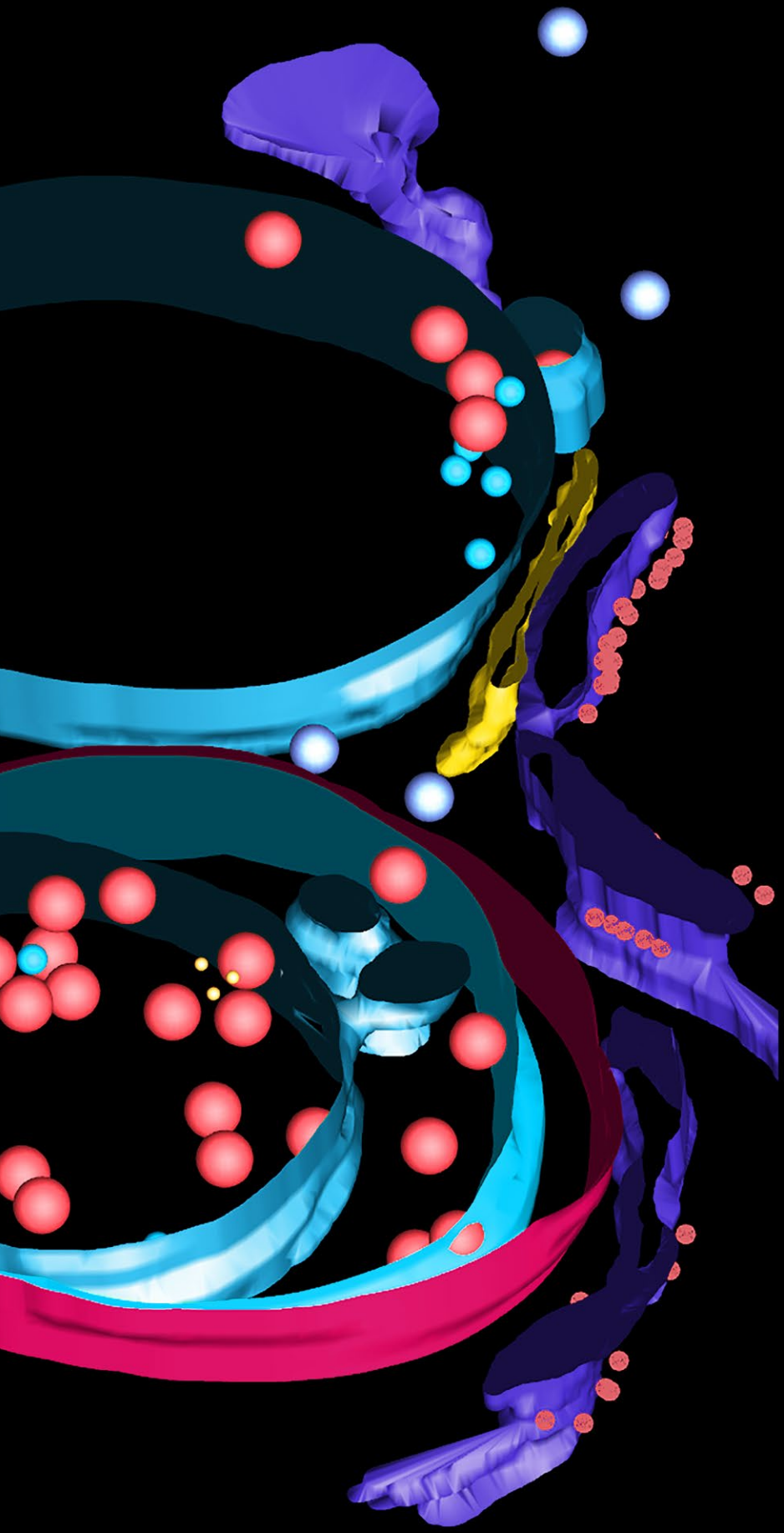


CanCell

ANNUAL REPORT 2020

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

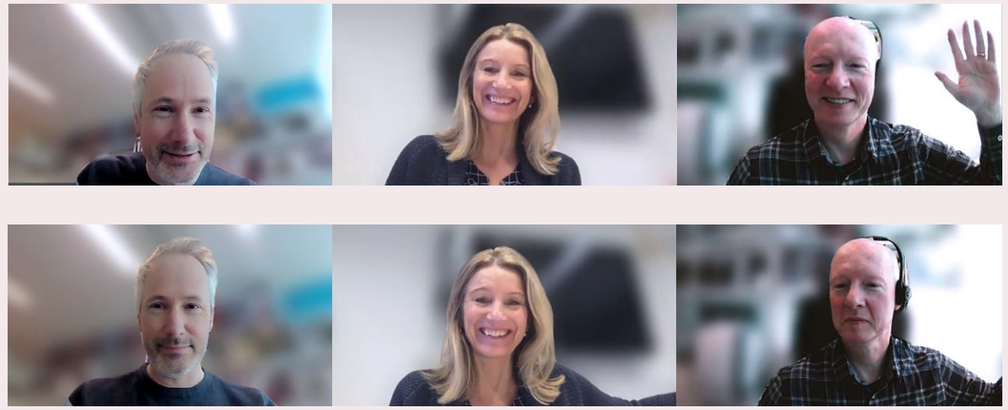
REPROGRAMMING CANCER
OMPROGRAMMERING AV KREFT

Cover image: 3D-model derived from EM tomogram depicting intracellular organelles belonging to the endo-lysosomal system with adjacent endoplasmic reticulum and cytosolic vesicles. Courtesy of Sebastian Schultz.

Contents

Interview with CanCell directors Harald Stenmark and Anne Simonsen

The CanCell administration sat down to discuss the status quo in CanCell – via Zoom



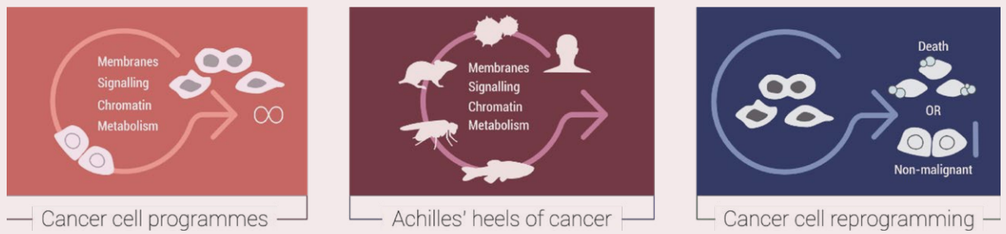
Anders: CanCell has now been running for three years. Is the research proceeding as planned?
Harald: Yes, when we compare CanCell's achievements so far with the milestones in the project proposal, I would say that we are, in most aspects, even ahead of schedule. The hallmark of basic experimental science is that there are surprises all the time. Sometimes these may come as technical problems or hypotheses that prove wrong. On other occasions, we may get positively surprised by interesting discoveries that we did not foresee, and which may give new directions for research. Therefore, a large and long-lasting project such as CanCell always has to take into account that certain subprojects have to be discontinued whereas new ones arise. That said, we are confident that we will reach our long-term goal of achieving reprogramming of cancer cells into harmless cells.

Anders: What does CanCell do to promote cooperations between the six participating groups?
Harald: The most important factor is that scientists from the different groups meet frequently to discuss science. The group leaders meet on a weekly basis to discuss both administrative stuff and scientific progress, although for the time being this is via Zoom. In addition, we encourage bottom-up initiatives for collaborations across groups by offering substantial grants to PhD students, postdocs and scientists from two or more groups who have good ideas for joint projects. *See also page 62.*

Anne: Joint workshops, meetings and social events are other arenas for CanCell scientists to meet across groups in order to develop fruitful collaborations. To facilitate interactions across the two locations (Institute of Basic Medical Sciences and Institute for Cancer Research) we alternate meetings, seminars and workshops between both places. As seminars are open to all staff at both institutes, we also hope to have an impact on the larger scientific environment.

Anders: How has the COVID-19 pandemic affected CanCell?
Anne: It is clear that this last year has been difficult for CanCell, as for everyone else. We have members from 23 countries and being far away from friends and family is obviously hard in the current situation. Moreover, many CanCell members have small children, which has made it difficult to plan laboratory work. Overall, the four groups based at Institute for Cancer Research have been less affected than the two groups based at Institute for Basic Medical Sciences, because the latter has been closed or partially closed at times. We are, however, impressed by the good spirit and effort shown by all CanCell members, even though many have had to do computer-based work from home offices. Obviously, the pandemic has prohibited physical meetings, conferences and planned visits to laboratories abroad, but we are happy that we managed to organize our annual CanCell symposium as a physical meeting although half of our members had to participate via Zoom. *See also page 52.*

CanCells three milestones



Anders: Which were the scientific highlights in 2020?
Harald: With respect to CanCell's aim to identify the Achilles' heels of cancer, two papers published in 2020 were particularly relevant. One was from Camilla Raiborg's project group with scientist Nina Marie Pedersen as first author. Camilla, Nina Marie and their co-workers identified a molecular mechanism responsible for formation of invadopodia, protrusions that cancer cells use to break through tissue barriers. The molecular machinery involved might represent one of the Achilles' heels we are looking for. Another paper, with senior scientist Marina Vietri as first author, concerned small cellular structures known as micronuclei, which contain single chromosomes. Micronuclei are rarely found in normal cells but are frequent in cancer cells and cells exposed to irradiation. Marina and her co-workers found that a molecular machinery that normally functions to seal the nuclear envelope hyper-accumulates on micronuclei when they rupture, and this causes collapse of the micronuclei and fragmentation of the chromosome they contain. This is similar to a condition known as chromothripsis, or chromosome shattering, which is strongly associated with cancer progression. In addition to being a driver of carcinogenesis, micronuclear breakdown might also represent an Achilles´ heel of cancer, and further work will clarify this. CanCell researchers have also made early progress in reprogramming cancer cells into harmless cells. Dagim Tedele in Jorrit Enserink´s group, who defended his PhD last year, identified a small-molecule compound that causes cellular depletion of c-Myc, a well-known driver of cancer progression and potential Achilles´heel of cancer. Dagim and his co-workers showed that this compound induces c-Myc-overexpressing cancer cells to differentiate, stop dividing, or die, exactly what we hope to achieve with cancer cell reprogramming. It will now be exciting to study if the new compound or its derivatives can show anti-tumour effects in preclinical studies. *See also page 44–46.*

Anders: Which advantages does CanCell offer to young scientists?
Anne: As members of CanCell, young scientists have access to an excellent research environment with extensive knowledge and expertise, as well as advanced methods and state-of-the art equipment. Most importantly, CanCell offers an arena for young scientist to interact and develop skills that are important for their future career. We have initiated several activities to promote exchange of know-how and interaction between the CanCell young scientists, including workshops on advanced techniques and career-promoting activities, such as grant writing and outreach. Young scientists in CanCell also have their own forum, CYS (CanCell Young Scientists), which has an independent budget to organize various events and an elected board that participates in CanCell PI meetings. Young scientists in CanCell have also formed the CanCell seminar committee, which is responsible for inviting speakers and chairing sessions. Moreover, each seminar starts with a "young shot talk" where one of our young scientists presents their data as "warm-up" for the subsequent "big shot" talk. As already mentioned, young scientists in CanCell can apply to CanCell Junior Grants (up to NOK 300.000) to initiate joint projects across groups. Last, but not least, CanCell offers a fun and inclusive environment with an overall aim to stimulate and support our young scientists to do excellent research. *See also page 10 and 62.*

Anders: Anne, you became elected member of the European Molecular Biology Organization, EMBO, in 2020. What does this mean to you?
Anne: Being elected a member of EMBO is of course a great honor, especially as new members are elected by existing members. Personally, it is satisfying to know that your work is recognized in the scientific community. I guess an EMBO membership also looks good on the CV. Most importantly, being a member of EMBO provides an opportunity to contribute to the important work done by EMBO, e.g. by serving on different committees and organizing courses and meetings.

Anders: Even though CanCell is a centre for basic cancer research, the centre has a panel of patient representatives. Why do you think this is necessary?
Harald: The idea of having a user panel is two-fold. Firstly, having our patient representatives sharing their experience is highly motivating for our scientists, since our people work mostly with flies, cultured cells, microscopes and computers and rarely meet those who are affected by cancer. Secondly, when our scientists present their projects for patient representatives, they often get valuable advice, especially regarding how to explain their project in layman's terms. *See also page 55.*

CanCell has an Equality Forum. What does this forum do?
Harald: CanCell's Equality Forum, which is led by Ragnhild Eskeland, has carried out a survey to map the landscape of equality issues in CanCell. The results of the survey were presented by Chara Charsou at our annual symposium. One obvious issue is that CanCell, like many other university centres, has a majority of women in lower academic positions and a majority of men in higher positions. The Equality Forum makes a strategy to address this issue as well as other issues related to gender equality. CanCell has a staff from 23 nationalities with diverse ethnic and cultural backgrounds, and the Equality Forum also focus on issues related to cultural differences and language-related challenges. *See also page 10.*

Anders: The Norwegian Centres of Excellence are expected to attract external funding. How has this been working for CanCell?
Anne: As expected, CanCell's group leaders have been very successful in obtaining external funding, and we thank the Norwegian Cancer Society, the Research Council of Norway, the South-Eastern Norway Regional Health authority, the EEA Norway Grants, the EU Marie Sklodowska-Curie Actions and the European Research Council for providing substantial funding.
Harald: We even have funding from private donations through the Radium Hospital Foundation, including a large donation from mr. Trond Paulsen to the InvaCell project, which concerns collaboration with the Institut Curie in Paris. We are especially pleased to see that some of the external funding has been obtained by CanCell's junior scientists, thereby promoting their careers towards becoming principal investigators. CanCell is also grateful for the continuous funding and support from our host institutions, the University of Oslo and Oslo University Hospital. *See also page 63.*

Anders: CanCell has several associate members. How are they involved?
Harald: Our seven associate members contribute to the interdisciplinary nature of CanCell by offering expertise that is complementary to those of the CanCell PIs, such as bioinformatics, biostatistics, biochemistry, animal models and clinical experience. They are involved at several levels – as collaborators, advisors and seminar speakers. We are happy to have some of the leading scientists in Norway on board to help us realize our ambition to achieve cancer cell reprogramming. *See also pages 34–40.*

Anders: The first CanCell PhD course was organized in 2020. How was the response?
Harald: The response from the students was very positive, and there was also enthusiasm among CanCell's junior staff, who contributed strongly to the course as teachers. We welcome a higher number of participants and will therefore promote the course more actively for 2021. *See also page 56.*

The online year

2020 was a different year due to the global pandemic caused by SARS-CoV-2 virus. When the COVID wave hit Europe and Norway, a new reality started to sink in also for CanCell members with lockdown and social distancing, limiting both our personal and professional life. Two vastly different aspects of the COVID year are presented here – the challenges of combining family and career and the possibility of hosting prominent speakers through online CanCell "Zoominars".

This piece was published in its entirety at our blog and reflects a survey conducted by the CanCell Equality Forum to address how COVID-19 had affected CanCell members. *Illustration by Chara Charsou and Carina VS Knudsen.*

Impact of COVID-19 on Centre for Cancer Cell Reprogramming mothers

by Chara Charsou and Ragnhild Eskeland

The coronavirus disease 2019 (COVID-19) has been part and parcel of our everyday reality for almost all of 2020. In early March, in an effort to contain the viral spread, most countries drifted one after the other into lockdowns and Norway was no exception. Overnight, the University of Oslo transitioned all the academic activities virtually and scientists were physically unable to reach their research laboratories and projects were put on hold. Kindergartens and schools remained closed for several weeks, displacing household labour and childcare and severely reducing PhD students' and academic staff's time to perform their work duties. Scientists and students in Centre for Cancer Cell Reprogramming (CanCell) had to adjust to the situation and work remotely from home, while others holding positions at the Oslo University Hospital were still able to go to work part-time depending on home situation. For some, this physical confinement could be 'utilised' to catch up on reading, writing and data analysis, since laboratory work was unfeasible while traveling and conferences were postponed or cancelled. For parents of young children though, this lockdown period became far more challenging. Members in the CanCell participated in a survey conducted by the CanCell Equality forum to map the impact of the COVID-19 restrictions.

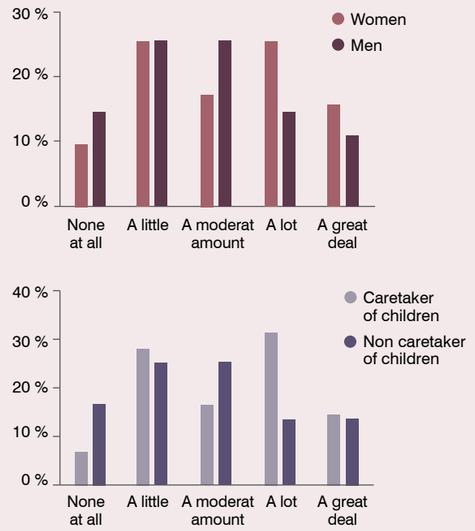


Figure 1. Women and caretakers of children more frequently report being severely affected by COVID-19 restrictions

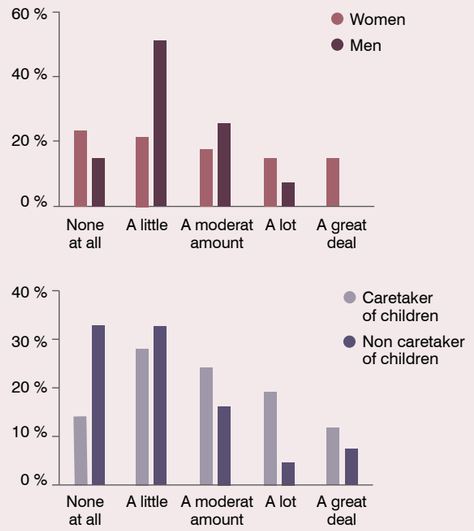


Figure 2. Women and caretakers of children more frequently report feeling too overwhelmed to fulfill their work duties during COVID-19 restrictions

Masks became a common sight during COVID in 2020, both while teaching...

...and in the lab.

CanCell mothers with small children most affected

Although undoubtedly in most cases both carers of children were affected by the COVID-19 situation, the CanCell survey confirmed a worldwide trend that mothers of underaged children were affected more severely (Figure 1).

A high number of CanCell members felt overwhelmed and faced difficulties in fulfilling their work duties during COVID-19 restrictions. The majority of those who answered that had been strongly affected were women and caretakers of children (Figure 2).

