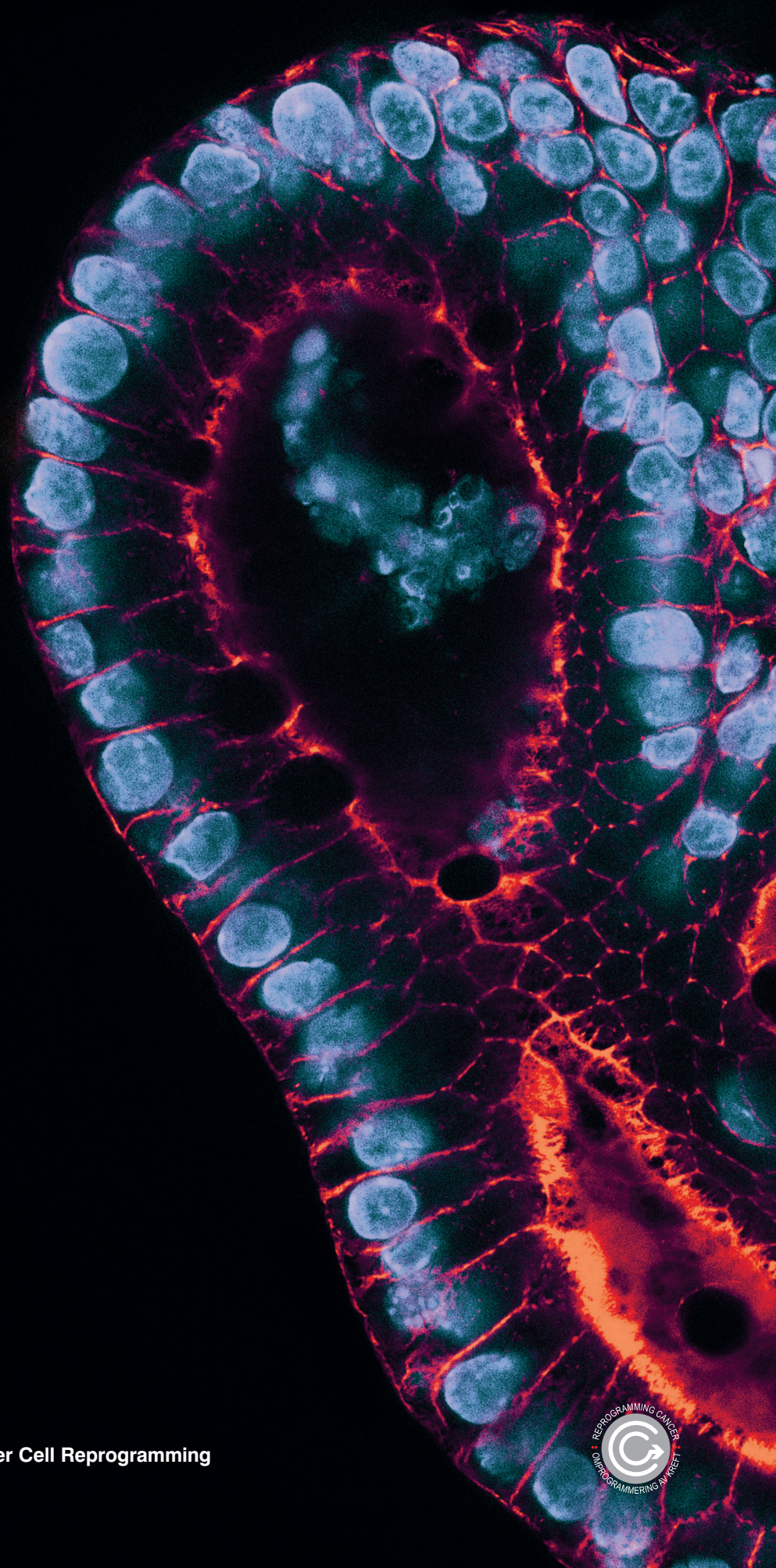
ANNUAL REPORT 2018

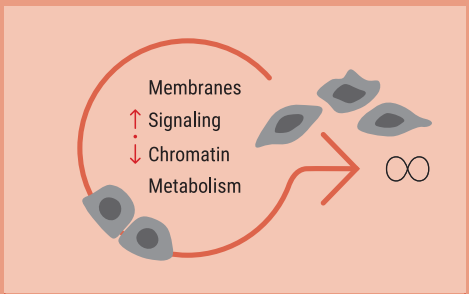
CanCell



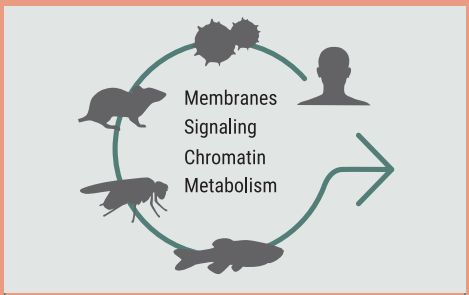
UiO : CanCell – Centre for Cancer Cell Reprogramming
University of Oslo

Cover: Intestinal stem-cell derived organoids from wild-type mouse labeled with Actin phalloidin **(purple)** and Hoechst **(blue)**.

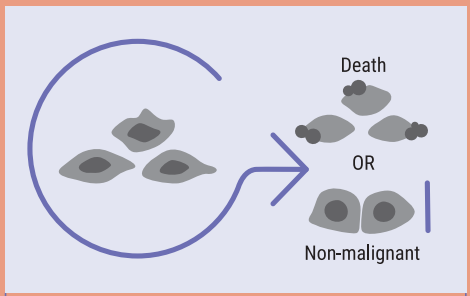
Image: Viola Lobert



Cancer cell programmes



Achilles' heels of cancer



Cancer cell reprogramming

CanCell's founding hypothesis is that interactions between chromatin regulation, cell signaling, membrane dynamics and cell metabolism represent potential vulnerabilities, or Achilles' heels, of cancer cells. CanCell's principal aim is therefore to identify such vulnerabilities and target these for reprogramming of cancer cells. How do we identify novel Achilles' heels of cancer? A good starting point is to initiate collaborations between experts on the abovementioned cellular programmes in order to pinpoint their interactions. CanCell's joint PI group holds expertise on chromatin regulation (Eskeland), membrane dynamics (Stenmark, Simonsen), cell signaling (Wesche, Enserink) and metabolism (Rusten) and is therefore in good position to identify novel vulnerabilities of the cancer cell.

REPROGRAMMING OF CANCER CELLS – A 10 YEARS PERSPECTIVE

We were thrilled to receive the announcement that Centre for Cancer Cell Reprogramming (CanCell) has been selected by the Research Council as a Norwegian Centre of Excellence (CoE). This means that we will receive substantial funding for 10 years (conditional on a successful midterm evaluation) for pursuing our ambitious goal of reprogramming cancer cells into harmless (or dying) cells. Writing the CoE application was a very positive experience, and the proposal was indeed the result of real teamwork among the 6 principal investigators (PIs) – Harald Stenmark, Anne Simonsen, Jorrit Enserink, Ragnhild Eskeland, Tor Erik Rusten and Jørgen Wesche.

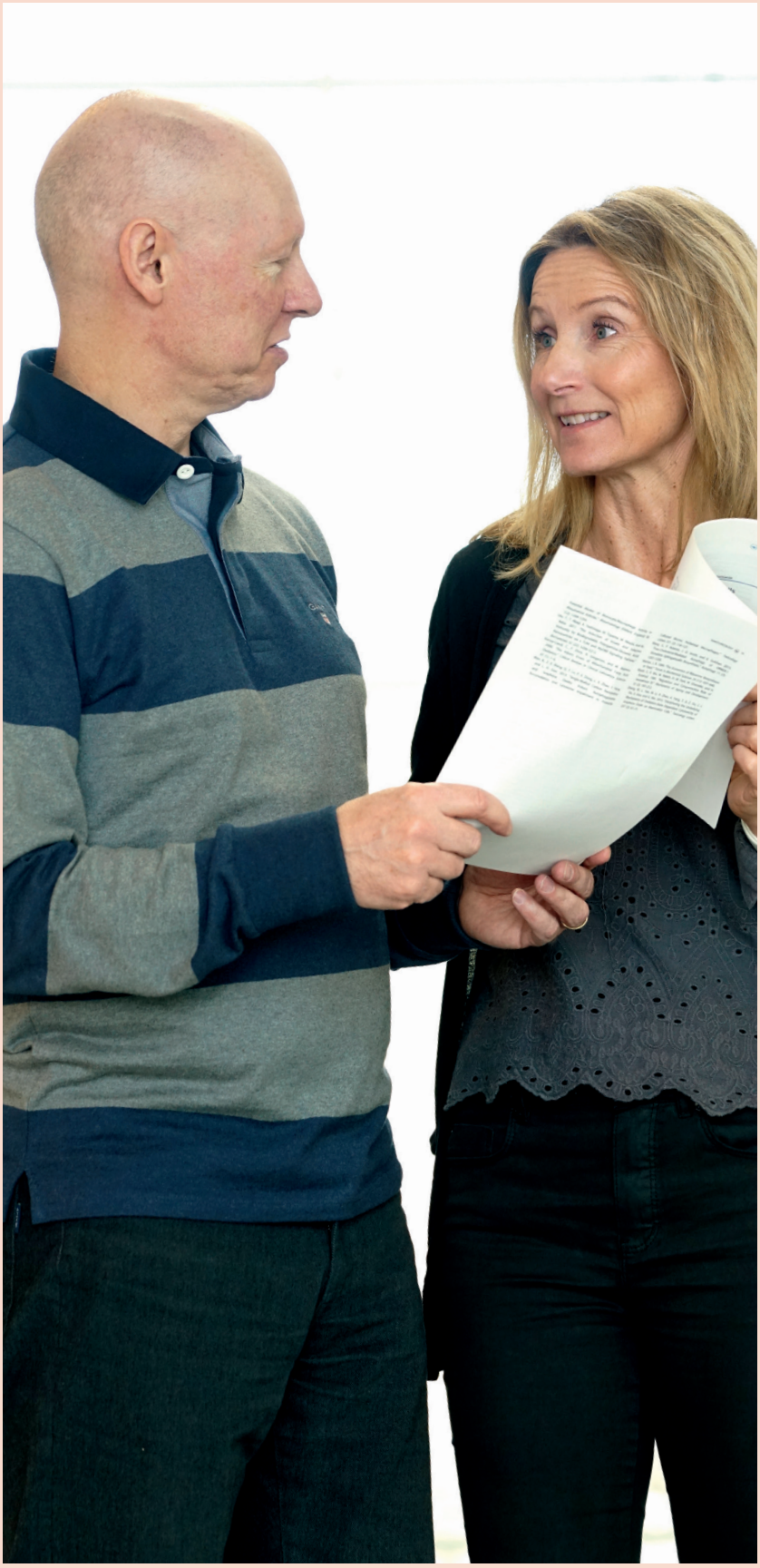
The societal challenge that motivated us was that, even in the era of whole-genome sequencing, personalized cancer medicine has so far proven inefficient. Our joint vision is that deeper knowledge of the cellular pathways that are rewired during cancer progression will enable reprogramming of cancer cells into harmless cells. In order to stimulate collaborations across different areas of cancer cell biology, CanCell's PIs meet every Friday for strategic and scientific discussions, and a number of exciting collaborative projects are now running.

Because modern cancer research requires a highly multidisciplinary approach, CanCell has a team of leading Norwegian scientists as associate members, with expertise that is mostly complementary to that of the PI group. These include Terje Johansen (molecular biology), Philippe Collas (chromatin dynamics), Eivind Hovig (bioinformatics), Arnoldo Frigessi (biostatistics), Emmet Mc Cormack (preclinical cancer models), Åslaug Helland (lung cancer medicine), and Yngvar Fløisand (leukaemia medicine). In addition, CanCell has world-leading visiting professors in Ivan Dikic (cellular membrane dynamics and cell signalling), Eyal Gottlieb (cell metabolism), Eileen White (cell signaling and metabolism) and Kristian Helin (chromatin regulation).

A lot has happened since CanCell's opening in January 2018. CanCell has published 20 papers in 2018, obviously on projects that were initiated prior to the establishment of the centre. These papers have been published in international journals of good reputation, such as *Cell, Nature Communications, EMBO Journal, EMBO Reports*, *Molecular and Cellular Proteomics, and Nucleic Acids Research* (see highlights elsewhere in this report). CanCell PIs have been invited to give 21 talks at international conferences in 2018, and Anne Simonsen co-organized a successful Keystone Symposium on "selective autophagy". Likewise, the centre's junior scientists have been active in presenting their work at conferences both as short talks and posters. CanCell has had 9 visits of excellent international scientists as guest speakers, and international ties have also been strengthened through international exchange of both junior and senior researchers.

Training and career development of junior cancer researchers is one of CanCell's main priorities, and together with 7 other present and former CoEs at University of Oslo, CanCell participates in a career development pilot programme intended at developing and strengthening the CoE's career support for younger scientists. So far, this has resulted in better routines for onboarding and checkout of young scientists, and further initiatives will be taken as the pilot programme continues. We have recently established a forum for young scientists, which will be a forum for both career-related, social and scientific activities. In addition, CanCell has been running a very successful course in scientific blog writing, which has already resulted in 11 blog entries on **www.cancell.no**. CanCell will announce two calls annually for project support for young scientists, the first one in March 2019.

