INSTITUTE FOR CANCER RESEARCH

ANNUAL REPORT 2019

Oslo University Hospital

HELSE SØR-ØST

UiO : University of Oslo

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The photographic theme of this year's Annual Report is *Humans at ICR*.
- The most important part of ICR is by far its human resources and our collective competence.

FRONT PAGE:
Optics inside a flow cytometer. Flow cytometry is used in our research in cancer immunology, immune-oncology and immune monitoring as well as in cell cycle and cell signalling analyses. Advanced technology and competence provided by the Department of Core Facilities is a pillar for cutting-edge research at the Institute for Cancer Research. Advanced infrastructure is financed by OUH, UoO, RCN, Radiumhospitalets Legater, and Norsk Hydros Fond.

PAPER: 150/300 Profimatt
CIRCULATION: 800

Contents

Taking our legacy into the future - Who we are and what we do

WHO WE ARE

1954

LEGACY IN RESEARCH, INNOVATION AND EDUCATION

The Institute for Cancer Research (ICR) was founded in 1954 representing 65 years of continuous advances in cancer research. Through the years, our work has significantly contributed to better understand cell cycle and cell division, cancer cell biology, cancer genetics, cancer immunology, radiation biology, molecular oncology, tumor biology, and metastasis. In addition, we have contributed to novel methods and implementation of a number of new technologies to help cancer diagnostics and monitoring.

RESEARCH

INNOVATION

There is also a proud history of translational research and innovation, for example on photomedicine leading to companies such as Photocure and PCI Biotech and with numerous other past and present translational and innovation projects at the ICR in various stages of development.

EDUCATION

Education and dissemination are an integrated part of ICR activities and many masters- and PhD-students and postdocs have received their training at the ICR and have pursued successful careers in research, clinical medicine, administration or in the biotech and pharma sector.

IN NUMBERS

350
RESEARCH STAFF

Approximately **350** research staff in **25** research groups, **6** core facilities and **1** admin unit (organization see pages 8-9)

PAST 5 YEARS (2015-2019)

ICR researchers have raised more than 1.0 billion NOK extramural funding (of total **1.5 billion** accounted)

1.00
BILLION NOK

1650
WORKING YEARS

Put in **1650** working years (FTEs)

150 EDUCATED PhDs and MScs

Educated **66** PhDs and **84** MScs that have graduated

1100
PUBLICATIONS

Leading to production of more than **1100** (**1112**) publications (mean IF **6.1**, median IF **4.5**)

(for 2019 Key Figures see pages 10-11).

WHAT WE DO

VISION: EXCELLENCE IN FIGHTING CANCER

WE AIM TO:

- Stay at the cutting edge of cancer research
- Educate the leaders of tomorrow in cancer research, cancer diagnostics and treatment
- Take a prominent part in developing of new OUH and national strategies for advanced molecular cancer diagnostics, cancer precision medicine and experimental cell therapy (see also page 15)

VALUES: QUALITY, INTEGRITY, TEAMWORK, VISION

GOALS 2019-2020

1. Strengthen translational research
2. Strengthen contact, coordination and collaboration with clinicians and diagnostic staff in OUH CCC and beyond
3. Build further excellence in research
4. Establish new SAB
5. Increase internationalisation and technology development

Introduction by the Director

I am proud to present you with our Annual Report for 2019. The Institute for Cancer Research (ICR) is an institution with approximately 350 employees plus students organised in 25 research groups complemented with cutting-edge core facilities. The ICR is a premier institution in basic and translational cancer research on a national and international arena and has a strong prior track record in translation and innovation. More than one third of the ICR staff is international and come from 37 different countries.

In 2019 we worked in the ICR Leadership group, among the Group Leaders and in all ICR departments and groups to set out and integrate our Vision and Values (Quality-Integrity-Teamwork-Vision, see the previous page). We also set out Goals for 2019-2020, both as presented under the heading "The ICR into the future!" in the 2018 Annual Report and on the preceding pages in this report. Among our goals for 2019 and 2020 are to (1) strengthen translational research, (2) to improve contact, coordination and collaboration with clinicians and diagnostic staff in the Oslo University Hospital Comprehensive Cancer Centre (OUH-CCC) and beyond, (3) to build further excellence in research where we would like to see originality, depth, quality, and international value.