"As many mothers during COVID19 pandemic lockdown, I ended up trapped at home, forced to do home office and at the same time take care of my 16 months old daughter. A new day at home. Same every morning: I must find a new fun activity to occupy my daughter, knowing that she gets bored of playing with the same toys for more than two weeks now. I decided to take out "the creativity box" and my daughter loves it. Maybe this will excite her a bit since she likes to draw and paint? Also, I need to keep her busy for a little while, to finalize some work before the group meeting at 14.00 pm on zoom.

At 09.00 am I finally manage to sit down and my daughter is sitting next to me. She is very excited about the drawing session. I am supposed to work, but it is almost impossible when my little girl saying, "mamma" every ten seconds. She wants another colour pencil, to show me her drawing or is simply looking for some attention. I am replying with a smile on the face, or quickly grabbing her the red pencil that went on the floor. Despite everything I am still trying to keep focused. Suddenly it's 11.00 am, and it is time for some lunch before my daughters' day-nap time. Finally, my daughter is sleeping, and can I enjoy this calm hour to be as productive as possible. I am hoping that my husband is back home from work on time to take my daughter to play outside while I attend my zoom meeting."

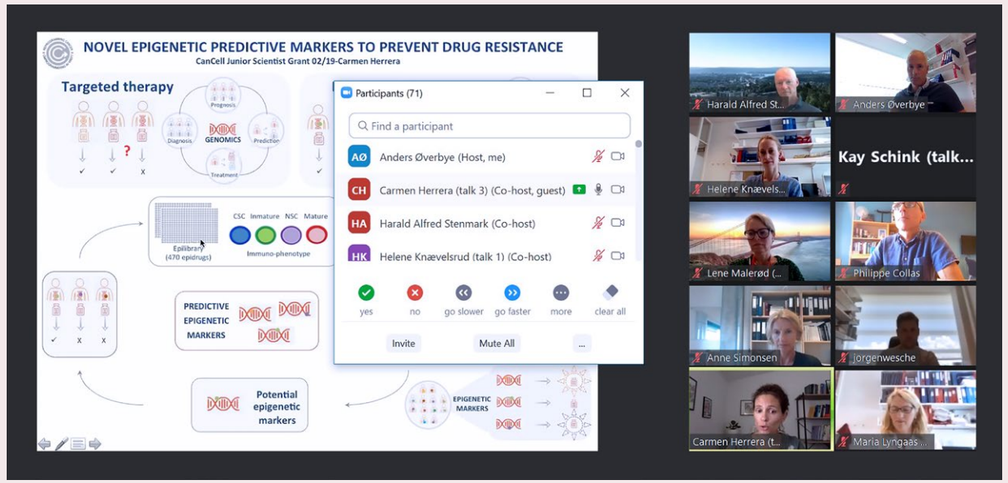
Those women devoted much of their time to home-schooling and taking care of younger children. And while many were able to make equal time arrangements with their partners, some had full time day-to-day responsibility for their household and children. Those mothers struggled to keep up their work, and instead of making progress on their research papers or thesis, they were stuck with other chores, increasing the gap to child-free peers and male scientists.

The pandemic deepens the gender gap in academia

Here it is important to point out that the difficulties female colleagues are facing amidst a pandemic, balancing childcare and career is not a "personal problem" but rather a systemic or structural constraint, the "motherhood penalty", defining the gap in pay, opportunities and benefits between working mothers and child-free women and men. In addition, we need to take into consideration that many of our female colleagues are working under precarious contracts of two or three years (Crook, 2020). In a large-scale study conducted in Europe and the US and published in Nature human behaviour, researchers found that scientists have been disproportionally affected by COVID-19. From those, female scientists being mothers of at least one child of five years or younger have reported 17% decline in their research and productivity (Myers et al., 2020). We are already aware of the productivity gap, measured by publications rate in academia between male and female researchers. Far less women are sitting high in the academic ladder, and those women are less likely to have family obligations compared to their male colleagues (Hunter & Leahey, 2010) (Mccarthy et al., 2013).

We and others have shown that women in academia carry a greater burden of COVID-19 restrictions. Although Norway has been considerably less affected by COVID-19 than other countries around the world, the national academic institutions ought to act and identify solutions to prevent the deepening of the gender gap upon reaching the end of the pandemic. The University of Oslo has extended the working contracts for many PhD students and postdocs for workhours lost during the lockdown period. However, these measures are gender neutral and gender equality is therefore not addressed.

A decrease in research productivity of female students and scientists following the COVID-19 pandemic will influence their merit, career opportunities, promotions and academic choices compared to their male peers. Moreover, the increased stress during the pandemic has also influenced work productivity and amplifies pre-existing inequality. Our female scientist mothers will not have been as successful in submitting and winning research grant applications during the COVID-19 period.



Recognising the impact of COVID-19 restrictions on gender bias is necessary to find appropriate solutions in academia upon our return to a relative normality. The academic institutions have to study and address the impact of COVID-19 measures on gender and other marginalized groups. Raising awareness and implementing policies that will help facilitate a reduction the gender gap in academia is a critical and necessary step. We believe in the necessity that reviewers of academic recruitment committees and funding bodies are made aware of the impact of this pandemic on gender imbalance in order to be able to conduct fear evaluations. Female PhD students and scientists must be given support and time to be able to complete their research publications, thesis or grant applications, potentially by being exempted from service or teaching duties for some time. Institutions have to act now to ensure a strong interdisciplinary, innovative and diverse academic environment.

CanCell Equality Forum

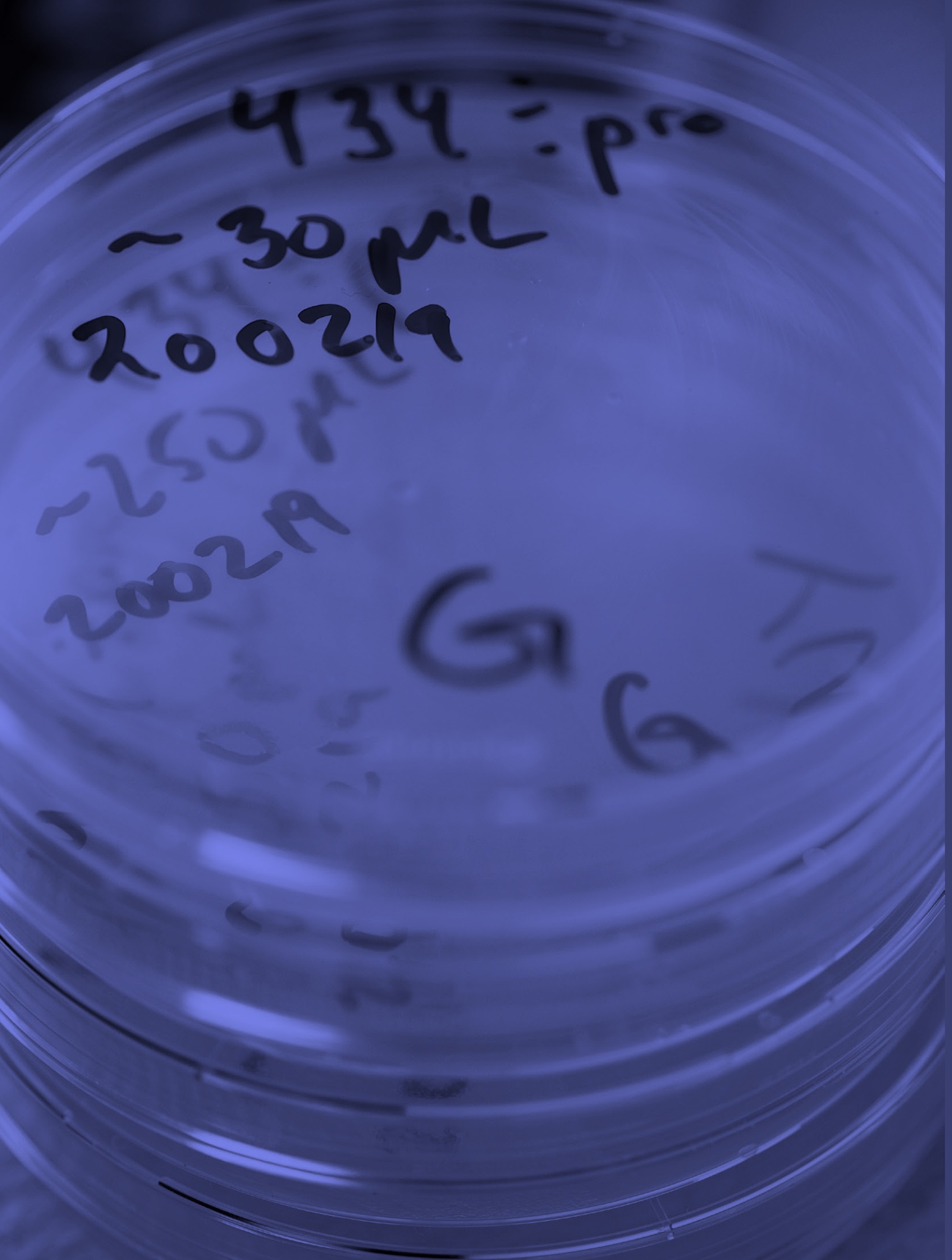
The Equality Forum is focusing on multilateralism and integration. Our aim is to promote gender equality, minorities and youth leadership in CanCell and academia to achieve transformative change.

This fall a questionnaire was performed among CanCell members to identify any potential inequalities that CanCell will work to resolve. The preliminary data from this report is presented in the Mothers and Covid blog piece and at our webpage. Briefly, it showed that although in general people feel safe and seen, certain issues that are problematic concerning inclusion and harassment were revealed and must be remedied. The Forum currently consists of Chara Charsou, Ragnhild Eskeland, Ashish Jain and Harald Stenmark.

"Zoominar" both internal and external, presenting flash talks and international guest seminars

'Zoominars' at CanCell

The seminar group consisted in 2020 of Lene Malerød, Carmen Herrera, Ellen Haugsten, Naima Azzouzi, Matthew Ng and Petter Holland. They hosted several seminars throughout the year, where only the first two were physical seminars. From March, we switched to digital seminars organized through Zoom. Although the interactions and social dimensions were reduced, these "Zoominars'' turned out to be very good alternatives to the physical seminars under the current circumstances. Being able to stay at home while lecturing and discussing science, it was easier to get busy invited guest speakers to accept our invitation. We also upheld the tradition of introducing eminent young shots speakers from CanCell before each invited speaker seminar.



Research groups presentations

Enserink Group

Cancer Molecular Medicine

@enserinklab

The Enserink group presently consists of the group leader, a project group leader, one senior researcher, nine post-docs, three PhD students,two research assistants, three MSc students, two medical research students, and two BSc students. In addition, there are four vacant post-doc positions that will be filled during 2021.

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 acquired resistance of cancer cells.
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.

To reach the 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 Research 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.

For the third goal, we are 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. Several lead compounds have been identified 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.

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).
- Developed a suite of novel small molecules that deplete c-Myc from cancer cells, resulting in apoptosis and differentiation of leukemic stem cells (Tadele et al, JBC 2020; Crispin et al, *in preparation*
- Acquired a research grant from the Research Council of Norway.
- Senior Scientist Dr. H Knævelsrud was appointed junior associate member of NCMM.
- Several DofIs submitted for compounds that selectively kill cancer cells, novel antimycotics and new immunotherapy tools.
- Three PhD students defended their thesis in 2020.
- Seven MSc students graduated from the group in the past two years.

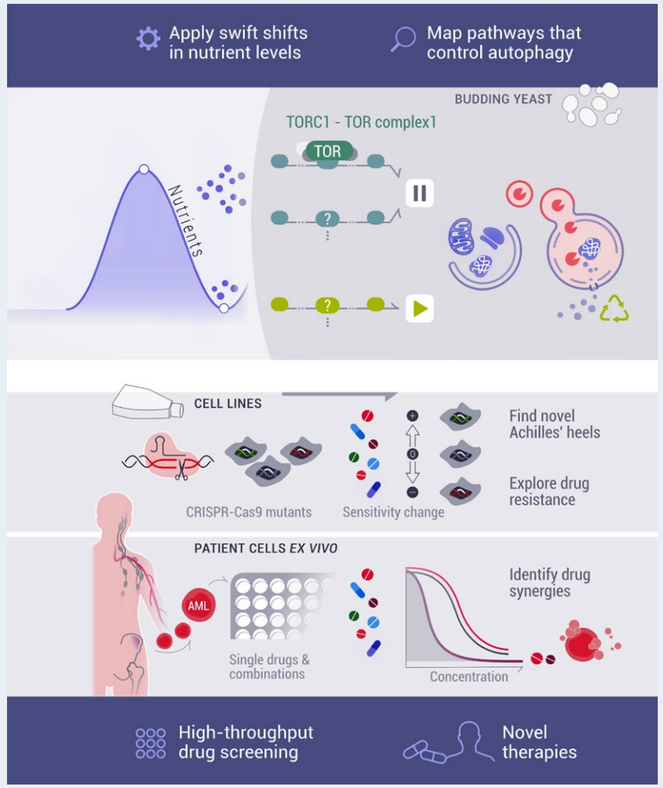
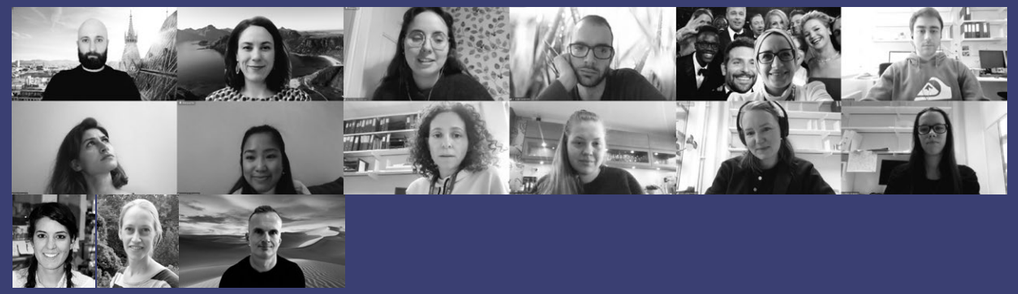


Illustration: Ellen Tenstad

Current projects

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



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.

New project group

In 2020 the project group "Mapping and disrupting cancer circuits" was established with Dr. H. Knævelsrud as the project group leader. The project group is focused on two main goals: 1) Unraveling the mechanisms of leukemia development and 2) Understanding how autophagy is switched off in vivo.

We employ Drosophila melanogaster as a model organism, to take advantage of the unique tools and ability for rapid unbiased in vivo screening that this organism offers. In addition, we are following up on results generated with our fly models in mammalian cell culture and patient samples, especially in relation to kidney cancer.

In 2020 two post-docs were recruited to the project group and both acquired independent co-funding through the Scientia Fellows Program. One MSc student graduated and continues in the team as a research assistant. Finally, two medical research students are starting their projects in the team from 2021.

Knævelsrud and her two new SF postdocs Miriam Formica and Amani al Outa

I am a naturally curious person, which is why I love science. I like being the person who discovers new things and the first to see something for the first time. For me it was great to be able to do what I love where the side effect is being able to help people.

Richard Crispin

Richard Crispin

Nationality: British
Position: Postdoc (former)
Group: Enserink
Molecular Cancer Medicine

One of the great things about being a scientist in CanCell is that you get to meet so many people that work with many different backgrounds working on so many different projects. "I am a naturally curious person, which

This is Richard Crispin who until recently worked as a postdoctoral fellow in Jorrit Enserink's lab. He came to Norway from Edinburgh, where he had just finished his PhD, to work in Jorrit's group in May 2017. Moving to Oslo was a whole new adventure for him and it was quite the coincidence that he landed in Jorrit's lab.

How is it to join CanCell as a scientist from abroad?
One of the things I like a lot with working in Norway compared with studying in Edinburgh is the work-life balance. I am still able to be active after work, whether it's kickboxing, snowboarding or meeting up with friends, but also getting to host gatherings for my lab group which meant a lot in the time before the Covid-19 pandemic hit. For me it was a nice thing that we were all in the same boat when coming new to a country where you do not know anyone or speak the language, so it was easy to connect to a lot of people. I web page before long.

It was also a great working environment in the lab, and I feel that when I entered the lab we all started out as colleagues, but we quickly became friends and that is rare and a huge bonus!

How can we exploit weaknesses in cancer cells to kill them?
This is the baseline for our work in Jorrit's lab where we work a lot with development and re-purposing of cancer drugs. My work followed the previous work from Dagim Tadale and Joe Robertson when they were in the lab. Dagim had completed big screen for new molecules that have selective anti-cancer activity in leukaemia and my job was to look at some of the molecules to figure out how they were working and if they were safe and efficacious enough to be a future cancer therapy.

In December 2020 I became a senior research scientist at Oncoinvent AS, which is a pharmaceutical company focusing on radio pharma. You can say that it is another adventure going from academia to a private pharmaceutical company, but I look forward to trying something new.

For more of Richard's past and current work and how he came to Jorrit's group, please see the full interview available at CanCell's home page this summer.

Wesche Group

Molecular Biology of Sarcomas

@Wesche_Lab

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

Achievements

- Members of the group published 7 papers in 2020.
- Research grant for a new Post-doctoral position was obtained from the South-Eastern Regional Health Authority (Boye).
- Wesche became part of a new consortium that obtained a Norway- Czech Republic EEA grant to develop targeted radio-therapy (ELECTTRA).
- Establishment of a new GIST collaborative project with Dr. César Serrano at Vall D'Hebron Institute of Oncology, Barcelona, Spain.