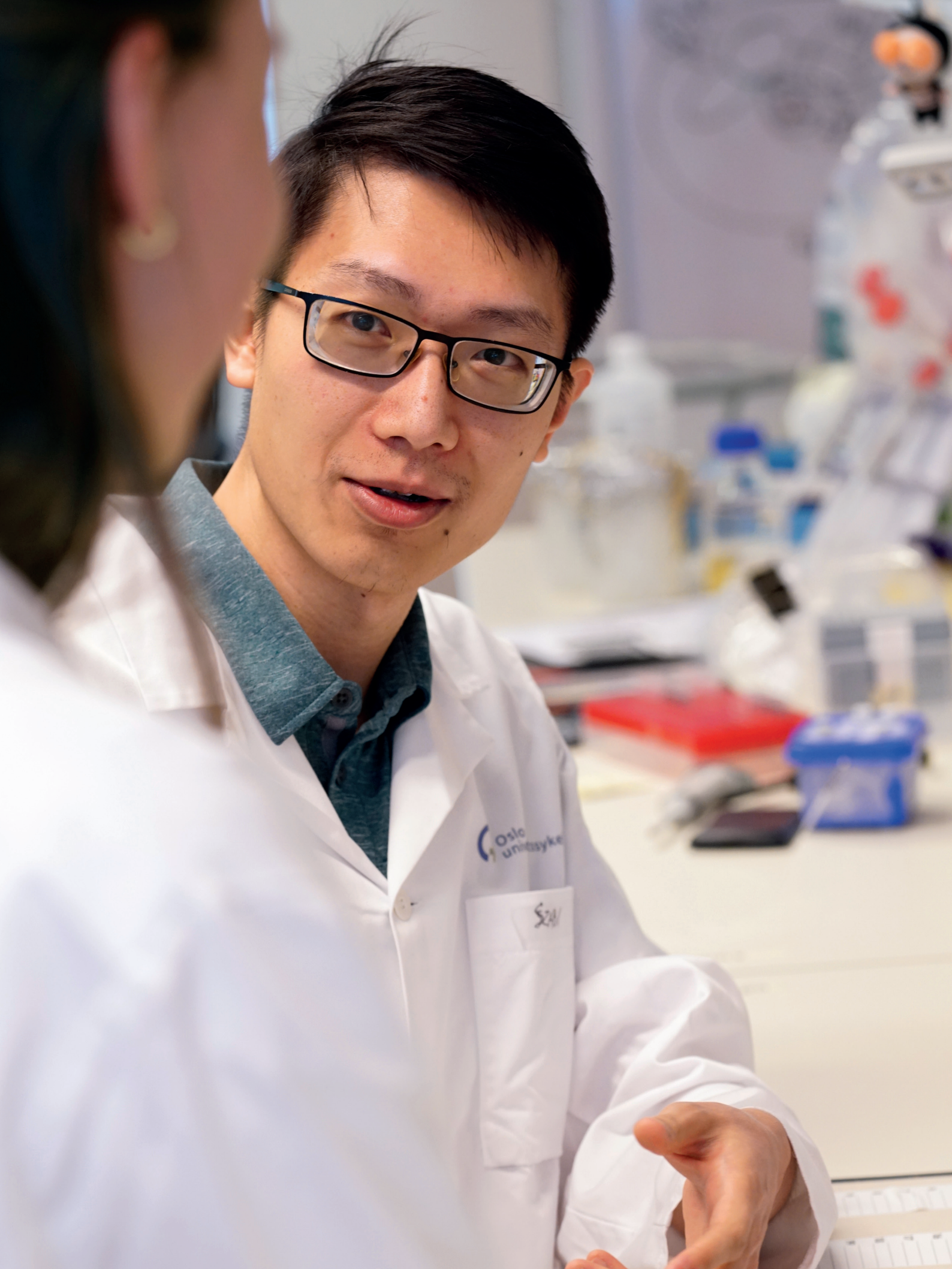
As a Norwegian CoE, CanCell is expected to obtain substantial external funding, and as many as 13 medium or large external CanCell projects were funded in 2018, including an ERC Advanced Grant to Harald Stenmark and a RCN "Toppforsk" grant to Tor Erik Rusten. We are particularly grateful to the Norwegian Cancer



Society and the South-Eastern Norway Regional Health Authority for funding several of our projects. Thanks are also due to our host institutions, the University of Oslo (Faculty of Medicine) and Oslo University Hospital, which provide excellent administrative support and infrastructures. Special thanks to our committee of patient representatives – Astrid Jahr (sarcoma society), Per Axel Ankre (prostate cancer society), Ole Knutzen (lung cancer society) and Trude Wetaas (blood cancer society) - who provide valuable advice from the patient's perspective and motivate our researchers with their own stories.

Looking into the immediate future, a top priority for CanCell is to implement successfully the collaborative projects that have already been initiated, and to launch new collaborations according to CanCell's research plan. We welcome "bottom-up" initiatives from the centre's junior researchers and anticipate that interactions with our associate members and visiting professors will contribute to research that leads us closer to the day when we can make cancer cells harmless.

Harald Stenmark, *director*
Anne Simonsen, *co-director*



RESEARCH GROUPS

Harald Stenmark
Twitter: @harald_stenmark

Stenmark Group

CELLULAR MEMBRANE DYNAMICS

About

The group has 36 members from 12 nations. It combines molecular biology methods such as transgenesis and genome editing in combination with advanced light and electron microscopy to understand the molecular biology that controls cellular membrane dynamics. Models include cell cultures, simple organoid models, invasion assays, and fruit flies.

Current projects (with co-ordinators in parentheses)

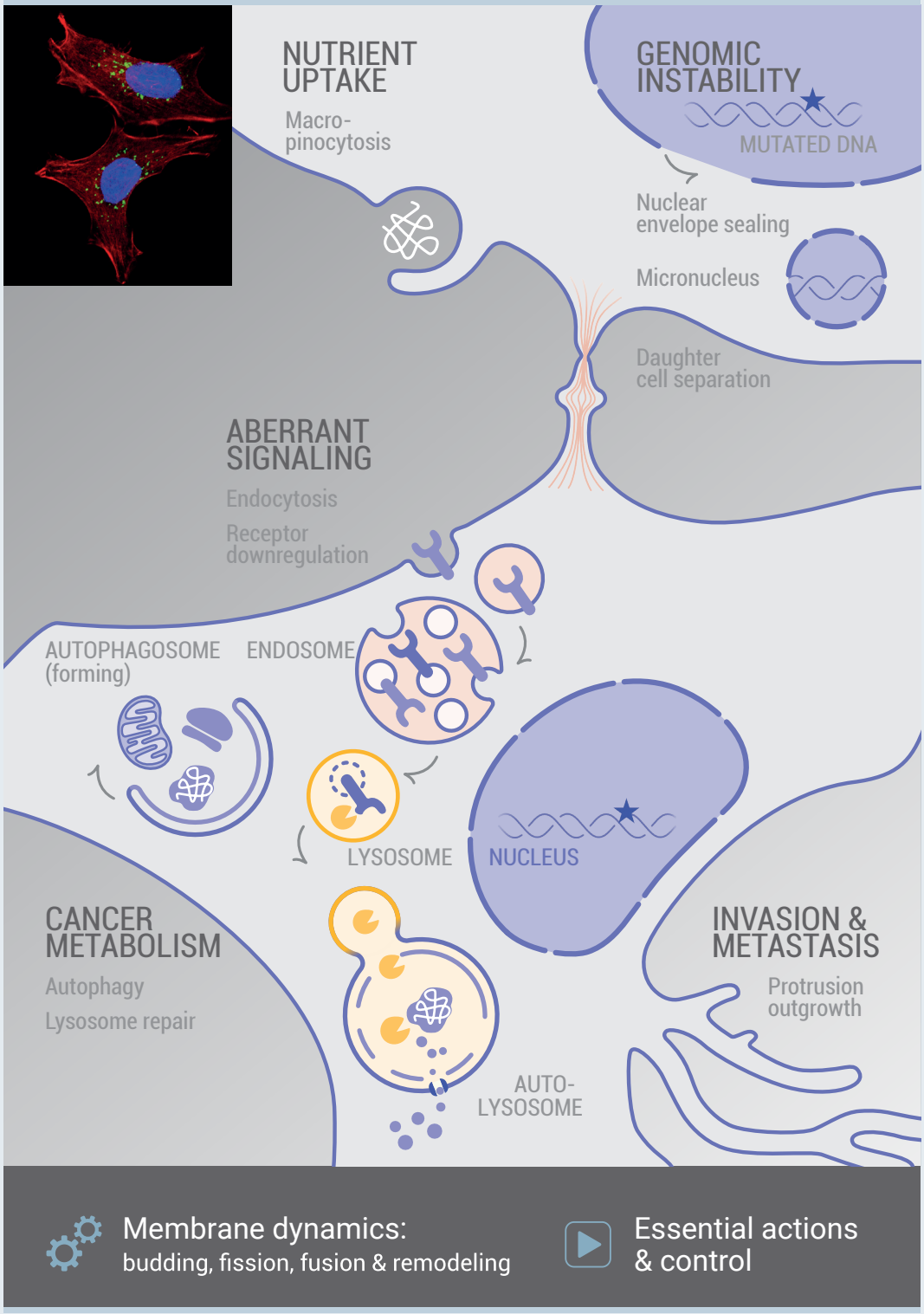
- Endosomal control of metastasis (Harald Stenmark)
- Coincidence detection of proteins and lipids in regulation of cellular membrane dynamics (Harald Stenmark)
- Autophagy and lipid droplets in regulation of cell metabolism (Harald Stenmark)
- Autophagy of large protein assemblies (Andreas Brech)
- Mechanisms and functions of lysosome repair (Harald Stenmark)
- Lysosome dynamics and their involvement in cancer invasion (Camilla Raiborg)
- Nuclear envelope dynamics in maintenance of genome stability (Marina Vietri)
- Phosphoinositides in control of macropinocytosis and endocytic recycling (Kay O. Schink)
- Multi-protein complexes in regulation of Wnt signalling (Eva M. Wenzel)
- Regulation of cytokinetic abscission in vivo (Kaisa Haglund)
- Fruit flies as model for understanding human cancer (Kaisa Haglund)

Recent achievements

- Establishment of protein dynamics during endosomal downregulation of growth factor receptors (Wenzel et al., *Nature Communications* 2018)
- Identification of a novel molecular mechanism for controlling positioning of the mitotic spindle (Malerød et al., *EMBO Journal* 2018)
- Identification of a novel molecular mechanism for repair of damaged lysosomes (Radulovic et al., *EMBO Journal* 2018)
- Research Prize of Oslo University to Harald Stenmark (2018)
- Dr. Ragnar Mørk´s Prize for excellent cancer research to Kaisa Haglund (2018)
- Research grants to Kaisa Haglund and Camilla Raiborg from the Norwegian Cancer Society and to Kaisa Haglund from the Research Council of Norway (2018)
- Advanced Grant from the European Research Council to Harald Stenmark (2018)
- Research Council funding of INTPART partnership with world-leading research laboratories in Beijing and Kunming, coordinated by Harald Stenmark (2018)

Aim

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



Simonsen Group
Twitter: @simonsen_lab

Simonsen Group

AUTOPHAGY

About
The Simonsen group is localized at the Institute of Basic Medical Sciences, Department of Molecular Medicine and includes 13 highly motivated scientists, all with research projects focusing on unraveling the molecular mechanisms involved in autophagy.

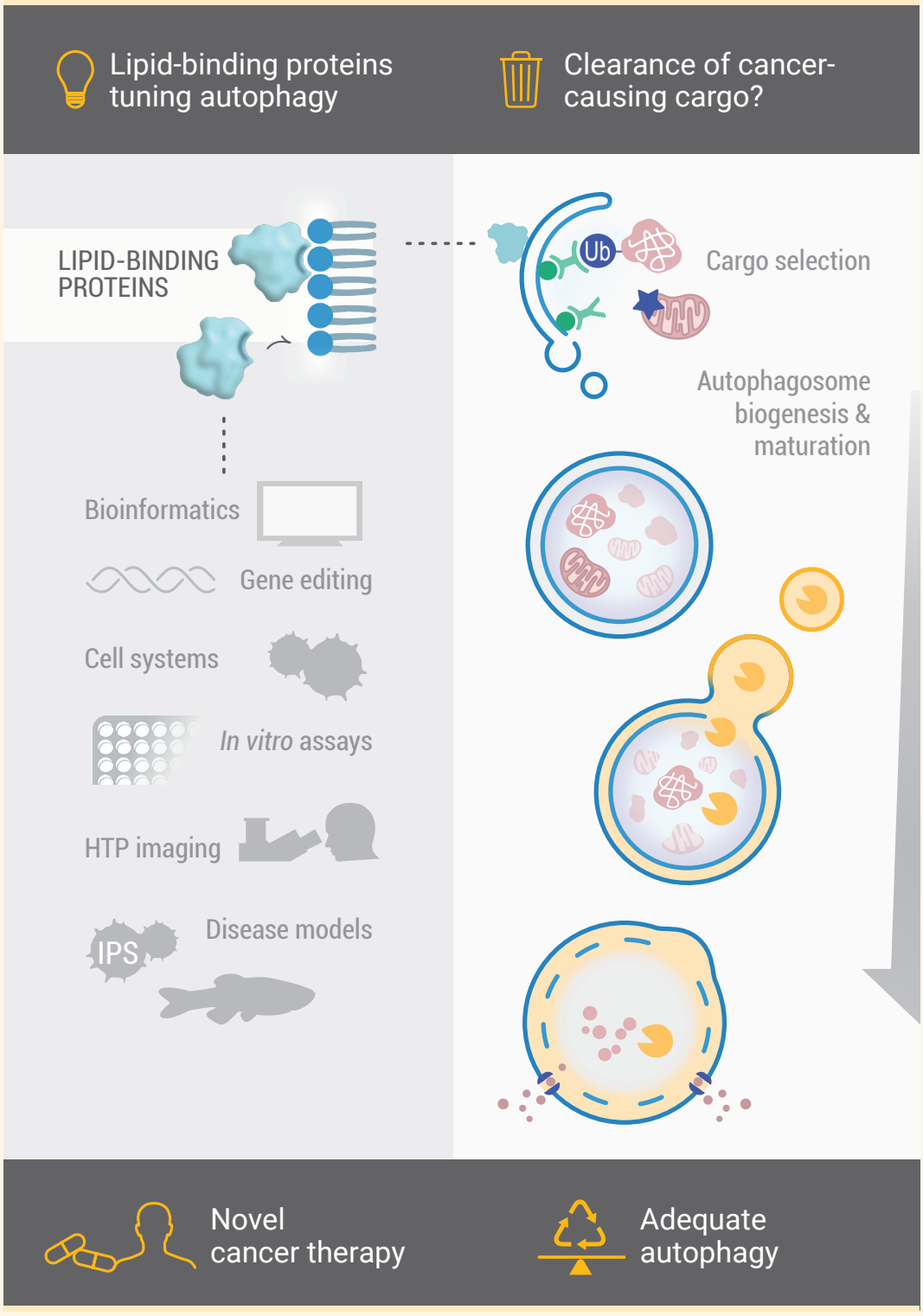
The role of autophagy in tumor suppression or progression is complicated and context-dependent, which makes it important to further characterize the molecular mechanisms underlying autophagy in different types and stages of cancer. Such knowledge might lead to identification of suitable targets for the development of future therapeutics. We use high-throughput imaging screens, in combination with molecular, biochemical and cell biological assays, as well as zebrafish as a model organism, to identify such mechanisms.