With respect to goals 1 and 2, I think there are numerous outstanding examples of collaborative translational and clinical projects throughout this report. Furthermore, the ICR is a central component in the new and developing strategies for precision medicine and for cell therapy in the Division for Cancer Medicine and the OUH-CCC. To build further excellence (goal 3), we would like to see a further increase in the quality of the scientific output. Against this backdrop, it is interesting to see that the median impact factor of the papers produced is up from 4.1 in 2017 to 5.0 in 2018 and 4.5 in 2019. Moreover, the fact that the output in terms of the number of papers is increasing, with 241 papers in 2019 and more than 40 in the two first months of 2020 (versus 220 and 186 papers in 2017 and 2018, respectively. This is excellent, particularly as almost half of the production also has first and/or senior authors from ICR. ICR innovation activities also appear to be progressing well with 10 new DOFIs, 7 new patent applications filed and 5 patents granted from ICR inventors. In addition, company collaborations and interaction appear to be increasing.

More than 2/3rds of the total ICR funding in 2019 (234.4 of 333.5 MNOK) came from extramural grants which are higher than ever before. ICR scientists have also been able to obtain substantial new funding and secured major new grants from the Norwegian Cancer Society, the Research Council of Norway, and the South-Eastern Norway Regional Health Authority as well as private and international sources.

We celebrate our victories at the ICR, and in 2019 we have marked the fact that two of the newly awarded OUH Strategic areas went to the ICR-led projects TEAM-ACT (led by Ragnhild A. Lothe) and STRATCELL (led by Karl-Johan Malmberg). We have celebrated a number of grants from the RCN including several young talent grants and including the start of Digital Life PINpOINT project, and multiple grants from the Cancer Society, the Regional Health Authority for South-Eastern Norway and other sources. ICR is also well represented in the new Cancer Society Expert Groups for Lung Cancer (headed by Åslaug Helland) and Pancreatic Cancer (headed by Caroline Verbeke). We have also had the official opening of the privately funded InvaCell project that formalized a collaboration between the ICR and the Curie Institute (with Harald Stenmark and Philippe Chavrier as PIs, donor Trond Paulsen). At Christmas, we celebrated the award of a highly prestigious ERC Consolidator Grant to Johanna Olweus. We have marked the fact that the University of Oslo (UiO)/OUH was granted a prestigious 6-mEUR Horizon2020 grant, RESCUER, for precision medicine research on breast cancer (headed by Vessela Kristensen and with strong ICR participation) and that Åslaug Helland received a large KLINBEFORSK grant. The ICR has also received very significant grants for new instrumentation from the Radium Hospital Foundation and from Norsk Hydro's Fund for Cancer Research in 2019. We also celebrated internally the award of the OUH Early Career Award to Anita Sveen, the EU Innovation Radar Prize to Kristian Berg and Theodossis Theodossiou, the award of the Ragnar Mørk's Prize for Outstanding Research to Karl-Johan Malmberg and the award of the new ICR Prizes Researcher-of-the-year and Employee-of-the-year for 2019 to Theodossis Theodossiou and Peter Wiedswang, respectively. Furthermore, OUH awarded prizes in their bi-annual assessment of best papers to ICR researchers Marthe Løvf and Rolf Skotheim (May 2019), Muhammad Ali, Zsofia Foldvari, Eirini Giannakopoulou and Johanna Olweus (Nov 2019) and Marte Sneeggen and Kay Oliver Schink (Nov 2019).

In the Department of Cancer Genetics, we welcomed Tero Aittokallio as a new Group Leader for the Computational Systems Medicine in Cancer Group from September 2019 (recruited from Finland) and in Department of Cancer Immunology, Jon Amund Kyte has been appointed Group Leader for the Immunotherapy Against Solid Cancers Group from 2020.

