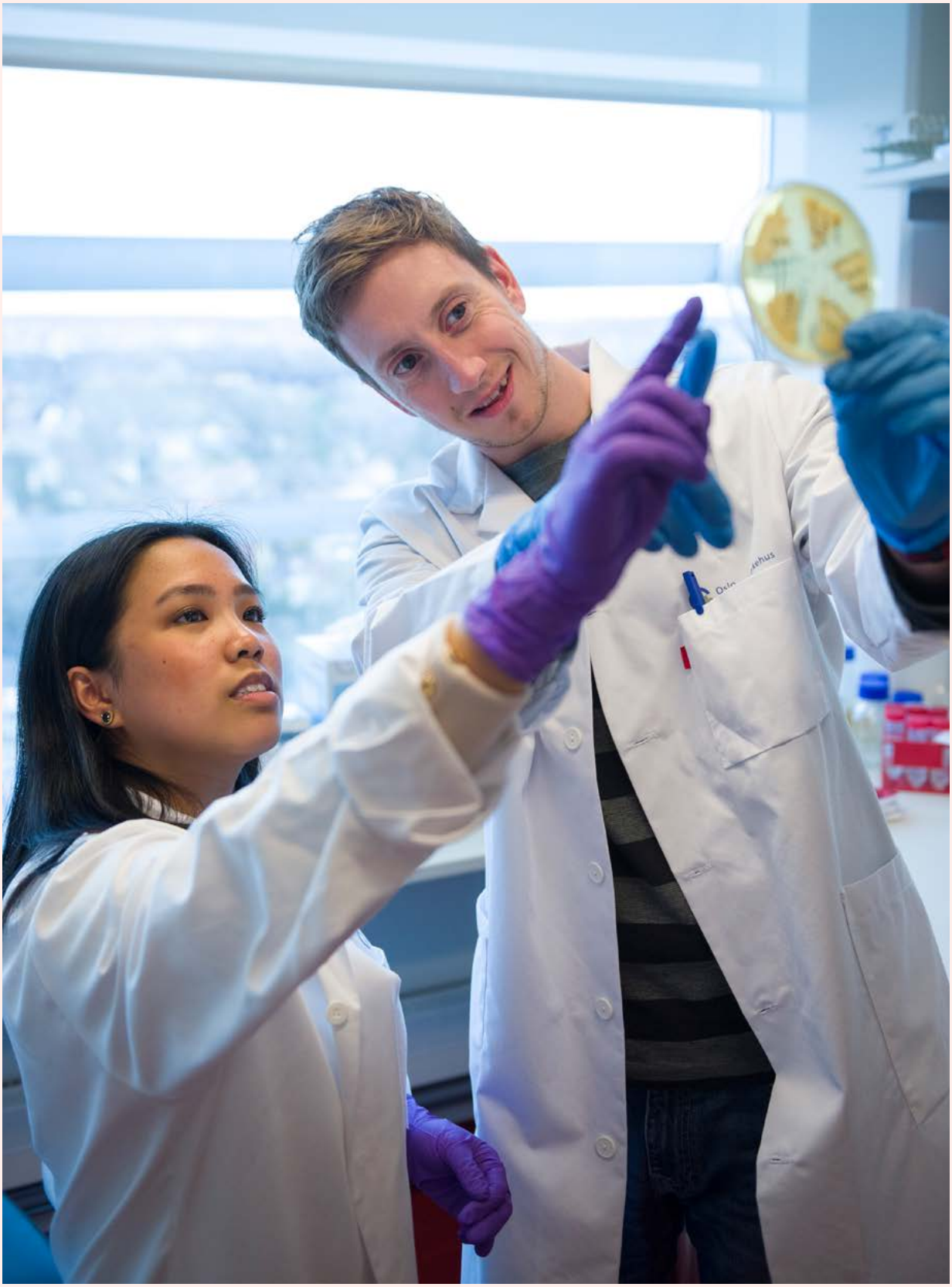
Recent achievements

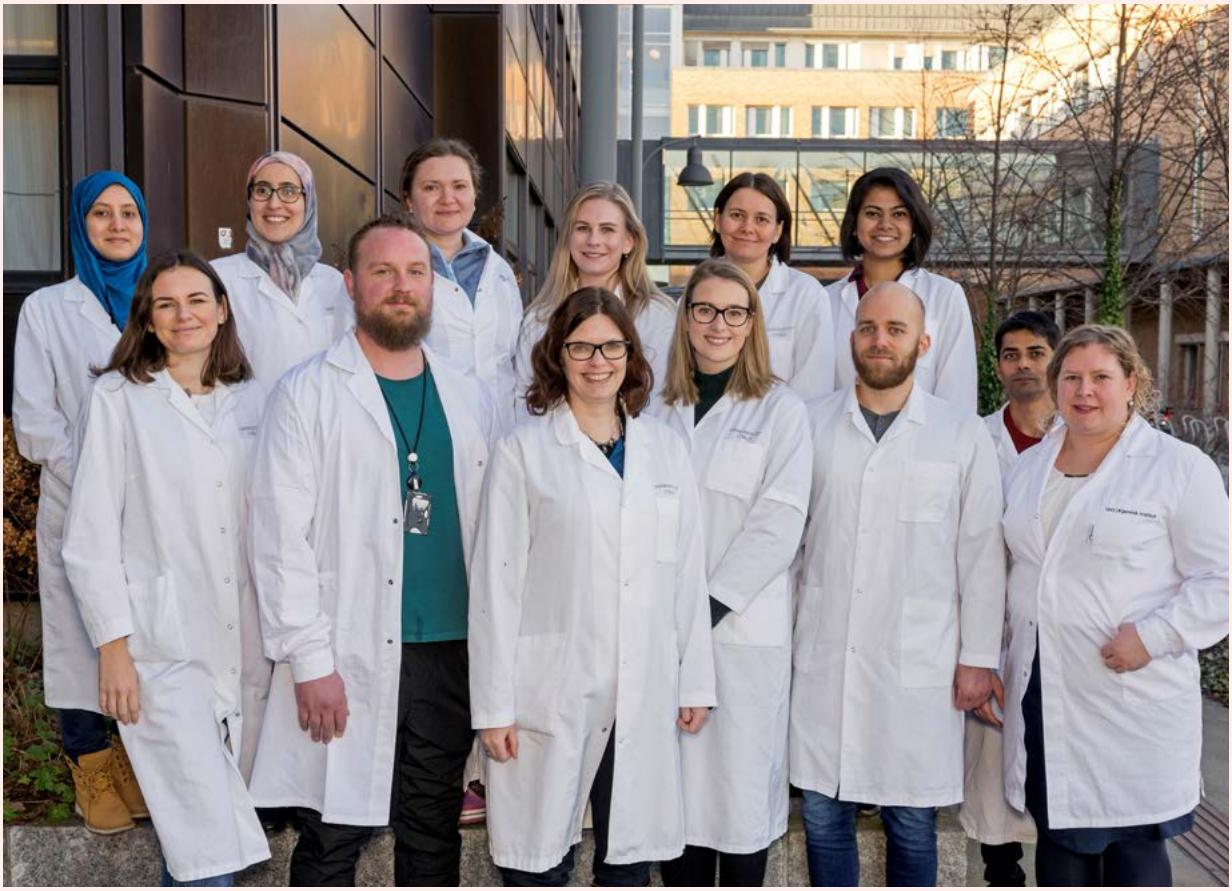
- Unraveled novel mechanistic pathways by which cells regulate transcriptional responses upon changes in nutrient levels and during cell cycle progression (Chymkowitch, PNAS 2017; Herrera, NAR 2018; Nguéa P, JBC 2019)
- Contributed to the discovery that centromeres regulate condensation of chromosome arms (Cell, 2018)
- Young Research Talent grant to Dr. H. Knævelsrud
- Establishment of the 'PINpOINT' node of the Norwegian Center for Digital Life
- Several DofIs submitted for compounds that selectively kill cancer cells, novel antimycotics and new immunotherapy tools.

Life in the group

At present, large amounts of data can be generated in short periods of time, and analysis and modelling of data are bottlenecks in research. This creates a challenge that requires intense collaboration within research teams to share ideas and findings, involves development of new analysis tools, and requires implementation of infrastructure for accessing and analysing the heterogeneous datasets that are created in the laboratory. A major focus of the Enserink team is therefore to be as collaborative and cross-functional as possible, where people readily share their expertise and contribute to each other's research projects. We pride ourselves of a flat, open and respectful atmosphere underpinned by a positive, can-do mindset.

Watch Helene and Pilar explain how personalised medicine for blood cancer can be achieved





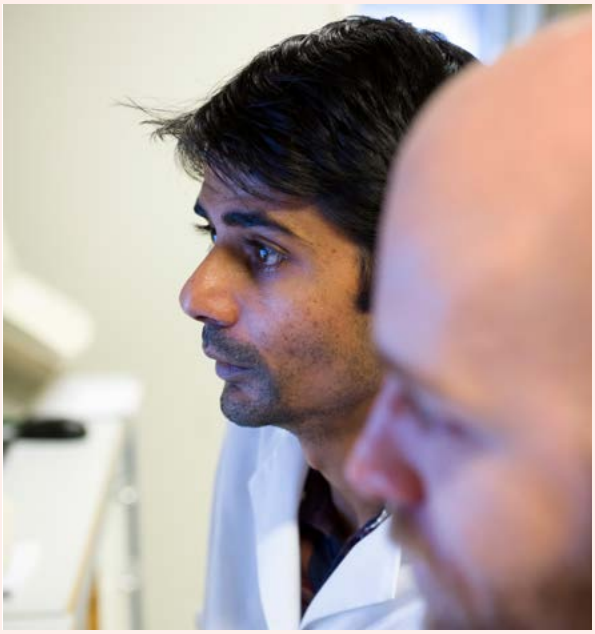
The Eskeland group consists of two researchers, two postdocs, two PhD students, one head engineer and six master students. Photo: Gunnar F. Lothe

Eskeland Group

Chromatin Biology

The aim of the Eskeland group is to understand how chromatin structure and nuclear organization is disrupted in the context of genomic variation and epigenetic remodelling in cancer to unravel molecular mechanisms that can form the basis for novel therapy strategies.

@EskelandLab **www.chromatome.no**



The Eskeland group work on different aspects of epigenetic regulation and chromatin through various molecular and biochemical methods.

Cancer remains a major disease group with over 30,000 new cases detected and more than 10,000 deaths in Norway each year. By deciphering the cell signatures of the initial cancer cells, we can gain new knowledge on how to reprogram or destroy the cancer cells before they develop into tumours. We have during the last year collaborated with Susanne Lorenz and Leonardo Meza-Zepeda (OUH) and used the most recent genomics analysis on thousands of single cells of Liposarcoma to look for these originating cells. Moreover, we have gained new knowledge on nuclear organisation of genomic aberrations in Liposarcomas in collaboration with CanCell bioinformatician Sigve Nakken, NoSarC and Ola Myklebost (UiB). To identify the transcription factor network in different sarcomas, our group has set up a pulldown assay that will be combined with mass spectrometry in a collaborative effort with Bernd Thiede (IBV). In parallel, we have studied aspects of gene regulation in prostate cancer and identified novel mechanisms of metastasis and proliferation. In collaboration with Sunniva Bjørklund, Thomas Fleicher and Vessela Kristensen (OUH), we have mapped expression of histone variants across breast cancer subtypes. Finally, we are developing a novel live-cell imaging tool for study of individual gene loci.

Our ambition is to establish new knowledge on various aspects of epigenetic aberrations and cross talk between cancer cell programmes and translate this knowledge to reprogram cancer cells into non-malignant cells.

To achieve this goal we have established state-of-the-art assays such as the auxin-inducible degron (AID) system and genome editing by CRISPR targeting, super-resolution and live-cell imaging, proteomics, genome-wide analysis and bioinformatics in the lab to assess the cancer specific epigenetic remodeling.

Projects

- Characterization of carcinogenic chromatin remodelling alterations, transcriptional networks and driver mutations of chromatin regulatory factors in sarcomas
- Gene regulation and chromatin organization in prostate cancer
- Regulation of histone variants in breast cancer
- Cell-based screens for identification of novel gene regulatory mechanisms
- Live-cell chromatin dynamics and function (Image-CRISPR, FRIPRO, The Norwegian Research Council)

Recent achievements

- We relocated and established the Eskeland lab at IMB
- Ignacio Cuervo successfully defended his PhD thesis focusing on the role of SUMOylation in gene regulation
- Guro C. Mustorp completed her master exam with distinction on her work to tune the activity of retrotransposable elements in cervical cancer cells.
- Marie Rogne and Naima Azouzi received CanCell's young research project grants

Life in the group

The Eskeland group is a young group of experienced researchers and students that have a positive, focused and friendly working environment. We renovated a new lab at IMB during the spring semester and moved from Department of Biosciences (IBV) in beginning of May. Everyone in the group did a great effort in packing and unpacking without loss of precious research material. We are grateful to our colleagues at IBV and IMB for making our renovation and relocation as smooth as possible. Marit Ledsaak started as head engineer in the group in August and has been instrumental in organizing our new lab. She also contributes to CanCell's joint project on CRISPR library amplification. Although the move to IMB has taken some time and effort we have set up all our project activities during autumn and are very happy in our new research environment.