Current projects

- ***The role of fibroblast growth factor receptor (FGFR) signalling in rhabdomyosarcoma and osteosarcoma*** (Wesche). FGFRs are mutated and overexpressed in rhabdomyosarcoma and osteosarcoma and potential targets for precision medicine. We are investigating the molecular determinants involved in relaying FGFR signalling. Currently, we are investigating how inorganic phosphate activates FGFR1 and the role of FGFR4 in regulating adhesion. By detailed understanding of oncogenic FGFR signalling, we aim to identify new strategies to inhibit sarcomas and other cancers dependent on FGFR signalling.
- ***Efficient Low-energy Electron Cancer Therapy with Terbium-161 (ELECTTRA) – targeted radiotherapy of cancers overexpressing FGFRs (***Wesche). Subsets of several cancer forms overexpress FGFRs (e.g. breast cancers and osteosarcoma). We have developed a vector based on the ligand FGF1, that can be loaded with Terbium-161, and is targeted to such cells. We have shown that FGF1/Terbium-161 is translocated to the nucleus of cancer cells, which brings the radioactivity close to its target; DNA. We are currently investigating if this could result in increased radiotoxicity.
- Establish new modalities for sensitive non-invasive monitoring of sarcoma patients by use of "liquid biopsies" (Meza-Zepeda). We have setup multiple protocols where we aim to evaluate the clinical impact of circulating tumour DNA (ctDNA) as biomarker for disease monitoring in soft tissue sarcomas (CircSarc STS) and gastrointestinal stromal tumours (CircSarc-GIST). The protocol has been implemented together with oncologists and pathologists at Oslo University Hospital, and we prospectively collect samples at the time of surgery or start of treatment, as well as blood samples at each routine control. Using high throughput sequencing we can monitor the presence and levels of ctDNA in plasma and correlate them to clinical behaviour, and thereby reveal tumor evolution.
- Characterise intratumour heterogeneity in relation to resistance in GIST, and reveal the molecular determinants linked to imatinib resistance (Meza-Zepeda). We have established different projects to study early drug adaptation and resistance to tyrosine kinase inhibitors. Using cell line and xenograft models of GIST, we have implemented technology to characterize transcriptional heterogeneity at the single cell level to reveal new dependencies for the development of resistance.
- Norwegian Sarcoma Consortium (NoSarC) – Biobanking (~500 samples) and genomic characterization (~300 normal/tumour pairs) of patient material and establishment of patient-derived sarcoma cell lines and mouse models (Myklebost, Boye and Meza-Zepeda). The characterization of the mutational landscape of different sarcomas is being performed in order to identify novel molecular subgroups and therapeutic options. This valuable biobank of sarcoma samples and models is being used worldwide to study different aspects of sarcoma biology.

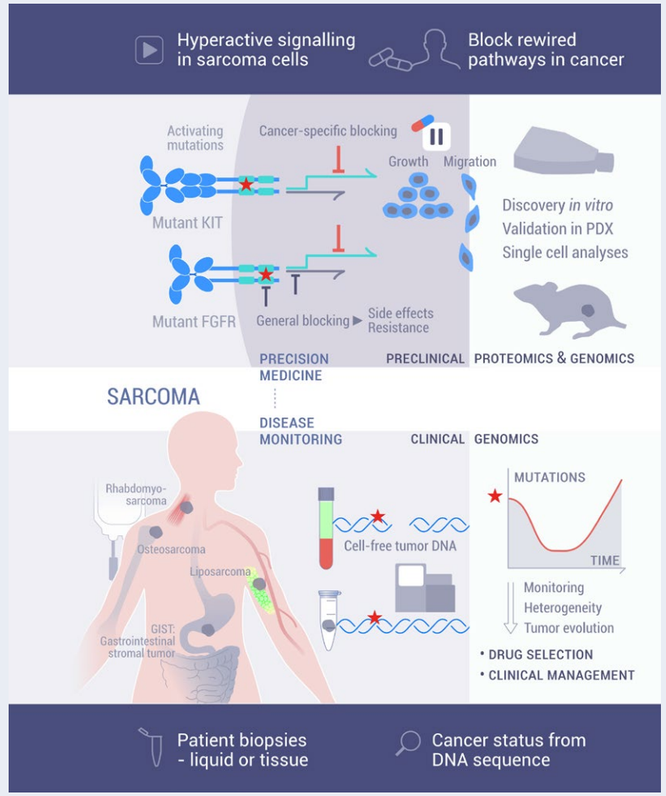


Illustration: Ellen Tenstad

Life in the group

The group has 12 members and has broad expertise in basic cell biology, genomcis 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-characterised sarcoma cell lines and patient derived xenograft mouse models to test novel anti-cancer drugs.

Dr. César Serrano from Vall D'Hebron Institute visited CanCell and the Wesche group in February to hold a seminar and initiate a research collaboration on GIST. From left: Heidi Namløs, Ellen Haugsten, Leonardo Meza-Zepeda, Cesar Serrano, Jørgen Wesche and Kjetil Boye.

I went from a lab which focuses on precision medicine and drugs to isolate and kill cancer cells to a lab which focused on basal research on how cells work.

Else Munthe

Else Munthe

Nationality: Norwegian
Position: Senior Technician
Group: Wesche – Molecular Biology of Sarcomas

It is great when you solve the puzzle and understand the science and if this can be used in the clinical setting, it is even better.

Else Munthe works as a senior technician and her typical workday is a mix between administration, keeping track of and ordering supplies for the lab and conducting research. She also supervises students and help them to learn new techniques.

A divergent career with much cross-lab experience
My path into academic science was not straight forward as I worked as a scientist at Dynal A/S for but soon missed the life in academic science again. Thus, I went back to working as a Post Doc. Before I got the opportunity to join the Stenmark lab I had been working as a Post Doc in several different labs and learned a lot of new techniques. This came in handy when I worked in the Stenmark lab as a technician. I have gone from a lab which focuses on precision medicine and drugs to isolate and kill cancer cells to a lab which focused on basal research on how cells work. Last year I returned to my previous group, which focuses on signalling that are important for sarcoma cancer cells.

What are the challenges of changing labs within CanCell during the last year?
Moving lab in the covid-19 year as I did was not as difficult as you might think. It can be because I knew many of my new colleagues from different projects already.

One of the pros about switching labs is that I learned many new things and to see things in other perspectives, and to get to work with many fantastic people. More challenging was it when we in Stenmark's lab were working with a revision of a paper before final publishing in Journal of Cell Science. This was during the period when the kindergartens were closed and my cohabitant and me had to come up with solutions so that there was always someone at home with our youngest kid. It worked surprisingly well. Eva (Wenzel) and I worked together good so that she was able to step in when I had to go home early. The most exhausting was that we had to go through everything at the lab in much shorter time and then be able to transition over to relaxation home after a stressing day.

How can we turn the weaknesses of sarcomas against them to treat cancers?
This question partially sums up our work here. What we do is to screen sarcomas to identify new therapeutic opportunities and develop precision medicine. I really love being in the lab and creating models. One of the things that motivates me to do science is that you gain a new understanding.

You can read more about Else's work and background, and how important skilled technicians are for CanCell in her full interview this summer at CanCell's own webpage.

Stenmark Group

Cellular Membrane Dynamics

@harald_stenmark

Many of the crucial biochemical reactions in the cell take place at its membranes – the plasma membrane or the membranes of the organelles. These membranes are highly dynamic and undergo continuous budding, fission and remodeling, and alterations in membrane dynamics can alter biochemical reactions. In our group we try to identify dysregulated membrane dynamics that leads to cancer progression. We are particularly interested in alterations of how the cells internalize large molecules by endocytosis, how they degrade molecules in lysosomes, and how dynamics of the membrane that surrounds the nucleus is regulated.

Achievements

- Characterization of Protrudin-dependent mechanism for formation of invadopodia –cellular protrusions that promote cancer cell invasion (Pedersen et al, *Journal of Cell Biology*, 2020). Dedicated commentary article in *Journal of Cell Biology*.
- Demonstration that unrestrained accumulation of ESCRT-III on ruptured micronuclei drives micronuclear catastrophe and chromosome fragmentation (Vietri et al., *Nature Cell Biology*, 2020). Dedicated "Highlight" in *Nature Reviews Molecular Cell Biology*. Awarded Article Prize of Oslo University Hospital.
- In collaboration with Andreas Carlson's group at Department of Mathematics, demonstration that protein crowding mediates ESCRT-induced formation of intraluminal vesicles in endosomes (Liese, Wenzel et al., *PNAS*, 2020).
- Demonstration that ESCRT proteins promote autophagy by mediating sealing of newly formed autophagosomes (Zhen et al., *Autophagy*, 2020).
- Comprehensive review on ESCRT proteins in sealing and scission of cellular membranes (Vietri et al., *Nature Reviews Molecular Cell Biology*, 2020).
- Major grants in 2020 to Kay O. Schink (Research Council of Norway), Harald Stenmark (Norwegian Cancer Society, EEA Romania-Norway grants), Antoni Wiedlocha (EEA Poland-Norway grants) and Marina Vietri (South-Eastern Norway Regional Health Authority).
- Patrycja Szybowska successfully defended her PhD thesis "Regulation of fibroblast growth factor receptor signaling" in January 2020. Anette Lie-Jensen successfully defended her PhD thesis "ALIX in cell division in vivo" in June 2020.
- Members of the group published 14 original papers, one review and one commentary article in 2020.

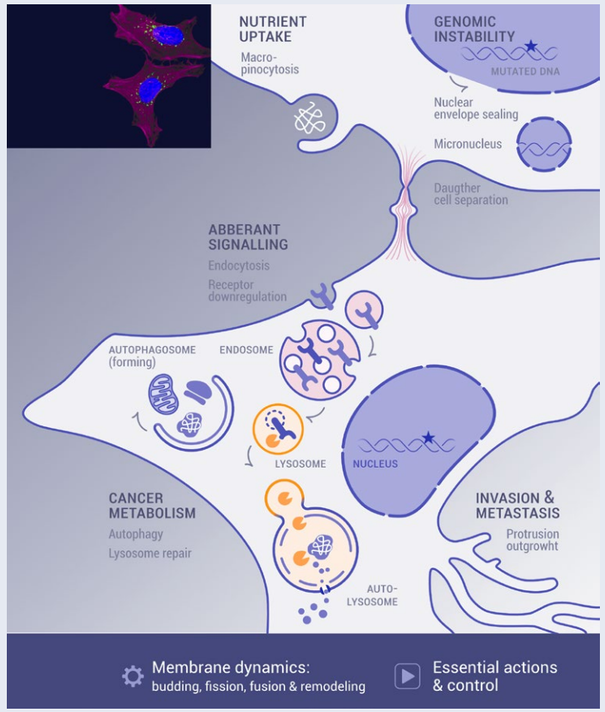


Illustration: Ellen Tenstad

Project groups

- ***Membrane contact sites, lysosomes and invadopodia in cancer cell invasion*** (Camilla Raiborg). The project group has identified a novel molecular mechanism that regulates the formation of invadopodia – cellular protrusions that help cancer cells breach through the extracellular matrix to invade other tissues. The mechanism involves transient contacts between the endoplasmic reticulum and lysosomes, loading of lysosomes with a motor protein, motor-driven translocation of lysosomes along microtubules towards the plasma membrane, and fusion of lysosomes with the plasma membrane to expose a protease that degrades extracellular matrix. Camilla and her co-workers are now trying to figure out how this process is controlled by lipids and kinases.This project is funded by the Norwegian Cancer Society, the South-Eastern Norway Regional Health Authority, and a private donation from Mr. Trond Paulsen, InvaCell.
- ***Nanoparticles and autophagic response*** (Maria L. Torgersen). Biodegradable nanoparticles show great promise as vehicles for cellular delivery of drugs and vaccines. Maria's project group has shown that nanoparticles can activate regulators of autophagy, and the group is currently characterizing the functional implications of such activation. The project is supported by the Research Council of Norway.
- ***Ultrastructural characterization of selective autophagy*** (Andreas Brech). It is well known that autophagy serves to degrade potentially harmful cytoplasmic objects such as protein aggregates, damaged organelles and pathogens, but we still do not know the molecular and cellular mechanisms in detail. This project group, which also includes electron microscopist Sebastian Schultz, is using advanced electron microscopy to understand how autophagic membranes sequester cytoplasmic objects, including fluid-like protein assemblies. The project is supported by Oslo University Hospital and the University of Oslo.
- ***Macropinocytosis and tumour cell feeding*** (Kay O. Schink). Some tumours, especially those expressing activated forms of the oncoprotein RAS, use macropinocytosis as a mechanism of "drinking" large amounts of extracellular fluid so that they can acquire sufficient nutrients for their further proliferation and tumour development. Kay and his project group are characterizing the molecular mechanisms that control macropinocytosis, with the aim of pharmacologically preventing nutrient acquisition by tumour cells. This project is supported by a project grant from the Research Council of Norway and a career grant from the South-Eastern Norway Regional Health Authority.
- ***Fibroblast growth factors in cell signaling and cancer therapy*** (Antoni Wiedlocha). Fibroblast growth factor receptors are overexpressed on some cancer cells to drive cancer progression. Antoni's project group has been characterizing mechanisms intracellular trafficking and cell signalling by fibroblast growth factors, and the group is currently investigating the possibility of using conjugates of fibroblast growth factor and cytotoxic drugs to selectively kill cancer cells that express high levels of fibroblast growth factor receptors. This project is supported by EEA Poland-Norway grants.

- ***Regulation of cell division in vivo*** (Kaisa Haglund). Dysregulated cell division is one of the major causes of cancer development, and Kaisa's project group focuses especially on the final stage of cell division, cytokinesis. Dysregulated cytokinesis is known to result in cells with abnormally high numbers of chromosomes, a driver a tumour development. The project group is currently trying to understand at a molecular level how cytokinesis is regulated, and which implications dysregulated cytokinesis has for tumour development. For these purposes, the project group employs cultured mammalian cells and a model organism, the fruit fly Drosophila melanogaster. This project is funded by the Research Council of Norway and the South-Eastern Norway Regional Health Authority.

Other projects

- Regulation of nuclear and micronuclear envelope dynamics in chromosome stability and cancer development (Marina Vietri, funded by career grant from the South-Eastern Norway Regional Health Authority)
- Mechanisms and importance of lysosome repair (Maja Radulovic)
- Migrasomes and cancer (Yan Zhen)
- Initiation of autophagy (Viola Nähse, funded by mobility grant from the Research Council of Norway)
- Autophagy and cell signalling (Simona Migliano)

Life in the group

The group currently has 37 members from 13 nations. Six of the group members are project leaders who supervise their own small teams. We have group meetings every week and make sure to celebrate whenever someone has published a paper or has an anniversary. We have had our annual lab retreats at interesting destinations in Norway and abroad but had to postpone our 2020 retreat because of covid-19.

Project leaders in the Stenmark Group: Camilla Raiborg, Andreas Brech, Kay O. Schink, Kaisa Haglund and Maria L. Torgersen

Kaisa Haglund

Nationality: Swedish
Position: Senior scientist,project leader
Group: Stenmark – Cellular Membrane Dynamics

In my project group we seek to understand mechanisms of cell division and cytokinesis in a multi-cellular context and how defects in these processes may be involved in cancer development

Kaisa Haglund is a project group leader in Harald Stenmark's lab. After completing her PhD degree at Uppsala University, Sweden, and a postdoctoral period in Ivan Dikic' lab (CanCell visiting professor) in Frankfurt am Main, Germany, she joined the Stenmark lab as an HFSP postdoctoral fellow in 2006. She believes Harald's lab is a very inspiring lab to work in because the research is forward-oriented and innovative.

How do cell division abnormalities lead to cancer?
The aim of the work in my project group is to elucidate mechanisms of cell division and cytokinesis in vivo and how their deregulation can contribute to cancer.

To gain new knowledge about the dynamics and mechanisms of cell division and cytokinesis we apply a combination of advanced light and electron microscopy, genetic, cell biological, proteomic and biochemical approaches. We investigate how cell division and cytokinesis are controlled in a multi-cellular context in vivo using Drosophila melanogaster as a model organism as well as human cancer cell lines. Already now we have indications that defects in several proteins we study can contribute to cancer-relevant phenotypes, but we need more detailed knowledge on how they do so and aim to perform long-term studies on this.

We have previously elucidated that ALIX and ESCRT-III promote the final cleavage step of cytokinesis, cytokinetic abscission, in Drosophila melanogaster. In short, we found that the ALIX scaffold protein interacts with the ESCRT-III complex to mediate cytokinetic abscission in a multi-cellular context in vivo. The ESCRT-III complex mediates scission of thin membrane necks in several different cellular processes. This was novel knowledge since it was not known in the field before that ALIX and ESCRT-III were important in cytokinetic abscission in a multi-cellular organism. How the abscission machinery, including ALIX, is recruited during abscission in Drosophila remained an unanswered question in the field, because the major protein recruiting ALIX in human cells is missing. We recently discovered that a conserved protein complex directly recruits Drosophila ALIX during cytokinesis via a mechanism similar to virus budding. This uncovered a previously uncharacterized mechanism of ALIX recruitment during cytokinetic abscission.

How have you been affected by the COVID situation?
This year has been affected by the COVID-19 pandemic, but I feel that we have managed to find constructive solutions to be able to perform our work and collaborate in this situation.

The vision of the work in my project group is to continue increasing the understanding of the spatiotemporal and molecular control of cytokinetic abscission, and to elucidate whether any of the proteins we investigate has tumour suppressive roles in vivo.

Make sure to read more about Kaisa and her current projects and her plans for the future in the full-length interview available at cancell.no towards the summer of 2021.

Simonsen Group

Autophagy

@simonsen_lab

The overall aim of the autophagy group is to characterize the basic mechanisms involved in recognition and clearance of cellular components by autophagy. Dysfunctional autophagy is linked to several pathophysiological conditions, including cancer and neurodegenerative disorders, and it is therefore important to identify novel regulators of autophagy that can be targeted for diagnosis or treatment of human disease. To investigate the mechanisms involved in autophagy we use a combination of cell biological, biochemical, imaging, genomic and computational approaches, as well as disease-related model systems, including zebrafish. The group has 17 members from 12 nations.