ICR's strong standing in Norwegian research is also illustrated by the fact that members of the institute lead a Centre of Excellence (CoE) Centre for Cancer Cell Reprogramming (CanCell, Director Harald Stenmark) and the three K.G. Jebsen centres for Cancer Immunotherapy (Director Johanna Olweus), Colorectal Cancer Research (Director Ragnhild A. Lothe), both

"Research and innovation with patient benefit in mind"

in the extension phase, and for B Cell Malignancies (Deputy Director June Myklebust), all with strong participation from ICR groups.

The recent advents of the Covid-19 pandemic have had major impacts world-wide and on the Norwegian society at large as well as on OUH and UiO research activity at this time. At the ICR, as part of the hospital and with good support from the leadership at all levels, we decided to keep the institute open throughout the pandemic. - This in recognition of the importance of the science we do and to support the hospital operations. With appropriate risk assessments, precautions and personal protection measures such as social distancing, hygiene measures, reduced density at work and somewhat reduced activity, this has so far gone well with strong efforts from all our employees in these difficult circumstances.

The ICR sets out to maintain the excellent science and outstanding production and to further build excellence by organising more collaborative efforts at all levels to deal with grand challenges in cancer medicine and to position the ICR in national and international alliances and consortia. We aim to be a significant partner for the clinical activities in the Division of Cancer Medicine and the OUS OECI-accredited Comprehensive Cancer Centre (CCC). We continue feeding results into a translational research path and to have **patient benefit** in mind in all aspects of research and innovation.

April, 2020
Kjetil Taskén, Head of the ICR

Organisation

Head of Institute
Kjetil Taskén

Chief Administrative Officer
Kari Aalrust Berger

- Administration
- Service Lab

Cancer Genetics
Therese Sørlie

- *Gry Aarum Geitvik* — Lab Technology
- *Therese Sørlie* — Breast Tumor Initiation
- *Tero Aittokallio* — Computational Systems Medicine in Cancer
- *Åslaug Helland* — Translational Studies in Solid Tumors
- *Vessela N. Kristensen* — Cancer Genome Variation (leave of absence from Q3 2019)
- *Hege E. G. Russnes* — Molecular Biology of Breast Cancer

Cancer Immunology
Johanna Olweus

- *Johanna Olweus* — Experimental Immunotherapy
- *Karl-Johan Malmberg* — NK Cell Biology and Cell Therapy
- *June Helen Myklebust* — Lymphoma Biology
- *Mouldy Sioud* — Immunomodulation and Targeted Therapies
- *Kjetil Taskén* — Cell Signalling and Immune Regulation
- *Jon Amund Kyte* — Immunotherapy against solid cancers — From 1st of January 2020

Molecular Cell Biology
Harald A. Stenmark

- *Harald Stenmark* — Cellular Membrane Dynamics
- *Jorrit Enserink* — Cancer Molecular Medicine
- *Tor Erik Rusten* — Tumor-host Biology
- *Kirsten Sandvig* — Intracellular Transport

The Institute for Cancer Research
Institute for Cancer Research is organized in 6 research departments with 25 research groups, and one Department of (6) Core Facilities.

Molecular Oncology
Ragnhild A. Lothe

- *Ragnhild A. Lothe* — Genetics
- *Guro Elisabeth Lind* — Epigenetics
- *Rolf I. Skotheim* — Genome Biology

Radiation Biology
Kristian Berg

- *Kristian Berg* — Photochemical Internalization
- *Heidi Lyng* — Clinical Radiation Biology
- *Einar Rofstad* — Radiation Biology and Tumor Physiology
- *Randi Syljuåsen* — Radiation Biology and DNA Damage Signaling

Tumor Biology
Gunhild M. Mælandsmo

- *Gunhild M. Mælandsmo* — Metastasis Biology and Experimental Therapeutics
- *Kjersti Flatmark* — Translational Cancer Therapy
- *Eivind Hovig* — Computational Cancer Genomics
- *Jørgen Wesche* — Molecular biology of Sarcoma