Watch an animation video about cancer epigenetics and research in the Eskeland group through this QR code


UNIVERSITETET
I OSLO

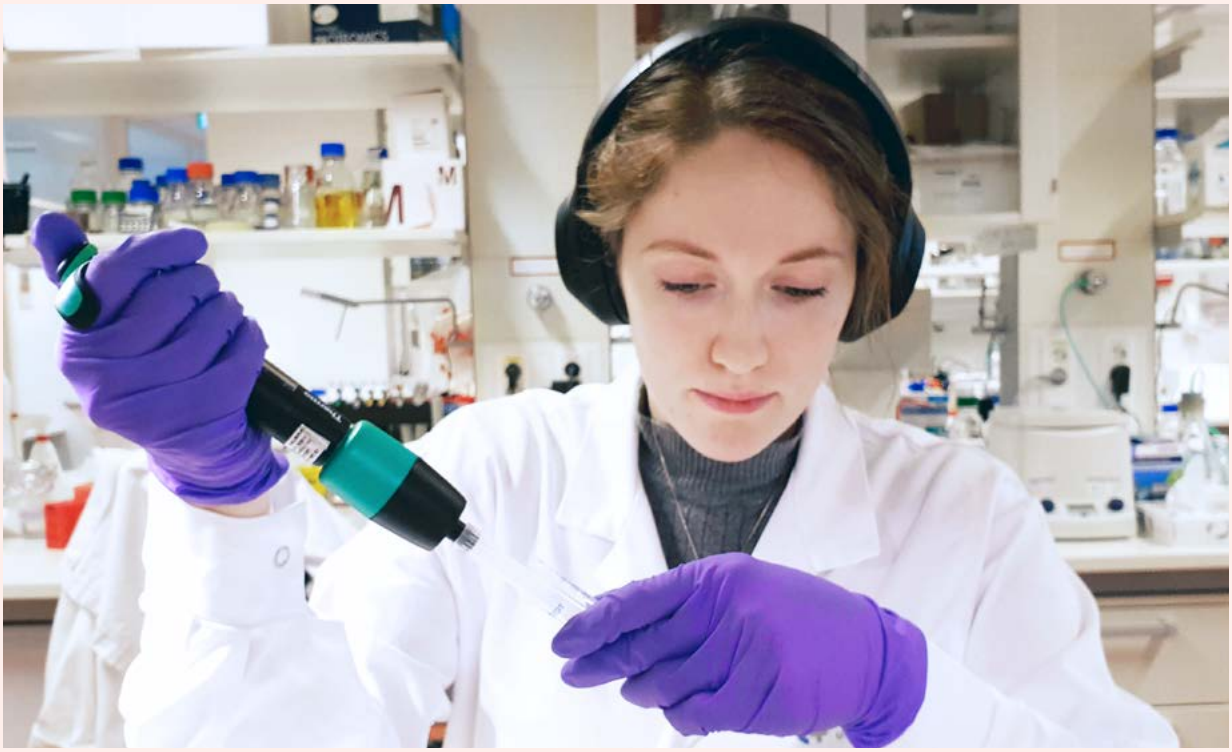
The group currently has 12 members (1 PI, 1 senior researcher, 5 postdocs, 1 PhD student, 1 master student, 2 ERASMUS exchange students, 1 technician). There is a postdoctoral and PhD position to be filled during 2020.

Rusten Group

Tumor-Host Biology

Our overarching interest is to understand the mechanisms by which tumor and host cells mutually engage each other in reciprocal interactions to facilitate carcinogenesis.

@rustenlab



Research

Tumor-host interactions occur both locally in the tumor microenvironment and systemically causing organ dysfunction such as in cancer cachexia - the metabolic reprogramming and catastrophic wasting of muscle and adipose tissue. We believe that studying these processes can uncover new ways to intercept carcinogenesis and systemic effects due to tumor presence.

In order to mechanistically understand how tumor and non-tumor cells and organs communicate to foster tumor growth and cause cancer cachexia we develop *novel* genetic tools in *Drosophila*. These tools will allow us to selectively and independently manipulate tumor and either tumor microenvironment or somatic organs *in vivo*. We employ a wide array of techniques and collaborate with experts in cell biology, genetics, imaging, tumor biology, metabolism, bioinformatics and clinical cancer cachexia in order to survey, measure and mechanistically understand these complex aspects of cancer biology.

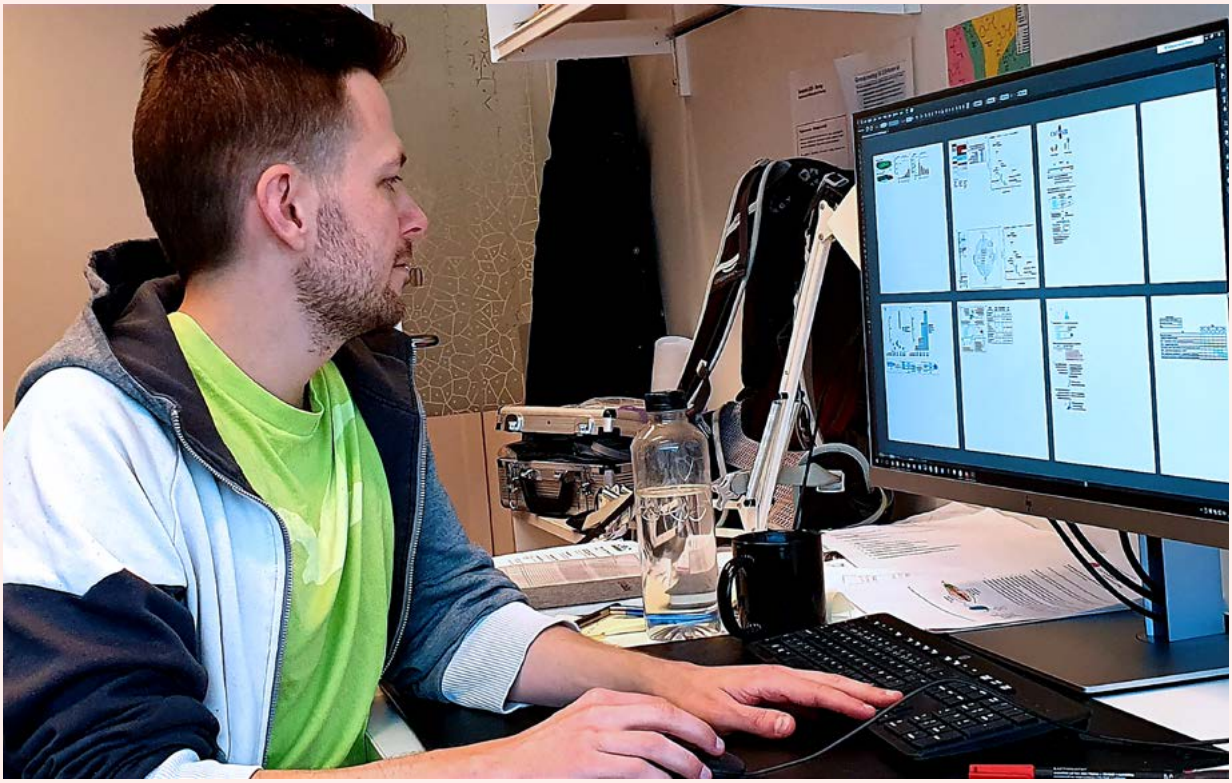
In parallel to *in vivo* work in flies, we utilize human organoid and spheroid cell culture to understand cellular mechanisms controlling cell polarity, morphogenesis and cell-cell communication, the disruption of which is set off by cancer-driving mutations and underlies early tumor development.

Projects and collaborations

- Tumor-microenvironment interactions and organ -organ communication during cancer cachexia
- Tumor-induced organ wasting
- Establishment of human organoids
- Mechanisms of non-autonomous tumor growth support

Collaborating groups

Harald Stenmark (OUH, cell biology, electron microscopy (Andreas Brech)), Kristian Berg (OUH, metabolism (T. A.Theodossiou)), Jorrit Enserink (OUH, protein phospho-proteomics), Anne Simonsen (UiO, autophagy), Stein Kaasa (OUH, clinical cachexia), Åslaug Hellland (OUH, clinical cachexia), Eivind Hovig (OUH, bioinformatics), Eyal Gottlieb (TICC, Haifa, Israel, metabolism), Heinrich Jasper (Genetech, California, US, organ-organ communication), Rita Sousa-Nunes (Kings College, London, UK, genetic tools, tumor-host communication), Eduardo Moreno (Champalimaud Centre for the Unknow, Lisbon, Portugal, tumor-microenvironment communication)



Recent achievements

- Discovery that malignant tumors induce a stress response in the microenvironment that supports tumor growth through nutrient-generating autophagy (Katheder, N.S., et al, *Nature* 2017).
- The tumor suppressor LKB1, responsible for the Peutz-Jegher cancer syndrome, is controlled by endocytic vesicle trafficking and its derailment contributes dysplasia and tumor growth (O´Farrell, F. et al. *Nature Cell Biology*, 2017).
- EMBO long term postdoctoral fellowship awarded to Swarupa Panda.
- 1 DOFI was filed 2019 regarding utilization of stable isotope labelling to trace transfer of organic building blocks from host to tumor.

Life in the group

The group is very international and includes a good mix of students, postdocs and a senior researcher with a wide set of expertise ranging from molecular biology, to cell biology, genetics, bioinformatics and organoid culture. We have weekly group meetings, celebrations and a yearly lab retreat on a remote location or another country for team building, project alignment and generation of new avenues of research. Lab members are encouraged to go to international meetings and develop their career and skills for professional development while in the group.

Watch scientist Viola Lobert present her project on gut organoids:


LEICA

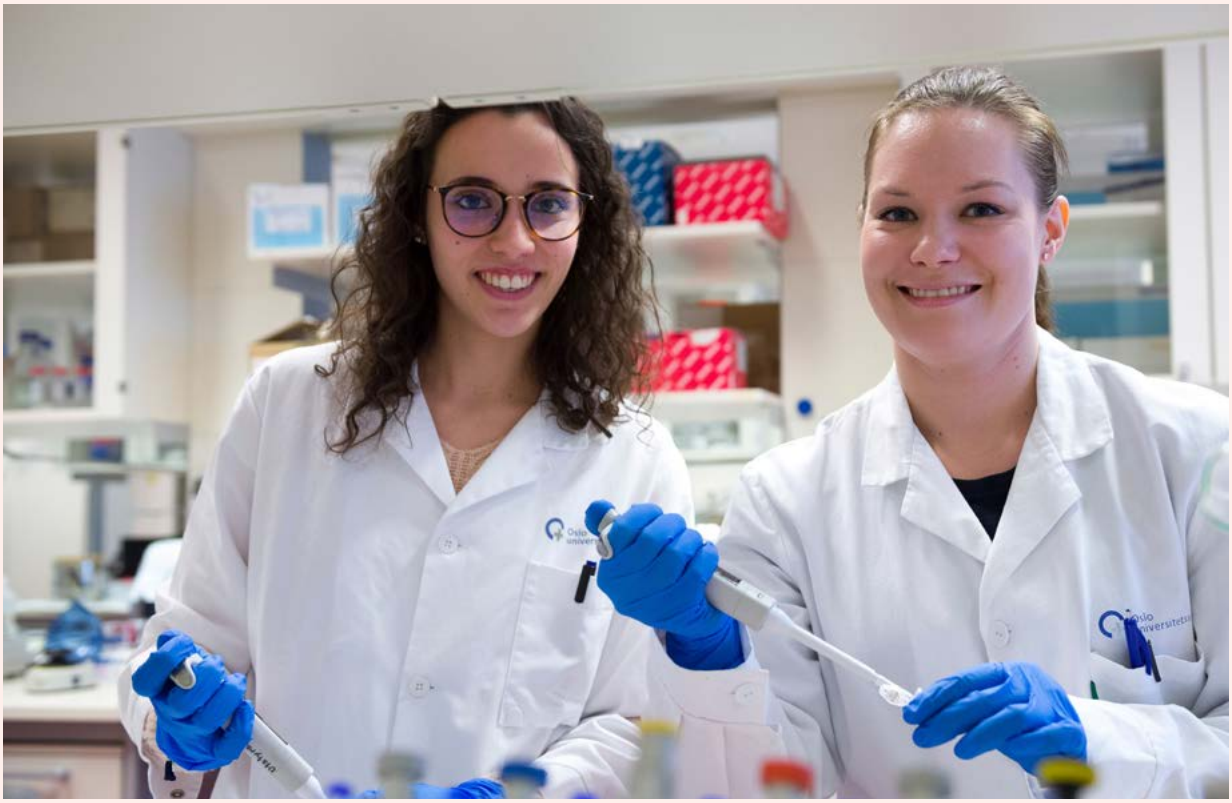
The group has 11 members, which includes 3 scientsist, two clinician, and postdocs in addition to the PI. Leonardo Meza-Zepeda, head of core facility department is also a part of the group with his team.

Wesche Group

Molecular Biology of Sarcomas

The group has its focus on the development of precision medicine for sarcoma patients. We study the hyperactive signalling of receptor tyrosine kinases in gastrointestinal stromal tumors and the childhood cancer Rhabdomyosarcoma. Since KIT and FGF receptors are frequently mutated in these sarcomas, they can be used as a target for therapy. In order to improve treatment, we are investigating how genetic changes (e.g. mutations) affect the signalling within the tumor, and how tumors evolve and become resistant. This will help identify new therapeutic strategies and novel drug targets, ultimately providing better treatment for sarcoma patients.