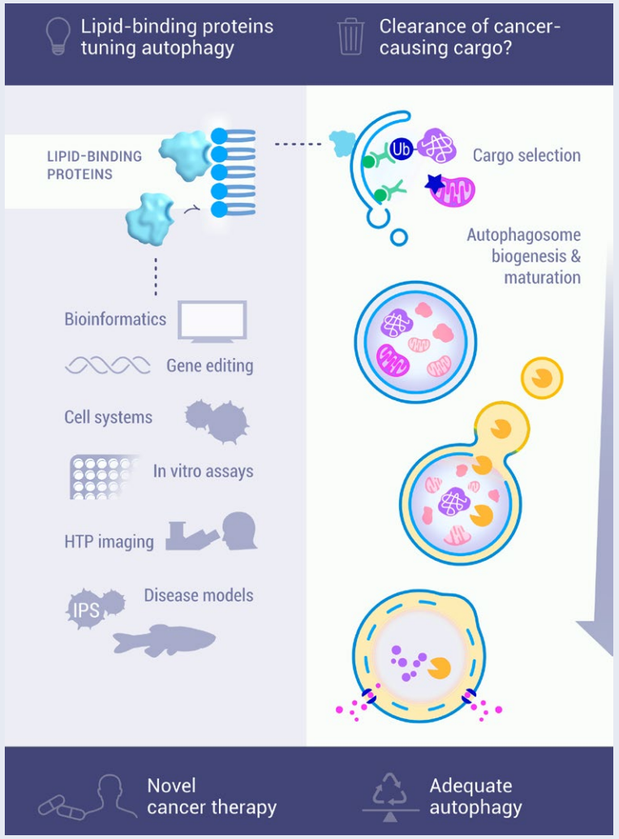


Illustration: Ellen Tenstad

Achievements

- Comprehensive review on Autophagosome biogenesis: From membrane growth to closure (Melia, Lystad and Simonsen, *Journal of Cell Biology* 2020)
- Contribution to a paper showing that AXL Targeting Abrogates Autophagic Flux and Induces Immunogenic Cell Death in Drug-Resistant Cancer Cells (Lotsberg et al., *Journal of Thoracic Oncology* 2020)
- Demonstration that the BEACH protein NBEAL1 controls SREBP2 processing and cholesterol metabolism and is a susceptibility locus for coronary artery disease (Bindesbøll et al., *Scientific Reports* 2020)
- In collaboration with CanCell visiting professor Ivan Dikic (Goethe University Frankfurt), we showed that TBK1-mediated phosphorylation of LC3C and GABARAP-L2 controls autophagosome shedding by ATG4 protease (Herhaus et al. *EMBO Reports* 2020)
- Demonstrated (in collaboration with Nico Dantuma, Karolinska Inst) that the Machado-Joseph disease deubiquitylase ataxin-3 interacts with LC3C/GABARAP and promotes autophagy (Herzog et al., *Aging Cel*. 2020)
- Members of the group published 7 original papers and two review articles in 2020.
- Camilla Bergsmark completed the Medical Faculty Forskerlinje program

Projects

Lipid Binding proteins in autophagy; molecular mechanisms and links to disease. A main focus of the lab is to identify lipids and lipid-binding proteins involved in autophagy and understand how these are regulated under various metabolic conditions and in disease. This project has been funded by the Research Council of Norway (RCN) and by UiO through the Toppforsk and Scientia Fellows programs and several lab members have been involved. We have carried out several imaging-based high content siRNA screens to identify regulators of non-selective starvation-induced autophagy and selective types of autophagy (e.g. mitophagy; degradation of dysfunctional mitochondria) and have discovered many novel regulators of autophagy that are further characterized in cellular and zebrafish models of disease (manuscripts in progress). We expect this project to reveal novel interactions between lipids and proteins in autophagy, which may pave the way for treatment of numerous severe diseases. Candidate lipid-binding proteins are also characterized in two projects funded by the Marie Sklodowska-Curie actions Innovative Training Networks (ITN), SAND (Secretion, Autophagy and their role in Neurodegeneration) and DRIVE; Driving next generation autophagy researchers towards translation.

The role of selective autophagy in tumor development. In this project, funded by the Norwegian Cancer Society, the objective is to investigate the mechanisms underlying the role of selective autophagy in cancer development. Autophagy can protect healthy cells against malignant transformation by selective degradation of toxic cellular components as damaged or dysfunctional mitochondria (mitophagy) and misfolded aggregated proteins (aggrephagy), but further insight into how autophagy affect tumorigenesis is needed. We have identified several novel regulators of mitophagy, including NIPSNAP proteins (Abudu et al., Developmental Cell 2019) and the kinases PRKCD and GAK (Munson et al, BioRxiv) and are currently investigating a role for HS1BP3, a negative regulator of autophagy, in gastric cancer.

Unraveling the role of mitophagy in cancer development (funded by HSØ, 2020–2023); In this project we will investigate whether hypoxia-induced mitophagy in tumor cells and/or stromal cells contribute to tumorigenesis. We aim to unravel the mechanisms involved in hypoxia-induced mitophagy and the role of mitophagy in tumorigenesis with a long-term goal to identify novel regulators of mitophagy for therapeutic targeting in cancer.

Unraveling the functions of BEACH-domain containing proteins (BDCPs) (funded by RCN and UiO);
This project is focused on characterization of the localization and function of human BEACH-domain containing proteins (BDCPs), which are very large proteins with largely unknown functions that are related to human disease. We have recently found that the BDCP NBEAL1 controls SREBP2 processing and cholesterol metabolism and is a susceptibility locus for coronary artery disease (Bindesbøll et al, Scientific Reports 2020) and are currently elucidating the localization and functions of other BDCPs in the endocytic and s ecretory pathways (unpublished).

Single Membrane ATG8 Conjugation (SMAC) in health and disease; SMAC, also referred to as non-canonical autophagy, involves conjugation of ATG8 proteins of the LC3 and GABARAP families to endo-lysosomal compartments in response to pathogens and other stress-inducing agents. Indeed, defective SMAC compromises our defense against pathogens and is linked to auto-inflammatory and autoimmune diseases. This project, headed by Dr. Alf Håkon Lystad, aims at elucidation of the mechanisms involved in SMAC and their role in protection against pathological conditions.

Life in the group

2020 started off very nice with welcoming two new lab members (Chiara and Sakshi) and celebration of three papers involving lab members. We were also excited to have a visiting Fulbright Scholar (Danielle Rose Jacobson) in the lab, where Anne and Danielle were invited to the American Embassy in February (picture 3v). Soon after Anne went to London to give a talk at the Crick Institute and then to California to co-organize the Gordon Research Conference, which was cancelled due to the pandemic. On March 12, the lab was closed for six weeks (on a 2 hrs notice), resulting in loss of several cell lines and ongoing experiments. We are happy that we have been able to come to work since May and that we even got to go out for dinner together in June. It has been a difficult year for everyone, especially for those being far away from friends and family, but we have managed to keep up the work, although at reduced capacity and most importantly, we have tried to support and help each other in these difficult times. Although we have become very familiar with group and project meetings on zoom, it was very nice to meet other CanCell members in person for the CanCell annual meeting in September and to be gathered for the CanCell Christmas event where we enjoyed beautiful music together. The year ended at a positive note with three new lab members (Arja, Santosh and Zahoor) and everyone getting presents from their secret Santa.

Celebrating online Christmas seminar with gifts from CanCell

It is cool to be the first person to see how a protein behaves under the microscope. It is like having a secret that only I know.

Matthew Ng

Matthew Ng

Nationality: Malaysian
Position: PhD student
Group: Simonsen – Autophagy

I immediately fell in love with autophagy when I was first introduced to it in my Master's degree.

Matthew Ng is a PhD student in Anne Simonsen's lab. Having grown up in Malaysia, on a tropical island city surrounded by warm sandy beaches, he did not know what he was in for when he decided to move to Norway in the winter. He was ecstatic to be accepted into the Bachelor program at the University of Oslo, and in the excitement, he did not read the fine print that studies were to be conducted completely in Norwegian! At that time, he barely knew how to order a coffee in Norwegian, but he can assure you that the stress of not passing exams is an amazing motivator for learning a new language.

How did you choose your field of study?
While completing my Master's project in another lab, I was fortunate to visit the Simonsen lab to learn more about autophagy. It was then I decided that this was the lab that I wanted to work in after my MSc and I have been in Anne's lab for four years now. The lab environment is conducive to excellent research in large part due to the many helpful and talented people from the lab who are passionate about science. These people are one of the main reasons I was attracted to this lab in the first place. Even though we are all working on different biological questions, we are still grounded on the autophagy side of everything and that makes it easy to get help when needed.

How are mitochondrial turnover regulated?
In a subsection of my work, we are looking at how mitochondrial proteins regulate mitochondrial turnover by autophagy (mitophagy). I think that this project will reveal how the mitochondrion itself regulates its own degradation in the face of cellular insults. We are currently working on several interesting mitophagy candidates, so stay tuned for more. In a recent publication from the lab, we discovered novel signals for mitochondrial damage in the form of two small mitochondrial proteins NIPSNAP-1 and -2. In short, these proteins associate to the outer mitochondrial surface on damaged mitochondria to act as "eat-me" signals for mitophagy. We have recently also identified two novel kinases involved in regulation of mitophagy. Importantly, Benan John Mathai, a postdoctoral fellow in the lab, has generated a Zebrafish line with fluorescent mitochondria to be able to visualise the mitochondrial turnover in every cell of the fish.

I believe that our findings will translate to better insights into how altered mitochondrial function contributes to diseases like cancer. While accumulation of damaged mitochondria contributes to tumorigenesis, mitochondrial function is also altered in tumour cells, leading to a shift towards more glycolysis dependent energy production. Understanding how mitochondrial health is maintained, or in the case of cancer, not maintained, can potentially reveal how the mitochondrion contributes to the pathogenesis of cancer.

Be sure to catch the rest of Matthew's interview to learn about the group's teamwork, his skiing skills and his plans for the future when it is published on CanCell's home page during the summer.

Eskeland Group

Chromatin Biology

@EskelandLab

www.chromatome.no

The Eskeland group presently consists of the two researchers, one post-doc, two PhD students, one senior engineer and three MSc students. We have had a large turnover in 2020, five master students, one Erasmus student, one PhD student and one post-doc finished and three new master students joined our team.

Our genome is packed into chromatin and just as places on the map of the world, genes have positions in the nuclear space. Like airplanes, proteins are able to travel between destinations in the nucleus. Chromatin associated proteins take off and land at different genomic regions and many can deposit modifications across the DNA-runways. This dynamic modulation of chromatin brings genes in close proximity. These gene contacts can modulate transcriptional activity. In our group, we focus on how gene expression is regulated, through the study of epigenetic modifications, histone variants, chromatin structure and nuclear organization. Our aim is to unravel molecular mechanisms that can form the basis for identification of novel biomarkers and cancer therapy strategies. Moreover, we also have an innovative focus on development of molecular tools.

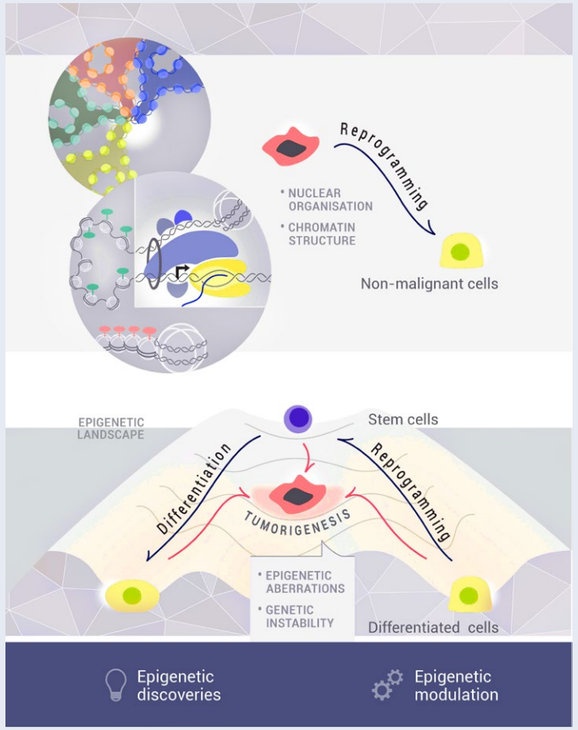


Illustration: Ellen Tenstad

Achievements

- Submitted two DOFIs on novel imaging tools, and one was accepted as a project.
- Mohamed Abdelhalim, Tasmia Jinnurine, Martine Mesel Isom, Hallvard Wæhler and Aruna Abraham successfully completed their master projects.
- Martin Falck defended his PhD.
- Cecile Palao completed her Erasmus traineeship.
- Anders Jahres fond til vitenskapens fremme (Dr. Naima Azouzi) and Cancell Junior grant (Dr. Marie Rogne).

Projects

Our projects employ different chromatin methods, high throughput sequencing and microscopy to gain insight into molecular mechanisms regulating gene expression in the context of chromatin and nuclear organisation. We focus our studies in embryonic stem cells that can undergo stem cell differentiation, different cancer cell lines and cells exposed to pharmaceuticals and develop novel tools to study chromatin structure *in vitro*, and in live cells.

The role of histone variants in Breast Cancer *Project team: Dr. N. Azouzi, T. Jinnurine and M. Ledsaak. Collaborators: Dr. T. Fleischer and Prof. V. Kristensen (OUH/UiO)*

Breast cancer is the one of the leading causes of death in females, second only to lung cancer. Gene expression profiling of breast cancer has identified five distinct molecular subtypes of breast cancer with different prognosis and response to therapy. We study the regulation of histone H2A.Z variants in a panel of breast cancer cell lines representing these subtypes to understand how these proteins might contribute to this heterogenous disease.

Chromatin structure and epigenetic deregulation in Sarcomas *Project team: Dr. M. Rogne, A. Abraham, E. Martiensen, M. Abdelhalim, Dr. A. Sharma. Collaborators: Dr. S. Nakken (UiO), Dr. L. Meza-Zepeda (UOH), Dr. S. Lorentz (UOH), Prof. O. Myklebost (UiB), Prof. P. Collas (UiO), Prof. B. Thiede (UiO), Prof. M. Costache and Dr. S. Dinescu (University of Bucharest, RO)*

Sarcomas are a rare cancers that comprise about 1% of adult cancers and arise in bones or soft tissues. There are more than 80 different subtypes of sarcomas. Due to frequent relapses of treatment resistant disease, the prognosis for patients is often poor. Sarcoma is understudied and there is a need for reliable molecular markers for precise diagnostic, prognostic and treatment purposes.

Liposarcoma, the second most common sarcoma, consists of over 50 different malignancies of mesenchymal adipose stem cell origin. To identify tumour initiating cells in Liposarcoma we employ single cell sequencing approaches to compare cell populations from adipose stem cells with populations from a liposarcoma patient cell line. This study has also led to the discovery of novel biomarkers. Cancer specific chromosomes, also termed neochromosomes, is a prominent feature of liposarcoma. By combining whole genome sequencing methods, and imaging we are able study the genomic makeup, chromatin structure and epigenetic regulation of these neochromosomes.

Osteosarcomas are aggressive malignancies of the bone that are primarily affecting children and young adults. Osteosarcoma genomes have a high number of aneuploidy and multiple mutations that are associated with disease development. In our lab, we characterise the transcriptional networks in osteosarcoma cell lines to establish knowledge on how these networks contributes to proliferation and metastasis.

Deciphering epigenetic gene regulation in sarcoma cells will enable us to identify cancer specific cell signatures that can be used to develop refined prognostic and predictive markers and improve current cancer treatment.

Novel tools for live-cell imaging of genomic loci (RCN FriPro 2017–2021) *Project team: Dr. B. Nadratowska-Wesolowska, Dr. N. Azouzi, M. Mesel, C. Palao and J. Rønneberg. Collaborator: Prof. K. Bystricky (University of Toulouse, FR)*

Chromatin is not a static entity within the nuclear space. Genes move and communicate with each other across genomic distances through looping. The cause and relationship of these connections and genome function is poorly understood but it has been correlated with modulation of transcriptional activity. A holy grail in the chromatin field is to be able to follow dynamic chromatin contacts in live cells by microscopy based methods. We focus on development of imaging tools to study the movement of indi-

vidual genes by live-cell imaging. This challenging project has been ongoing for many years in our lab and in 2020 we had major breakthroughs that led to two DOFI applications, one of which is accepted as a project.

Epigenetic regulation of 'Jumping genes' in Embryonic Stem Cells and Disease *Project team: H. Wæhler, M. Gornitzka and M. Ledsaak. Collaborators: Dr, S. Nakken (UiO), Dr. A. Mathelier (NCMM), Dr. R. B. Lemma (NCMM), Prof. G. K. Sandve (UiO), Diana Domaska (UiO), Dr. Simon Elsasser (Karolinska Institutet, SE), Dr. J. Garcia-Perez (University of Edinburgh, UK)*

Almost half of our genome is made up of repetitive sequences derived from ancient viruses called transposable elements (TEs). In contrast, only about 2 % of the human genome is gene encoding. TEs are able to become expressed and jump from one position to another in our genome. Although several molecular mechanisms have been identified that maintain silencing of these jumping genes, we find it intriguing that mobilisation of TEs occur in the early embryos, neuronal cells and in cancer. We wish to better understand how these ancient genes utilise the cells own machinery to be able to spread across the human genome and look for drugs that can modulate this activity.

Life in the group

The group currently has ten members from four nations. 2020 has been a challenging year and negatively affected our scientific progress. But maybe also this stressful time has promoted some major breakthroughs in our research? Our lab was closed for six weeks under the national lockdown and after reopening members have worked in shifts for long periods and some of us has been in home office for longer periods. We have become good at keeping distance at work but at rare occasions we have been able to celebrate final exams and a leaving do. Digital group meetings is the new normal and we also enjoy a digital coffee together every Friday. Some of our group members were able to attend CanCell annual meeting and presented their projects. We have enjoyed CanCell digital seminars but we look forward to meet everyone in person again some time in 2021.

A group gathering in the summer consisted with social distancing

What I love the most about science is solving the unknown riddles of chromatin and discovering new connections that increase our knowledge on gene regulation.

Ragnhild Eskeland

Ragnhild Eskeland

Nationality: Norwegian
Position: Group leader
Group: Eskeland – Chromatin Biology

I have worked in excellent scientific environments throughout my career and I think this has challenged me to push myself, always do better, and to be critical about my scientific work.

Ragnhild Eskeland is the group leader of The Chromatin Biology group in CanCell and associate professor at Institute of Basic Medical Sciences, UiO. She has throughout her whole career been focusing chromatin which is the structure of DNA wound up around proteins.

It has been a long journey to establish my own group here at University of Oslo. Funding from the Norwegian Research Council through the Young Research Talents program and a researcher grant from Norwegian Cancer Society has been pivotal for this to happen.

How are our genes regulated and how does deregulation lead to cancer?
We focus on gene regulation in stem cells and cancer cells. Establishing a method to light up specific genes in living cells to be able to study their movement is one of our projects. Imagine the DNA in your cells fy– the first thought that comes in mind is that our genome is static and don't move around much. What if I tell you this is wrong? That genes in our body in fact "meet and talk" together. Not literally but they meet with other regions in the genome, and this movement affect the level of gene expression. Very few methods are currently available to study gene-gene interactions by live-cell imaging, and researcher Beata Nadratowska-Wesolowska and postdoc Naima Azouzi in my lab have invested many years to develop two novel methods which will expand this toolbox. With our newly developed methods we can now follow gene expression in the living cell, and understand how and if gene-to-gene contacts are altered in cancer cells.