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

Recent achievements
- Distinct functions of ATG16L1 isoforms in membrane binding and LC3B lipidation in autophagy-related processes (Lystad et al., *Nat Cell Biol.* 2019)
- NIPSNAP1 and NIPSNAP2 act as "eat-me signals" for mitophagy (Abudu et al., *Dev Cell. In press*).
- ATG9A trafficking from recycling endosomes by recruiting Dynamin-2. (Søreng et al. *EMBO Rep.* 2018)
- Kristiane Søreng received the best paper award of the Department of Molecular Medicine and CanCell, as well as the CanCell annual poster prize
- Matthew Yoke Wui Ng received the poster prize at the Nordic Autophagy Society meeting.
- Benan John Mathai defended his thesis (03.10.2018) entitled: "Novel-modulators of non-selective and selective autophagy".
- 1 DOFI was filed regarding a product to study mitophagy
- Partner in the RCN INTPART project "Chinese-Norwegian Partnership for Education and Research in Cancer Cell Biology (ChiNoCell)" (2018)

Aim

The overall goal of the Simonsen group is to characterize the signals and mechanisms involved in recognition and targeting of cancer-promoting cargo, including damaged mitochondria and aggregate-prone proteins, for degradation by autophagy. In particular, we are interested in the role of lipids and lipid-binding proteins in these processes.



Jorrit Enserink
Twitter: @jenserink

Enserink Group

CANCER MOLECULAR MEDICINE

About

The Enserink group consists of two senior researchers, seven post-docs, two PhD students, six MSc students and one BSc student, in addition to a clinician in a 20% affiliated position. In addition, there are two vacant post-doc positions and one PhD student position that will be filled during 2019.

Most projects in the group employ high-throughput screening methods to gain insight in two main research problems: i) understanding how cells respond to sudden changes in nutrient levels, particularly focusing on reprogramming of transcriptional networks; and ii) development of novel therapeutic strategies that bypass development of drug resistance in leukemia.

Projects

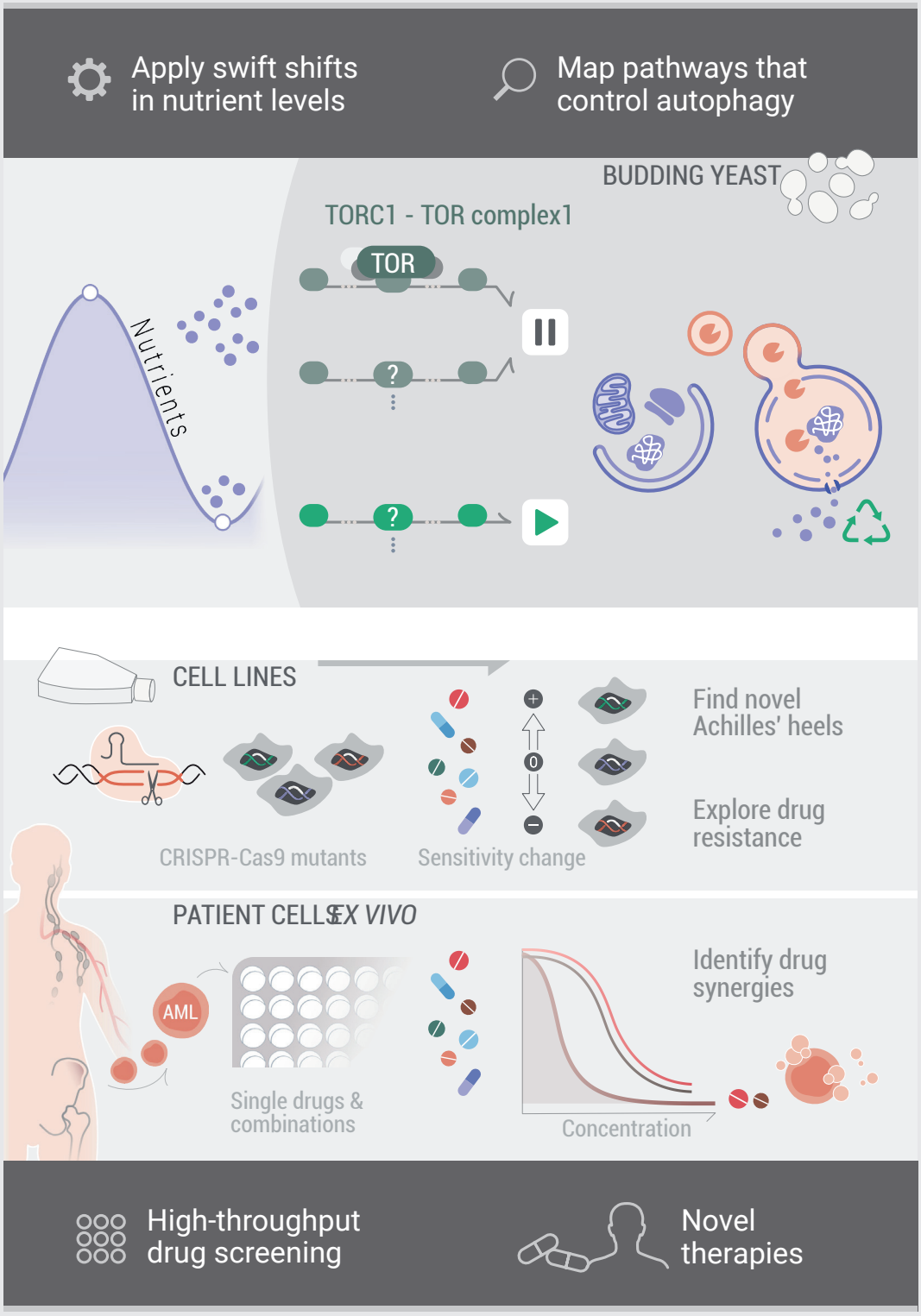
- Identification of the upstream pathways that switch on and switch off autophagy.
- Unraveling genetic networks that determine the response of cancer cells to anticancer drugs using genome-wide CRISPR/Cas9 screens.
- Identification of synergistic drug combinations to overcome drug resistance of cancer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

Recent achievements

- Centromeres License the Mitotic Condensation of Yeast Chromosome Arms (Kruitwagen T*, Chymkowitch P* *et al. Cell.* 2018).
- Cdk1 gates cell cycle-dependent tRNA synthesis by regulating RNA polymerase III activity (Herrera MC *et al. Nucleic Acids Res.* 2018).
- TORC1-dependent sumoylation of Rpc82 promotes RNA polymerase III assembly and activity (Chymkowitch P *et al. Proc Natl Acad Sci U S A.* 2017).
- Norwegian Research Council, Centre for Digital Life, Biotek2021 program (2019-2023, 19.9 MNOK, with Prof. Arnoldo Frigessi and Prof. Kjetil Tasken): "Pipeline for individually tailoring new treatments in hematological cancers"
- Norwegian Health Authority South-East (2019-2021; 3.7 MNOK): "Evading drug resistance in cancer treatment" Norwegian Health Authority South-East, Innovation grant (2019, 0.5 MNOK). "Development of Novel Immune Therapy for Acute Myeloid Leukemia".
- Norwegian Health Authority South-East, awarded to senior scientist Nacho Garcia (2019-2021, 3.3 MNOK). "Development of Novel Antimycotics to Treat drug-resistant Fungal Infections in Leukemia Patients"
- Senior scientist Helene Knævelsrud was elected to the Young Academy of Norway.

Aim

- Unraveling the regulation of nutrient responses using the model organism budding yeast.
- Development of new strategies for treatment of leukemia, with particular focus on drug resistance.



Ragnhild Eskeland
Twitter: @EskelandLab

Eskeland Group

CHROMATIN BIOLOGY

About
The Eskeland group consists of two researchers, two postdocs, two PhD students, five master students and one engineer from 9 nations.

The goal of the Eskeland group is to understand how chromatin organization is disrupted in the context of genomic variation and epigenetic remodeling in cancer to unravel molecular mechanisms that can form the basis for new novel therapy strategies. Nuclear shape and chromatin organization are frequently abrogated in cancer. Thus, nuclear structure is well known diagnostic hallmark of many cancers, but the underlying mechanisms are poorly understood. An important feature of epigenetic mechanisms is that, in contrast to genetic factors, they are reversible and thus can be changed upon exposure to stimuli. Identification of underlying epigenetic mechanisms in cancer cells will therefore be an essential component in understanding chromatin organization and function in tumour development and promote earlier diagnosis and more efficient cancer treatments.

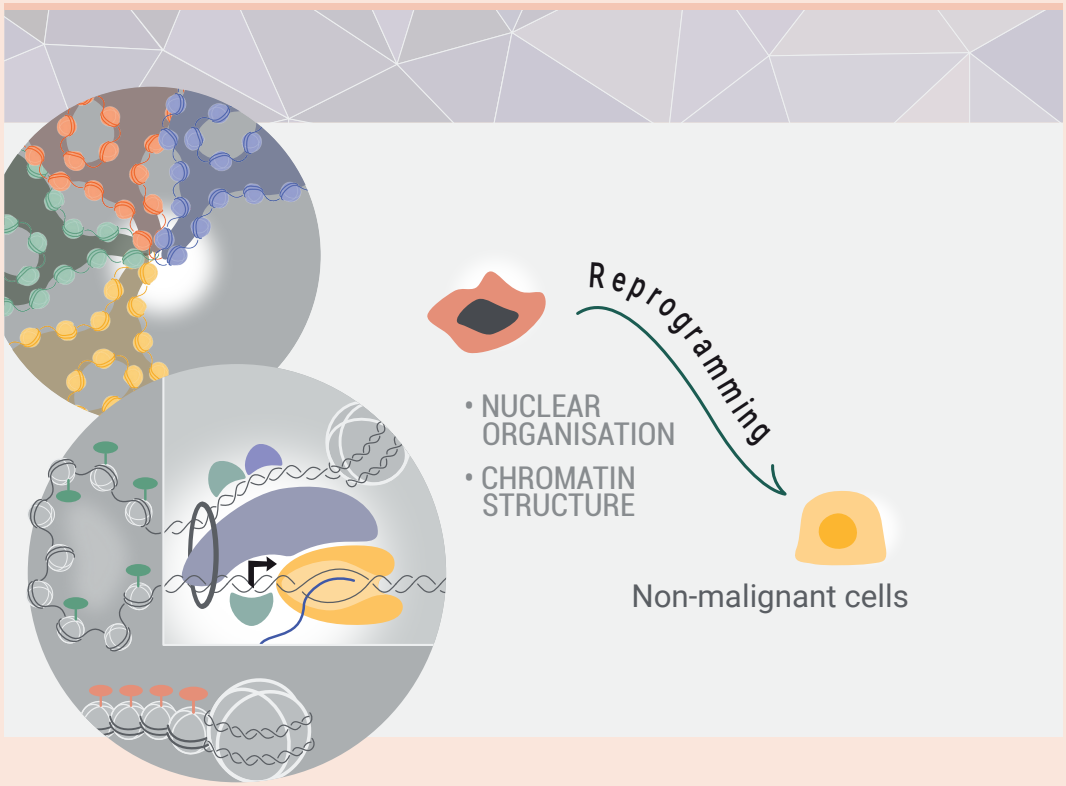
To achieve this goal we have established various molecular and biochemical methods in the lab to assess the cancer specific epigenetic remodeling. This includes state-of-the-art assays such as the auxin-inducible degron (AID) system and genome editing by CRISPR targeting, super-resolution and live-cell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

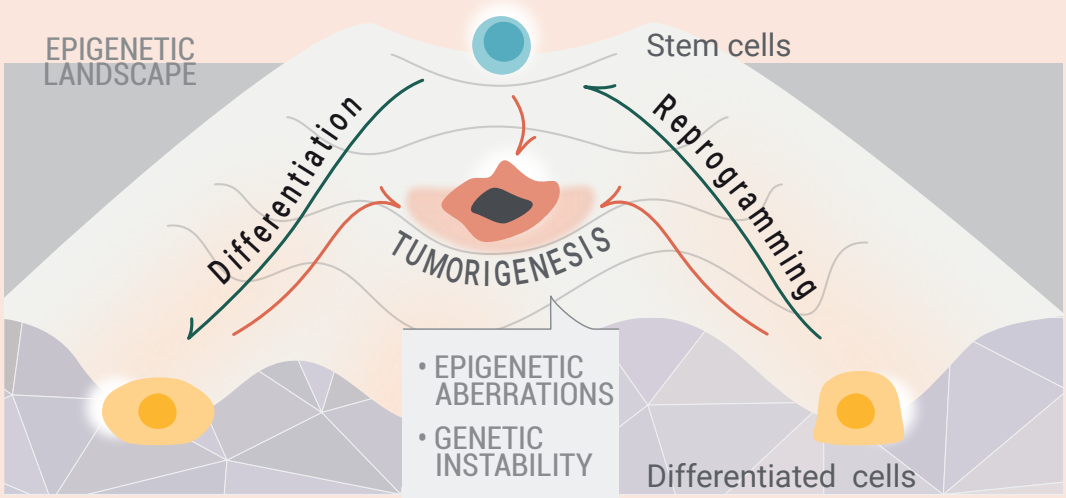
Projects
- Characterization of carcinogenic chromatin remodelling alterations and driver mutations of chromatin regulatory factors in Sarcomas
- Gene regulation and chromatin organization in prostate cancer
- Regulation of histone variants in breast cancer
- Live-cell chromatin dynamics and function (ImageCRISPR, FRIPRO NFR)

Recent achievements
- Eskeland hired as Associate Professor at Institute of Basic Medical Sciences, MedFak, UiO in September 2018.
- Eskeland is co-applicant and member of management committee of a new COST Action CA18127: *"International Nucleome Consortium"*.
- The pioneer factor activity of c-Myb involves recruitment of p300 and induction of histone acetylation followed by acetylation-induced chromatin dissociation. (Fuglerud et al.)
- *Epigenetics Chromatin.* 2018)
- The SUMO protease SENP1 and the chromatin remodeller CHD3 interact and jointly affect chromatin accessibility and gene expression (Rodríguez-Castañeda et al. *J Biol Chem.* 2018).

Aim

Our aim is to investigate how chromatin organization is disrupted in the context of genomic variation and epigenetic remodelling in cancer to unravel molecular mechanisms that can form the basis for new novel therapy strategies.





Epigenetic discoveries

Epigenetic modulation

Tor Erik Rustenlab
Twitter: @rustenlab

Rusten Group

TUMOR-HOST BIOLOGY

About
Current group size is 11 (1 PI, 2 senior researchers, 4 postdocs, 1 PhD student, 2 master students, 1 technician).

Our overarching interest is to understand the mechanisms by which tumor and host cells mutually engage each other in reciprocal interactions to facilitate carcinogenesis. These interactions occur locally in the tumor microenvironment, but also 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 of tumor growth.