@Wesche_Lab

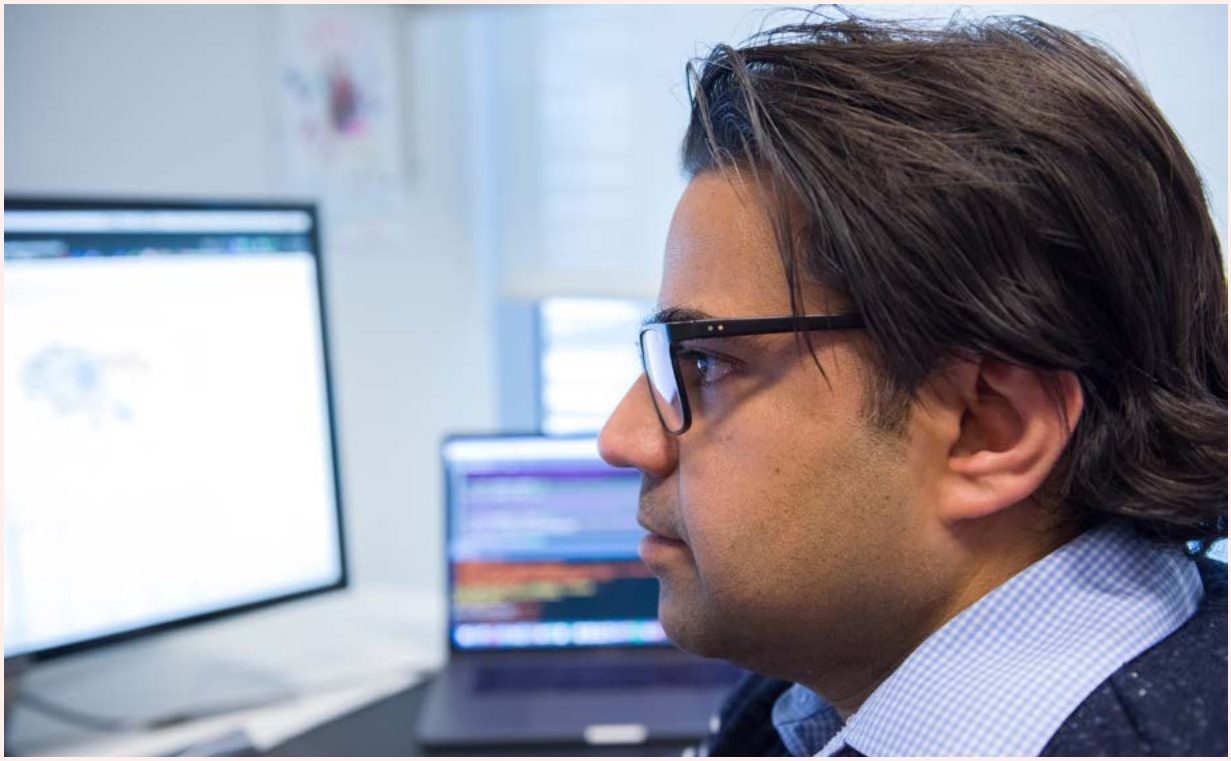


Projects

- Study the role of fibroblast growth factor receptor (FGFR) signalling in rhabdomyosarcoma, liposarcoma and osteosarcoma. By detailed understanding of oncogenic FGFR signalling, we hope to identify new strategies to inhibit sarcomas and other cancers dependent on FGFR signalling.
- Establish new modalities for sensitive non-invasive monitoring of sarcoma patients by use of "liquid biopsies".
- Characterize intratumor heterogeneity in relation to resistance in GIST, and reveal the molecular determinants linked to imatinib resistance.
- Norwegian Sarcoma Consortium (NoSarC) – Bio-banking (~500 samples) and genomic characterization (~300 normal/tumor pairs) of patient material and establishment of patient-derived sarcoma cell lines and mouse models.

Recent achievements

- Characterization of aberrant FGFR signalling in cancer (Kostas et al., Mol Cell Proteomics, 2018; Szybowska et al., Cells, 2019).
- Non-invasive analysis of circulating tumor DNA (ctDNA) was employed to analyse the progression and heterogeneity of gastrointestinal stromal tumors (GIST) (Namløs et al., Mol Cancer Ther 2018, Namløs et al., Mol Aspects Med 2019).
- Research grant for a new PhD-student was obtained from the South-Eastern Regional Health Authority.
- A well-functioning user panel for sarcoma research is established.
- Establishment of a new GIST collaborative project with Dr. César Serrano at Vall D'Hebron, Barcelona, Spain.



Life in the group

The group has 12 members and has broad expertise in basic cell biology and translational research and, importantly, one MD in a shared clinical position. This multidisciplinary approach will help ensure that basic findings will be translated to clinical use whenever possible. In addition, collaborations internationally, nationally and within CanCell, open up exciting possibilities for high qualitative research.

The group uses advanced technologies, including bulk and single-cell sequencing, to genetically characterize sarcoma patient material to identify and monitor druggable targets. Advanced proteomic methods and imaging are applied to study oncogenic sarcoma signalling. Our work utilizes well-characterized sarcoma cell lines and patient derived xenograft mouse models to test novel anti-cancer drugs.

Here you can find an explanation of the role of aberrant signalling in sarcomas by Leonardo Meza Zepeda

Associated members

The centre is proud to have close collaborations with seven outstanding research groups. These all have complimentary expertise to the core research groups in order to reach the centre's ambitions for cancer cell reprogramming. Each group leader is considered an associated member of CanCell, and is beneficiated by a CanCell grant of 100 000 NOK per annum.

Åslaug Helland

Translational Research on Solid Tumours

is head of transdisciplinary research group at OUH. They focus their studies on molecular analyses on biological material from patients included in clinical studies, in particular pancreatic cancer, lung cancer and colorectal cancer.

Emmet McCormack

Translational Molecular Imaging in Cancer)

is a professor at UiB and heads a group that focus on the development and effective translation of novel therapies and imaging strategies for the treatment of cancer.

Yngvar Fløisand

Hematology and Acute Myeloid Leukemia

is head physician at OUH and does research acute myeloid leukemia (AML) and allogeneic stem cell transplantation, especially with regard to acute graft versus host disease He currently also holds a 20% position in Enserink group.

Eivind Hovig

Computational Cancer Genomics and Melanoma Systems Biology

is a professor at OUS. His main focus is computational analysis of clinical data and provides support for large-scale scientific computing and storage of high-throughput datasets (primarily cell imaging, transcriptomics, and genomics) for CanCell scientists.

Terje Johansen

Molecular Cancer Research

is a professor at UiT. His group performs basic research with main focus on molecular mechanisms and roles of selective autophagy in cell signaling and disease.

Arnoldo Frigessi

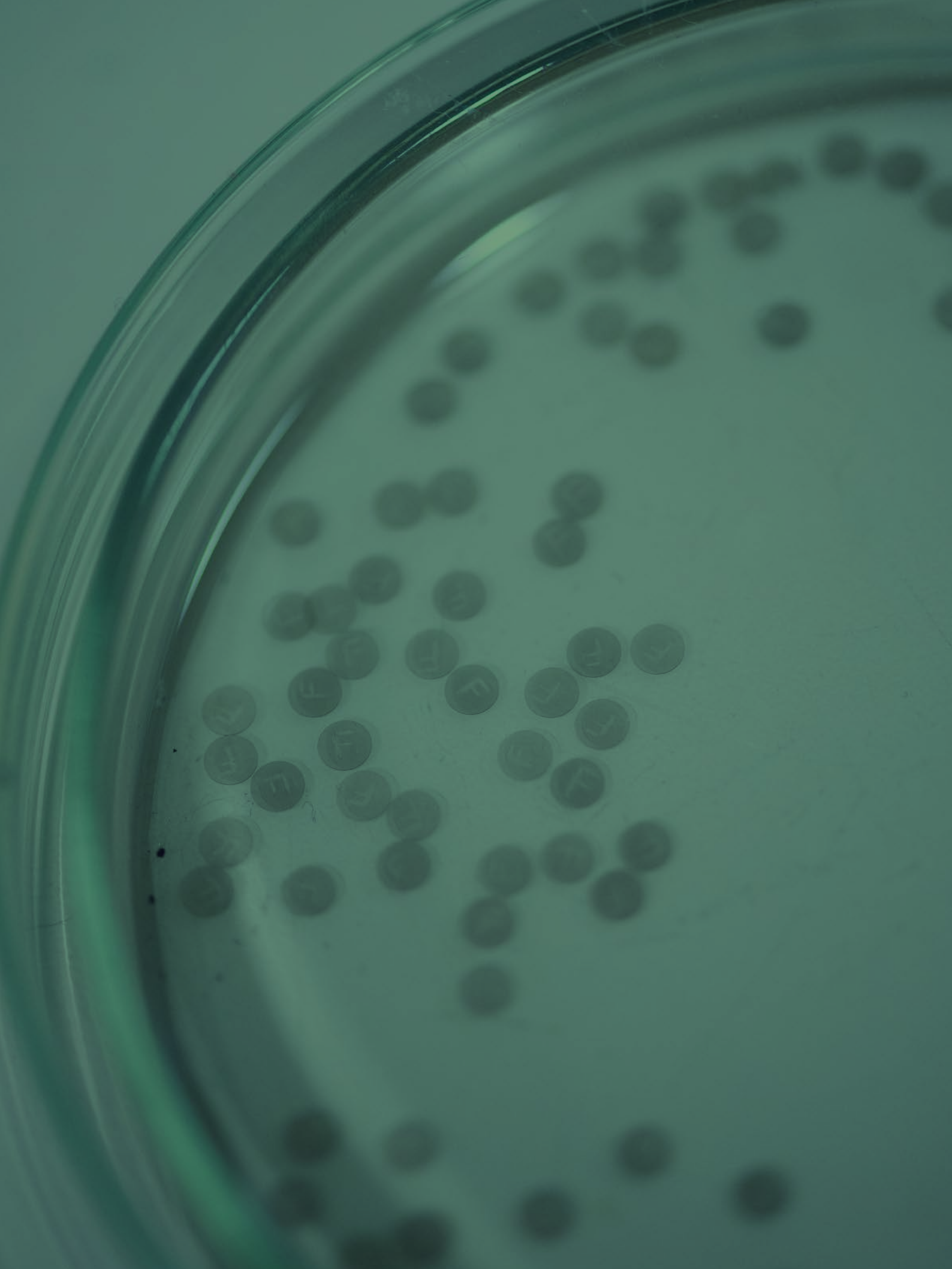
Stochastic Models and Inference

is a professor of statistics at UiO and director of BigInsight. Frigessi and his group develop statistical methodology and stochastic models to study principles, dynamics and patterns of complex dependence in biomedicine.

Phillipe Collas

Chromatin Regulation in Adipose Stem Cells

is a professor at UiO, and have a research group that investigates how disease states such as metabolic syndrome and cancer affect the spatial conformation of the human genome.



Scientific highlights

Scientific highlights

CanCell scientists made several outstanding scientific contributions in 2019. Among these three papers were bestowed the ''Excellent Article Award" at the Annual Meeting (see also page 60):

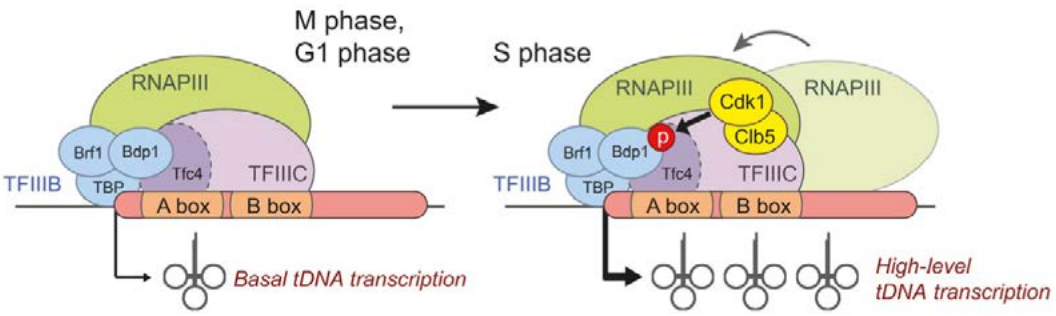


Figure 1. Model for cell cycle-induced stimulation of tDNA transcription. While basal tDNA transcription takes place during most or all of the cell cycle, it peaks during S phase due to recruitment of Clb5-Cdk1. Cdk1-dependent phosphorylation of Bdp1 promotes Tfc4 recruitment, leading to enhanced RNAPIII turnover and increased tDNA transcription.

Cell cycle dependent control of protein synthesis

Herrera MC, Chymkowitch P, Robertson JM, Eriksson J, Bøe SO, Alseth I, Enserink JM. ***Cdk1 gates cell cycle-dependent tRNA synthesis by regulating RNA polymerase III activity***. Nucleic Acids Res. 2018.

Under optimal growth conditions Cdk1 gates tRNA synthesis in S phase by regulating the RNAPIII machinery, revealing a direct link between the cell cycle and RNAPIII activity. This study demonstrates that under optimal growth conditions Cdk1 gates tRNA synthesis in S phase by regulating the RNAPIII machinery, revealing a direct link between the cell cycle and RNAPIII.