Is academia free from gender disparity?
We enjoy scientific freedom and have a fantastic research group that challenges me and keep me young at mind. Although we see a gradual improvement, there is still a large overweight of men in permanent positions in academia in Norway. This is in part due to the fact that female scientists are compared with their male peers on their publication records and the impact of extramural activities, maternity leave and raising young children is not taken into account. Being a mother always put you in a time squeeze. Especially, I think these "COVID-times" promote inequality between women and men in academia as the women are doing more of the household chores. You can read more about the impact of COVID-19 on the mothers working in CanCell in this annual report that is co-written by Eskeland and Chara Charsou.

Read more about Ragnhild's thoughts on how COVID affects scientists, her long and winding road towards chromatin research and her concerns and advice for aspiring scientists at our CanCell web page before long.

Rusten Group

Tumor-Host Biology

@rustenlab

In 2020, the group had 11 members (1 PI, 1 senior researcher, 6 postdocs, 1 PhD student, 1 master student, 1 ERASMUS exchange student, 1 technician). There are 2 postdoctoral and one senior scientist position to be filled during 2021.

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

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 initiated by 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*. We now have tools in hand 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.

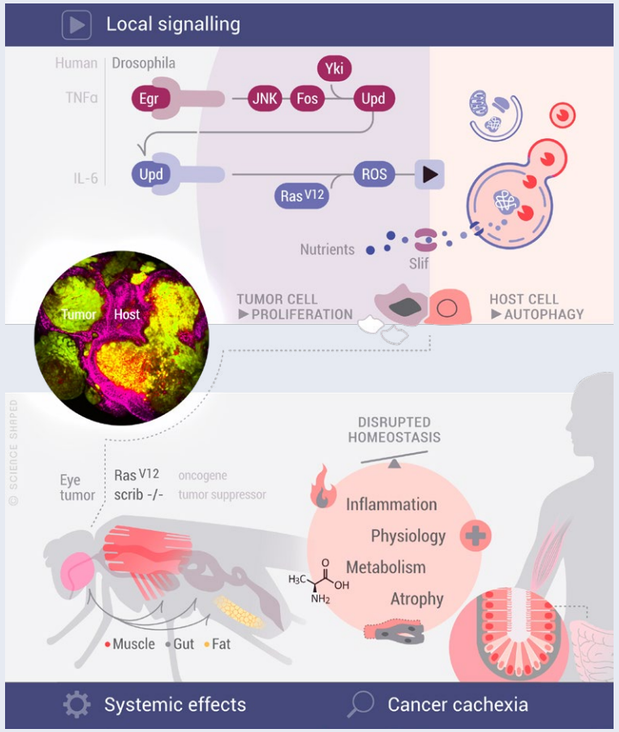


Illustration: Ellen Tenstad

Achievements

- Rojyar Khezri successfully defended her PhD “Host autophagy mediates organ wasting and nutrient mobilization from tumor growth” in September
- Julia Simensen defended her Master thesis in June
- Eduardo Martin Quintana finalized his ERASMUS exchange visit from the University of Madrid. Thank you for your contribution Eduardo!
- New project “Uncovering Nutrient Vulnerabilities to stall tumor growth in vivo” (2021–2024, 6.7 MNOK, South-Eastern Norway Regional Health Authority)

Collaborative works:

- Mammalian Atg8 proteins and the autophagy regulator IRGM control mTOR and TFEB at a regulatory node critical for responses to pathogens (Kumar S, Jain A, et al, Nat Cell Biol, 2020)
- Autoimmunity gene IRGM suppresses cGAS-STING and RIG-I-MAVS signalling to control interferon response (Jena KK, et al, EMBO Rep, 2020)

Life in the group

The group is very international and includes a 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 cell culture. We have weekly group meetings, celebrations and a yearly lab retreat on a remote location nationally 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. In 2020, due to the pandemic, we felt the lab retreat was more important than ever and managed to hold a responsible and productive lab retreat downtown Oslo at The Hub hotel. We are pleased that the hospital has worked hard to implement mechanisms so that all members with critical lab work functionality could continue work during the pandemic.

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 Helland (OUH, clinical cachexia), Eivind Hovig (OUH, bioinformatics), Eyal Gottlieb (TICC, Haifa, Israel, metabolism), Heinrich Jasper (Genentech, California, US, organ-organ communication), Rita Sousa-Nunes (King’s College, London, UK, genetic tools, tumor-host communication), Eduardo Moreno (Champalimaud Centre for the Unknown, Lisbon, Portugal, tumor-microenvironment communication)

Roji receives her much deserved PhD «hat« after her PhD defence.

Current projects

Deciphering Tumor-Host Biology (2018–2023) funded by the Research Council of Norway and University of Oslo.

Through our long-standing interest in the lab in understanding the process of autophagy and relevance to disease, we found that the lipid kinase, PIK3C3 complex acts as a tumor suppressor to control epithelial integrity through the tumor suppressor kinase, LKB1 (O'Farrell, F., Lobert, V. et al, NCB, 2017). In a Drosophila tumor model where complex aspects of carcinogenesis can be modeled, we uncovered that tumor cells induce an autophagy stress response locally in the microenvironment and systemically in distant tissues. The local autophagy response supports tumor growth, in part through providing amino acids (Katheder, N., et al Nature, 2017). In this "Toppforsk" project, we characterize the reciprocal communication between tumor and host metabolically and transcriptionally in order to infer the communication between tumor and host, both locally and systemically. We develop novel genetic tools to enable independent manipulation of tumor and host tissues in order to systemically interrogate what cellular mechanisms are required for tumor-microenvironment interaction in order to support tumor growth and what are the mechanisms for long-distance detrimental effects on systemic tissues, including cachexia. Current avenues pursued include the role of inflammation and reactive oxygen species stress signaling on tumor growth, cell competition, and systemic effects.

Mechanisms of tumor-induced wasting (2018–2021) funded by South-Eastern Norway Regional Health Authority.

80% of late-stage cancer patients suffer severe cachectic muscle and adipose tissue wasting. This condition is characterized by immune and metabolic reprogramming that collectively and dramatically worsens prognosis, decreases quality of life, prevents cytostatica treatment and accounts for more than 20% of cancer-related deaths. The mechanisms of tumor-induced wasting remain obscure and there is currently no effective treatment. We have found that tumors trigger peripheral organ stress responses (Katheder, N., et al Nature, 2017) in muscle and adipose tissue akin to that of cancer cachexia in humans. The overall aim of this project is to functionally and mechanistically decipher tumor-host interactions and cell biology underlying organ wasting. We have developed a novel stable isotope tracing method and show that tumors source the majority of their building blocks from host and not food during tumor growth (Holland P., et al BMC Biology, accepted). We have found that organ (muscle) atrophy is mediated by autophagy and lead to serum nutrient mobilization to "feed" the tumor during cachexia-like wasting in Drosophila (Khezri, R., et al BioRxiv). We currently study the role of lipid and sugar mobilization during cachexia and its effects on organ wasting and tumorigenesis *in trans*.

Uncovering Nutrient Vulnerabilities to stall Tumor Growth in vivo (2021–2024, South-Eastern Norway Regional Health Authority, and EMBO).

Tumors do not grow in isolation, but depends on extracellular nutrients for *energy, redox control, cellular signaling* and *building blocks* in order to increase biomass and sustain cell survival and proliferation. Upon transformation, tumor cells reprogram their metabolism for growth, and at the same time creates *tumor cell vulnerabilities* that can be targeted. Herein lies the proven potential to harvest the ability to interfere with nutrient access and metabolism to stall tumor growth. In this project, initially funded by a EMBO long-term postdoctoral fellowship to Swarupa Panda, we aim to uncover tumor metabolic vulnerabilities *in vivo* under physiological conditions by way of targeting nutrient (SLC) transporters and metabolism in preclinical animal cancer models (Drosophila and mouse Xenograft).

It is a privilege to do advanced microscopy and to be able to visualize the structures I am working on.

Riccarda (Ricci) Katharina Schimanski

Riccarda (Ricci) Katharina Schimanski

Nationality: German
Position: MSc Student
Group: Rusten – Tumor-Host Biology

Ricci is a master student in the group of Tor Erik Rusten, and is currently doing her thesis on novel regulators of Hedgehog signaling in primary cilia under supervision of Viola Lobert. The proteins Ricci studies are known to act as tumor suppressors. They control epithelial cell polarity and structure, and their absence seems to have a direct impact on Hedgehog signaling. Ricci's task is to find out how they are involved in the regulation of this important pathway. A wide range of diseases such as polycystic kidney disease or medulloblastoma are associated with aberrant ciliary function.

What models are you using during your project? What is your favorite method?
I am using human RPE-1 and mouse IMCD3 cell lines for my in vitro studies, and the fruit fly *Drosophila Melanogaster* for *in vivo* experiments. As many others here at MCB, I really love to do microscopy. One node of the Advanced Light Microscopy Core Facility at the Oslo University Hospital is located at the Institute for Cancer Research. The core facility is on the same floor as our department and offers imaging techniques such as laser scanning confocal microscopy (LSCM), spinning disk confocal microscopy (SDCM), super-resolution microscopy including structural illumination microscopy (SIM) or stochastic optical reconstruction microscopy (STORM). I am just so astonished about how advanced and amazing these instruments and techniques are. I am very thankful that I have received training for the LSCM, the SDCM as well as the super-resolution microscope. The training at the core facility is provided by Ellen Skarpen and Vigdis Sørensen. They are both lovely and always happy to help. It is a privilege to do advanced microscopy and to be able to visualize the structures I am working on.

Would you recommend other students to do a master thesis at an external institution such as the Institute for Cancer Research?
Absolutely. It is good to get away from the campus and to be in a new environment. As I mentioned before, the facilities at the institute are outstanding and the scientists working here are very skilled, hard-working and supporting. As a student I can participate in weekly meetings, as well as department and institute seminars. This is not only interesting, but also very educational.

You can read more about Ricci and her work, her Tekna grant and floorball world championship at CanCell featuring her full interview this summer.

Associated members

CanCell is proud to collaborate with seven outstanding researchers having excellent complementary competence to our own core knowledge. Here are a brief summary of their CanCell related activities for 2020.

Philippe Collas

Chromatin Regulation in Adipose Stem Cells

2020 has been relatively slow in CollasLab, which does not mean we have been sleeping. Two PhDs have graduated after, of course, zoom defenses (Frida Forsberg and Tharvesh M. Liyakat Ali). New people have started, including Mohamed Abdelhalim, our new bioinformatician (coming from the Eskeland lab), and Natalia Galigniana, postdoc from Buenos Aires who joined us to work on the regulation of adipocyte differentiation in an obesity context. Focusing on the nuclear periphery (where we as a group like to gather), we have shown that a subset of interactions of chromatin with the nuclear lamina follow a circadian rhythm (1), adding to growing evidence that large-scale genome organization is under influence of the circadian clock. On a theoretical physics side, we have examined how biophysical properties of chromatin as a polymer may influence interactions with the nuclear lamina (2). We are also complementing our –omics approaches to understanding 3D genome organization in stem and cancer cells, by FISH-based imaging of large-scale chromatin architecture. Functional studies gradually provide clues on how the nuclear lamina influences chromatin topology, not only at the nuclear periphery but also in the nuclear interior. The nucleolus (like it or not) is of increasing interest in the lab, as it is majorly remodeled during (adipogenic) differentiation of adipose stem cells. Inasmuch as lamina-associated domains (LADs), nucleolus-associated domains (NADs) are preferred anchor sites for heterochromatin, so nucleolar remodeling may affect large-scale chromatin domains, including the relationship between LADs and NADs. We are combining –omics and imaging approaches to address the functional significance of this relationship. To learn more about the nuclear periphery, you may want to check out our latest review on chromatin-lamina interactions (3).

We have a number of going collaborations with the group of Ragnhild Eskeland at CanCell, on projects dealing with 3D genome organization in liposarcomas, radial distribution of specific genomic elements and histone variants, cell fate and various interesting technical aspects such as chromatin accessibility assays (ATAC) or single-cell RNA-seqzanalysis methods. Our plans related to CanCell entail 1) investigations of the 3D cancer genome by combining genomics and imaging approaches, 2) strengthening our collaboration with the Eskeland group (Chromatome) by contributing to their ongoing research and manuscripts, and leveraging their expertise in single-cell RNA-seq and ATAC-seg analyses. Lastly, we would like to offer our expertise in grant application writing to the Research Council of Norway in particular, with a "workshop". CollasLab is looking forward to 2021!

Yngvar Fløisand

Hematology and Acute Myeloid Leukemia

The last year was dominated by clinical trials in acute myeloid leukemi and allogeneic stem cell transplantation. We set up two new trials in first-line treatment of AML with FLT3-inhibitors and IDH 1/2-inhibitors added to conventional chemotherapy for AML or myelodysplastic syndromes. Our graft versus host disease prophylaxis trial with the integrin a4b7 antagonist, Vedolizumab included up to February 2020 and was targeting a total of > 500 patients worldwide. Also, we have set up a novel cellular therapy concept with decidual stroll cells from placentas from healthy donors and treated two patients for refractory GvHD waiting for the start of a randomized clinical trial.

In the Enserink group we have continued to sample blood and bone marrow from all newly diagnosed patients with acute leukemias and have now collected close to 300 patient samples. These are a part of several ongoing PhD and Post doc projects.

From Spring of 2021, I will be taking up a new position as the Clinical Research Lead and Ass. Director of Stem Cell Transplant and Cellular Therapy at the Clatterbridge Cancer Centre in Liverpool UK. Our work with the Enserink group and CanCell will continue in this international setting.

Åslaug Helland

Translational Research in Solid Tumours

Lung cancer is a disease with a poor prognosis. Using material from our lung cancer biobank, we have analysed tumour samples for differences in protein expression using a pipeline developed at MDAnderson (Gordon Mils). This analysis investigates 295 cancer-relevant phosphorylated and non-phosphorylated proteins, using reverse phase protein arrays. We identified different proteins associated with RFS depending on molecular subtype, smoking- and mutational-status, with PKC-α, PKC-β, and PKC-δ showing the strongest correlation. (Frontiers in Oncology, Halvorsen et al, 2020). We have also initiated collaboration with professor Simonsen, and are part of the HSØ-funded project in her group, analysing PKC's involvement in cancer. This project just recently started.

In addition, we have an ongoing collaboration with Janne Lethio, investigating proteomics in lung carcinomas. This is ongoing work. The analyses are being done in Janne Lethio's lab, and we will collaborate on the data analyses.

I have supported Holland's application to the Research Council. I have also supported applications on cachexia in cancer with Prof Rusten.

In my group, we have recently initiated work on the LTK and its' role in lung cancer. We have an ongoing collaboration with prof Hesso Fahran at UiO (just recently moved to Austria). Mouse models have been established from two patients, and cell line work is ongoing. We have one postdoc working on this project. The idea is based on similarities between the LTK tyrosine kinase and the ALK. ALK-inhibitors are very effective drugs for tumours with an ALK-activating gene alteration. Functional studies have indicated that tumours with ER stress and LTK activation, also might respond to ALK-inhibitors. This is currently being analysed in cell lines, with mouse model work in the planning. This project might benefit from collaboration with the CanCell-groups.

Terje Johansen

Molecular Cancer Research

Terje Johansen is PI and leader of The Molecular Cancer Research Group, Department of Medical Biology, University of Tromsø – The Arctic University. Johansen and coworkers study molecular mechanisms and roles of selective autophagy in cell signaling and disease. During 2020 the group has discovered a novel selective autophagy receptor named CALCOCO1. In a paper published in The EMBO Journal we showed that CALCOCO1 is acting as a soluble receptor for degradation of tubular endoplasmic reticulum (ER) by autophagy acting by binding to ER-resident VAPA and VAPB proteins on one hand, and to ATG8 family proteins on the other. We contributed to a collaborative paper published in Nature Communications involving the group of Carsten Sachse in Jülich, Germany, and Andreas Brech and Sebastian Schultz in CanCell on the structure and function of the autophagy receptor p62/SQSTM1. Collaborating with Ioannis Nezis in Warwick, UK, we have contributed to several papers on autophagy in the fruit fly model system. We also have an ongoing collaboration with Zhixun Dou at Massachusetts General Hospital, Harvard University and collaborated on a paper published in Nature Cell Biology last year on SIRT1 being downregulated by autophagy in senescence and ageing.

We presently have ongoing collaborations on several projects with groups at CanCell. We collaborate with Andreas Brech and Sebastian Schultz on the selective autophagy receptors p62 and NBR1 where we plan to complete studies that have been ongoing for some time now. We also collaborate with Harald Stenmark, Viola Nähse, Kay Schink and Camilla Raiborg on another autophagy project. Future plans is to continue the collaborations and interactions with groups at CanCell and also expand these collaborations.

Arnoldo Frigessi

Exploring clonal heterogeneity in blood cancers for personalised treatment.

Our goal is to develop a data-driven modelling framework to improve treatment strategies in blood cancers. WE collaborate with Jorrit Enserink group and others at OUS. One major obstacle to developing personalized medicine is the presence of cellular heterogeneity within the cancer cell population of each patient. In such situations, a therapy initially succeeds at reducing disease burden, but then the cancer grows again due to the development of a drug-resistant clone. To address this obstacle, we are working on new methods to estimate and quantify the heterogeneity present in each particular patient. We use high-throughput drug screening data to infer the subpopulation substructure. We will develop a statistical platform to help identify the number of distinct clones present as well as how these clones respond to specific drugs based on drug screens of patient samples. This information then will feed into mathematical models of drug response to therapy, to predict the effect of a drug. The collaboration with Enserink's team is fundamental for the development of our statistical mixture methodology.

Eivind Hovig

Computational Cancer Genomics and Melanoma Systems Biology

We are in the process of finalising our comprehensive bioinformatics tool for the interrogation and prioritization of gene lists from high-throughput genome-scale screens. The tool, which is coined oncoEnrichR, and developed in collaboration with the Wesche group, provides a suite of annotation modules for which a list of genes/proteins can be prioritized for cancer relevance. At its core, oncoEnrichR combines functionality from basic gene enrichment tools e.g. DAVID or MetaScape) with various data visualizations of cancer aberration data (e.g. cBioPortal). In addition, oncoEnrichR provides functionality to i) explore a potential enrichment of the target set with respect to subcellular localizations, ii) explore a potential enrichment of the target set with respect to tissue or cell-type specific gene expression patterns, as obtained from the Human Protein Atlas, iii) explore the protein-protein interactions in the target set and potential interactions with other cancer-relevant proteins (tumor suppressors, oncogenes), iv) explore potential prognostic associations in the target set with respect to tumor gene expression (i.e. high versus low in relation to survival). All of these elements make up distinct analytical modules that ultimately provide the prioritization of candidate genes in an interactive report and a multi-sheet Excel workbook. The oncoEnrichR tool is implemented as an R package, and through a collaboration with ELIXIR Norway (Oslo node), we have also managed to set up a web interface for the tool through the Galaxy framework. This framework is widely used in bioinformatics, and ensures transparency and reproducibility for a number of computational workflows. The establishment of a Galaxy instance for oncoEnrichR will make the tool more easily accessible to users with limited training in bioinformatics. Importantly, we plan to expand further on the work performed with Galaxy, enabling web interfaces to other computational tools developed in the CanCell environment.