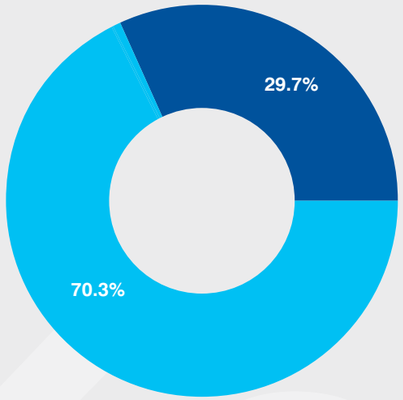
Core Facilities
Leonardo A. Meza-Zepeda

- *Trond Stokke* — Flow-Cytometry and Pre-Clinical Imaging
- *Susanne Lorenz* — Genomics and Bioinformatics
- *Ellen Skarpen* — Advanced Microscopy

Key figures 2019

Funding

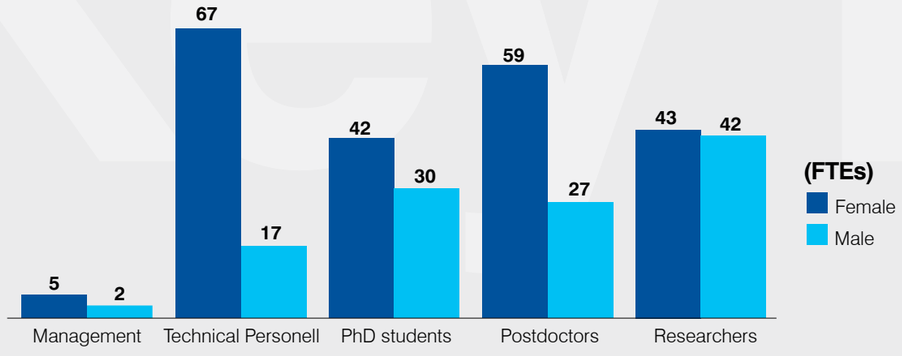
Percent



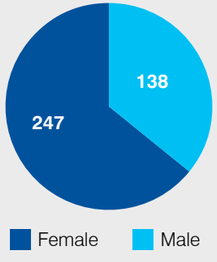
Actual Institute expenditure for 2019 by internal and external funding sources (total 333,5 MNOK = approx. 32,8 M€)

- Internal funding
- External funding

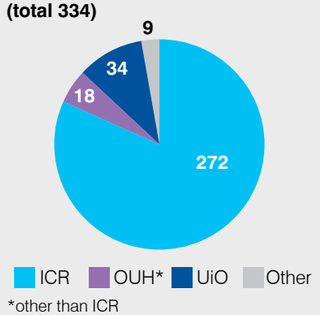
Employees



Employees by Gender
(total 385)

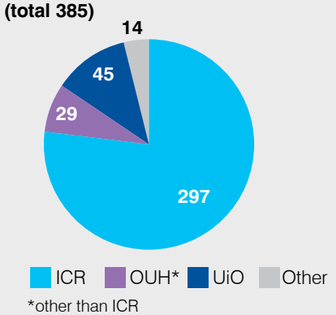


FTEs by Employer
(total 334)



*other than ICR

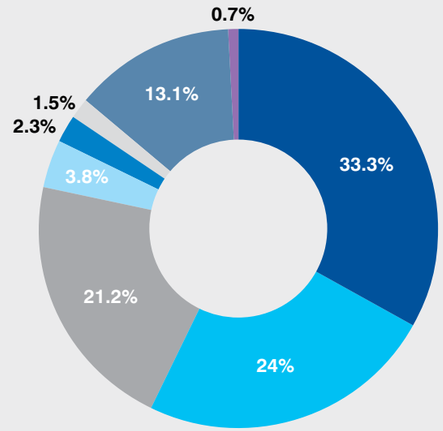
Employed by
(total 385)