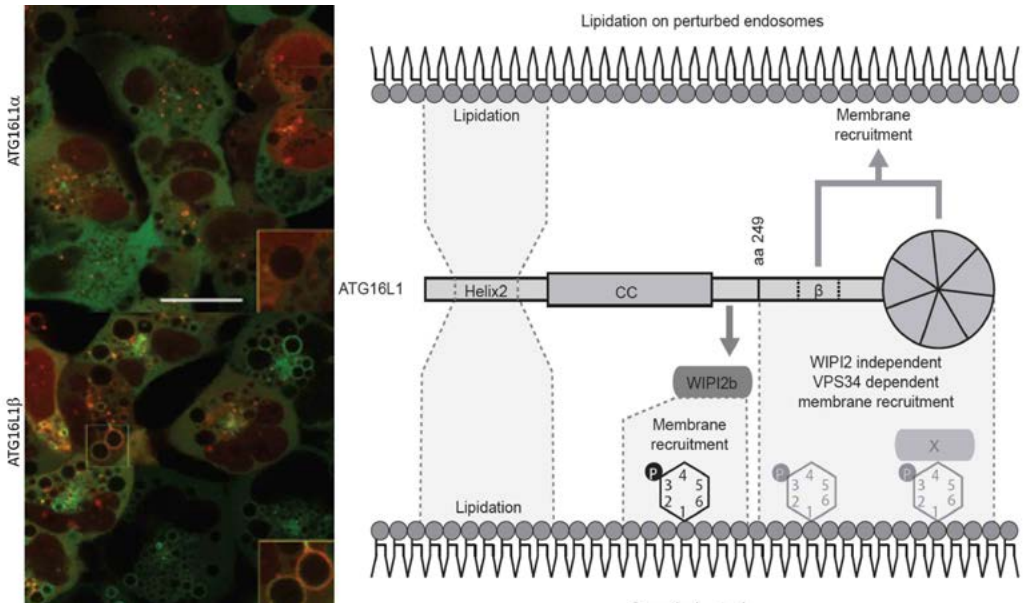


Figure 2. Left: Confocal images of ATG16L1–KO HEK293 cells rescued with eGFP–ATG16L1α or eGFP–ATG16L1β expressing mTAGBFP2–LC3B, showing that the C-terminal β-isoform-specific membrane-binding region of ATG16L1 is required for LC3B lipidation to membranes of perturbed endosomes (inset). Green EGFP Atg16L1, red LC3B. Right: Model of Atg16L1 domains involvement in ATG16L1 membrane recruitment and LC3/GABARAP lipidation.

Protein lipidation in control of autophagy

Lystad AH, Carlsson SR, de la Ballina LR, Kauffman KJ, Nag S, Yoshimori T, Melia TJ, Simonsen A. ***Distinct functions of ATG16L1 isoforms in membrane binding and LC3B lipidation in autophagy-related processes.*** Nat Cell Biol. 2019 Mar;21(3):372-383.

Lystad and co-workers now show that the β-isoform specific membrane-binding region of ATG16L1 is important for conjugation of LC3 and GABARAP to perturbed single layered endo-lysosomal membranes. Interestingly, this autophagy-related process is independent of ULK and VPS34 protein complexes that are required for conventional autophagy.

Tumor suppression by control of endocytic recycling

Sneeggen M, Pedersen NM, Campsteijn C, Haugsten EM, Stenmark H and Schink KO. ***WDFY2 restrains matrix metalloproteinase secretion and cell invasion by controlling VAMP3-dependent recycling***. *Nature Comm.* 2019 10: 2850.

WDFY2 is frequently lost in cancers, especially in high grade ovarian and prostate cancers. If WDFY2 is lost – an event that often happens in metastatic cancers - cells lose control over the recycling of MT1-MMP. More MT1-MMP is transported to the cell surface and allows normally non-invasive cells to become invasive. Using CRISPR/Cas9, Sneeggen et al showed that deletion of WDFY2 in normal cells is sufficient to allow these cells to become invasive, whereas overexpression of WDFY is able to "re-program" highly invasive prostate cancer cells to a non-invasive phenotype. This shows that WDFY2 is a key factor regulating tumor cell invasion and metastasis.

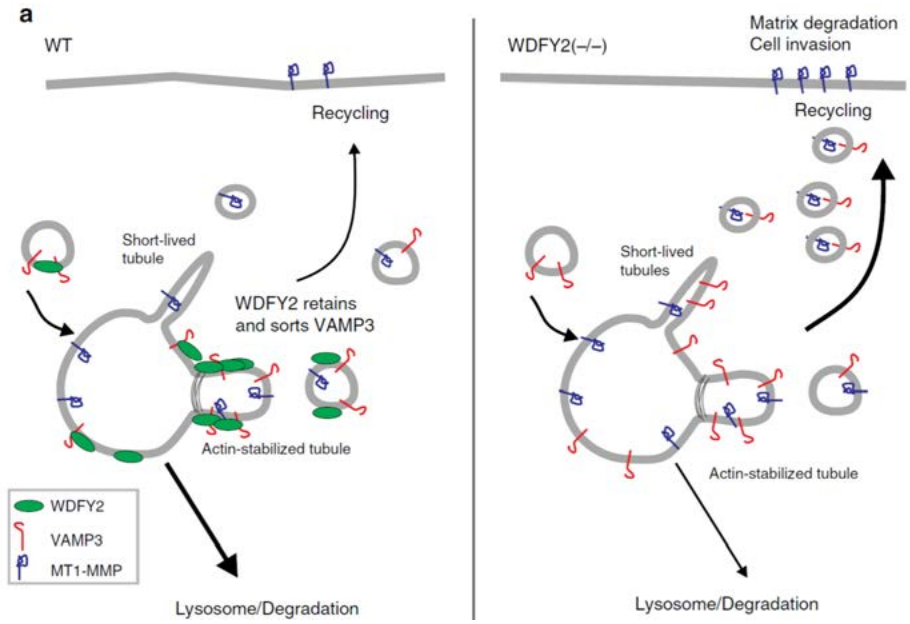
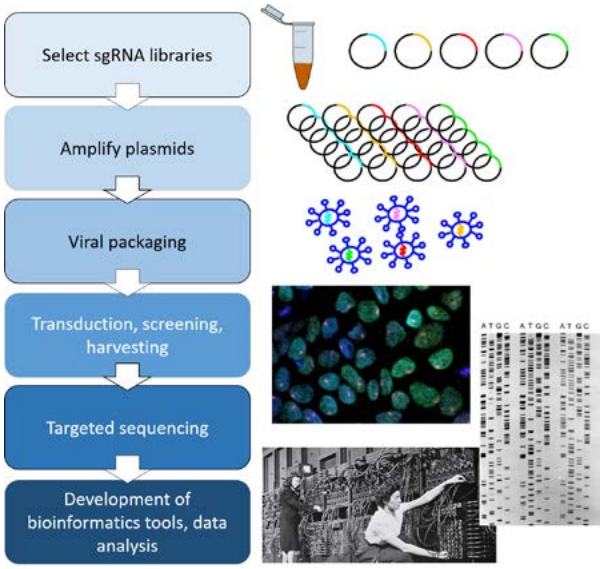


Figure 3: Model of WDFY2 action in the endocytic system. In WT cells, WDFY2 interacts with VAMP3 and preventssorting into bulk recycling tubules. This limits the amounts of VAMP3-positive recycling vesicles transporting MT1-MMP. In cells lacking WDFY2, more VAMP3 can be sorted into recycling vesicles, allowing more MT1-MMP to be recycled to the cell surface.

Figure 4:
Workflow of the CRISPR/Cas9 project



Additional outstanding contributions to the scientific community include a collaboration between the groups of Anne Simonsen and CanCell associate member Terje Johansen which resulted in the identification of a molecular mechanism for selective autophagy of damaged mitochondria, the power stations of the cell (***Developmental Cell***, 2019). Yan Zhen and her co-workers in Harald Stenmark's group collaborated with Anne Simonsen's group to reveal a molecular mechanism that closes the autophagosome and that is essential for autophagy of mitochondria (***Autophagy***, 2019).

PhD student Patrycja Szymbowska, supervised by Antoni Wiedlocha in Harald Stenmark's group and Ellen Haugsten in Jørgen Wesche's group, identified a negative feedback loop that prevents hyperactivation of fibroblast growth factor receptor 2 and showed that this negative regulation is abrogated by mutations found in cancers (***Cells,*** 2019).). PhD student Aurélie Nguéa and her colleagues in Jorrit Enserink's group identified a mechanism that shuts down production of new proteins under stress conditions (***Journal of Biological Chemistry***, 2019). PhD student Anette Lie Jensen, supervised by project leader Kaisa Haglund in Harald Stenmark's group, uncovered a new mechanism for regulation of cytokinesis, the final stage of cell division, in vivo (***Current Biology***, 2019). The article on SNX18 and ATG9a authored by Kristiane Søreng in the Simonsen Lab from last year was one of the top cited articles in EMBO Reports in 2019.

In total, CanCell published 39 papers in peer-reviewed international journals in 2019, with 14 of these senior authored by CanCell members. Many of these papers were published in high-quality open-access journals such as ***Nature Communications, PLoS Biology, Elife*** or ***Cell Reports***.

A common collaborative project on ***CRISPR/Cas9 screen*** was started in 2019. CRISPR/Cas9-gene editing technology enables screening of effectors of cellular processes in many types of cancer development and will be an invaluable tool for all of the CanCell research groups. Each group provides their expertise to a certain protocol during the project and in addition to the scientific contribution this project will have great teamwork benefits, enable spin-off projects and exchange of knowledge across labs.

CanCell Young Scientists Board 2019. From left:
Marie Rogne, Viola Lobert, Aram Nikolai Andersen,
Heidi Namløs, Anthony Ravussin, Kristiane Søreng.

CanCell Young Scientists (CYS)

This year saw the inauguration of Cancell Young Scientists (CYS). CYS is a forum for all affiliates to the Centre for Cancer Cell Reprogramming, focusing on the early stage career scientists.

Our board is made up of 6 members; one from each of the research groups within the Centre of Excellence. Our vision is that scientists within CanCell come together to get excited about the broader aspects of science. We hope that this will promote scientific discourse and collaboration since this is a more social setting than the traditional scientific lectures. We have so far organised several events, from inspirational talks at our kick-off and a workshop focusing on skill building.

Kick-off at Litteraturhuset

Anne Marthe Pensgaard has a joint position at the Norwegian School of Sports Sciences and the Norwegian Olympic Training Centre. Her research focuses on motivation and coping with stress among elite athletes. She gave us a presentation on the parallels between the psychology of professional athletes and of researchers. She asked us to think about how we define success, as this is tightly linked with motivation. It was inspiring to hear that the best achievers do not define success as the final destination (publication, grant, position), but rather milestones along the way.

Ruslan Medzhitov is a professor of immunobiology at Yale School of Medicine, USA. He is famous for the discovery Toll-like receptors and the role they play in controlling adaptive immunity, infections and tumor growth. His current research includes host-pathogen interactions, inflammation and the role of epigenetic regulation in developmental plasticity. He shared his thoughts on what makes successful scientific progress, and how to ask the right questions in research.

Next-level Scientific Writing Workshop

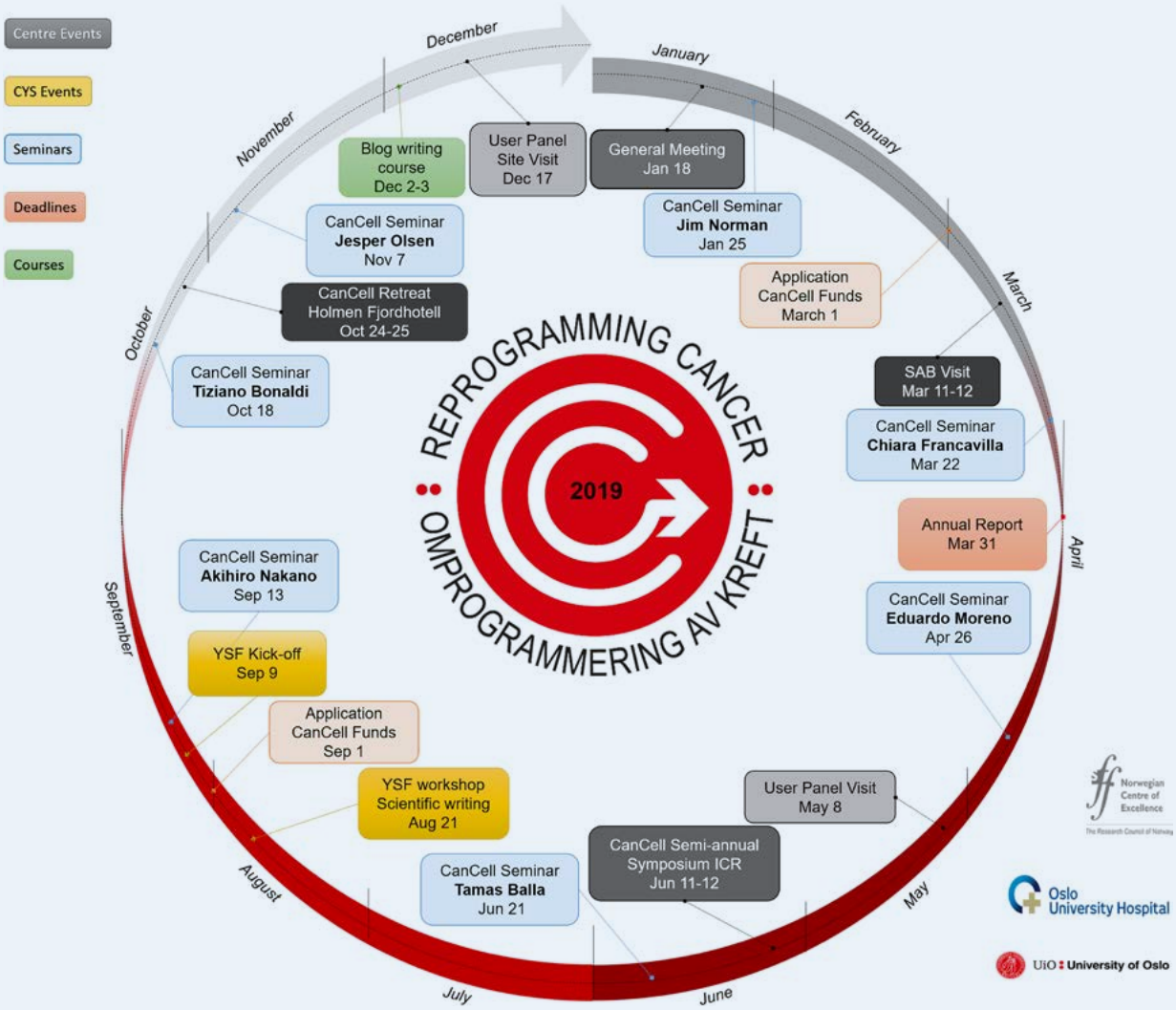
This writing workshop had several sessions focusing on different aspects of scientific writing: grant applications, abstract and cover letter, journal article and CV. We thank the group leaders who participated for excellent sessions where they shared their expertise in these different categories. We also had a very interesting talk by Per Seglen who told us about how the impact factor can be manipulated by journals, as well as scientific misconduct and retractions. Bottom line – do rigorous science, and you should still be able to get citations independently of where you publish! We look forward to bringing together the young scientists of CanCell for more exciting events in 2020.