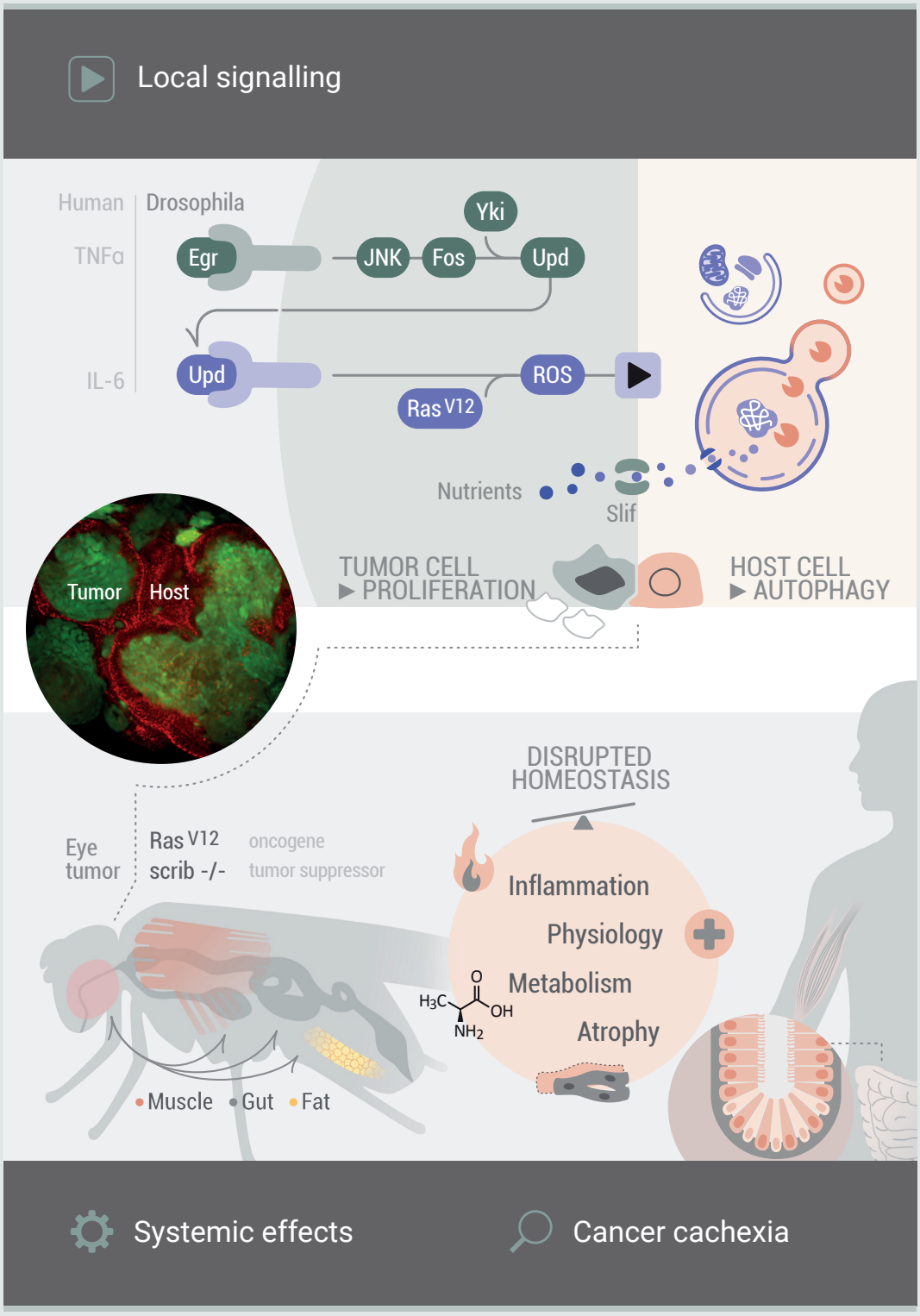
In order to mechanistically understand how tumor cells and non-tumor cells and organs communicate to foster tumor growth and cause cancer cachexia we develop novel genetic tools in Drosophila. These tools allow us to selectively and independently manipulate tumor and either tumor microenvironment or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

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 (OUS, clinical cachexia), Åslaug Hellland (OUS, clinical cachexia), Eivind Hovig (OUS, bioinformatics), Eyal Gottlieb (TICC, Haifa, Israel, metabolism), Heinrich Jasper (Genetech, California, US, organ-organ communication), Rita Sousa-Nunes (Kings College, London, UK, genetics tumor-host communication)

Recent achievements
- Discovery that malignant tumors induce a stress response in the tumor microenvironment that supports tumor growth through nutrient-generating autophagy (Katheder, N.S., et al, *Nature 2017*).
- The tumor suppressor LKB1, responsible for the Peutz-Jegher cancer syndrome, is controlled by endocytic vesicle trafficking and its derailment contributes dysplasia and tumor growth (O´Farrell, F. et al. *Nature Cell Biology, 2017*).
- "Toppforsk" grant (Norwegian Research Council, 25 MNOK, 5 years 2018-2022), Research project (Helse Sør-Øst, 8 MNOK, 3 years 2018-2020)

Aim

- Uncover mechanisms of oncogene-induced epithelial disintegration and delamination using in vivo (Drosophila melanogaster) and in vitro (human organoid cell culture) approaches.
- Uncover how tumor-microenvironment interactions foster tumor growth in vivo (D. melanogaster).
- Uncover molecular mechanisms of cancer cachexia in vivo using the animal model Drosophila melanogaster.



Jørgen Wesche
Twitter: @Wesche_Lab

Wesche Group

MOLECULAR BIOLOGY OF SARCOMAS

About
The group has 11 members and has its focus on the development of precision medicine for sarcoma patients.

To achieve this, the group has broad expertise in basic cell biology and translational research and, importantly, one MD in a shared clinical position. The group uses modern sequencing methods to genetically characterize sarcoma patient material to identify and monitor druggable targets. Advanced proteomics methods are applied to study oncogenic sarcoma signalling. Sarcoma cell and mouse models are used to test anti-cancer drugs.

Projects

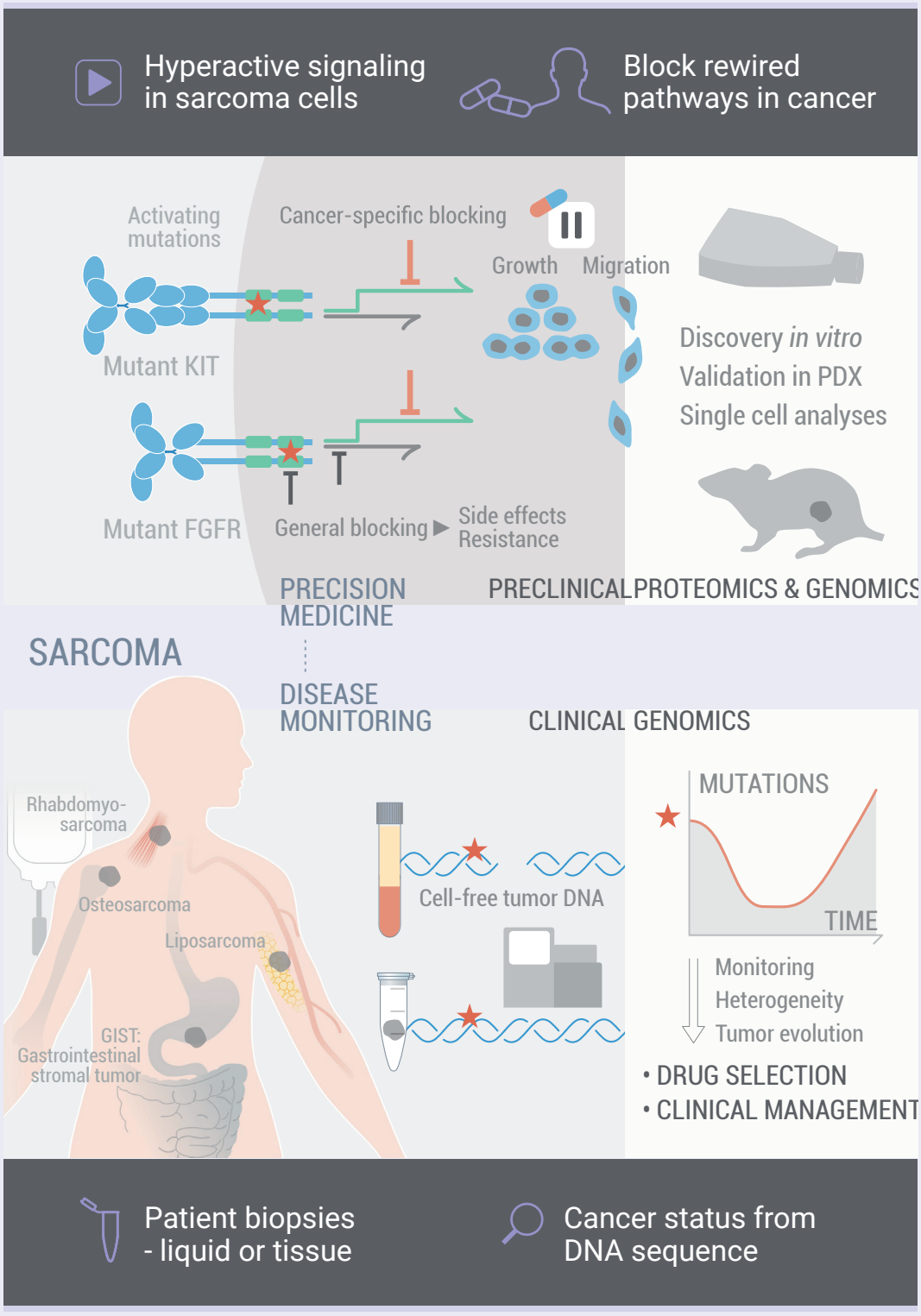
- Study the role of fibroblast growth factor receptor (FGFR) signalling in rhabdomyosarcoma, liposarcoma and osteosarcoma. By detailed understanding of oncogenic FGFR signalling, we hope to identify new strategies to inhibit sarcomas and other cancers dependent on FGFR signalling.
- Using "liquid biopsies", as a non-invasive method for detection of tumour-derived DNA in blood, to monitor disease progression, treatment response and tumour evolution.
- 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.

Recent achievements

- We have found that the tyrosine phosphatase PTPRG controls FGFR signalling and influences the activity of FGFR kinase inhibitors (Kostas et al., *Mol Cell Proteomics 2018*).
- Non-invasive analysis of circulating tumour DNA (ctDNA) was employed to analyse the progression and heterogeneity of gastrointestinal stromal tumors (GIST) (Namløs et al., *Mol Cancer Ther 2018*).
- Research grants to Jørgen Wesche and Leonardo Meza-Zepeda were obtained from the Norwegian Cancer Society and to Kjetil Boye and Leonardo Meza-Zepeda from the Southern and Eastern Regional Health Authority.
- 1 DOFI was filed regarding the exploration of a method to target cancer cells overexpressing FGFRs.

Aim

We aim to unravel new oncogenic mechanisms in sarcomas. Genetic and proteomic screens in sarcoma cells and models lay the basis for the discovery of cancer cell programs that can be targeted.



ASSOCIATED MEMBERS

Eivind Hovig

Eivind Hovig

Computational Cancer Genomics and Melanoma Systems Biology

We have, with support from the University Center for Information Technology (USIT), established a computing server for CanCell, which provides support for large-scale scientific computing and storage of high-throughput datasets (primarily cell imaging, transcriptomics, genomics). We are continuously maintaining and expanding the software portfolio available on the server, driven by the various needs of CanCell scientists.

We are collaborating with the Eskeland group with respect to a mechanistic analysis of copy number events in cancer, and how these can disrupt chromatin domains and the three-dimensional nuclear genome organization. Using soft tissue cancers (sarcoma) as the disease model, we have screened "The Cancer Genome Atlas" (TCGA) for significant copy number amplifications of genes with chromatin-regulatory functions. In addition, a whole-genome sequence of a liposarcoma cell line has been analyzed for focal copy number breakpoints, which is making the foundation for downstream experiments (Hi-C, ChIP-Seq etc) initiated by the Eskeland lab.

A high-throughput screen to identify synergistic drug combinations in melanoma have been initiated in collaboration with the Enserink group. A total set of 18 different melanoma cell lines available from the Hovig group have been the subject of genomic and transcriptomic characterization (kinome and exome sequencing and RNA-seq). The Enserink group is piloting the robustness and reproducibility of the drug screening assay.

We are establishing a prototypic web-based tool for the interrogation and prioritization of cancer relevance among a set of human candidate proteins, e.g. as found through (phospho)-proteomics screens performed by CanCell groups (e.g. Wesche/Simonsen). Public resources on known protein-protein interactions (BioGRID), evidence on protein subcellular localizations (COMPARTMENTS), and the landscape of genomic tumor aberrations (TCGA) are integrated in a manner that permits interactive visualization and ranking of cancer-related targets in the context of the underlying cell biology.

Sigve Nakken has been a key driver in these undertakings.

Emmet Mc Cormack

Emmet Mc Cormack

Translational Molecular Imaging in Cancer (UiB)

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.
- Through the InoVa project, the group is developing the application of imageguided surgery, whereby fluorescent dyes will target biomarkers on surgically amenable cancers to aid their greater resection.

Terje Johansen

Terje Johansen

Molecular Cancer (UiT)

The Molecular Cancer Research Group, Institute of Medical Biology, University of Tromsø – The Arctic University of Norway led by professor Terje Johansen performs basic research with main focus on molecular mechanisms and roles of selective autophagy in cell signaling and disease. The group consists of 17 dedicated people. Our work on the signaling scaffold protein p62/SQSTM1 led to the discovery of autophagy receptors that specifically direct protein aggregates, organelles, nucleic acids and pathogens for degradation in the lysosome. Autophagy is an evolutionary conserved renovation process in cells, acting as a key regulator of cell survival or death in response to a variety of internal and external signals. Disabled autophagy plays a major role in human diseases including cancer, heart failure, metabolic, inflammatory and neurodegenerative diseases. The Norwegian Cancer Society and the Norwegian Research Council in addition to the support we receive from UiT fund our research.

Following our discovery of the first mammalian selective autophagy receptors p62/SQSTM1 and NBR1 we have focused our research on selective autophagy. We have enjoyed a long standing close contact and collaboration with the groups of Harald Stenmark, Anne Simonsen and Tor Erik Rusten in CanCell and have published a number of papers together with these groups from 2005 and onwards. Andreas Brech has been heavily involved in all of our published studies involving electron microscopy. In 2018 we published a paper in J. Cell Biology on the finding that amino acid starvation induces rapid degradation of selective autophagy receptors by endosomal microautophagy involving ESCRT-III components together with Harald Stenmark and Andreas Brech. Throughout 2018 we have worked together with Anne Simonsen and her group on a large study on the role of NIPSNAP1 and -2 proteins as “eat me” signals for autophagic degradation of damaged mitochondria (*in press* in Developmental Cell).