*other than ICR

External funding by source

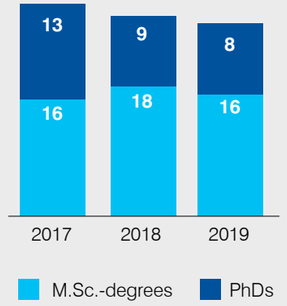
Percent



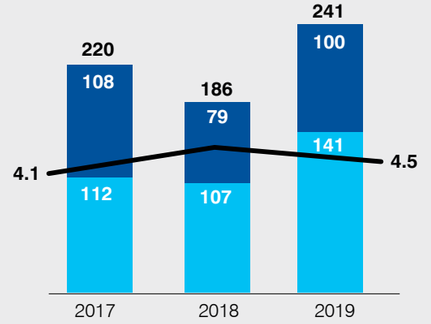
Sources of external competitive funding for 2019, based on actual expenditure (total 234,4 MNOK= approx. 23 M€)

- South-Eastern Norway Regional Health Authority
- The Research Council of Norway
- The Norwegian Cancer Society
- University of Oslo
- EU
- Other international sources
- Other private sources
- Other public sources

Completed PhDs and M.Sc.-degrees



Articles published

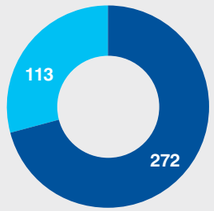


IMPACT FACTOR

Mean	5.8	6.5	6.1
Median	4.1	5	4.5

International Staff Distribution

37 nations are represented
113 people in total are from outside Norway



- Norwegian: **272 (71%)***
- International: **113 (29%)**

*Including naturalised foreigners

01
Countries represented by one person

Bosnia
Colombia
Croatia
Czech Republic
Equador
Estonia
Finland
Ireland
Iceland
Latvia
Macedonia
Mexico
Netherlands
Pakistan
Russia
Singapore
Slovakia
Switzerland

02
People
Denmark
Japan
Portugal
USA

03
People
Austria
Greece
Iran
Serbia

04
People
France
Hungary

05
People
Great Britain
Lithuania
Poland

06
People
Italy

07
People
China
Spain

08
People
Sweden

11
People
India

13
People
Germany

Oslo University Hospital Comprehensive Cancer Centre

Oslo University Hospital was designated a Comprehensive Cancer Centre by the OECI in 2017, after a process where activities both in clinical practice and in research were evaluated. The cancer research performed by the Institute for Cancer Research (ICR) is a corner stone in our OECI-accredited Comprehensive Cancer Centre (CCC).

The Institute is situated in close proximity to clinical cancer departments and diagnostic laboratories at the Radium Hospital, a cancer-oriented part of Oslo University Hospital where also the Cancer Registry of Norway is located. The collaboration between the ICR and clinical research groups in Oslo University Hospital is an important factor to increase our activities in clinical research. More patients into clinical trials is an expressed aim for our Comprehensive Cancer Centre, and several investigator initiated clinical trials have been developed in collaboration between researchers at ICR and clinical research groups at all locations of Oslo University Hospital. Another of ICR's neighbours is Oslo Cancer Cluster, - which consist of several biotech and pharmaceutical companies. The proximities between all these actors, provides an excellent environment for synergies and collaboration.

Several Centres of Excellence also including basic research are located at the Institute for Cancer Research, enriching the Comprehensive Cancer Centre with competence and expertise. The extensive international collaboration involving researchers at ICR is also an important asset for the CCC.

Further development of the tight bonds between ICR, clinical researchers and the Cancer Registry, will be important in the coming years and with the new hospital building and proton center that will open for patients in 2023/24. In the integrated organisation of cancer-related activities, the ICR will be a key participant in the further development of Oslo University Hospital as a leading cancer centre in Europe.