Link to a video presentation of CYS:

The year at CanCell

The year at CanCell

Here is an overview over the events at CanCell in 2019:



Disputations

Two new PhDs were completed at CanCell in 2019.

Ignacio Cuervo at his defense with supervisors Ragnhild Eskeland and Odd Stokke Gabrielsen.

M.Sc. Ignacio Cuervo from Ragnhild Eskeland's group defended his thesis "Unravelling transcriptional regulation through chromatin interacting proteins and SUMOylation" on April 29th. His defense included a trial lecture on the topic: "Transcriptional control of cellular identity and functions through mitosis".

His work studied different aspects of the transcriptional regulating processes implicated in embryonic stem cell differentiation and in the regulation and dysregulation of cancer cells. This thesis also studied the role of SUMOylation of a transcription factor, FOXA1, involved in prostate cancer regulation as well as other targets regulated by SUMOyaltion.

His adjudication committee consisted of Associate Professor Erna Magnúsdóttir, University of Iceland, Project Group leader Pierre Chymkowitch, Oslo University Hospital and Professor Emeritus Tom Kristensen, University of Oslo. Ignacio Cuervo was co-supervised by Odd Stokke Gabrielsen, Department of Biosciences, UiO. He has since his defense moved to Arne Klunglands group to work on DNA repair.

Marte Sneeggen defended her thesis at ICR.

M.Sc. Marte Sneeggen of Harald Stenmark's group defended her thesis "Regulation of Epithelial Organization and Cell Invasion by the Endosomal Protein WDFY2" on November 8th.

In this work she studied the endocytic pathway and how this pathway is involved in regulation of cell polarization and invasion. The focus was on the early-endosomal protein WDFY2, which was found to regulate localization to early endosomes of proteins relevant to cancer development.

The trial lecture held by Marte was titled "Targeting autophagy in cancer therapy – what are the prospects for the patient?"

Her public defense was evaluated by Professor James Norman, Beatson Institute for Cancer Research, UK, Assistant Professor Olof Idevall-Hagren, Department of Medical Cell Biology, Uppsala University, Sweden and chaired of the by Professor II Therese Sørlie, Institute of Clinical Medicine, University of Oslo. Marte started a post-doc scholarship with Cinzia Progida at University of Oslo.

Seven new MSc completed their exams at CanCell in 2019:

- Guro Mustorp (Eskeland)
- Aurora Karlsen Vikan (Wesche)
- Jeanne Corrales (Enserink)
- Marketa Chlubnova (Enserink)
- Linda Håkensbakken Sønsterud (Enserink)
- Desmond Mfua Abono (Enserink)
- Nora Rojahn Brathen (Enserink)

The seminar committee in 2019: Naima Azouzi, Carmen Herrera, Petter Holland, Ellen Haugsten, Matthew Yoke Wui Ng, Lene Malerød

The CanCell seminars hold the attention of the audience.

CanCell seminars

The seminars held at CanCell are hosted by the seminar committee. Each group is represented by one member and their responsibilities are to suggest, invite and present the guest speakers.

In 2019 we had visits from 8 highly acclaimed speakers:

- James Norman | Beatson Institute, Glasgow University, UK
- Chiara Francavilli | University of Manchester, UK
- Eduardo Moreno | Champalimaud Research Centre, POR
- Tamas Balla | NIH, USA
- Akihiro Nakano | RIKEN, JP
- Tiziana Bonaldi | University of Milano, IT
- Jesper Olsen | University of Copenhagen, DK
- Thomas Vaccari | University of Milan, IT

Many of the speakers were preceded by a talk from one of CanCell young scientist (Young shot talk)

- Marte Sneeggen
- Ellen Haugsten
- Kay Schink
- Marie Rogne

CanCell Junior Scientists Grant

As part of CanCell's programme for support of junior scientists, this year it was announced the first two CanCell's project grants for researchers and postdocs (with a minimum of 2 year's postdoctoral experience). The grant could cover for up to 100 000 NOK of expenses related to libraries, screens, core facility services, minor equipment and short-term lab visits.

Applicant	Group	Project
Alf Håkon Lystad	Simonsen	Lab visit to learn secretory autophagy at Deretic-lab
Heidi Marie Namløs	Wesche	To establish single nuclei sequencing methodology for fresh frozen material
Helene Knævelsrud	Enserink	Pilot screen in S2 insect cell
Kay Oliver Schink	Stenmark	CRISPR/Cas9 toolbox for high-efficiency endogenous tagging including instrumentation
Marie Rogne	Eskeland	Single cell Assay for Transposase-Accessible Chromatin sequencing (scATAC-seq) in liposarcoma cell lines
Viola Lobert	Rusten	Establishment of human colon organoids
Petter Holland	Rusten	Establishing *in vivo* tissue-specific translatomics in Drosophila
Sigve Nakken	Hovig	Large-scale combinatorial drug screening in malign melanoma
Carmen Herrera	Enserink	Differentiation drug screening pilot
Lene Malerød	Stenmark	E3 Ubiquitin ligases: novel markers to stratify prostate cancer patients for effective therapy – siRNA library
Laura Rodriguez de la Ballina	Simonsen	Automated siRNA solid-phase reverse transfection for high throughput analysis of lipid-binding proteins in autophagy
Naima Azouzi	Eskeland	The role of QKI protein in epigenetic regulation of breast cancer

Recipients of the CanCell Jr Grants 02/19: Sigve Nakken, Naima Azouzi, Carmen Herrera, Petter Holland and Laura Rodriguez de la Ballina.

SAB members (from left): Stephan Beck, Marja Jäättelä, Michael Boutros, Johanna Ivaska, Pier Paolo Di Fiore.

Scientific advisory board visit

The Scientific Advisory Board supports our Centre with valuable input on strategy and science that helps us achieve our goal of becoming one of Europe's leading centres for cancer research. In the spring of 2019 (March 11–12) we were fortunate to have the SAB visit us for the first time. The program included presentations from group leaders, site visits and discussions with junior scientist in plenary and project development.

The SAB members are:

- Johanna Ivaska | University of Turku, Finland
- Marja Jäättelä | Head of Research Unit Cell Death and Metabolism, Danish Cancer Society Research Center, Copenhagen, Denmark
- Pier Paolo Di Fiore | European Institute of Oncology, Italy
- Stephan Beck | University College London, UK
- Michael Boutros | DKFZ, Heidelberg, Germany

Visitors to the semiannual symposium (from left – Eileen White, Ragnhild Eskeland, Harald Stenmark, Ivan Dikic, Irep Gözen and Tor Erik Rusten). Photo: Per-Marius Didriksen, OUH.

Semi-annual symposium

One of the highlights of the year was the semiannual symposium titled «Autophagy and metabolism in cancer" (June 11–12). With keynote lectures from our guest professors Eileen White (Rutgers Institute, USA) and Ivan Dikic (Göthe University, GER), it was a very well received and attended event. We very also fortunate to have several excellent presentation from our own scientists, including Roji Khezri, Marie Rogne, Alf Håkon Lystad and Aram Andersen. Further interesting talks from Irep Gözen (NCMM, UiO) and Per Seglen (NCMM, UiO) completed the program, which also had time for project discussions and poster presentation where our invited guests gave feedback.

CanCell has four internationally leading scientists as visiting professors

- Kristian Helin | BRIC, Copenhagen, Denmark
- Ivan Dikic | Goethe University, Frankfurt, Germany
- Eileen White | Rutgers Cancer Institute, NJ, USA
- Eyal Gottlieb | Metabolomics Center, Technion Integrative Cancer Center, Haifa, Israel

The CanCell members joined for the Annual Meeting at Holmen.

Annual meeting

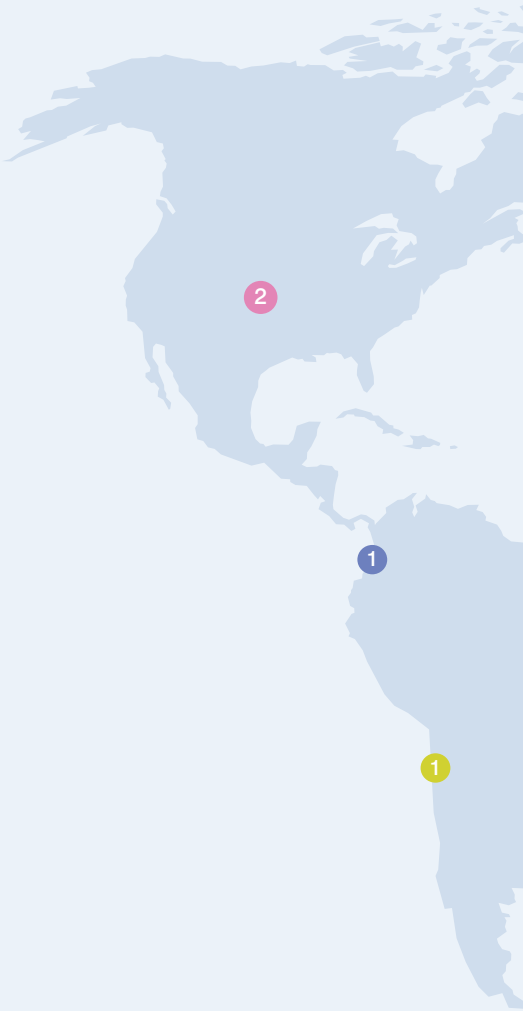
Viola Nähse, Eva Wenzel and Sara Orellana Munoz won the CanCell poster prizes for 2019

October 2019 saw the second CanCell annual meeting take place at the Holmen Fjordhotell in Oslo, Norway. With a great turnout (85 CanCell members from both core and associated groups), the meeting provided an excellent opportunity for sharing current research progress and establishing collaborations for future projects. This year we had presentations on precision medicine from two our associated clinical members, **Åslaug Helland** and **Yngvar Fløisand**. We also invited two prominent keynote lectures from **Marcus Baumbusch** (Jose Carreras Leukemia Institute, ESP) and **Marja Jäättelä** (Danish Cancer Society Research Institute, DK). Our associated members **Emmet McCormack** and **Terje Johansen** gave us valuable insight on the developments in their respective labs. Members were also given detailed overviews on the latest technology and specialist techniques available within the centre courtesy of **CYS,** including high throughput siRNA screening, zebrafish methodology, Cut and tag and AID degron methods for chromatin studies, single cell sequencing, superresolution microscopy, organoid research and drug sensitivity screening joined with bioinformatics. The CanCell Paper awards were presented and the recipients were Marte, Alf and Carmen (see also **Scientific highlights**). CanCell Junior grants were awarded for the second time in 2019 to six young researchers, simultaneously the recipients of the first grants held flash talks on their project progress. Three poster presenters were announced during dinner as this year's winners: Viola Nähse, Eva Wenzel and Sara Munoz.

User panel

The user panel consists of representatives from the sarcoma, prostate cancer, lung cancer and leukemia patient organizations and is a very valuable asset for CanCell scientist. The user panel will provide the perspective of users to our research and dissemination. In 2019 we had two meetings, one feed-back session on research applications (May 8th) and one site visit (Dec 17th). The CanCell user panel main organizer is Helene Knævelsrud (Enserink group). The panel consists of Per Axel Ankre (prostate cancer), Astrid Jahr (sarcoma), Ole Knutzon (lung cancer, first meeting), Kari Grønås (lung cancer, second meeting) and Trude Wetaas (leukemia). We are highly grateful for their contributions.

CanCell Equality Forum



CanCell consists of scientists from different ethnic, gender and social backgrounds. The Centre has members from 34 nationalities with 69% female and 31% male. However, these numbers are not equally distributed throughout the centre: Only 30% of the leadership and 37% of senior staff are female whereas the numbers move to 65-75% female at student level, technical staff and in post-doctoral positions (see Fact and figures).