Arnoldo Frigessi

Arnoldo Frigessi

Stochastic Models and Inference

Arnoldo Frigessi is professor of statistics at the University of Oslo, leads the Oslo Center for Biostatistics and Epidemiology and is director of BigInsight. BigInsight is a centre of excellence for research-based innovation, a consortium of industry, business, public actors and academia, developing model based and machine learning methodologies for big data. Frigessi and his group develop statistical methodology and stochastic models to study principles, dynamics and patterns of complex dependence in biomedicine. Inference is usually based on computationally intensive stochastic algorithms. Frigessi's research has focused on Bayesian statistics, both methodological and applied. Currently, he has research collaborations in genomics, personalised therapy in cancer, infectious disease models, eHealth research, but also in personalised and viral marketing, sensor data and recommender systems. He has published more than 100 papers in peered reviewed journals and has supervised 41 PhD students and 14 postdocs.

Recent achievements

- A multi-scale pharmacokinetic and pharmacodynamic model informed by multi-type patient data for personalized computer simulation of breast cancer treatment.
- A new Bayesian parametric model for integrative, unsupervised clustering across data sources, with application to a Norwegian breast cancer cohort of ductal carcinoma in-situ and invasive tumors, comprised of somatic copy-number alteration, methylation and expression data

Frigessi is involved in integration biostatistical methods for large scale omics-studies within CanCell.

Åslaug Helland

Åslaug Helland

Translational Research on Solid Tumours

Our group of 17 members consist of both oncologists and biologists, and we focus our studies on molecular analyses on biological material from patients included in clinical studies. We have studies on pancreatic cancer, lung cancer and colorectal cancer. We have several investigations initiated clinical trials ongoing. Predictive and prognostic biomarkers can be of great importance for treatment stratification, and we have investigated microRNA and proteins in both tumour tissue and blood samples. We have also investigated the immunological tumour microenvironment analysing expression profiles, immunohistochemistry and flow cytometry. This is of special interest in lung cancer, where some patients have a long-lasting effect, while many patients do not respond.

We have recently identified protein profiles in lung cancer samples pointing at a role for the PKC group of proteins and have initiated a collaboration with Professor Anne Simonsens group aiming at elucidating the roles of PKCs in lung cancer.

Ex vivo drug screening of tumour cells is already established in collaboration with Jorrit Enserink's group. This drug panel includes currently approved lung cancer drugs, many FDA/EMA-approved anticancer compounds, and a large collection of emerging drugs. The group has performed pilot assays on several lung cancer patient samples, providing proof of principle of this method for lung cancer.

Yngvar Fløisand

Yngvar Fløisand

Hematology and Acute Myeloid Leukemia

Yngvar Fløisand is senior consultant hematologist at Oslo University Hospital. His main research areas are in acute myeloid leukemia (AML) and allogeneic stem cell transplantation, especially with regard to acute graft versus host disease. AML is a cancer of the myeloid line of blood cells, characterized by the rapid growth of abnormal cells that build up in the bone marrow and blood and interfere with normal blood cells.

He is running several clinical trials in first line treatment of AML, maintenance treatment and treatment of relapsed/refractory AML. He is currently also running trials in the prophylaxis and treatment of acute graft versus host disease. Recent studies include vedolizumab-efficacy and integrin implications in graft-vs-host disease establishment and mAB-development for blood cancer treatment.

As an associate member, he is collaborating with the group of Jorrit Enserink in basic biology of acute and chronic leukemias, especially with regard to ex vivo drug sensitivity testing and elucidating basic pathogenetic mechanisms. He has also been involved in CanCell's establishment of a user panel of cancer patients for basic, translational and clinical research input.

Philippe Collas

Philippe Collas

Chromatin Regulation in Adipose Stem Cells

The 3- and 4-dimensional layout of chromatin plays important roles in the establishment and control of gene expression programs that govern cell fate decisions. These programs are altered in disease contexts. Our laboratory studies how disease states such as metabolic syndrome and cancer affect the spatial conformation of the human genome at multiple scales – that is, at the nucleus level, and at the gene locus level. We are addressing how changes in 3D genome conformation regulate adipose differentiation, mutations in nuclear lamins and histones affect nuclear architecture, sugars and fatty acids regulate gene expression and cells regulate the nuclear envelope and genome integrity.

Our work combines molecular, high-throughput genomics and cell imaging approaches, as well as developments in computational genome modeling, using patient material and engineered stem cells.

In collaboration with CanCell researchers, we are investigating:

- the mechanisms of changes in spatial genome conformation during somatic stem cell differentiation (*postdoc Thomas Germier, co-funded by UiO and CanCell*)
- the role of regulators of autophagy in the nucleus
- the impact of the spatial distribution of cancer-linked mutations and genetic variants on genome organization and function in pediatric gliomas, breast cancer and liposarcoma

Recent achievements

- Computational 3D genome modeling using Chrom3D (Paulsen et al. P. *Nature Protoc 2018*)
- Ribosomal DNA copy loss and repeat instability in ATRX-mutated cancers. (Udugama et al. *PNAS 2018*)
- The lipodystrophic hotspot lamin A p.R482W mutation deregulates the mesodermal inducer T/Brachyury and early vascular differentiation gene networks. (Briand et al., *Hum Mol Genet 2018*)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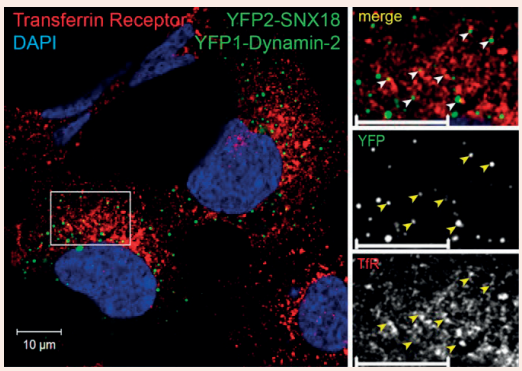
SCIENTIFIC HIGHLIGHTS

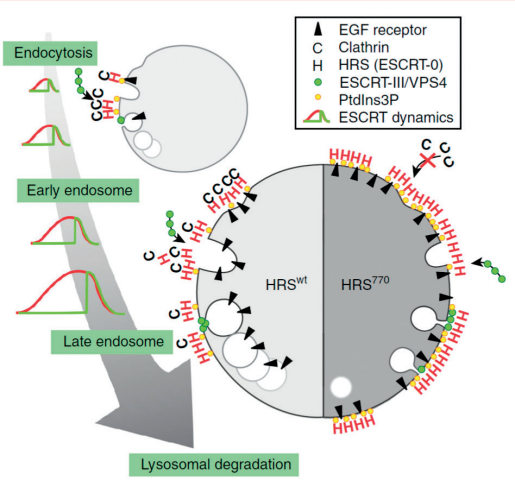
Although 2018 was the inaugural year for CanCell, several major scientific achievements were made. Here is a presentation of the three papers awarded 'Best Article' at the Annual Meeting



The split-YFP bimolecular fluorescence complementation assay reveals that SNX18 and Dynamin-2 interacts in close proximity to TfR-positive recycling endosomes

Regulation of autophagosome biogenesis involves trafficking of mammalian ATG9A between the Golgi apparatus, endosomes and peripheral compartments.
Paper from Kristiane Søreng from the Simonsen group in *EMBO Reports* (EMBO Rep. 2018 Apr;19(4).

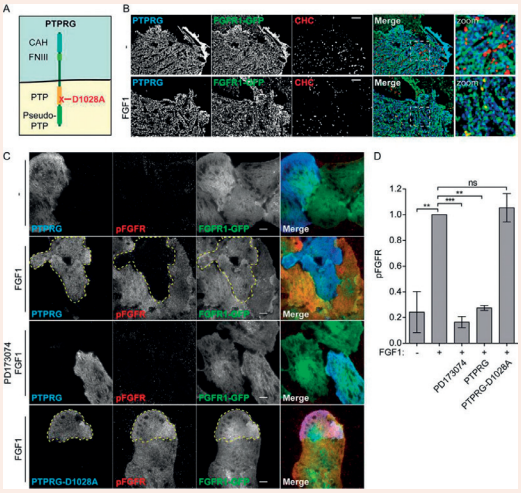
Søreng and co-workers have reported that the membrane remodelling protein SNX18, previously identified as a positive regulator of autophagy, regulates ATG9A trafficking from recycling endosomes by binding to Dynamin-2. Their data support a model where upon autophagy induction, SNX18 recruits Dynamin-2 to induce budding of ATG9A containing membranes from recycling endosomes that traffic to sites of autophagosome formation.



Model of ESCRT-dependent ILV formation and the role of clathrin

Timing of growth factor receptor downregulation. Article from Eva Wenzel from Stenmark groups in *Nature Communications* (Nat Commun. 2018 Jul 26;9(1):2932.

Binding of growth factors to their receptors is known to cause endocytosis and degradation of the receptors and their ligands by a mechanism that involves the endosomal sorting complex required for transport (ESCRT) machinery. Failure of this mechanism can lead to cancer development. The team led by project leaders Eva Wenzel and Camilla Raiborg has used advanced microscopy methods to reveal the dynamics of ESCRT recruitment and formation of multivesicular endosomes (MVEs) into which the receptor-ligand complexes are sorted for subsequent degradation.



TIRF images of U2OS-R1-GFP cells transfected with MYC-FLAG-tagged PTPRG or PTPRG-D1028A, and stimulated with FGF1 in the presence of heparin or FGFR1 tyrosine kinase inhibitor PD173074, as tweeted by the MCP journal when published.

Protein Tyrosine Phosphatase Receptor Type G (PTPRG) Controls Fibroblast Growth Factor Receptor (FGFR) 1 Activity and Influences Sensitivity to FGFR Kinase Inhibitors. Publication from Michal Kostas in the Wesche group in *Molecular & Cellular Proteomics* (MCP) (Mol Cell Proteomics. 2018 May;17(5):850-870).

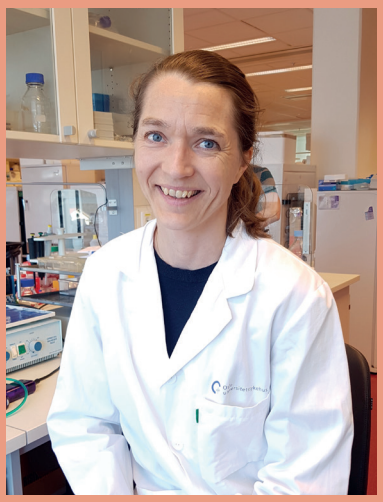
Although it is well known that FGFR1 plays crucial physiological roles and is an important oncogene in several cancers, the mechanism of how the receptor is regulated after activation remains largely unknown. Kostas, Haugsten, Zhen and co-workers have performed a proteomic study of FGFR1 in osteosarcoma cells. The team identified the protein tyrosine phosphatase receptor type G (PTPRG) as an important regulator of FGFR activity. PTPRG regulates sarcoma cancer cell growth, and interestingly, seem to be a determinant for the efficacy of FGFR kinase inhibitors. Thus, the expression level of PTPRG in cancer cells may have future clinical relevance by being a predictor of the success of kinase inhibitor treatment.

AWARDS

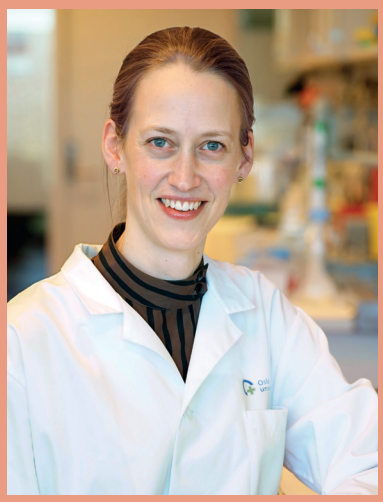
- **Nadja Katheder** from Tor Erik Rusten's group at the Centre for Cancer Cell Reprogramming was awarded H.M. the King's Gold Medal 2018 for best thesis of the Faculty of Medicine. It was the third time in four consecutive years that a PhD student from the Centre for Cancer Biomedicine (CCB) or the Centre for Cancer Cell Reprogramming (CanCell) environments receives H.M. the King's Gold medal, as Sigrid Bratlie Thoresen and Marina Vietri won this medal in 2015 and 2016 respectively.

Nadja Katheder at the doctoral conferment ceremony where she received the HM King's Gold Medal with supervisor Tor Erik Rusten

- Harald Stenmark received the UiO research prize. The prize was awarded by the University Board for Stenmark's excellent research within the field of cancer and cell biology.
- The 2018 Dr. Ragnar Mørk's legacy prize went to **Kaisa Haglund**, head of the Cytokinesis in development and carcinogenesis project group at the Department of Molecular Cell Biology, for her outstanding research on cell division and cancer.
- This year one of the recipients of the OUH's excellent articles award was **Fergal O'Farrel**, scientist at Tumor-Host Biology group, for his article on PI3K control over LBK1 regulation in fruitflies. The works reflect the good quality and the interdisciplinary that characterizes several research environments at Oslo University Hospital and is presents important finding on both-short and long-term scales.
- The Academy for Young Scientists extended their membership to include 8 new members for the period 2018-2022. Among the carefully selected members is CanCell's **Helene Knævelsrud** from Jorrit Enserink's group at the Department of Molecular Cell Biology. Helene was also granted a Nansen Foundation-funding for her work on fruitfly model for leukemia treatment.
- **Kristiane Søreng** in the Autophagy group received the best paper award of the Department of Molecular Medicine at the Institute for Basic Medical Sciences for her paper on SNX18 in EMBO Reports.
- Several junior CanCell members have given short talks at international conferences in 2018, and PhD student **Anette Lie Jensen** from Stenmark's group won the "best short talk award" at the Biochemical Society conference "new horizons in ESCRT biology" in London.
- PhD student **Matthew Yoke Wui Ng** won the "best poster award" at the Nordic Autophagy meeting in Riga. He is a member of Anne Simonsen's group.
- Marketa Chubnova (master student in the Enserink lab) won Gold medal for Best diagnostics project while participating at iGEM in Boston in November.