Sigbjørn Smeland

Head of Division of Cancer Medicine,
Chair, OUH CCC Board

Åslaug Helland

Research Director, Division of Cancer Medicine
Head OUH, CCC Research Committee

Oslo University Hospital
Comprehensive Cancer Centre

OECI COMPREHENSIVE Cancer Centre

Precision Cancer Medicine at OUH Comprehensive Cancer Centre

The implementation of genomic medicine and individualised treatment has been lagging behind in Norway and other countries in Northern Europe with publicly funded health care systems. Against this backdrop, the Head of the Division for Cancer Medicine and Chair of the OUH Comprehensive Cancer Centre appointed a PCM working group[1] that started its activities in January of 2019. The working group decided to make a concrete plan for PCM implementation and delivered the results of its work to the Division and the CCC Board in June 2019:

VISION AND OBJECTIVES FOR IMPLEMENTATION OF PRECISION CANCER MEDICINE

- *Patients who are referred to OUH with cancer and where advanced molecular cancer diagnostics will be instrumental for selection of treatment should be offered such diagnostics at the right time during the course of the disease.*
- *Cancer patients should have opportunity to receive individualised treatment where this is shown to impact on clinical outcome or where it is probable that it would give patient benefit.*
- *OUH will learn and build competence in advanced molecular cancer diagnostics and individualised treatment and contribute to development and production and dissemination of knew knowledge in this area.*

ACTION POINTS NECESSARY FOR IMPLEMENTATION OF PCM, THREE MAIN AREAS:

I. Establishment of a platform that can provide advanced (experimental) molecular cancer diagnostics. Develop such service also in the standard process to examine and diagnose patients.
II. Increase the volume of clinical trials and number of patients in trials in the precision medicine area (industry studies, researcher-initiated trials).
III. Offer individualised cancer treatment in the ordinary standard of care in OUH according to national and international guidelines.


Dagens Medisin — Nyheter | Debatt | Pharma | DM Arena | DMTV | Om oss

VIL TILBY NY BEHANDLING: Nylig møttes mange av Norges mest fremstrebende kreftleger og forskere for å diskutere mulighetene for en norsk studie som skal inkludere kreftpasienter som blant annet har brukt opp behandlingsmulighetene som finnes. Fra venstre: Sigbjørn Smeland, Kjetil Taskén, Hege E.G Russnes og Åslaug Helland. Foto: Vidar Sandnes

Vil starte nasjonal studie på kreftpasienter

En studie på presisjonsdiagnostikk innen kreft kan komme til å inkludere 250 norske kreftpasienter.

Anne Grete Storvik
agst@dagensmedisin.no
Publisert: 2020-02-12 — 04.34

RADIUMHOSPITALET (Dagens Medisin): – Vi undersøker muligheten for å starte en nasjonal studie som bruker avansert molekylær kreftdiagnostikk. Vi vil finne nye behandlingsmuligheter som vil tilbys pasienter med langtkommen kreftsykdom og som ikke har et annet behandlingstilbud – eller har brukt opp det som er av andre

PROGRESS:

- In the spring of 2019, the Division for Laboratory Medicine responded to the needs of the cancer area with respect to action points I and II (above) and decided to establish a Section for Experimental Diagnostics and Research Support in the Department of Pathology to provide a genomic medicine platform to ensure delivery of necessary molecular cancer diagnostics (Head Hege Russnes). The CCC PCM working group also on behalf of the CCC in June organized a national meeting on implementation of advanced molecular cancer diagnostics.

- In the fall of 2020, the PCM working group was reinforced and expanded[2] and now reports directly to the CCC Governing Board. The work has next focussed on attracting PCM clinical trials (action point II). Specifically, the CCC PCM working group has looked at the possibility of establishing a national PCM trial modelled on the DRUP study in the Netherlands (IMPRESS-Norway trial, national coordinator and PI, Åslaug Helland) matched by a national infrastructure for precision diagnostics, InPreD. The work has involved raising national support, discussion with key stakeholders, planning of a public-private partnership with industry participation and national consensus as well as organising a second national meeting in January 2020.