CanCell Equality Forum was established in autumn 2019 to focus on multilateralism and integration in our centre. Our overall aim is to promote gender, ethnic and social equality in CanCell and academia to achieve transformative change. The Equality Forum, led by Ragnhild Eskeland, has regular meetings with the forum members and will work to improve working culture within our centre and in academia.

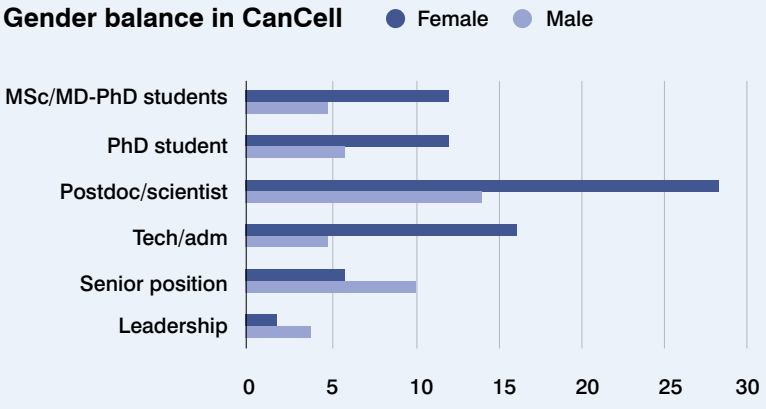
Women are under-represented in leadership positions in academia. CanCell Equality Forum will raise awareness about gender equality in science at research institutions and in our society, to promote the view that diversity, inclusive leadership and team work, is paramount for excellent research and best patient care. We are also developing measures for strengthening career development and to promote young leaders in our Centre.

The CanCell Equality forum: Ashish Jain, Chara Charsou, Harald Stenmark and Ragnhild Eskeland.

Country of origin for CanCell members.

NOR	41	NED	1	MAL	1
AUT	1	POL	5	PHIL	1
CZE	1	POR	1	RUS	1
EIRE	1	SERB	1	SING	1
ESP	8	SWE	3	CHI	1
FIN	1	SWISS	1	COL	1
FRA	2	UK	2	US	2
GER	9	UKR	1	EGY	1
GRE	1	BANG	1	ETH	1
HUN	1	CHN	2	MAR	1
ITA	3	IND	8		
LIT	1	IRQ	1		

Gender balance in CanCell



Outreach

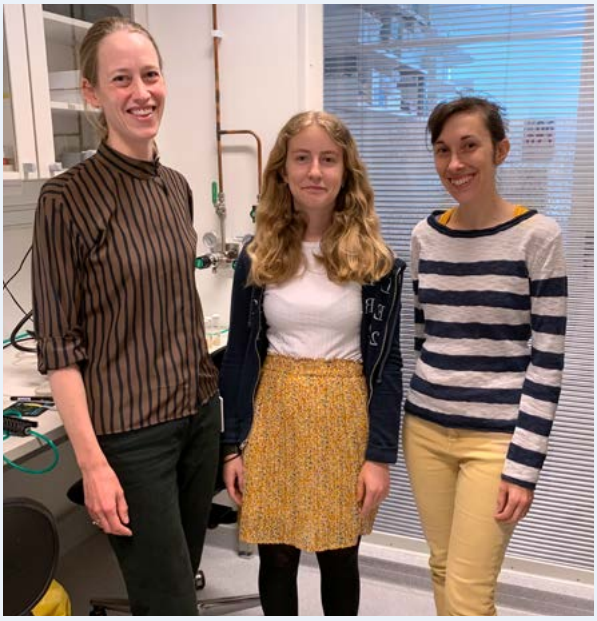
CanCell aims at reaching out the public and is engaged in several outreach projects in schools and to a wider audience.

Ragnhild Eskeland together with colleagues at UiO, Bioteknologirådet and Bergen International Film Festival (BIFF) had a public showing of the CRISPR documentary "Human Nature" at Vega scene and participated in the following panel debate of the implications of CRISPR/Cas9 technology for society. She also participated in another debate – "The secrets of cells" in September regarding the impact of epigenetics.

CanCell scientist Maria del Pilar Ayuda Duran is involved in "Spanish Researchers in Norway" who arrange popular science events such as "Tapas of Science". She also administered a visit to Oslo Cancer Cluster and Ullern High School for Erasmus +eligible professional from Spain in April. In June 2019, the CanCell fly facility hosted Emma Thompsen from the French High School in Oslo for a work-week internship. She got hands-on experience with two CanCell projects using fruit flies to understand cancer, led by Helene Knævelsrud and Caroline Dillard.

Anne Simonsen held a popular science talk arranged by the Norwegian Cancer Society on the purpose of cellular recycling and its role in cancer.

Viola Nähse, Camilla Raiborg, Kaisa Haglund, Kay Oliver Schink, Nina Marie Pedersen and Lene Malerød enjoyed showing students at "Forskerlinja" vgr1, Ullern High Scool how we study cancer development in the lab. Outreach to high schools across the country in general is a priority at CanCell – several further visits were made in 2019, and Ragnhild Eskeland coauthored a textbook on biology for this level.



Emma flanked by Helene and Caroline in the fly lab

Curious students from Ullern VGS in the lab

Educational activity

The members of CanCell have teaching duties both domestically and abroad. Anne Simonsen and several of her group members participate in lectures and courses for The Medical School at UiO, where also Jørgen Wesche, Ragnhild Eskeland, Tor Erik Rusten and Harald Stenmark held lectures. Jorrit Enserink is a course leader at Faculty of Natural Sciences at UiO, and Tor Erik lectured at several courses on different levels at the same faculty. CanCell junior staff is often asked to participate in teaching, both as lecturers and course holders. Andreas Brech and Sebastian Schulz at the electron microscopy facility organized and taught two CLEM courses, open to the institute and CanCell.

Conferences

All CanCell PIs have been invited to visit international laboratories in 2019. Both Anne Simonsen and Harald Stenmark were invited speaker at 6 international conferences in 2019, including EMBO. Tor Erik Rusten held a keynote lecture at the 3rd Nordic Autophagy Society Conference in Utrecht, the Netherlands.

CanCell scientists and young research representatives participated in the Career Development Programme discussions KUPP, an initiative by and for Centres of Excellence on Nov 15. This was initiated by The Hylleraas Centre and a follow-up engagement from last year where many important aspects of career development were discussed. CanCell will implement many of the measures in our centre in the near future.

Awards and grants

Anne Simonsen received the award from H.M. King Harald V. Photo: Håkon Mosvold.

Marte received her prize.

CanCell co-director Anne Simonsen received the King Olav Vs Cancer Research Prize for outstanding contribution to the research on autophagy. The award was granted by His Majesty King Harald V at a ceremony at Domus Academica on April 9th, the research prize is 1 000 000 NOK. The prize is awarded to persons that excels in promoting the quality and expansion of cancer research in Norway.

Every half-year, six of the very best papers authored by scientists working on the hospital (first or last author must be affiliated to OUS) are selected. The six selected articles are of especially high quality, and they present important finding on both-short and long-term scales. This year one of the recipients was **Marte Sneeggen** from the group of Harald Stenmark and Kay Schink's project group. The works reflect the good quality and the interdisciplinarity that characterizes several research environments at Oslo University Hospital.

Helene Knævelsrud, Kay O. Schink, Viola Nähse and Swarupa Panda received research grants in 2019.

Alf Lystad with coauthor Laura R. de la Ballina. Photo: Terje Heiestad.

Anne Simonsen was invited to the 9th International Symposium on Autophagy (ISA) in Taiwan, where CanCell colleagues Yan Zhen and Andreas Brech both won poster awards.

Helene Knævelsrud achieved a Young Research Talent grant from the Norwegian Research Council (RCN) on a project "Turning off autophagy in a multicellular organism". **Kay Schink** received a Career grant from Helse Sørøst on his project "Hitting the supply lines – targeting macropinocytosis as source for nutrients in pancreatic cancer", and **Viola Nähse** a Mobility Grant from RCN on "The composition and function of lipid droplet contact sites". **Swarupa Panda** arrived at CanCell afer obtaining an EMBO grant, currently working in Rusten research group.

CanCell also had three senior researchers receiving National grants in 2019: Anne Simonsen ("Open Project Grant", HSØ), **Leonardo Meza-Zepeda** (a PhD Student, HSØ) and Harald Stenmark ("Researcher Grant", RCN).

Alf H. Lystad was awarded with the 2019 publication prize from the IMB Biochemistry section for his paper on Atg16L in Nature Cell Biology. It was also selected as one of the **scientific highlights** of CanCell in 2019. This was the second year in a row a Simonsen lab worker won this prize as Kristiane Søreng won last year.

International grants and collaborations

CanCell scientists participate in several COST networks. Anne Simonsen is MC of the TransAutophagy COST network, in which also Harald Stenmark participates, and Ragnhild Eskeland is MC of the International Nucleome COST Consortium. Jorrit Enserink is MC of COST CA17104 – New diagnostic and therapeutic tools against multidrug resistant tumors. Anne Simonsen is member of the Marie Curie training network (H2020-MSC-ITN2017) DRIVE and received funds from this initiate in 2019. She is also participating in another Marie Curie training network (H2020-MSC-ITN2018) SAND, starting in Nov 2019. Through a private fund donated by Trond Paulsen, Harald Stenmark was awarded 10 MNOK to form Invacell with a collaboration at Institut Curie, France.

National

Several CanCell members were recipients of grants from the three largest national funding organizations during 2019 (listed below), with a total amount of 48.9 million NOK.