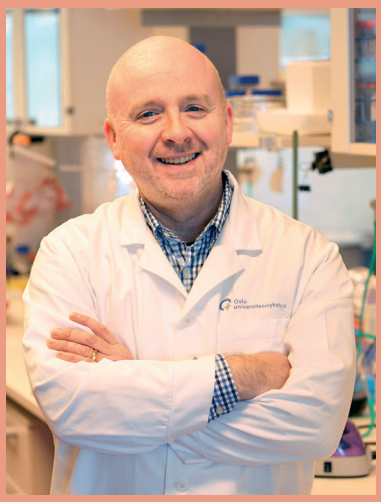


Kaisa Haglund



Helene Knævelsrud

Anette Lie Jensen



Fergal O´Ferral

Kristiane Søreng

Matthew Yoke Wui Ng

Educational activity

During the year, CanCell was involved in three events bringing science to high school students. The fly facility at CanCell hosted Tiril Garshol, high school student at Oslo By Steinerskole, for a research project related to genetics. At Grefsen High School young research talents (9-13 years) presented their research at the Science Fair "Hvorfor det?" where Helene Knævelsrud and Tor Erik Rusten participated as judges. In addition, Max Tau German School in Oslo received a visit from our 5 German scientists to improve both understanding of science and language. The members of CanCell have teaching duties both domestically and abroad. Anne Simonsen and several of her group members participate in lectures and courses for The Medical School at UiO, where also Ragnhild Eskeland, Tor Erik Rusten and Harald Stenmark held lectures. In addition, Anne was invited to give lectures at The Spanish National Research Council in Madrid. Jorrit Enserink is a course leader at Faculty of Natural Sciences at UiO, and both Ragnhild and Tor Erik lectured at several courses on different levels at the same faculty.

Disputation

M.Sc. Benan John Mathai from Anne Simonsen's group in CanCell defended his thesis "Novel-modulators of non-selective and selective autophagy" on October 3. His trial lecture was titled "Using model organisms to determine the physiological implications of autophagy" and Ian Ganley (School of Life Sciences, University of Dundee) and Claire Russel (Royal Veterinary College, University of London) opposed him. He was the first PhD granted at CanCell.

Conferences

All CanCell PIs have been invited to visit international laboratories in 2018. Harald Stenmark was invited speaker at 7 international conferences in 2018, including FASEB, Biochemical Society and Keystone conferences. Anne Simonsen co-organized the Keystone Symposium on "Selective autophagy" in Kyoto in 2018 (280 participants), and was invited speaker at 8 high-profile international conferences in 2018, such as the Keystone Symposium on Selective autophagy, Gordon Research Conference on autophagy and the Cold Spring Harbor Symposium on autophagy. Jorrit Enserink was invited speaker at a FASEB conference in Steamboat, Colorado, "Cell Signaling in Cancer: from Mechanisms to Therapy". Researcher/clinician Kjetil Boye in Jørgen Wesche's group was invited speaker at the Connective Tissue Oncology Society Annual Meeting in Rome. Tor Erik Rusten was invited speaker at 4 conferences in 2018, including the Gordon conference on Autophagy, the Cold Spring Harbor Laboratory Banbury meeting, and the annual congress of the Europan Association for Cancer Research.

Innovation

The patenting and possible commercialisation of discoveries made by CanCell scientist is an important contribution. Several DOFI (Disclosure of inventions) were filed - regarding the exploration of a method to target cancer cells overexpressing FGFRs (DOFI 18154), development of novel antimycotics against drug-resistant fungi (DOFI 18098), GRP94 CAR (DOFI 18104), and products to analyze mitophagy (DOFI 18144). In addition, Jorrit Enserink has a pending patent application: "A compound for the treatment and/or prevention of cancer and, more specifically, to the treatment of cancerous cell populations in which c-Myc activity is upregulated".

Annual meeting

October 2018 saw the very first CanCell annual meeting take place at the Holmen Fjordhotell in Oslo, Norway. With a great turnout (85 CanCell members from both core and associated groups), the meeting provided an excellent opportunity for sharing current research progress and establishing collaborations for future projects. Members were also given detailed overviews on the latest technology and specialist techniques available within the centre, including proteomics, live cell imaging approaches and genome-wide perturbation screens. The first CanCell Paper awards were presented and the recipients were Michal, Kristiane and Eva (see also **Scientific highlights**).

Outreach

The first meeting of the CanCell user panel was held on November 23rd, organized by Helene Knævelsrud from the Enserink group. The user panel consists of representatives from the sarcoma, prostate cancer, lung cancer and leukemia patient organizations. The user panel will provide the perspective of users to our research and dissemination.

RCN CoE invited CanCell directors Harald Stenmark and Anne Simonsen, and fellow PIs Tor Erik Rusten and Ragnhild Eskeland to "KUPP" (Career development pilot project), where they were introduced to ways to encourage recruitment and career pathways within the Centre.

The CanCell workshop on scientific writing "Write without fear, edit without mercy" led by Åsmund Eikenes gave this and some other good tips and formed the basis for the CanCell blog. CanCell has a dedication for weblogging and several of the centre's members contributed to blog about various aspects of their science at CanCell Blog (https://cancell.no/english/news-and-events/blog/). Among the entries, you can come across thoughts on precision cancer, the universality of the language of science, and why we should learn from our intracellular self of the value of recycling and much more.

The center also operates a Twitter-account @CanCell_UiO, where exciting and informative news are shared. Currently followed by 187 it has 78 tweets with a total of 310 likes, and 45 retweets. The home page of CanCell is hosted by University of Oslo and can be found at (http://cancell.no). Here a collection of people, science and events are presented and updated daily and is the hub of the CanCell information platforms and the interface to interact with external and internal interested parties.

From left to right: Tor Erik Rusten, Ole Knutzen, Anne Simonsen, Per Axel Ankre, Helene Knævelsrud, Astrid Jahr, Camilla Raiborg, Yngvar Fløisand and Jørgen Wesche.

Twitter:
@CanCell_UiO

Web:
CanCell.no

Visiting Professors

Professor Kristian Helin visiting CanCell in dialogue with our young scientists

CanCell has four professors associated to the Centre.

- KRISTIAN HELIN | BRIC, Copenhagen, **Denmark**
- IVAN DIKIC | Goethe University, Frankfurt, **Germany**
- EILEEN WHITE | Rutgers Cancer Institute, NJ, **USA**
- EYAL GOTTLIEB | Beatson Institute, Glasgow, **UK**

Scientific Advisory Board

The Scientific Advisory Board supports our Centre with valuable input on strategy and science that helps us achieve our goal of becoming one of Europe's leading centres for cancer research. The SAB will have their first visit to CanCell in March 2019.

The SAB members are:

- JOHANNA IVASKA | University of Turku, **Finland**
- MARJA JÄÄTTELÄ | Head of Research Unit Cell Death and Metabolism, Danish Cancer Society Research Center, Copenhagen, **Denmark**
- PIER PAOLO DI FIORE | European Institute of Oncology, **Italy**
- STEPHAN BECK | University College London, **UK**
- MICHAEL BOUTROS |DKFZ, Heidelberg, **Germany**

Invited speakers and seminars

Invitations of international guest speakers is an additional way of increasing CanCell's international visibility. CanCell has a programme for invitations of international guest speakers, led by a committee of junior scientists. In 2018, 8 guest speakers were invited. A guest professor, Nuria Cassals Farré (UIC Barcelona, Spain) visited Stenmark's lab for 6 months in 2018 for a collaboration on membrane contact sites in metabolic regulation. We also had four interns visiting.

- ERIC BAEHRECKE | University of Massachusetts, **USA**
- ESTEBAN BALLESTAR| Bellvitge Biomedical Research Institute (IDIBELL), **Spain**
- IAN GANLEY | University of Dundee, **UK**
- KAPIL N. BHALLA | MD Anderson Cancer Center, **USA**
- TERESA A. ZIMMERS | Indiana University, **USA**
- RAFAEL CANTERA | University of Stockholm, **Sweden**
- PABLO WAPPNER | Leloir Institute, Buenos Aires, **Argentina**
- RITA SOUSA NUNES | Centre for Developmental Neurobiology, Kings College London, **UK**

Grants

Harald Stenmark is the leader of one of 25 research projects receiving a total of 100 million NOK from the Research Council of Norway and the Norwegian Agency for International Cooperation and Quality Enhancement in Higher Education (Diku), that run the program INTPART together. The aim of INTPART is to strengthen collaborations with Brazil, Canada, India, Japan, China, Russia, South Africa and USA. The project led by Stenmark, with Anne Simonsen as a partner, is the ChineseNorwegian Partnership for Education and Research in Cancer Cell Biology (ChiNoCell). The ChiNoCell project is supported with 3.8 million NOK over a 3-year period. Harald Stenmark was also awarded the prestigious ERC Advanced Grant for the second time. Through this grant from the European Research Council, Stenmark's research project "Coincidence detection of proteins and lipids in regulation of cellular membrane dynamics (CODE)" is supported with 2.5 million Euros over a 5-year period. CanCell scientists participate in several COST networks.

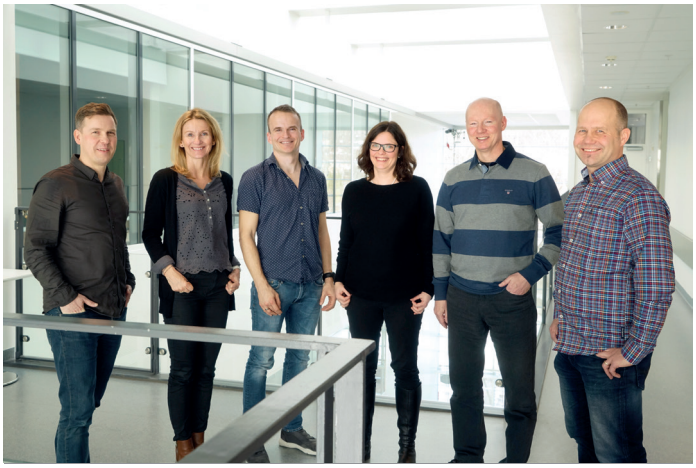
Anne Simonsen is MC of the TransAutophagy COST network, in which also Harald Stenmark participates, and Ragnhild Eskeland is MC of the International Nucleome COST Consortium. Both Anne Simonsen and Harald Stenmark were MCs of the Proteostasis COST network, which ended in 2018. Jorrit Enserink is MC of COST CA17104 - New diagnostic and therapeutic tools against multidrug resistant tumors. Anne Simonsen is member of the Marie Curie training network (H2020-MSC-ITN2017) DRIVE and received funds from this initiate in 2018.

CanCell Principle Investigator Tor Erik Rusten achieved the substantial RCN "TOPPFORSK" funding grant for the project "Tumor-Host Biology" within the FRIPRO program. FRIPRO is an open competitive arena for all research areas and disciplines, where there are no thematic guidelines and no requirements relating to the applicability or immediate utility of the research. The competition in FRIPRO is tough, and only the best researchers with particularly good projects and very well written proposals have a chance at succeeding. CanCell PI Anne Simonsen as well as associate members Philippe Collas and Terje Johansen also hold a RCN "TOPPFORSK" grant.

Several CanCell members were recipients of grants from the three largest national funding organizations during 2018 (listed below), with a total amount of 70.6 million NOK."

Grantee	Type	Funding organization	Amount
Harald Stenmark	Advanced grant	European Research Council	2.5 MEUR
Anne Simonsen	ITN grant	H2020-MSCA	0.4 MEUR
Tor Erik Rusten	"Toppforsk" grant	Research Council of Norway	25.0 MNOK
Kaisa Haglund	Project grant	Research Council of Norway	6.2 MNOK
Jorrit Enserink	Postdoc position	Research Council of Norway	3.3 MNOK
Camilla Raiborg	Project grant	Norwegian Cancer Society	7.7 MNOK
Kaisa Haglund	Project grant	Norwegian Cancer Society	5.0 MNOK
Jørgen Wesche	Project grant	Norwegian Cancer Society	5.5 MNOK
Leonardo Meza-Zepeda	Project grant	Norwegian Cancer Society	5.7 MNOK
Leonardo Meza-Zepeda	Postdoc position	South-Eastern Norway Regional Health Authority	3.3 MNOK
Kjetil Boye	Clinical project grant	South-Eastern Norway Regional Health Authority	2.3 MNOK
Jorrit Enserink	Postdoc position	South-Eastern Norway Regional Health Authority	3.3 MNOK
Ignacio Garcia	PhD student position	South-Eastern Norway Regional Health Authority	3.3 MNOK

ABOUT CanCell



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

Anette Sørensen is the Administrative coordinator for CanCell

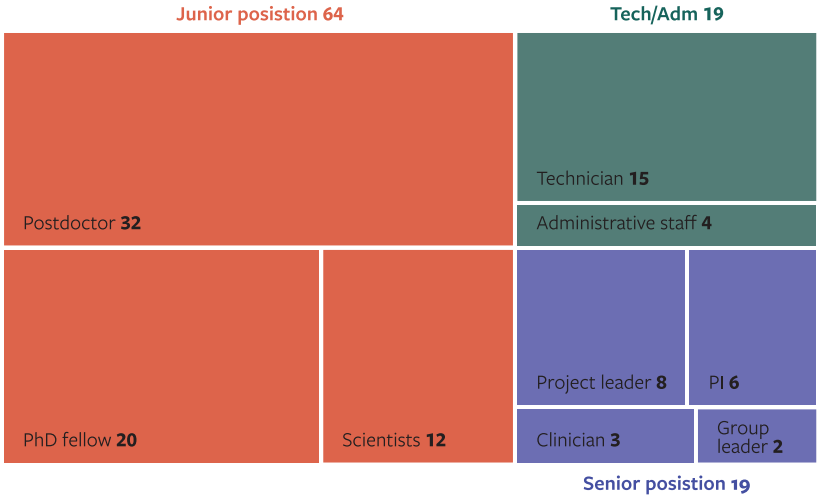
Centre for Cancer Cell Reprogramming was established in December 2017 as a Centre of Excellence appointed by the Research Council of Norway with the University of Oslo as host institution. Our Centre has a presence at two locations; the Institute for Cancer Research at Norwegian Radium Hospital, Oslo University Hospital and Institute for Basic Medical Sciences, University of Oslo. The two campuses are located about 6 km apart, and commuting between the two sites is easy (including a free shuttle bus service every 20 minutes). 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.

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. Stenmark, Enserink, Rusten and Wesche are based at Institute for Cancer Research, whereas Simonsen and Eskeland are at Institute of Basic Medical Sciences. Six independent groups are associated with CanCell. These are the groups of Emmet Mc Cormack, Arnoldo Frigessi, Terje Johansen, Eivind Hovig, Åslaug Helland, and Phillippe Collas. Additionally, head clinician Yngve Fløisand's research is funded as an associate member. Oncologist Kjetil Boye is associated with the Wesche group, and both the core facility for advanced light microscopy (Ellen Skarpen and Vigdis Sørensen) and for genomics (Leonardo Meza-Zepeda and Suzanne Lorenz) are integrated in the Centre.

Management

Director Harald Stenmark, co-director Anne Simonsen, and administrative coordinator Anette Sørensen (2017-2018) perform the regular management of CanCell. Together with the four other PIs, the management team forms the Steering Group of CanCell. The Centre management reports to the CanCell board.