The software portfolio available on the CanCell server for high-throughput computing is subject to continuous maintenance by our group, as initiated through the needs of different CanCell scientists. We are further continuing our collaboration with the Eskeland group with respect to a mechanistic analysis of copy number events in soft tissue sarcoma, and have started the co-supervision of a PhD student (H. Wæhler) with respect to bioinformatics. Our collaboration with the Enserink group on combinatorial drug screening in melanoma has progressed significantly after extensive quality control procedures, with available combinatorial drug response data for more than 60 anti-cancer drugs measured across 18 different melanoma cell lines. A PhD student in biostatistics (L. Rønneberg), who is co-supervised by our group, is actively contributing in this project with methodologies on how to robustly estimate drug synergy or antagonism. We are now investigating the variation with respect to molecular properties of the cell lines (genomic aberrations and transcriptomic signatures) in relation to the drug screening datasets, with the goal of identifying novel biomarkers for promising synergistic drug combinations.

Emmet McCormack

Translational Molecular Imaging in Cancer)

Main motivation of the group is the development and effective translation of novel therapies and imaging strategies for the treatment of cancer, particularly cancers with limited therapeutic options. It is the group's belief that the current dogma of rushing novel pharmaceuticals through inappropriate preclinical models is one of the major reasons for their limited clinical penetration. This can only be solved through multidisciplinary development of preclinical surrogates, models and diagnostic tools that more accurately mimic clinical conditions. Subsequently, the development of patient derived xenograft models in haematological malignancies, gynecological cancers and pancreatic cancer in Bergen has been performed, in addition to application of multimodal imaging for use in evaluation of novel therapies. The group now has multimodal imaging of over 40 personalized cancer models, spanning most cancer phenotypes in addition to lab-on-a-chip scaffolds for greater in vitro understanding of the bone marrow microenvironments.

Our group is involved in several projects:

- SonoCURE explores the application of Sonoporation (the transient formation of pores in cells by microbubbles activated by ultrasound) in the treatment of Pancreatic Ductal AdenoCarcinoma (PDAC). The application aims to preclinically elucidate, evaluate, and potentiate a new era of sonoporation theranostics for PDAC through application of innovative biomarker mining, organoid models and preclinical modelling.
- PreLIM focuses on the development of novel preclinical models of leukemia and lymphomas in the development of novel targeted and immune therapies, and exploration of microenvironmental factors critical to disease development and emergence of resistant clones. Active collaboration with the Enserink group has resulted in the evaluation of several novel therapeutic strategies in PDX models of AML. The collaboration has been on hold due to Covid19, but is set to resume in early 2021.
- Through the InoVa project, the group is developing the application of image-guided surgery, whereby fluorescent dyes will target biomarkers on surgically amenable cancers to aid their greater resection.

Highlights of CanCell 2020

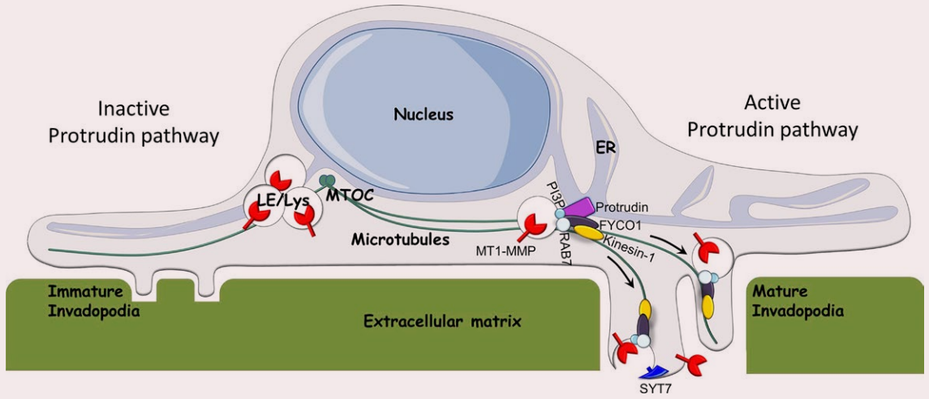
Scientific highlights

Three exceptional papers were celebrated during the CanCell annual retreat.

Scientist Nina Marie Pedersen and her co-workers in the Cellular Membrane Dynamics (Camilla Raiborg's project group) group identified a new mechanism of how cancer cells grow invadopodia. Their findings were published in an article on June 1st 2020 in Journal of Cell Biology.

They found that invadopodia growth and the exposure of MT1-MMP at the invadopodial tip are controlled by contact site formation between Protrudin in the endoplasmic reticulum and MT1-MMP containing endosomes. This contact triggered the translocation of the endosomes to the cell periphery, and their subsequent fusion with the plasma membrane provided membrane for the growing invadopodia. In addition, MT1-MMP was exposed at the cell surface, mediating degradation of the extracellular matrix.

By overexpressing this pathway in a non-cancerous cell line, Pedersen et al found that the cells grew invadopodia and became invasive. When the Protrudin pathway was inhibited by CRISPR/Cas9 mediated knock down of Protrudin, highly invasive breast cancer cells failed to develop invadopodia and lost their invasiveness.

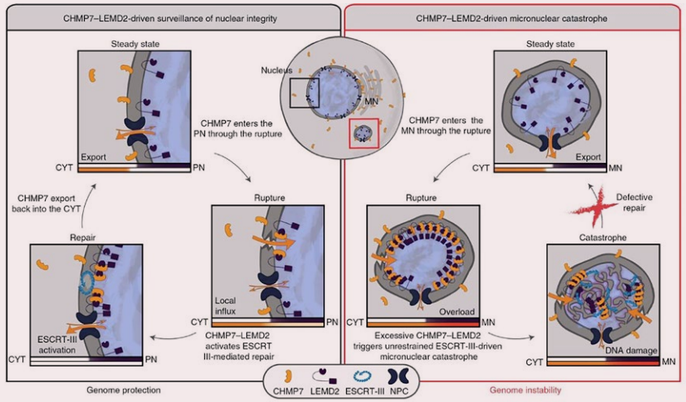


Model of how contact between Protrudin in the endoplasmic reticulum and MT1-MMP containing endosomes facilitate invadopodia growth, MT1-MMP exocytosis and extracellular matrix degradation

Marina Vietri and her colleagues published "Unrestrained ESCRT-III drives micronuclear catastrophe and chromosome fragmentation" in Nature Cell Biology in July showing that the ESCRT machinery is also recruited to damaged micronuclei, which contain single chromosomes enclosed by a micronuclear envelope.

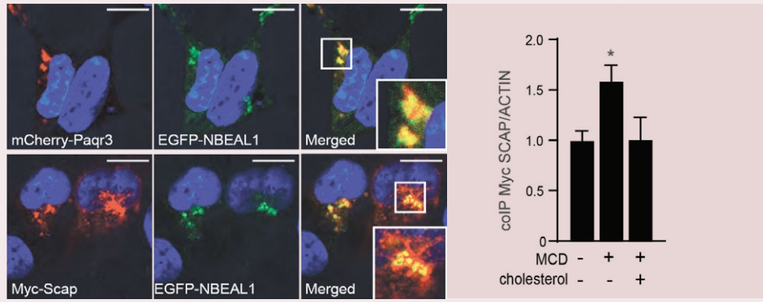
Micronuclei are typically found in cancer cells and are thought to represent a mechanism for harnessing single chromosomes that fail to be incorporated into the nucleus. However, when the ESCRT machinery is recruited to damaged micronuclei, this does not result in their repair but instead causes massive membrane rearrangements that, probably because of physical strains, lead to chromosome fragmentation. This resembles a process known as chromothripsis, a chromosome shattering condition strongly associated with cancer progression. The reason why the membrane repair machinery goes awry at micronuclei appears to be related to accumulation of factors that recruit ESCRTs due to the small size of micronuclei with respect to primary nuclei. This causes local hyper-recruitment of the ESCRT machinery and results in distorted membranes – with catastrophic consequences for the underlying chromosome.

This work was a close collaboration between the groups of Harald Stenmark at CanCell and Coen Campsteijn at Institute of Basic Medical Sciences and also involved cytogeneticists at Oslo University Hospital and an international team of biophysicists and computational biologists. Their paper went on to win the OUH's prize for Outstanding Article for the fall of 2020 as well.



Model for ESCRT-III function at the nuclear envelope of primary nuclei and micronuclei. At ruptured micronuclei, an inherent inability to restrict CHMP7–LEMD2 causes unrestrained ESCRT-III activity along the membrane, resulting in failure to repair the membrane and instead driving extreme membrane deformation, causing micronuclear catastrophe and DNA damage. CYT, cytoplasm. From Vietri et al. 2020, Nature Cell Biology ©

Marina Vietri is first author of the article



NBEAL1 is a positive regulator of SREBP2 activity. EGFP-NBEAL1 colocalizes with two proteins involved in processing of SREBP2, SCAP and PAQR3. Scientific Reports 2020 (C)

Christian Bindesbøll and co-authors Margret Ogmundsdottir and Anne Simonsen

Christian Bindesbøll and coworkers in Anne Simonsen's lab was the third recipients of this year's Excellent Paper at the CanCell Retreat. Their paper entitled "NBEAL1 controls SREBP2 processing and cholesterol metabolism and is a susceptibility locus for coronary artery disease" was published in Scientific Reports in March 2020.

Dysregulated cholesterol homeostasis promotes the pathology of atherosclerosis, myocardial infarction and strokes. Cellular cholesterol is mainly regulated at the transcriptional level by SREBP2, but also through uptake of extracellular cholesterol from low-density lipoproteins (LDL) via expression of LDL receptors (LDLR) at the cell surface. The authors identified genetic variants in the large and poorly characterized BEACH domain protein NBEAL1 associated with decreased expression of NBEAL1 in arteries and increased risk of coronary artery disease in humans. They could show that NBEAL1 is a Golgi-associated protein that regulates cholesterol metabolism by modulating LDLR expression in a mechanism involving interaction with SCAP and PAQR3 and subsequent SREBP2-processing. Thus, low expression of NBEAL1 may lead to increased risk of coronary artery disease by downregulation of LDLR levels.

CYS in 2020: Anthony, Aram, Viola, Kristiane, Heidi and Marie

CanCell Young Scientists (CYS) in 2020

Although 2020 was a challenging year, CYS has still worked hard to organise scientific events bringing the young scientists of CanCell together.

Rigorous scientific methodology

The first event of this year was a workshop on quantitation and statistics with a basis in experimental methods widely used in CanCell. The audience was guided from data quantitation to hypothesis testing and the cutting edge of data analysis in biology.

For this workshop we used the knowledge within CanCell and the invited speakers were all among our own young scientists. Marie Rogne gave a talk about proper quantitation of qRT-PCR and western blotting data followed by Kay O. Schink presenting standard techniques and advanced methods for analysing microscopy data. Aram N. Andersen showed us how to properly choose statistical tests and Nacho Garcia guided us through function fitting and machine learning for analysing biological data.

CYS' successful Alumni Day was held amidst COVID-restrictions

CRISPR Workshop

CanCell is investing in technologies for advanced genetic manipulation, and is currently facilitating a centre-wide collaboration effort on the preparation and execution of pooled CRISPR screens. Our next workshop thus focused on exposing some of the newest technologies available in the centre, and to explore and discuss novel ideas, setting seeds for potentially new and exciting projects amongst the young scientists in the CanCell.

Alumni Day

For our last event of the year, CYS had the pleasure to arrange an Alumni Day, an event where the young scientist of CanCell could come and find out about opportunities outside of academia. With only 3% of PhDs that obtain professor positions, it was high time to discuss new attractive possibilities.

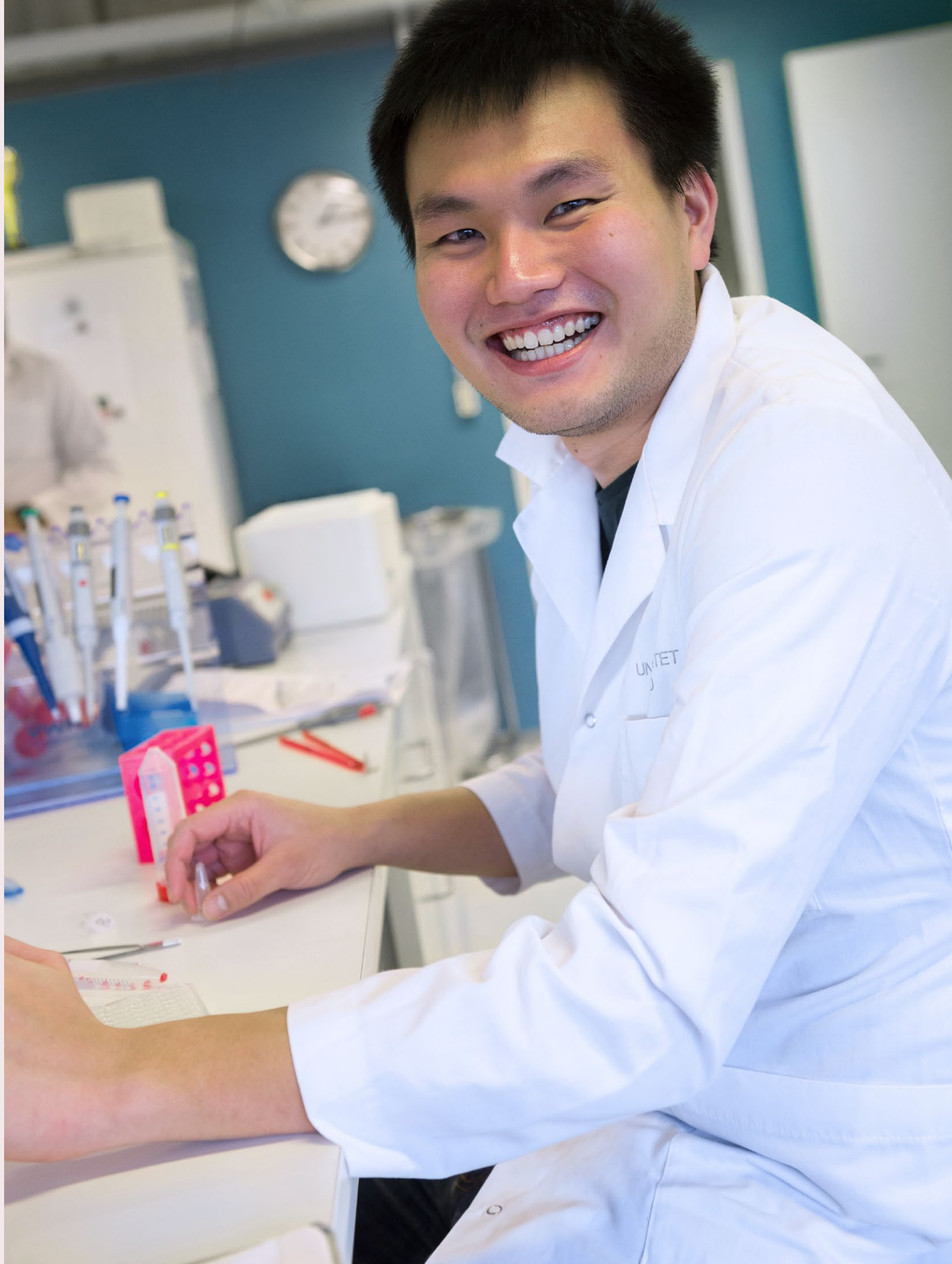
The event was initiated by an inspirational talk by Lars Christian Lassen who has an MD and PhD from the University of Copenhagen. He wor-ked as the medical director at Novo Nordisk, before transitioning into Human Resources as senior vice president. He has developed leadership programmes at international business schools and is now the leader of Mobilize Strategy Consulting, a company that helps individuals and companies mobilise and unfold their true strategic potential.

We had invited six scientists who presented their scientific journey: Ingrid Roxrud (Norwegian Research Council), Iwona Grad (Thermo Fisher), Anne-Mari Håkelien (The Norwegian Medicines Agency), Christian Bindesbøll (Roche), Hilde Abrahamsen Enserink (MSD) and Raimonda Viburiene (CEPI). All of them gave us their story on how they got to where they are, with an honest focus on the transition process from academia towards a non-academic position.

All the participants had outlined challenges they encountered when moving away from academia, which triggered a lot of questions and fruitful discussions from the audience.

As we are now stepping down, we want to thank for all the support and positive feedback on our events. At the same time, we want to welcome the new CYS board that is already in the progress of organizing fruitful events for the young scientists of CanCell for the coming years.

On behalf of CYS,
Aram, Marie, Heidi, Anthony, Viola and Kristiane



The year at CanCell

CanCell Annual Retreat

This year's Annual retreat was held at Quality Hotel 33 in Oslo amidst COVID-restrictions in October, and was reduced in size compared to previous retreats. We restricted the number of participants in the physical events to 50, divided into strict cohorts, and simultaneously live-streamed the events through Zoom.

The "online year" enabled us to have several international experts in their field as key speakers that all held their talks via Zoom. Visiting professor Eyal Gottlieb (Technion institute, Israel) spoke about metabolism and cancer and Jayanta Debnath (UCSF, USA) held a lecture on "Autophagy and Secretion in Cancer", while SAB-member Johanna Ivaska (University of Turku, Finland) talked about endosomal trafficking in breast cancer progression and drug resistance. In addition to the international keynote speakers we had an excellent presentation from associated member Arnoldo Frigessi, and both Leonardo Meza-Zepeda and Marie Rogne presented their exciting new work. This year we had a focus on three-minute long flash talks, of which there were 25 in total. Among these, a committee awarded three talks as winners: Aruna Abraham (Eskeland), Simona Miglioni (Stenmark) and Amani Al Outa (Enserink). During the banquet, the inaugural prize for "Communicator of the year" was awarded to Viola Lobert for her contribution to scientific outreach. Finally, the three papers selected as pre-eminent in 2020 were rewarded and presented by their first authors, i.e. Nina Marie Pedersen, Marina Vietri and Christian Bindesbøll (*see also "Scientific highlights" page 46–48*). Despite the restrictions, the participants who physically attended the retreat praised the gathering as scientifically and socially rewarding.