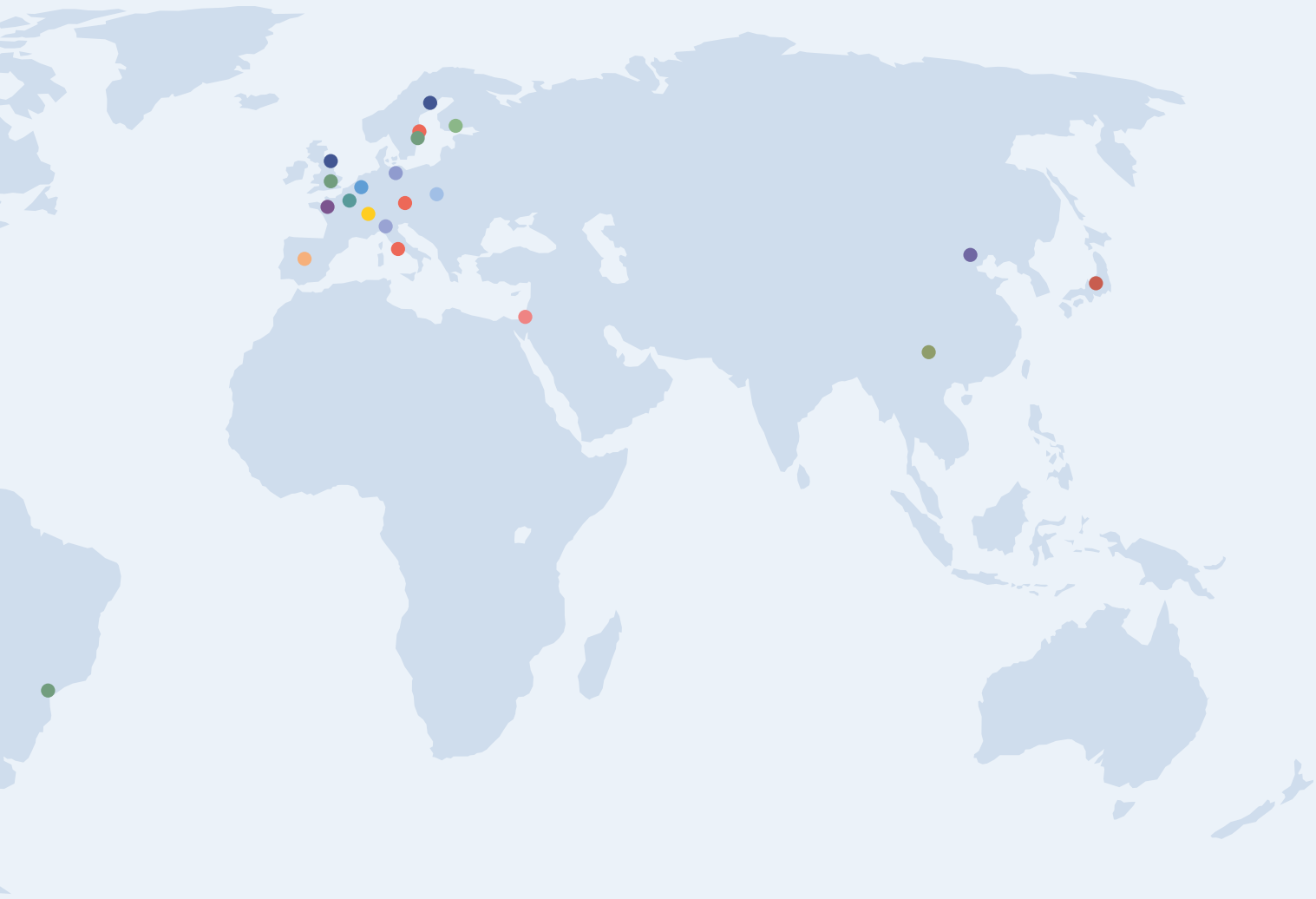
List of grants 2019

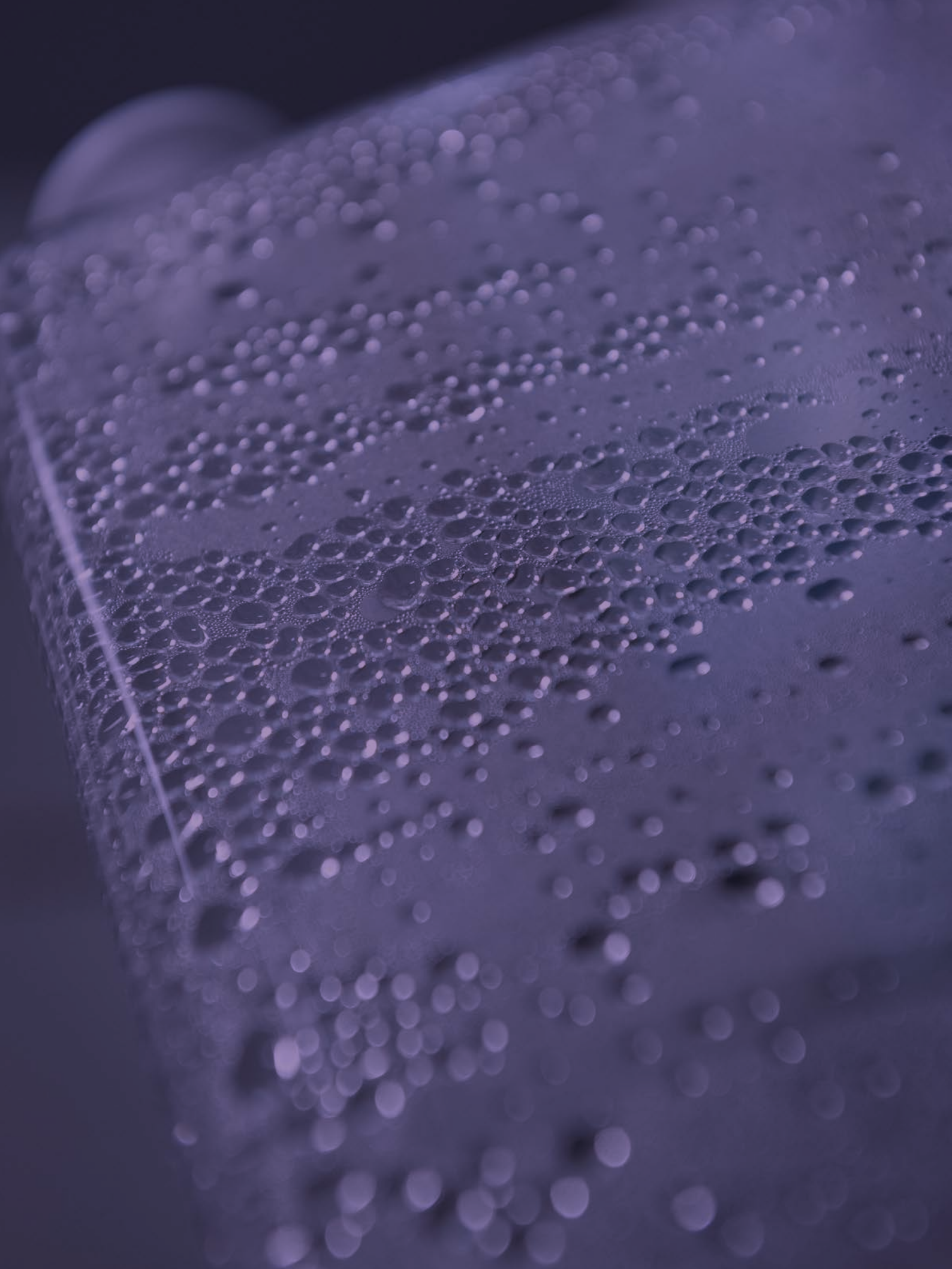
Grantee	Type	Funding organization	Amount
Kay O. Schink	Career Fellowship	HSØ	9 MNOK
Viola Nähse	Mobility grant	RCN	3.2 MNOK
Harald Stenmark	Research Project	RCN	12 MNOK
Anne Simonsen	Open Call	HSØ	10 MNOK
Leonardo Meza Zepeda	PhD Student	RCN	4 MNOK
Helen Knævelsrud	Young Researcher Talent	RCN	9 MNOK
Jorrit Enserink	Research Project	Cancer Society	8 MNOK
Swarupa Panda	Long-term EMBO fellowship	EMBO	1.7 MNOK

CanCell in the world

All CanCell groups have active international collaborations, and among the 39 CanCell papers published in 2019, 23 were collaborations with international research laboratories.

- Tom Melia | Yale School of Medicine, New Haven, CT, **USA**
- Ai Yamamoto | Columbia University, New York, **USA**
- Roberto Zoncu | UC Berkeley, San Francisco, CA, **USA**
- Chris Eide | University of Portland, OR, **USA**
- Jonathan A. Fletcher | Harvard Medical School, MA, **USA**
- Heinrich Jasper | Genentech, CA, **USA**
- Todd Schoborg | NIH, Bethesda, ML, **USA**
- Nasser M. Rusan | NIH, Bethesda, ML, **USA**
- Pablo Wappner | Leloir Institute, Buenos Aires, **Argentina**
- Sven Carlsson | Umeå University, **Sweden**
- Nico Dantuma | Karolinska Institute, **Sweden**
- Christos Samakovlis | University of Stockholm, **Sweden**
- Patricia Boya | Spanish National Research Council, Madrid (CSIC), **Spain**
- Sharon Tooze |Francis Crick Institute, London, **England**
- Jose L. Garcia-Perez | University of Edinburgh, **Scotland**
- Christian Behrends | Ludwig-Maximilians-Universität (LMU) München, **Germany**
- Ole Pless |Fraunhofer IME ScreeningPort (IME SP), Hamburg, **Germany**
- Ivan Dikic |Göthe Univ, Frankfurt, **Germany**
- Yves Barral | ETH Zurich, **Switzerland**
- Kimmo Porkka | FIMM, Helsinki, **Finland**
- Pavel Krecji | Masaryk University, Brno, **Czech Republic**
- Eyal Gottlieb | Israel Institute of technology, Technion, **Israel**
- Tiziana Bonaldi | European Institute of Oncology, **Italy**
- Kerstin Bystricky | University of Tolouse, **France**
- Vojo Deretic | Univ New Mexico, Albuquerque, NM, **USA**
- Susan Ferro-Novick | UCSD, La Jolla, **USA**
- Tamotsu Yoshimori | Osaka University, **Japan**
- Li Yu | Tsinghua University, Beijing, **China**
- Chonglin Yang | Yunnan University, Kunming, **China**
- Philippe Chavrier | Institut Curie, Paris, **France**





About CanCell

Group leaders Harald Stenmark, Anne Simonsen, Jørgen Wesche, Jorrit Enserink, Ragnhild Eskeland, and Tor Erik Rusten. Photo: Terje Heiestad.

About CanCell

Centre for Cancer Cell Reprogramming was established in December 2017 as a Centre of Excellence appointed by the Research Council of Norway with the University of Oslo as host institution. It resides at two different locations: Institute for Cancer research at Norwegian Radium Hospital (ICR) and Institute for Basic Medical Sciences (IMB) at Domus Medica, University of Oslo. The sites are connected by a regular shuttle bus service. A consortium agreement regulates cooperation between the University of Oslo and Oslo University Hospital with the intention to make conditions favorable for fulfilling the scientific aims and strategic plans of CanCell.

Emilie Einertsen works as a laboratory technician at ICR

Anne Engen is head engineer and responsible for the cell lab at ICR

Anders Øverbye is the administrative coordinator for CanCell. Photo: Terje Heiestad

Research Groups

CanCell is formed by 6 principal investigators (PIs):

- Harald Stenmark (director)
- Anne Simonsen (codirector)
- Jorrit Enserink
- Tor Erik Rusten
- Jørgen Wesche
- Ragnhild Eskeland

Management

Director Harald Stenmark, co-director Anne Simonsen, and administrative coordinator Anders Øverbye perform the daily management of CanCell. The Centre management reports to the CanCell Board. The Board consists currently of Dag Kvale, the Head of Institute of Clinical Medicine, University of Oslo (official host institute of CanCell), the Head of Department of Biosciences Rein Aasland, University of Oslo, and the Research Director of the Division of Cancer Medicine, Oslo University Hospital, Gunnar Sæter. From 2020 the Head of Institute for Basic Medical Sciences, Lene Frost-Andersen will join the Board.

Support staff

CanCell also relies on the support of administrative and technical staff at both locations. The technical staff are invaluable to ensure functions and safety in the laboratories. The administration take care of procurement, budgets, HR-functions and communications.

Facts and figures 2019

CanCell staff

The total number of people registered in the centre in 2019:

FTE, excluding students:

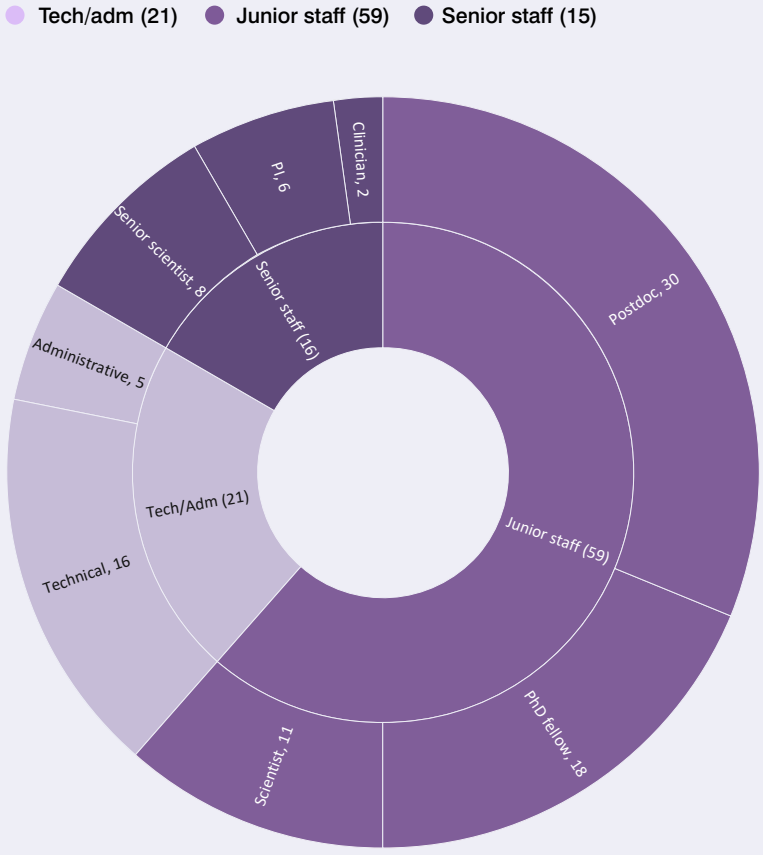
86

Headcount, including students and associated members:

125

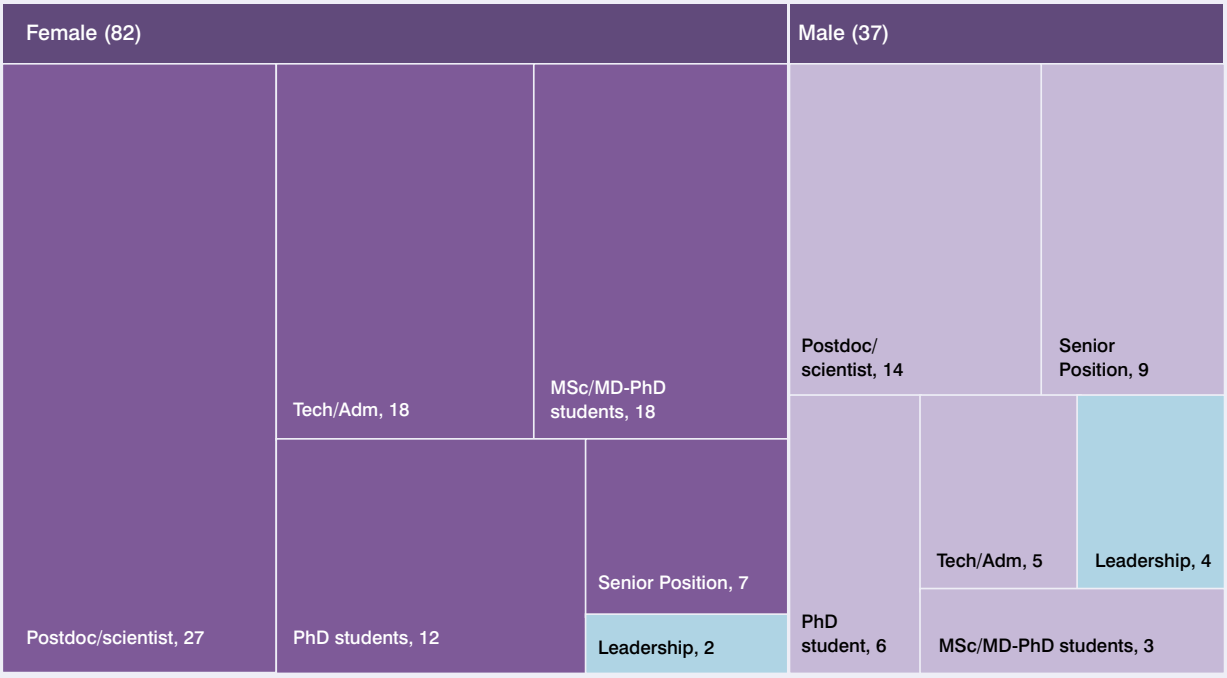
CanCell staff distribution

The chart shows the categorization of our staff by position. In addition, the centre harbored 21 Master students throughout 2019.