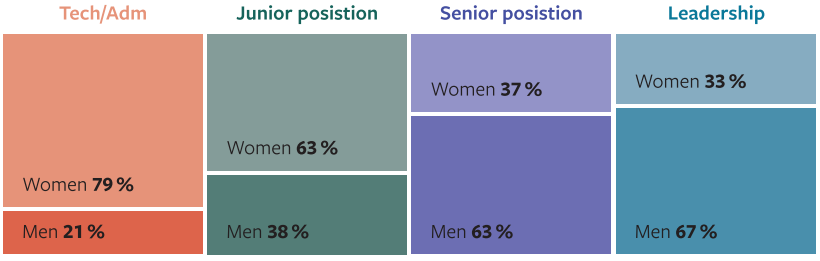
THE TOTAL NUMBER OF PEOPLE REGISTERED IN THE CENTRE IN 2018:

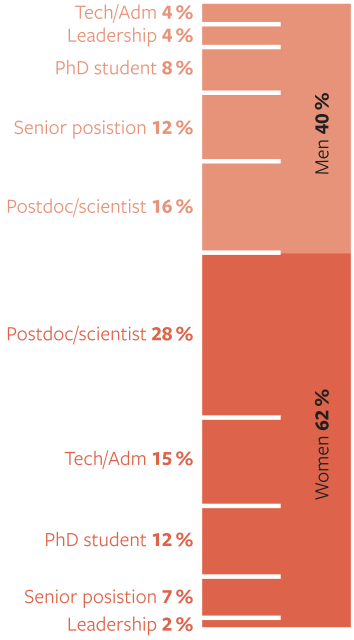
Man-years, excluding students: 86
Headcount, including students: 102+7

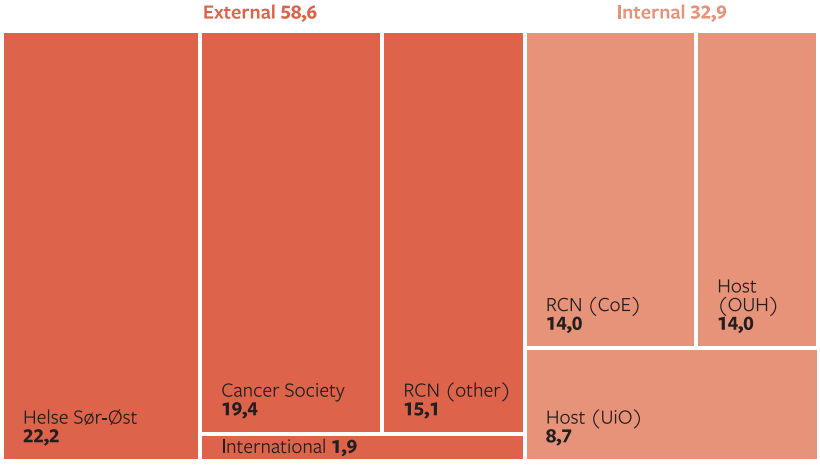
CanCell currently houses 29 different nationalities from five continents (Asia (9), N America/S America (2), Africa (2), Australia (1), Europe (88). The chart shows the categorization of our staff by position. In addition, the centre harbored 7 Master students throughout 2018.

GENDER BALANCE

The gender balance in CanCell is 61% women and 39% men among our total staff. Approximately the same percentages account for the postdoc category as well as for the PhD student category. However, for the highest scientific categories our male colleagues constitute the majority (principal investigators 67% men, all senior positions 63% men (group leader, project leader, clinicians, professor). CanCell has a majority (63%) of women among the junior scientist category (postdocs, PhD students, non-tenured scientists) and technicians (79%), whereas there is a good gender balance among all CanCell's scientist positions (50% each). Two out of 6 CanCell PIs are women (33.3%), and 31.9% of professors at the University of Oslo are women. It is a concern for the University, and for CanCell, that too few talented female scientists progress to group leader positions. CanCell will stimulate its best female junior scientists to pursue a scientific career by offering "bridging" grants for talented women in transition periods between grant funding. However, no such funding has yet been allocated.



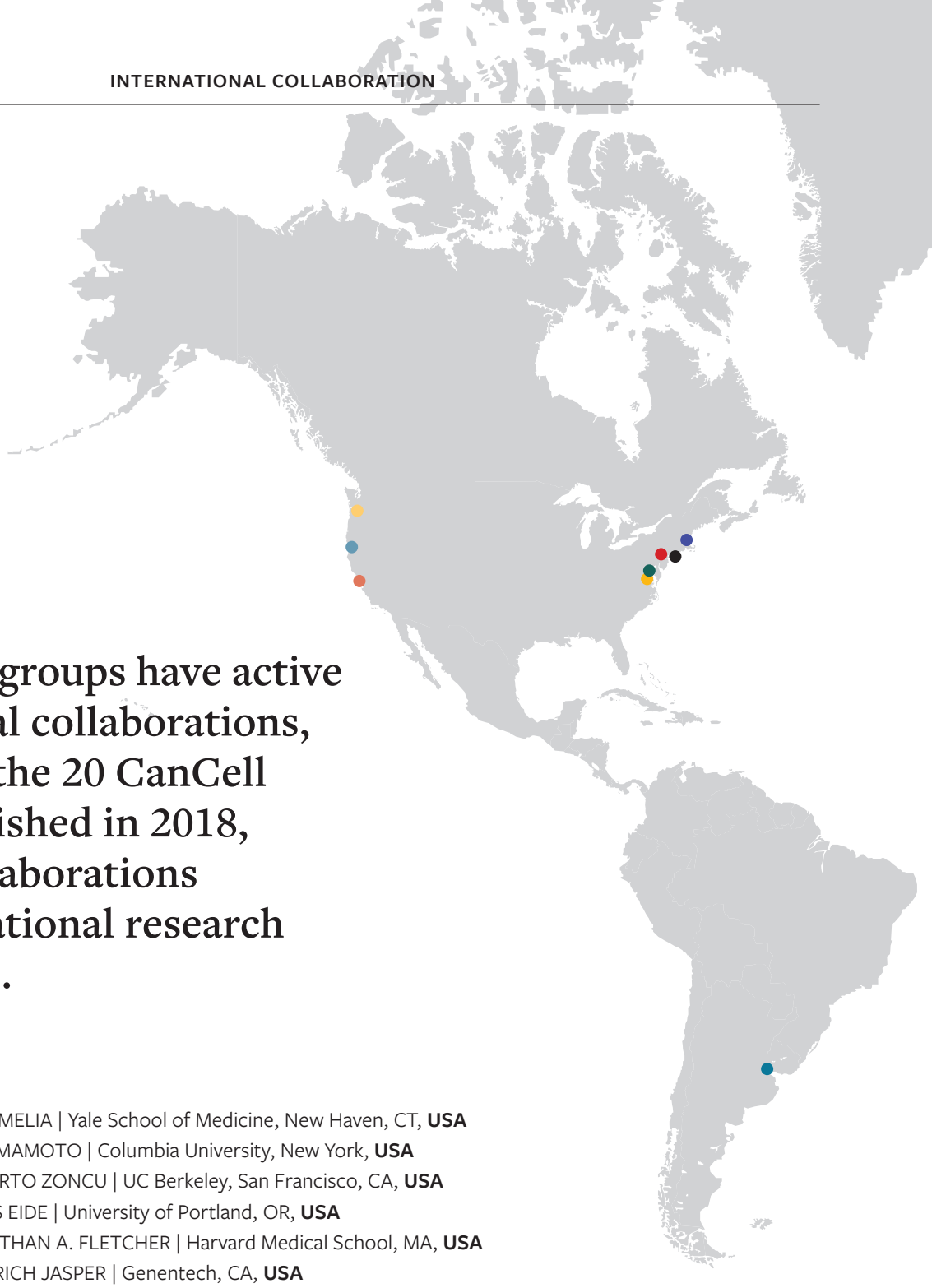




(MNOK)

TOTAL FUNDING

The total funding for 2018 was 91.5 MNOK. The funding situation for CanCell is stable and with the granting of several large funds during 2018 the centre has succeeded to obtain sufficient financial resources to implement all its planned activities. CanCell's Centre of Excellence funding from the Research Council of Norway (RCN) amounts to 14 MNOK in 2018 and is due to increase of 16.7 MNOK from 2019 onwards.



All CanCell groups have active international collaborations, and among the 20 CanCell papers published in 2018, 13 were collaborations with international research laboratories.

- TOM MELIA | Yale School of Medicine, New Haven, CT, **USA**
- AI YAMAMOTO | Columbia University, New York, **USA**
- ROBERTO ZONCU | UC Berkeley, San Francisco, CA, **USA**
- CHRIS EIDE | University of Portland, OR, **USA**
- JONATHAN A. FLETCHER | Harvard Medical School, MA, **USA**
- HEINRICH JASPER | Genentech, CA, **USA**
- TODD SCHOBORG | NIH, Bethesda, ML, **USA**
- NASSER M. RUSAN | NIH, Bethesda, ML, **USA**
- PABLO WAPPNER | Leloir Institute, Buenos Aires, **Argentina**

- SVEN CARLSSON | Umeå University, **Sweden**
- NICO DANTUMA | Karolinska Institute, **Sweden**
- CHRISTOS SAMAKOVLIS | University of Stockholm, **Sweden**
- PATRICIA BOYA | Spanish National Research Council, Madrid (CSIC), **Spain**
- SHARON TOOZE | Francis Crick Institute, London, **England**
- JOSE L. GARCIA-PEREZ | University of Edinburgh, **Scotland**
- CHRISTIAN BEHRENDS | Ludwig-Maximilians-Universität (LMU) München, **Germany**
- OLE PLESS | Fraunhofer IME ScreeningPort (IME SP), Hamburg, **Germany**
- IVAN DIKIC | Göthe Univ, Frankfurt, **Germany**
- YVES BARRAL | ETH Zurich, **Switzerland**
- KIMMO PORKKA | FIMM, Helsinki, **Finland**
- PAVEL KRECJI | Masaryk University, Brno, **Czech Republic**
- EYAL GOTTLIEB | Israel Institute of technology, Technion, **Israel**
- TIZIANA BONALDI | European Institute of Oncology, **Italy**
- KERSTIN BYSTRICKY | University of Tolouse, **France**
- FRANK LAFONT | Pasteur Institute of Lille, Lille, **France**
- ROLAND LE BORGNE | University of Rennes, Rennes, **France**

Name	Position	Group
Andersen, Aram Nikolai	PhD student	Enserink
Anker, Liv Dammann	PhD student	Stenmark
Asp, Nagham T.	Lab manager	Simonsen
Ayuda-Duran, Maria del Pilar	Postdoctoral fellow	Enserink
Azouzi, Naima	Postdoctoral fellow	Eskeland
Bassols, Jose Maria	ICT specialist	Stenmark
Boye, Kjetil	Oncologist	Wesche
Brech, Andreas	Project leader, senior scientist	Stenmark
Brinch, Ulrikke Dahl	Technician	Stenmark
Charsou, Chara	Postdoctoral fellow	Simonsen
Chica-Balaguera, Nathalia	Scientist	Enserink
Crispin, Richard	Postdoctoral fellow	Enserink
Dillard-Eple, Caroline Marie Claude	Postdoctoral fellow	Rusten
Engen, Anne	Head engineer	Stenmark
Enserink, Jorrit	PI, professor	Enserink
Eskeland, Ragnhild	PI, associate professor	Eskeland
Falck, Martin	PhD student	Eskeland
Fiorito, Elisa	Postdoctoral fellow	Wesche
Fløisand, Yngvar	Head clinician	Enserink
Garcia Llorente, Ignacio	Senior scientist	Enserink
Georgiesh, Tatiana	PhD student	Wesche
Grad, Iwona	Postdoctoral fellow	Enserink
Greni, Eivind Andreas	Advisor (20%)	Admin
Haglund, Kaisa	Project leader, senior scientist	Stenmark
Halnes, Isabel	Laboratory assistant	Stenmark
Hanes, Robert	PhD student	Enserink
Haugsten, Ellen Margrethe	Scientist	Wesche
Helland, Åslaug	Clinician, group leader	Helland
Herrera, Maria Carmen	Postdoctoral fellow	Enserink
Holland, Peter	Postdoctoral fellow	Rusten
Hovig, Eivind	Group leader, professor	Hovig
Ignacio, Cuervo	PhD student	Eskeland
Ivanauskiene, Kristina	Postdoctoral fellow	Wesche
Jain, Ashish	Postdoctoral fellow	Rusten
Khezri, Rojyar	PhD student	Rusten
Kjos, Ingrid	Engineer	Stenmark
Knævelsrud, Helene	Senior scientist	Enserink
Kostas, Michal Janusz	Postdoctoral fellow	Wesche
Lapao, Ana	PhD student	Simonsen
Lie-Jensen, Anette Christensen	PhD student	Stenmark
Lindeberg, Mona Mari	Engineer	Wesche
Lobert, Viola	Postdoctoral fellow	Stenmark
Log, Ingeborg	Research technician	Stenmark
Lorenz, Susanne	Project leader, scientist	Wesche
Lystad, Alf Håkon	Scientist	Simonsen
Malerød, Lene	Scientist	Stenmark
Mateo Tortola, Maria	PhD student	Stenmark
Mathai, Benan John	PhD student/ Postdoctoral fellow	Simonsen
Migliano, Simona	Postdoctoral fellow	Stenmark
Muñoz, Sara Orellana	Postdoctoral fellow	Enserink
Munson, Michael	Postdoctoral fellow	Simonsen