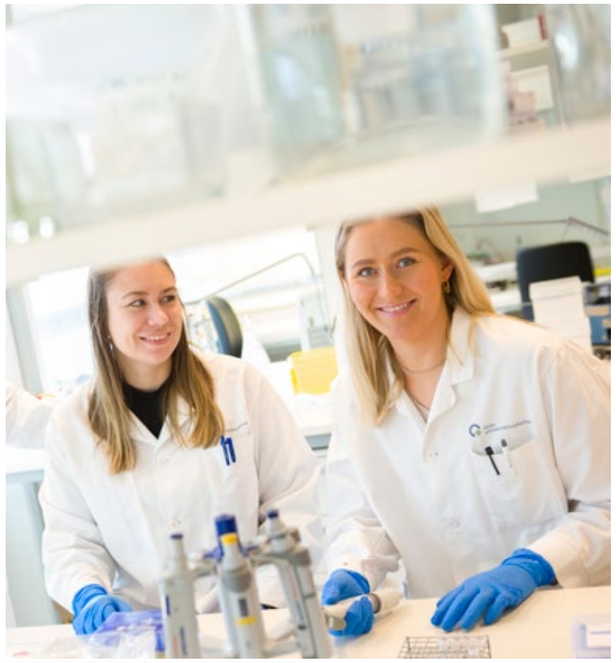
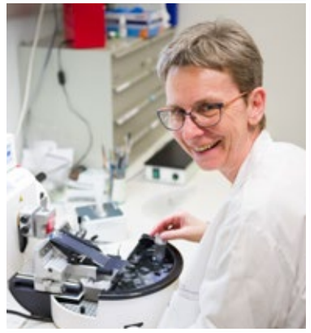
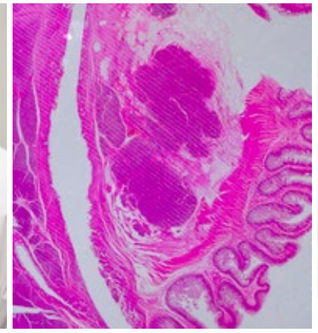
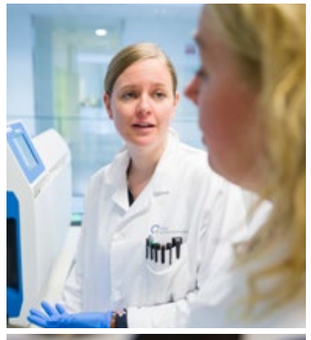
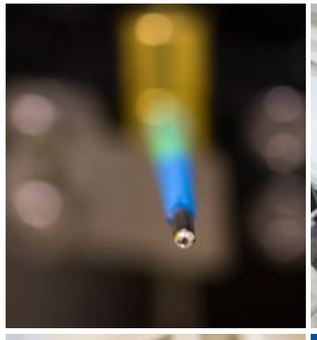
[1] The Cancer Precision Medicine Working Group (Jan-Sept 2019) has consisted of Kjetil Taskén (ICR, chair) Tormod Guren (Onc), Ragnhild Lothe (ICR), Per Magnus Mæhle (CCC), Hege Russnes (ICR/Pat), Gunnar Sæter (CCC), and with Live Fagereng (ICR) as secretary.

[2] From Oct 2019 the CCC PCM Working Group consists in addition to the above members of: Monica Cheng Munthe-Kaas (Ped), Nils Tore Vethe (ClinPharm), Ben Davidson (Pat), Espen Enerly (CRN), Åslaug Helland (Onc/CCC), Yngvar Fløysand (Hem), Kristina Lindemann (GynOnc), Turid Vederhus (Rad), Torunn Berge (HSE, observer)

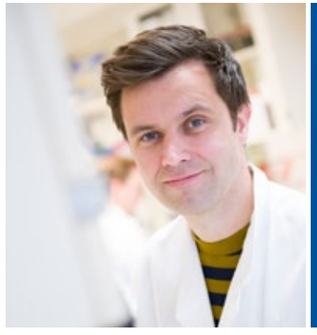
Departments









"Our mission is to improve the lives of cancer patients through translational research in precision oncology"

Department of

Cancer Genetics

Headed by Therese Sørlie

Our aim is to improve risk estimation, achieve earlier diagnosis and improve prediction of treatment responses and other clinical outcomes for patients with early and advanced stages of both solid tumors and hematologic malignancies. Our research is translational in nature and include functional studies, molecular classification, data integration and pan-cancer analyses. We work towards facilitating the implementation of discoveries into clinical use. A common theme across groups is to achieve a deeper molecular understanding of inter- and intra-tumor heterogeneity and tumor evolution using patient cohorts and mouse models.