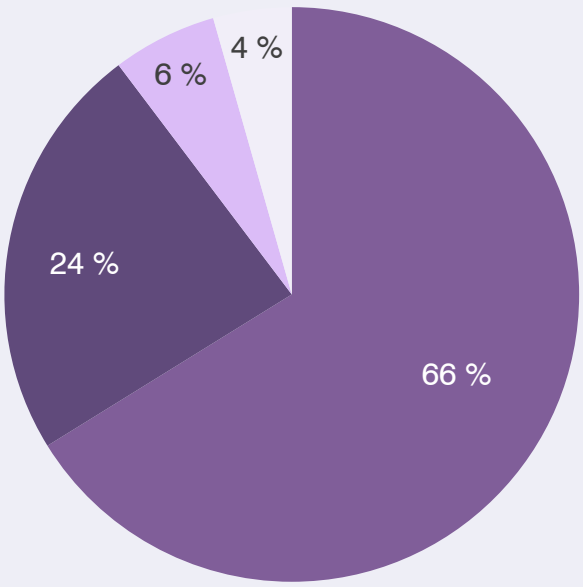
Gender distribution in total headcount

● Female (82) ● Male (37)



The leadership consisting of the six PIs are in addition to the other categories (in green)

Gender distribution in % of total headcount



Non-Norwegian Continent of origin

Europe Asia Americas Africa

Gender balance

The gender balance in CanCell is 69% female and 31% male among our total staff. Approximately the same percentages account for the postdoc category as well as for the PhD student category. The junior positions, which include post-doctors, scientist (tenured) and PhD students, are held by a woman in 67% of the instances. In terms of recruiting, the female proportion is prominent at entry level, encompassing 78% of our students and technical staff. Through the initiative of the ***Equality Forum*** CanCell hope to address challenges posed by this skewedness

Diversity

CanCell members have background from most of the world's continents and about a third come from countries outside the western hemisphere. We have this diversity in mind when we set out to create a common culture and understanding for all of CanCell.

Income 2019 (MNOK)

Funding in MNOK

The total funding for 2019 was 92.8 MNOK. The funding situation for CanCell is stable and with the granting of several large funds during 2019, the centre has succeeded to obtain sufficient financial resources to implement all its planned activities and are ahead of the target for income set by the CoE long-term plan. CanCell's Centre of Excellence funding from the Research Council of Norway (RCN) amounts to 16 MNOK in 2019.

@cancell_uio

Our twitter account focuses on research news, recruitment and announcements. It has 330 followers, and 41.2 K impressions in 2019 (Twitter Analytics). An Instagram profile was initiated in Dec 2019, with the same handle @cancell_uio, this also applies to our YouTube channel where we will feature shorts on projects and methods in the Centre.

List of members 2019

Name	Position	Group
Aas, Aleksander	MD-PhD student	Simonsen
Abdelhalim, Mohamed	Master student	Eskeland
Abono, Desmond Mfua	Master student	Enserink
Abraham, Aruna Thankam	Master student	Eskeland
Andersen, Aram Nikolai	PhD student	Enserink
Anker, Liv Dammann	PhD student	Stenmark
Asp, Nagham T.	Head technician	Simonsen
Ayuda-Duran, Maria del Pilar	Postdoc	Enserink
Azouzi, Naima	Postdoc	Eskeland
Bassols, Jose Maria	IT advisor	Stenmark
Bergersen, Anne Gro	Head engineer	Admin/support staff
Bergsmark, Camilla	MD-PhD student	Simonsen
Boye, Kjetil	Oncologist	Wesche
Brathen, Nora Rojahn	Master student	Enserink
Brech, Andreas	Project leader, senior scientist	Stenmark
Brinch, Ulrikke Dahl	Research technician	Stenmark
Brodersen, Andrea Moen	Master student	Enserink
Charsou, Chara	Postdoc	Simonsen
Chica-Balaguera, Nathalia	Postdoc	Enserink
Chlubnova, Marketa	Master student	Enserink
Collas, Phillippe	Group leader, professor	*Associated member*
Corrales, Jeanne	Master/PhD student	Enserink
Crispin, Richard	Postdoc	Enserink
Cuervo, Ignacio	PhD student	Eskeland
Dillard-Eple, Caroline Marie Claude	Postdoc	Rusten
Einertsen, Emilie	Laboratory assistant	Admin/support staff
Engelfriet, Melanie	Engineer	Eskeland
Engen, Anne	Head engineer	Admin/support staff
Enserink, Jorrit	PI, professor	Enserink
Eskeland, Ragnhild	PI, Associate professor	Eskeland

Name	Position	Group
Fiorito, Elisa	Postdoc	Rusten
Fløisand, Yngvar	Head physician	Enserink
Frigessi, Arnoldo	Group leader, professor	*Associated member*
Gan, Yili	Advisor	Admin/support staff
Garcia Llorente, Ignacio	Senior scientist	Enserink
Georgiesh, Tatiana	PhD student	Wesche
Gornitzka, Mari B.	Master student	Eskeland
Greni, Eivind Andreas	Advisor	Admin/support staff
Haglund, Kaisa	Project leader, senior scientist	Stenmark
Hallstensen, Ida Sundsøy	Master student	Enserink
Halnes, Isabel	Laboratory assistant	Stenmark
Hanes, Robert	PhD student	Enserink
Haugsten, Ellen Margrethe	Scientist	Wesche
Heintz, Karen-Marie	Head engineer	Wesche
Helland, Åslaug	Head physician, group leader	*Associated member*
Herrera, Maria Carmen	Postdoc	Enserink
Holland, Petter	Postdoc	Rusten
Hovig, Eivind	Group leader, professor	*Associated member*
Ivanauskiene, Kristina	Postdoc	Stenmark
Jain, Ashish	Postdoc	Rusten
Jain, Preeti	Laboratory assistant	Stenmark
Jinnurine, Tasmia	Master student	Eskeland
Johannessen, Julie Aarmo	Master student	Enserink
Johansen, Terje	Group leader, professor	*Associated member*
Khezri, Rojyar	PhD student	Rusten
Kjos, Ingrid	Postdoc	Stenmark
Knævelsrud, Helene	Senior scientist	Enserink
Kostas, Michal Janusz	Postdoc	Wesche
Kresse, Stine Henrichson	Postdoc	Wesche
Lapao, Ana	PhD student	Simonsen

Name	Position	Group
Ledsaak, Marit	Head engineer	Eskeland
Lie, Maren	Master student	Rusten
Lie-Jensen, Anette Christensen	PhD student	Stenmark
Lobert, Viola	Scientist	Rusten
Log, Ingeborg	Laboratory assistant	Stenmark
Lorenz, Susanne	Senior scientist	Wesche
Lystad, Alf Håkon	Scientist	Simonsen
Malerød, Lene	Scientist	Stenmark
Martinsen, Emily	Master student	Eskeland
Mateo Tortola, Maria	PhD student	Stenmark
Mathai, Benan John	Postdoc	Simonsen
McCormack, Emmet	Group leader, professor	*Associated member*
Mesel, Martine	Master student	Eskeland
Meza-Zepeda, Leonardo	Project leader, senior scientist	Wesche
Migliano, Simona	Postdoc	Stenmark
Muñoz, Sara Orellana	Postdoc	Enserink
Munthe, Else	Head technician	Stenmark
Mustorp, Guro	Master student	Eskeland
Nadratowska-Wesolowska, Beata	Scientist	Eskeland
Nähse-Kumpf, Viola	Postdoc	Stenmark
Nakken, Sigve	Scientist	Hovig
Namløs, Heidi Maria	Postdoc	Wesche
Ng, Matthew Yoke Wui	PhD student	Simonsen
O'Farrel, Fergal	Scientist	Rusten
Øverbye, Anders	Administrative coordinator (02-12/19)	Admin/support staff
Panda, Swarupa	Postdoc	Rusten
Pankiv, Serhiy	Senior engineer	Simonsen
Pedersen, Nina Marie	Postdoc	Stenmark
Piechaczyk, Laure Isabelle	PhD student	Enserink
Radulovic, Maja	Postdoc	Stenmark
Raiborg, Camilla	Project leader, senior scientist	Stenmark
Ravussin, Anthony	Postdoc	Stenmark
Robertson, Joseph	Postdoc	Enserink

Name	Position	Group
Rodriguez de la Ballina, Laura	Scientist	Simonsen
Rogne, Marie	Scientist	Eskeland
Rønning, Eva Simonsen	Head technician	Stenmark
Rusten, Tor Erik	PI, Associate professor	Rusten
Schimanski, Riccarda	Research technician	Rusten
Schink, Kay Oliver	Project leader, senior scientist	Stenmark
Schultz, Sebastian	Senior engineer	Stenmark
Sharma, Ankush	Postdoc	Eskeland
Sharma, Sakshi	Postdoc	Simonsen
Simensen, Julia Elisabeth	Master student	Rusten
Simonsen, Anne Gjøen	PI, professor	Simonsen
Singh, Sachin Kumar	Postdoc	Wesche
Smestad, Marianne	Research technician	Stenmark
Sneeggen, Marte	PhD student	Stenmark
Sønsterud, Linda Håkensbakken	Master student	Enserink
Søreng, Kristiane	Postdoc	Simonsen
Sørensen, Anette	Admin coordinator (01/19)	Admin/support staff
Sørensen, Vigdis	Scientist	Stenmark
Spangenberg, Helene	PhD student	Stenmark
Stenmark , Harald Alfred	PI, professor	Stenmark
Szybowska, Patrycja	PhD student	Stenmark
Tadele, Dagim Shiferaw	PhD student	Enserink
Takáts,Szabolcs	Postdoc	Rusten
Tan, Kia Wee	PhD student	Stenmark
Thorvaldsen, Thor Espen	Postdoc	Stenmark
Trachsel Moncho, Laura	PhD student	Simonsen
Vietri, Marina	Senior scientist	Stenmark
Vikan, Aurora Karlsen	Master student	Wesche
Wæhler, Hallvard	Master student	Eskeland
Wang, Ling	Research technician	Stenmark
Wenzel, Eva	Scientist	Stenmark
Wesche, Jørgen	PI, professor	Wesche
Zhen, Yan	Scientist	Stenmark

Publications from CanCell 2019

Yellow = review/commentary
Red = first/senior author from CanCell
Blue = both

1. Scorrano L, De Matteis MA, Emr S, Giordano F, Hajnóczky G, Kornmann B, Lackner LL, Levine TP, Pellegrini L, Reinisch K, Rizzuto R, Simmen T, Stenmark H, Ungermann C, Schuldiner M. Coming together to define membrane contact sites. ***Nat Commun***. 2019 Mar 20;10(1):1287.

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10. Lystad AH, Carlsson SR, Simonsen A. Toward the function of mammalian ATG12-ATG5-ATG16L1 complex in autophagy and related processes. ***Autophagy***. 2019 Aug;15(8):1485-1486.

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12. Goodridge JP, Jacobs B, Saetersmoen ML, et al. Remodeling of secretory lysosomes during education tunes functional potential in NK cells. ***Nat Commun***. 2019 Jan 31;10(1):514.

13. Dominguez-Valentin M, Sampson JR, Seppälä TT, Ten Broeke SW, Plazzer JP,Nakken S, et al. Cancer risks by gene, age, and gender in 6350 carriers of pathogenic mismatch repair variants: findings from the Prospective Lynch Syndrome Database. ***Genet Med***. 2020 Jan;22(1):15-25

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15. Möller K, Sigurbjornsdottir S, Arnthorsson AO, Pogenberg V, Dilshat R, Fock V, Brynjolfsdottir SH, Bindesboll C, Bessadottir M, Ogmundsdottir HM, Simonsen A, Larue L, Wilmanns M, Thorsson V, Steingrimsson E, Ogmundsdottir MH. MITF has a central role in regulating starvation-induced autophagy in melanoma. ***Sci Rep***. 2019 Jan 31;9(1):1055.

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23. Seppälä TT, Ahadova A, Dominguez-Valentin M, et al. Lack of association between screening interval and cancer stage in Lynchs yndrome may be accounted for by over-diagnosis; a prospective Lynch syndrome database report. ***Hered Cancer Clin Pract***. 2019 Feb 28;17:8.

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38. Sneeggen M, Schink KO, Stenmark H. Tumor suppression by control of matrix metalloproteinase recycling. ***Mol Cell Oncol***. 2019 Aug 14;6(6):e1646606.

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CanCell Code of Conduct

We are happy to share our knowledge and expertise.

We aim for a clear and constructive way to communicate.

We always treat people with respect regardless of background.

We have zero tolerance for condescension, harassment and ridicule.

We all do our best to create a friendly, inclusive and safe working environment.

The code extends equally to all of CanCell including guests and visitors.

If you have any concerns, please do not hesitate to contact CanCell's management or use UiOs Speak Up.

Acknowledgements

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by several external sources
to CanCell in 2019.

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Helse Sør Øst (South-East Norway
Regional Health Authority) (SENRHA)
European Research Council (ERC)
European Union (EU)

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REPROGRAMMING CANCER
OMPROGRAMMERING AV KREFT

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