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Name	Position	Group
Munthe, Else	Head technician	Stenmark
Myklebost, Ola	Project leader, professor (3%)	Wesche
Nakken, Sigve	Postdoctoral fellow	Hovig
Namløs, Heidi Maria	Postdoctoral fellow	Wesche
Nardatowska-Wesolowska, Beata	Scientist	Eskeland
Ng, Matthew Yoke Wui	PhD student	Simonsen
Nguéa P, Aurélie Alyssa Yolaine	PhD student	Enserink
Nähse-Kumpf, Viola	Postdoctoral fellow	Stenmark
O´Farrel, Fergal	Scientist	Rusten
Pankiv, Serhiy	Technician	Simonsen
Pedersen, Nina Marie	Postdoctoral fellow	Stenmark
Piechaczyk, Laure Isabelle	PhD student	Enserink
Radulovic, Maja	Postdoctoral fellow	Stenmark
Raiborg, Camilla	Project leader, senior scientist	Stenmark
Ravussin, Anthony	Postdoctoral fellow	Stenmark
Robertson, Joseph	Postdoctoral fellow	Enserink
Rodriguez de la Ballina, Laura	Scientist	Simonsen
Rogne, Marie	Scientist	Eskeland
Rusten, Tor-Erik	PI, associate professor	Rusten
Rønning, Eva Simonsen	Head technician	Stenmark
Schimanski, Riccarda	Technician	Rusten
Schink, Kay Oliver	Project leader, senior scientist	Stenmark
Schultz, Sebastian	Senior engineer	Stenmark
Sharma, Ankush	Postdoctoral fellow	Eskeland
Simonsen, Anne Gjøen	PI, professor	Simonsen
Singh, Sachin Kumar	Postdoctoral fellow	Wesche
Skarpen, Ellen	Scientist	Stenmark
Smestad, Marianne	Technician	Stenmark
Sneeggen, Marte	PhD student	Stenmark
Spangenberg, Helene	PhD student	Stenmark
Stenmark , Harald Alfred	PI, professor	Stenmark
Stratford, Eva Wessel	Postdoctoral fellow	Wesche
Szybowska, Patrycja	PhD student	Stenmark
Søreng, Kristiane	Postdoctoral fellow	Simonsen
Sørensen, Anette	Administrative coordinator	Admin
Sørensen, Vigdis	Core facility manager	Wesche
Tadele, Dagim Shiferaw	PhD student	Enserink
Takáts,Szabolcs	Postdoctoral fellow	Rusten
Tan, Kia Wee	PhD student	Stenmark
Thorvaldsen, Thor Espen	Postdoctoral fellow	Stenmark
Toft Bjørndahl, Gunnveig	Head engineer	Simonsen
Trachsel Moncho, Laura	PhD student	Simonsen
Vietri, Marina	Scientist	Stenmark
Wang, Ling	Technician	Stenmark
Weisheit, Sabine	Postdoctoral fellow	Rusten
Wenzel, Eva	Project leader, senior scientist	Stenmark
Wesche, Jørgen	PI, professor	Wesche
Wiedlocha, Anthoni	Project leader, senior scientist	Stenmark
Zepeda, Leonardo Andres Meza-	Core facility leader	Wesche
Zhang, Beibei	Postdoctoral fellow	Enserink
Zhen, Yan	Postdoctoral fellow	Stenmark

indicate steering group

PUBLICATIONS

Reviews and commentaries are in blue, papers from 2019 emphasized.

Abudu YP, Pankiv S, Mathai BJ, Lystad AH, Bindesbøll C, Brenne HB, Thiede B, Yamamoto A, Nthiga TM, Lamark T, Esguerra CV, Johansen T and Simonsen A.

NIPSNAP1 and NIPSNAP2 act as "eat me" signals for mitophagy.

In press Dev Cell.

Deretic V, Prossnitz E, Burge M, Campen MJ, Cannon J, Liu KJ, Sklar LA, Allers L, Garcia SA, Baehrecke EH, Behrends C, Cecconi F, Codogno P, Chen GC, Elazar Z, Eskelinen EL, Fourie B, Gozuacik D, Hong W, Hotamisligi G, Jäättelä M, Jo EK, Johansen T, Juhász G, Kimchi A, Ktistakis N, Kroemer G, Mizushima N, Münz C, Reggiori F, Rubinsztein D, Ryan K, Schroder K, Simonsen A, Tooze S, Vaccaro MI, Yoshimori T, Yu L, Zhang H, Klionsky DJ.

Autophagy, Inflammation, and Metabolism (AIM) Center of Biomedical Research Excellence: supporting the next generation of autophagy researchers and fostering international collaborations.

Autophagy. 2018;14(6):925-929

Fafilek B, Balek L, Bosakova MK, Varecha M, Nita A, Gregor T, Gudernova I, Krenova J, Ghosh S, Piskacek M, Jonatova L, Cernohorsky NH, Zieba JT, Kostas M, Haugsten EM, Wesche J, Erneux C, Trantirek L, Krakow D, Krejci P.

The inositol phosphatase SHIP2 enables sustained ERK activation downstream of FGF receptors by recruiting Src kinases.

Sci Signal. 2018 Sep 18;11(548). pii: eaap8608.

Fuglerud BM, Ledsaak M, Rogne M, Eskeland R, Gabrielsen OS.

The pioneer factor activity of c-Myb involves recruitment of p300 and induction of histone acetylation followed by acetylation-induced chromatin dissociation.

Epigenetics Chromatin. 2018 Jun 28;11(1):35.

Goodridge JP, Jacobs B, Saetersmoen ML, Clement D, Hammer Q, Clancy T, Skarpen E, Brech A, Landskron J, Grimm C, Pfefferle A, Meza-Zepeda L, Lorenz S, Wiiger MT, Louch WE, Ask EH, Liu LL, Oei VYS, Kjällquist U, Linnarsson S, Patel S, Taskén K, Stenmark H, Malmberg KJ.

Remodeling of secretory lysosomes during education tunes functional potential in NK cells.

Nat Commun. 2019 Jan 31;10(1):514.

Herrera MC, Chymkowitch P, Robertson JM, Eriksson J, Bøe SO, Alseth I, Enserink JM.

Cdk1 gates cell cycle-dependent tRNA synthesis by regulating RNA polymerase III activity.

Nucleic Acids Res. 2018 Dec 14;46(22):11698-11711.

Johannessen TC, Hasan-Olive MM, Zhu H, Denisova O, Grudic A, Latif MA, Saed H, Varughese JK, Røsland GV, Yang N, Sundstrøm T, Nordal A, Tronstad KJ, Wang J, Lund-Johansen M, Simonsen A, Janji B, Westermarck J, Bjerkvig R, Prestegarden L.

Thioridazine inhibits autophagy and sensitizes glioblastoma cells to temozolomide.

Int J Cancer. 2019 Apr 1;144(7):1735-1745.

Kostas M, Haugsten EM, Zhen Y, Sørensen V, Szybowska P, Fiorito E, Lorenz S, Jones N, de Souza GA, Wiedlocha A, Wesche J.

Protein Tyrosine Phosphatase Receptor Type G (PTPRG) Controls Fibroblast Growth Factor Receptor (FGFR) 1 Activity and Influences Sensitivity to FGFR Kinase Inhibitors.

Mol Cell Proteomics. 2018 May;17(5):850-870.

Kostas M, Lampart A, Bober J, Wiedlocha A, Tomala J, Krowarsch D, Otlewski J, Zakrzewska M.

Translocation of Exogenous FGF1 and FGF2 Protects the Cell against Apoptosis Independently of Receptor Activation.

J Mol Biol. 2018 Oct 19;430(21):4087-4101.

Kraft C, Boya P, Codogno P, Elazar Z, Eskelinen EL, Farrés J, Kirkin V, Kruitwagen T, Chymkowitch P, Denoth-Lippuner A, Enserink J, Barral Y.

Centromeres License the Mitotic Condensation of Yeast Chromosome Arms.

Cell. 2018 Oct 18;175(3): 780-795.e15. doi: 10.1016/j.cell.2018.09.012. Epub 2018 Oct 11.

Jungbluth H, Martinez A, Pless O, Primard C, Proikas-Cezanne T, Simonsen A, Reggiori F.

Driving next-generation autophagy researchers towards translation (DRIVE), an international PhD training program on autophagy.

Autophagy. 2018 Sep 13:1-5.

Kumar S, Jain A, Farzam F, Jia J, Gu Y, Choi SW, Mudd MH, Claude-Taupin A, Wester MJ, Lidke KA, Rusten TE, Deretic V.

Mechanism of Stx17 recruitment to auto-phagosomes via IRGM and mammalian Atg8 proteins.

J Cell Biol. 2018 Mar 5;217(3):997-1013.

Kumar S, Gu Y, Abudu YP, Bruun JA, Jain A, Farzam F, Mudd M, Anonsen JH, Rusten TE, Kasof G, Ktistakis N, Lidke KA, Johansen T, Deretic V.

Phosphorylation of Syntaxin 17 by TBK1 Controls Autophagy Initiation.

Dev Cell. **2019** 019 Feb 27. pii: S1534-5807(19)30055-3.

Lystad AH, Carlsson SR, de la Ballina LR, Kauffman KJ, Nag S, Yoshimori T, Melia T, Simonsen A.

Distinct functions of ATG16L1 isoforms in membrane binding and LC3B lipidation in autophagy-related processes.

Nat Cell Biol. **2019** Mar;21(3):372-383.

Malerød L, Le Borgne R, Lie-Jensen A, Eikenes ÅH, Brech A, Liestøl K, Stenmark H, Haglund K.

Centrosomal ALIX regulates mitotic spindle orientation by modulating astral microtubule dynamics.

EMBO J. 2018 Jul 2;37(13). pii: e97741.

Mejlvang J, Olsvik H, Svenning S, Bruun JA, Abudu YP, Larsen KB, Brech A, Hansen TE, Brenne H, Hansen T, Stenmark H, Johansen T.

Starvation induces rapid degradation of selective autophagy receptors by endosomal microautophagy.

J Cell Biol. 2018 Oct 1;217(10):3640-3655.

Ogmundsdottir MH, Fock V, Sooman L, Pogenberg V, Dilshat R, Bindesbøll C, Ogmundsdottir HM, Simonsen A, Wilmanns M, Steingrimsson E.

A short isoform of ATG7 fails to lipidate LC3/GABARAP.

Sci Rep. 2018 Sep 26;8(1):14391.

Olsvik HL, Svenning S, Abudu YP, Brech A, Stenmark H, Johansen T, Mejlvang J.

Endosomal microautophagy is an integrated part of the autophagic response to amino acid starvation.

Autophagy. **2019** Jan;15(1):182-183.

Radulovic M, Stenmark H.

ESCRTs in membrane sealing.

Biochem Soc Trans. 2018 Aug 20;46(4): 773-778. Review

Radulovic M, Schink KO, Wenzel EM, Nähse V, Bongiovanni A, Lafont F, Stenmark H.

ESCRT-mediated lysosome repair precedes lysophagy and promotes cell survival.

EMBO J. 2018 Nov 2;37(21). pii: e99753.

Rodríguez-Castañeda F, Lemma RB, Cuervo I, Bengtsen M, Moen LM, Ledsaak M, Eskeland R, Gabrielsen OS.

The SUMO protease SENP1 and the chromatin remodeler CHD3 interact and jointly affect chromatin accessibility and gene expression.

J Biol Chem. 2018 Oct 5;293(40):15439-15454.

Skah S, Richartz N, Duthil E, Gilljam KM, Bindesbøll C, Naderi EH, Eriksen AB, Ruud E, Dirdal MM, Simonsen A, Blomhoff HK.

cAMP-mediated autophagy inhibits DNA damage-induced death of leukemia cells independent of p53.

Oncotarget. 2018 Jul 13;9(54):30434-30449.

Simonsen A.

Confidence to go the way science takes you.

Nat Cell Biol. 2018 Sep;20(9):1009.

Søreng K, Munson MJ, Lamb CA, Bjørndal GT, Pankiv S, Carlsson SR, Tooze SA, Simonsen A.

SNX18 regulates ATG9A trafficking from recycling endosomes by recruiting Dynamin-2.

EMBO Rep. 2018 Apr;19(4). pii: e44837.

Søreng K, Neufeld TP, Simonsen A.

Membrane Trafficking in Autophagy.

Int Rev Cell Mol Biol. 2018;336:1-92. Review

Vietri M, Stenmark H.

Orchestrating Nuclear Envelope Sealing during Mitosis.

Dev Cell. 2018 Dec 3;47(5):541-542.

Wenzel EM, Schultz SW, Schink KO, Pedersen NM, Nähse V, Carlson A, Brech A, Stenmark H, Raiborg C.

Concerted ESCRT and clathrin recruitment waves define the timing and morphology of intraluminal vesicle formation.

Nat Commun. 2018 Jul 26;9(1):2932.

Zhen Y, Haugsten EM, Singh SK, Wesche J.

Proximity Labeling by a Recombinant APEX2-FGF1 Fusion Protein Reveals Interaction of FGF1 with the Proteoglycans CD44 and CSPG4.

Biochemistry. 2018 Jul 3;57(26):3807-3816.

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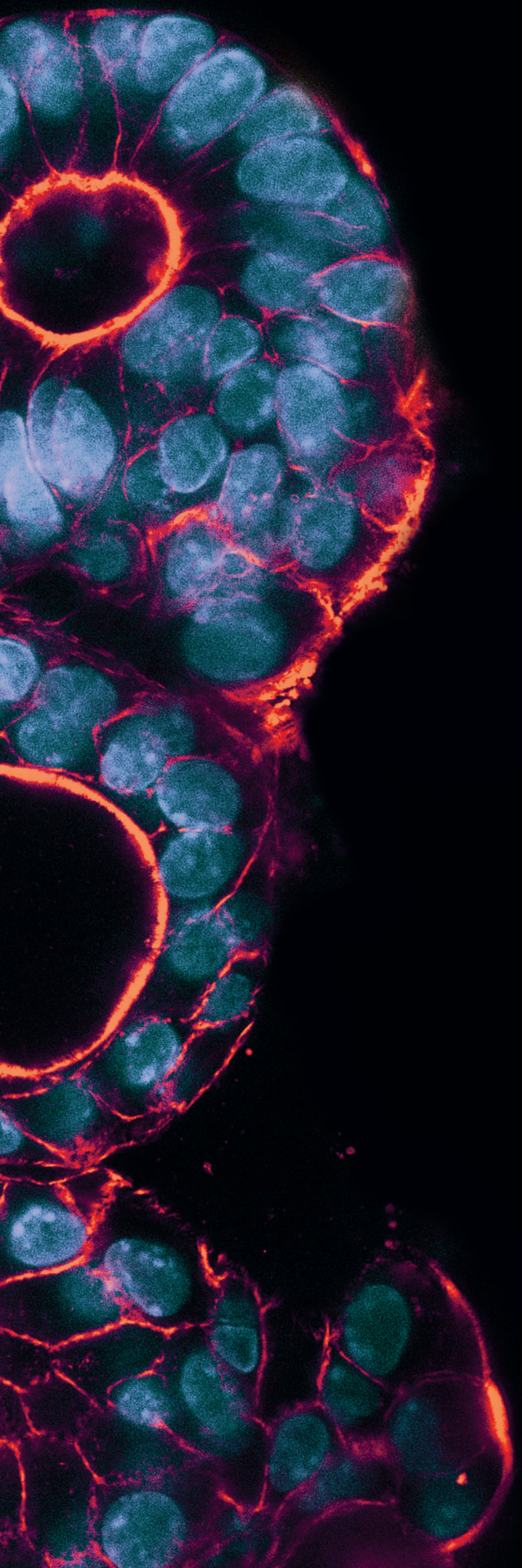

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