Top: Flash talk winners: Aruna Abraham, Amani al Outa and Simona Migliano

Middle: Attentative crowd at Hotel 33 during the combined zoom-annual retreat

Bottom: Staff always prepared: Anders Øverbye, Nagham Asp, Ulrikke Dahl Brinch

Paper awards

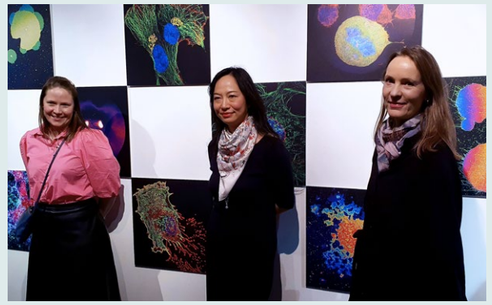
- Nina Marie Pedersen et al. – Protrudin-mediated ER–endosome contact sites promote MT1-MMP exocytosis and cell invasion (Journal of Cell Biology 2020).
- Marina Vietri et al. – Unrestrained ESCRT-III drives micronuclear catastrophe and chromosome fragmentation (Nature Cell Biology, 2020).
- Christian Bindesbøll et al. – NBEAL1 controls SREBP2 processing and cholesterol metabolism and is a susceptibility locus for coronary artery disease (Scientific Reports, 2020).

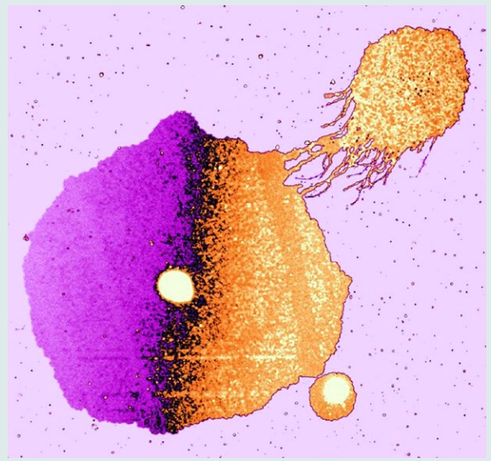
Nanocosmos

CanCell scientists from the Stenmark Lab participated in the exhibition "Nanocosmos" at Kunstplass Akersgata, as a part of the UiO:Life Science Programmable Cell-like Compartments convergence environment.

The event featured images of biological origin, such as cell micrographs, lipid droplets and fluorescently labelled intracellular components. In particular, cell art from Vigdis Sørensen, Yan Shen and Nina Marie Pedersen represented science from CanCell at the exhibition.

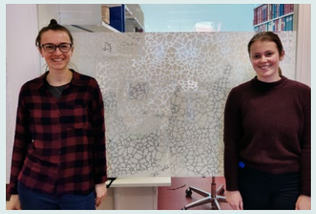
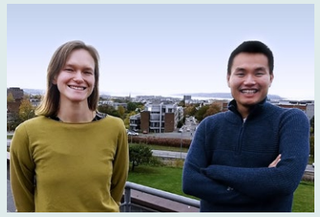
The exhibition was opened by UiOs rector, Svein Stølen on February 11th and lasted until Feb 16th as part of the UiO:life Science conference week. The initiative was undertaken by Irep Gözen at NCMM, and other partners in the Convergence environment, and curated by the art gallery Kunstplass Contemporary Art. The event was also featured at forskning.no.

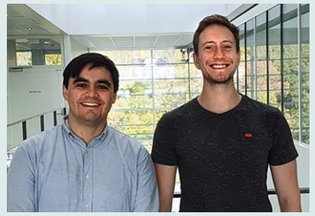




Top: Exhibitors from CanCell Nina Marie Pedersen, Yan Zhen and Vigdis Sørensen. Bottom: Poster image from the exhibit

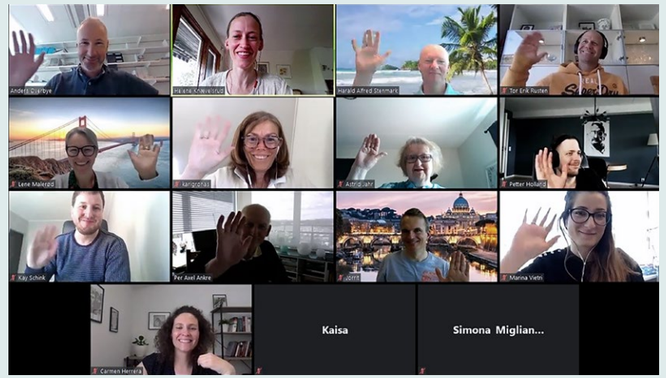



CanCell Buddies

Every new person arriving to CanCell in 2020 was offered a CanCell Buddy to welcome her/him to the group, Centre and Norway, and provide guidance, tips and a social fundament. Here are some of the Buddy duos:



User panel

On May 6th, several of CanCell's scientists convened by Zoom to receive feedback from representatives from three different cancer patient organizations. Per Axel Ankre (Prostate Cancer Society), Astrid Jahr (Sarcoma Society) and Kari Grønaas (Lung Cancer Society) all gave valuable input on abstracts, which was used to improve grant applications to various funding agencies. In addition, Trude Wetaas (Leukemia Society) gave feedback via email. Kari shared her experience both from the perspective of participant in grant evaluation committees and from her background as a patient. Her views were greatly appreciated and very useful to our scientists, both in grant writing and for their cancer research in general. We would like to express our gratitude to our user panel members for their important contributions to our Centre!

ESCRT symposium

The Stenmark group hosted a "zoomposium" online, with guest lectures from Jeremy Carlton (Francis Crick Insitute, UK) and Arnaud Echard (Institut Pasteur, France) that was held on June 11th. The main topic was ESCRT proteins and their regulation, with great local input from CanCell scientist Marina Vietri.

Harald 60

CanCell director Harald Stenmark turned 60 in October, and was honored with a symposium in OCCI Friday Oct 23. The program touched upon his early career, recent achievements and untold stories from several people close to him in various stages of his professional life. The event was a both physical as well as digitally broadcasted with several guests from abroad linking in.

Molecular Cancer Medicine (MF9235)

A new course for Master and PhD-level on molecular cancer biology was established and taught for the first time this fall. In four weeks the students were introduced to subjects including biology of cancer, tumorigenesis, invasion and metastasis, therapeutic outcomes, and cutting edge molecular and cellular techniques. CanCell junior and senior scientists gave lectures, demonstrations and assignments. The course organiser was CanCell PI Tor Erik Rusten. The first course had just a small number of students, but was very well received, holding the promise for increased student interest for future courses.

ChiNoCell

Harald and Anne have initiated an INTPART collaboration with two Chinese research group led by Chonglin Yang from Yunnan and Li Yu from Tsingtua Universities – called ChiNoCell (Chinese-Norwegian Partnership for Education and Research in Cancer Cell Biology), and had their first visit to China in 2019. This year CanCell was host to a reciprocal seminar, which due to the pandemic was held as a zoominar on December 17-18. More than 100 persons attended the event, which featured lectures from all four involved research groups thematically revolving around autophagy, migrasomes and endocytic membrane traffic. The ChiNoCell project also hosts courses and several workshops in addition to encouraging knowledge exchange. It runs until 2023, with the possibility for extension.

Outreach

We aim to reach out to a broad part of the public and encourage our members to reach out about their work. In accordance with this we are visible on YouTube, Twitter, Instagram and our webpage.

Lab tour videos

Students from Ullern high school and the University of Oslo visit CanCell labs as a part of their teaching every year. Due to the pandemic, this was not possible in 2020. CanCell members instead took the initiative to create a series of videos with virtual tours of our laboratories.

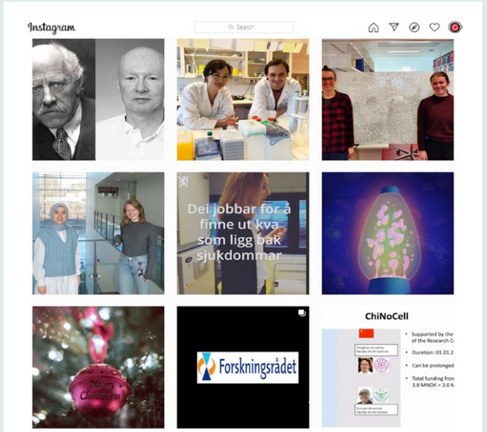
This included guided tours to the fish lab, plant lab and fly lab. A lab tour featuring Anne Simonsen's lab was posted online by the Department of Education (KD) to advertise for grant application deadlines and part of their infomercial for their grants.

Instagram

At our Instagram account: cancell_uio, you can follow glimpses of CanCell life, activities and people. The account holds a selection of posts ranging from information about scientific events, new discoveries, publications and life of a scientist.

Twitter

Twitter is our main "science" platform and where we seek to reach both active scientists and science aficionados. Here we comment on papers from CanCell and related work, scientific events and conferences.



CanCell News

At our official UiO webpage, you will find CanCell News, where you can get up to date and accurate information about our publications, grants and events happening in CanCell.

Through our blog written by our members, you get the chance to see another side of life at CanCell. The blog post Impact of COVID-19 on Centre for Cancer Cell Reprogramming mothers received praise from many of our members which felt that it captured their experiences under the pandemic.

Pilar Ayuda has promoted science at several high schools the last year and is active as president of Spanish Researchers Association in Norway (IENO-SFNO)

Fulbright scholar Danielle Jacobsen accompanying Anne Simonsen at the US Embassy

Seminars

During 2020 many "physical" seminars and conferences were cancelled, but several CanCell members gave talks at virtual conferences and webinars, including the Keystone symposium on Autophagy: Mechanisms and Disease (Anne), the AIN-ILS autophagy Webinar series (supported by EMBO) (Anne). Anne was also invited to hold a talk at the CRICK Institute, London, UK in person. Jorrit Enserink was invited as speaker at '2020 FASEB SRC on Cell Signaling in Cancer: From Mechanisms to Therapy'. In addition, we arranged 5 CanCell seminars, with the last 3 being virtual Zoominars.

- Professor Marta Miączyńska (International Institute of Molecular and Cell Biology, Warsaw) – Inflammatory signalling from endosomes in cancer cell biology.
- Professor César Serrano (Vall'd Hebron Institute of Oncology (VHIO), Barcelona) – Deciphering the crossroads of KIT oncogene in gastrointestinal stromal tumor.
- Professor Andrea Ballabio (TIGEM institute of Pozzuoli, Italy) – A substrate-specific mTORC1 pathway drives kidney cytogenesis and tumorigenesis.
- Professor Philippe Collas, (Institute for Basic Medical Sciences UiO, associated member at CanCell) – Aspects of 3D genome topology during differentiation.
- Claus Jørgensen (Group leader of the Systems Oncology Group, Cancer Research UK Manchester Institute) – Heterocellular interactions in the tumour microenvironment.

CanCell members in the news and media

Our members have contributed to the public discussion via chronicles or guest entries in large Norwegian newspapers. Examples are Morgenbladet (Helene Knævelsrud – twice), Klassekampen (Helene Knævelsrud) and Aftenposten. The piece "Ett steg nærmere tryggere genredigering" featured in Aftenposten was written by CanCell PI Ragnhild Eskeland and her Master student Martine Mesel Isom, and featured a discussion on gene-editing. Anne Simonsen was invited to the American Embassy in Oslo in connection with her Fulbright Scholar Danielle Jacobsen (from Haverford College, USA) who stayed in Anne's lab for a year.

Disputations, awards and honours

Six new PhDs were completed at CanCell in 2020. Due to the on-going pandemic five of the disputations were arranged digitally as public events on Zoom.


Patrycja Szybowska


Anette Christensen Lie-Jensen


Dagim Tadele


Rojyar Khezri


Aurélie Nguéa P.


Laure Isabelle Piechaczyk

Patrycja Szybowska

MSc Patrycja Szybowska defended her thesis – ***Regulation of Fibroblast Growth Factor Receptor signalling*** the 24th of January 2020. Her defence included a trial lecture in the topic – *Exosomes, their formation and role in intercellular communication in physiology and oncogenesis.* Both the trial lecture and thesis defence were held as a public event in the research building at the Radium Hospital. In her work she focused on identifying novel mechanisms that regulate FGFR signalling. A process which is regulated by endocytosis, pathway-specific regulatory proteins, phosphatases, and negative feedback loops. Her Principal Supervisor was research group leader Antoni Wiedlocha, at the Oslo University Hospital. Szybowska is now working as a postdoctoral fellow in Jørgen Wesche's group Molecular Biology of Sarcomas.

Anette Christensen Lie-Jensen

MSc Anette Christensen Lie-Jensen was first out defending her thesis on Zoom – ***ALIX in cell division in vivo*** on the 12th of June. Her defence included a trial lecture in the topic *Mechanisms of asymmetric cell division and role in development and homeostasis.* She worked in the Stenmark lab on cell division in fruit flies (*Drosophila melanogaster*) with Kaisa Haglund as her principal supervisor and project leader. The PhD defence was held as a digital public defence on Zoom. Lie-Jensen is currently working as a senior lecturer at Østfold University College.

Dagim Tadele

On the 26th of August MSc Dagim Tadele defended his thesis on Zoom – ***Development of novel approaches for treatment of leukemia***. Included in his thesis defence was also the trial lecture – *Preventing and overcoming resistance to targeted therapies in cancer.* In his work he focused on possible drugs to treat leukaemia's characterized by the BCR-Abl oncoprotein, performed drug screens based on competition between isogenic untransformed cells and BCR-Abl transformed cells. Tadele performed his research in the Cancer Molecular Medicine group of Jorrit Enserink.

Aurélie Nguéa P.

The 28th of August MSc Aurélie Nguéa P. defended her thesis on Zoom – ***Nutrient stress responses in the budding yeast. Saccharomyces cerevisiae***. Her defence included a trial lecture in the given topic – *Transcription and metabolism interplay: Dysregulation in Cancer and therapeutic opportunities* and one in the chosen topic – *Exosome-mediated functions of short non-coding RNAs.* Nguéa's work focused on revealing mechanisms by which Sumoylation and TORC1 support survival upon nutrient stress in Saccharomyces cerevisiae. She worked in the lab of Jorrit Enserink.

Laure Isabelle Piechaczyk

On the 16th of September, MSc Laure Isabelle Piechaczyk defended her thesis – ***Identifying new avenues for leukemia treatment using genome wide CRISPR/Casg and ex vivo drug sensitivity screens*** via Zoom. Her thesis defence included a trial lecture on the theme – *Mechanisms of drug resistance in cancer.* Piechaczyk's work focused on understanding the mechanisms behind resistance and sensitivity to tyrosine kinase inhibitors (TKIs) which are used to treat patients suffering from Chronic Myeloid Leukaemia and Ph+ Acute Lymphoblastic Leukaemia. She used genome wide CRISPR/Cas9 screens to study these mechanisms. Piechaczyk worked in the Cancer Molecular Medicine lab with Jorrit Enserink as her Principal Supervisor.

Rojyar Khezri

On the 25th of September, MSc Rojyar Khezri defended her thesis – ***Host autophagy mediates organ wasting and nutrient mobilization for tumor growth***. Her thesis defence included a trial lecture on – *Trafficking in Eukaryotic Cells.* Khezri's work focused on and demonstrated that autophagy has a complex role in cancer. She worked in the Tumor-Host Biology, and associate professor Tor Erik Rusten from the institute of Clinical Medicine (UiO) was her Principal Supervisor and Co-supervisor was Professor Harald Stenmark from the Stenmark lab. The PhD defence was held as a digital conference over Zoom. She continues to be a vital part of Rusten's group as a post doc.

Master students

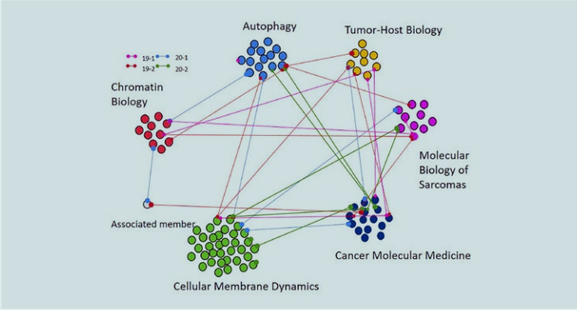
CanCell also had nine MSc students successfully completing their exams:

- Mesel Isom (Eskeland)
- Mohamed Abdelhalim (Eskeland)
- Aruna Abraham (Eskeland)
- Hallvard Wæhler(Eskeland)
- Tasmia Jinnurine (Eskeland)
- Julia Elisabeth Simonsen (Rusten)
- Julie Aarmo Johannesen (Enserink)
- Aleksander Aas (Simonsen)
- Camilla Bergsmark (Simonsen)


Four completed MScs from Eskeland's lab (from left): Hallvard Wæhler, Mohamed Abdelhalim, Tasmia Jinnurine, Martine Mesel

CanCell Junior Grants

To strengthen CanCell's programme support of junior scientists, it was announced that the project grants for researchers and postdocs from 50.000 to 300.000 NOK for joint applications from two or more groups. The grants could cover expenses related to libraries, screens, core facility services, minor equipment and short-term lab visits, but CRISPR-Cas9-screens was prioritized. The grants had the effect of increasing the interactions between the groups as indicated by the interaction map (right).



Applicant	Group	Project
Marie Rogne, Sigve Nakken	Eskeland, Hovig	Identify and assess mechanisms of genomic amplifications of liposarcoma
Sakshi Singh, Ankush Sharma	Simonsen, Eskeland	Analyzing the mitophagy transcriptome
Michal Kostas, Kay Schink	Wesche, Stenmark	Single molecule tracking of FGFR1 dimers at the surface of living cells
Kristiane Søreng, Nina Marie Pedersen	Simonsen, Stenmark	Cell migration and invasion in gastric cancer cells, elucidating the role of HS1BP3
Eva Maria Wenzel, Pilar Ayuda-Durá	Stenmark, Enserink	Drugging the Protrudin pathway to identify the Achilles heel of cancer cells
Nathalia Chica, Petter Holland	Enserink, Rusten	Identification of causation directed gene expression networks as a predictive factor for changes in autophagy dynamics
Jonathan Arias, Vigdis Sørensen	Enserink	Optimization of nuclear translocation and kinetics of the novel CRISPR nuclease CN-05
Matthew Ng, Laura R. de la Ballina, Nathalia Chica Balaguera	Simonsen, Enserink	The role of cholesterol in autophagy membrane dynamics
Ellen Margrethe Haugsten, Aram Nikolai Andersen, Nina Marie Pedersen	Wesche, Enserink, Stenmark	CRISPR screen to identify vulnerabilities in cancer cell invasion
Sebastian Schultz	Stenmark	Accelerated Sample processing for Advanced Electron Microscopy (minor grant)
Yan Zhen	Stenmark	Migrasomes in the cancer immune checkpoint (minor grant)

Funding Grants:

- Kay Schink (RCN) – FRIPRO - Open Call (12 MNOK)
- Anne Simonsen (RCN) – FRIPRO - Open Call (12 MNOK)
- Jorrit Enserink (RCN) – FRIPRO - Open Call (12 MNOK)
- Harald Stenmark (DNK) – Project grant (7.7 MNOK)
- Marina Vietri (HSØ) – Career grant (9.0 MNOK)
- Tor Erik Rusten (DNK & HSØ) – Open Call – project grant (6.7 MNOK)
- Kjetil Boye (HSØ) – Postdoctoral Fellowship (4.6 MNOK)

Awards

- Anne Simonsen elected EMBO member proving scientific excellence and pioneering research.
- Helene Knævelsrud appointed young associate investigator at NCMM.
- Riccarda Schimanski received Tekna Masters grant.
- Ulrikke Dahl Brinch was awarded the prestigious UiO HSE Prize for her excellent efforts to improve the working environment.
- Marina Vietri's paper in Nature Cell Biology received OUH' prize for outstanding article





From top left: Anne, Marina, Ricci, Helene and Ulrikke

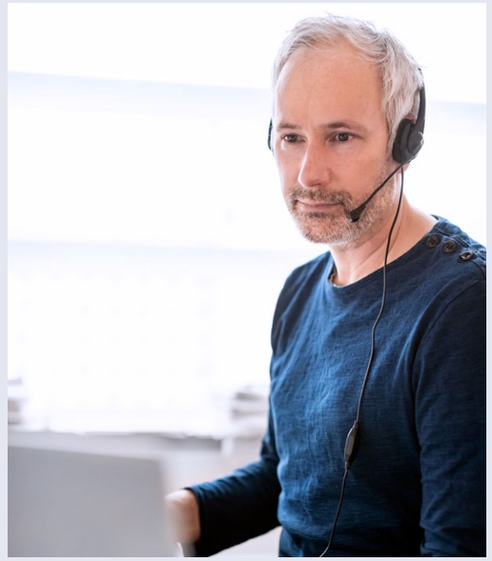
About CanCell

The leader group in 2020. From left: Tor Erik Rusten, Jørgen Wesche, Harald Stenmark (director), Anne Simonsen (co-director), Anders Øverbye (administrative coordinator), Jorrit Enserink and Ragnhild Eskeland.

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 6 km distance is covered 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.

Top: Susanna Ferizi is CanCell's communication advisor
Bottom: Lab technician Mats Kleppe at work in the hood



Anders Øverbye is the administrative coordinator for CanCell.

Research Groups

CanCell is formed by 6 principal investigators (PIs): Harald Stenmark (director), Anne Simonsen (co-director), Jorrit Enserink, Tor Erik Rusten, Jørgen Wesche and Ragnhild Eskeland. The PIs have weekly meetings to discuss all issues related to the Centre. Furthermore, seven independent groups or research teams are associated with CanCell. These are the groups of Emmet McCormack, Arnoldo Frigessi, Terje Johansen, Eivind Hovig, Yngvar Fløisand, Åslaug Helland, and Phillippe Collas.

Management

The CanCell PIs acts as executive board for CanCell together with administrative coordinator Anders Øverbye. 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, Åslaug Helland, and the Head of Institute for Basic Medical Sciences, Lene Frost-Andersen.

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. Since October 2020 CanCell also has it's own communcation advisor Susanna Ferizi, responsible for sosial media, blogs and various output.

Facts and figures 2020

Key figures

Full-time equivalent (FTE), excluding students: 83

Headcount, including students: 128

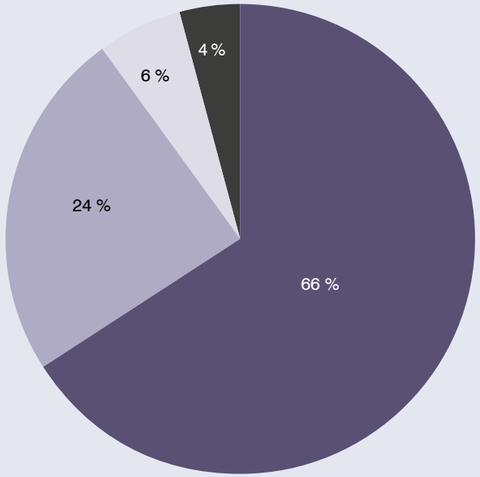
Publications 37

Funding 91.1 MNOK

Global background

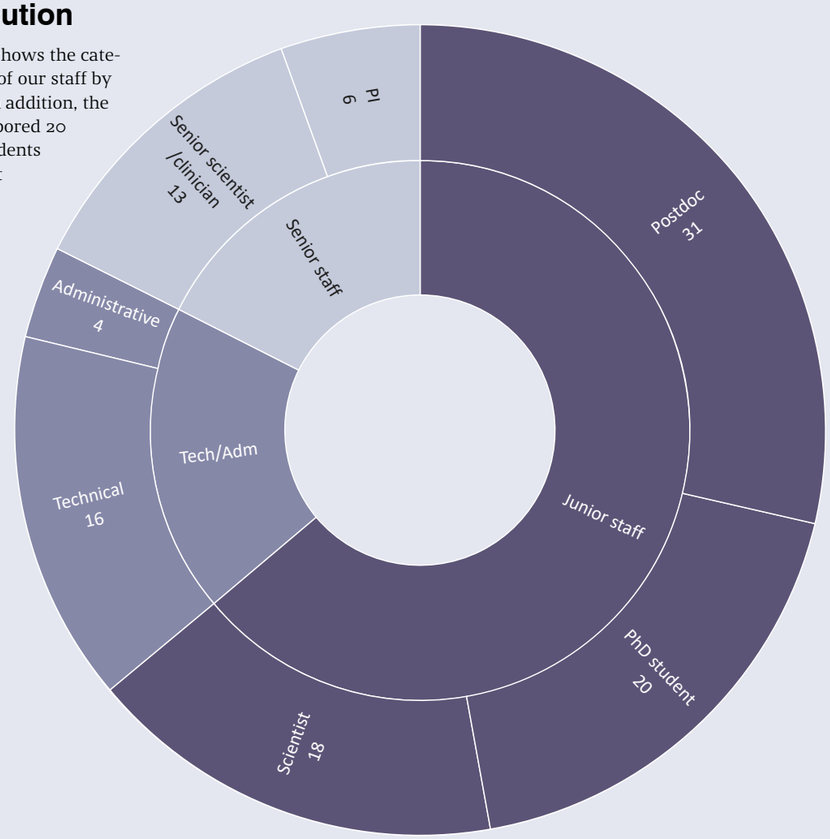
CanCell members have background from most of the world's continents. We have this diversity in mind when we set out to create a common culture and understanding for all of CanCell.

- **Europe**
- **Asia**
- **Americas**
- **Africa**



CanCell staff distribution

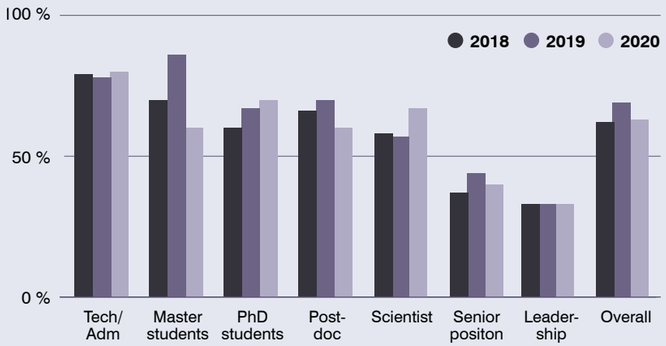
The chart shows the categorization of our staff by position. In addition, the centre harbored 20 Master students throughout 2020.

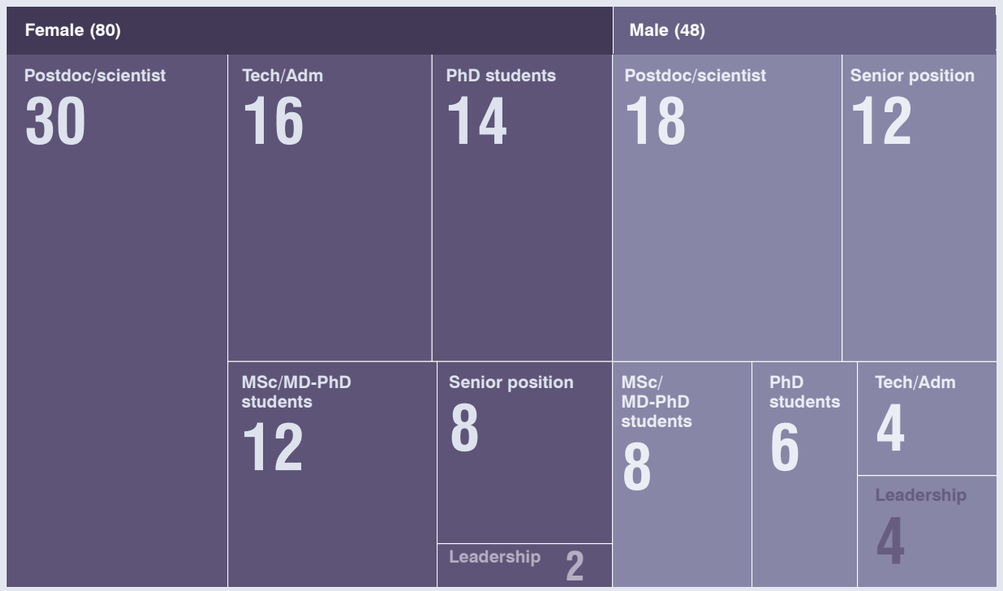


Gender balance

CanCell consists of eighty women and forty-eight men in 2020, resulting in an overall gender balance of 62.5% women and 37.5% men. Women are over-represented in supportive and junior positions, following the tendency seen in student recruitment. There is a marked decrease in female presence in senior positions; this trend has been constant throughout the last three years. Through the initiative of the Equality forum CanCell hope to address challenges posed by this skewedness.

Gender balance development (5% women per category)

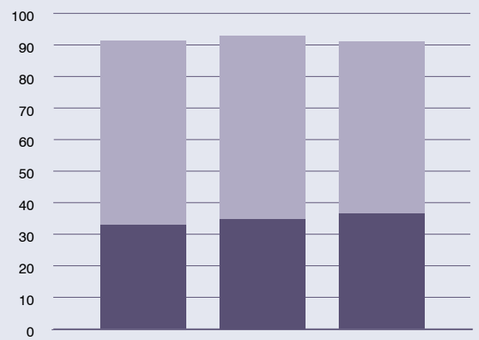




Funding

The total funding for 2020 was 91.1 MNOK, a minor change since 2019. The funding situation for CanCell is in general stable and with the granting of several large funds during 2020, 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 2020.

Funding development (MNOK)



Funding 2020 (MNOK)

CanCell and the world

The world at CanCell – international members by continent

CanCell in the world – international collaborations by continent

List of CanCell Collaborators

- Ai Yamamoto | Columbia University, **New York, USA**
- Chris Eide |University of Portland, **OR, USA**
- Christian Behrends | Ludwig-Maximilians-Universität (LMU) München, **Germany**
- Christos Samakovlis | University of Stockholm, **Sweden**
- Eyal Gottlieb | Israel Institute of technology, Technion, **Israel**
- Heinrich Jasper | Genentech, **CA, USA**
- Ivan Dikic |Göthe Univ, Frankfurt, **Germany**
- Jonathan A. Fletcher | Harvard Medical School, **MA, USA**
- Jose L. Garcia-Perez | University of Edinburgh, **Scotland**
- Kerstin Bystricky | University of Tolouse, **France**
- Kimmo Porkka | FIMM, Helsinki, **Finland**
- Nasser M. Rusan | NIH, Bethesda, **ML, USA**
- Nico Dantuma | Karolinska Institute, **Sweden**
- Ole Pless |Fraunhofer IME ScreeningPort (IME SP), Hamburg, **Germany**
- Pablo Wappner | Leloir Institute, Buenos Aires, **Argentina**
- Patricia Boya | Spanish National Research Council, Madrid (CSIC), **Spain**
- Pavel Krecji | Masaryk University, Brno, **Czech Republic**
- Roberto Zoncu | UC Berkeley, San Francisco, **CA, USA**
- Sharon Tooze |Francis Crick Institute, London, **England**
- Sven Carlsson | Umeå University, **Sweden**
- Tiziana Bonaldi | European Institute of Oncology, **Italy**
- Todd Schoborg | NIH, Bethesda, ML, **USA**
- Tom Melia | Yale School of Medicine, New Haven, **CT, USA**
- Yves Barral | ETH Zurich, **Switzerland**
- Swati Chauhan | Institute of Life Sciences, Bhubaneswar, **India**

List of members

Persons in CanCell during 2020 by group

Name	Position	Group
Ferizi, Susanna	Advisor	Admin
Gan, Yili	Advisor (OUH)	Admin
Øverbye, Anders	Administrative Coordinator	Admin
Khan, Abdushakoor	Executive officer	Admin
Karlsrud, Lady Nina	Executive officer	Admin
Enserink, Jorrit	**PI, Professor**	**Enserink**
Al Outa, Amani	Postdoc	Enserink
Andersen, Aram Nikolai	PhD Student	Enserink
Arias, Jonathan	Postdoc	Enserink
Ayuda-Duran, Maria del Pilar	Postdoc	Enserink
Brodersen, Andrea	MSc Student	Enserink
Caulier, Benjamin	Postdoc	Enserink
Chica-Balaguera, Nathalia	Postdoc	Enserink
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Publications

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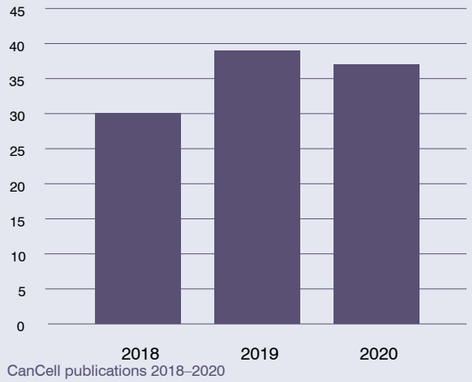

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CanCell Code of Conduct

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.

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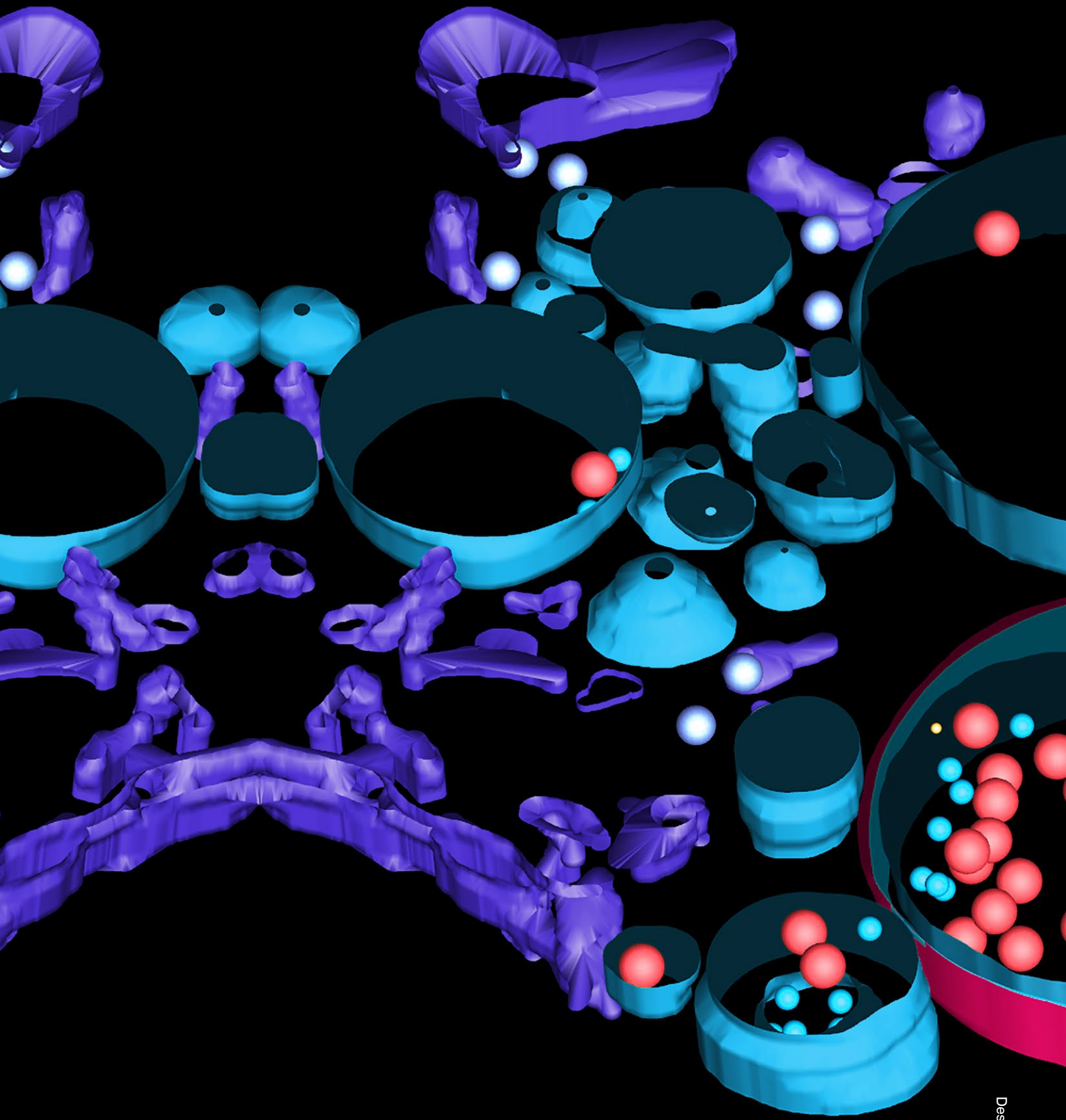

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