We are an interdisciplinary team of 50 researchers, including medical doctors, molecular biologists, computational biologists and highly specialized engineers organized in four research groups and one lab-technology unit. Two of the group leaders hold part-time clinical positions and three have affiliated positions at UiO. The lab technology unit reinforces the department's expertise in state of the art technology and improves exchange of knowledge across research groups and cancer types. This is a key asset leading to increased quality of the department's laboratory work and project management.

For translational studies, we have established a pipeline for high-quality biobanking and secure data handling of patient cohorts with long-term follow-up that enables omics analysis of tumors down to single cell levels. Our clinical database consists of > 3000 subjects from consecutive studies and clinical trials with high quality follow-up information. We are involved in the following studies:

- NeoAva - Neoadjuvant chemotherapy in breast cancer with/without bevacizumab.
- IBCT - Improved Breast Cancer Therapy in the neoadjuvant and metastatic setting
- EMIT -Establishment of Molecular profiling for Individual Treatment decisions in Early BC; three-phase study including randomized and observational clinical trials.
- OPTIMA-optimal personalized treatment of early breast cancer using multi-parameter analysis
- ComIT - evaluation of the benefit of radiation in combination with immune therapy for lung cancer
- TREM – Lung cancer patients with EGFR mutations and primary TKI-resistance
- ThoRaT - Lung cancer patients receiving radiotherapy
- NorPACT-1 and 2 - Neo-adjuvant chemotherapy for pancreatic cancer
- ICON - A randomized phase IIb study evaluating immunogenic chemotherapy combined with ipilimumab and nivolumab in patients with luminal B breast cancer
- ALICE – atezolizumab combined with immunogenic chemotherapy in patients with metastatic triple-negative breast cancer
- Oslo2- observational study with comprehensive biobanking

We are part of extensive collaborations at the institutional, national and international levels, and partnering in several national and international networks and consortia; for instance, the National Breast Cancer Research Network, the Norwegian Cancer Society expert groups on lung and pancreatic cancer, the Regional Research Network on Extracellular Vesicles, Personalized Cancer Treatment and Metaflammation, International Cancer Genome Consortium (ICGC), EuroPDX, the Breast Cancer Association Consortium (BCAC); EU funded projects (EpiMark, Cancer-ID, Gender Net Plus, HERCULES and RESCUER). The total number of publications in 2019 was 68.

Department of Cancer Genetics

Breast Tumor Initiation

Group Leader: Therese Sørlie

“Understanding cell fate decisions in tumor progression”

ABOUT

Our group studies molecular aspects of breast tumor initiation and progression with a special emphasis on identifying cell(s) of origin of molecular subtypes and the transition from in situ to invasive breast cancer. The group counts 10 members, including the group leader and professor (TS), three postdocs , three PhD students, one master student, and two engineers as well as two affiliated scientists (in 20% and 10% positions) and one affiliated breast surgeon. Two members are MDs and one is DVM. We have a broad expertise in laboratory technologies that includes high-throughput genomic technologies, in vivo lineage-tracing, 2D and 3D in vitro culture techniques, in situ hybridization, confocal microscopy, and FACS analysis. We use patient cohorts and mouse models (transgenic and patient derived xenograft - PDX) in our studies. We also have expertise in bioinformatics and statistical modeling.

AIMS

Our aim is to identify the cellular origins of breast tumors and the mechanisms underlying tumor initiation and further development into the heterogeneous molecular subtypes. Through an increased understanding of how early lesions progress to more advances stages, we aim to contribute to improved strategies for early intervention and more precise treatment.

PROJECTS

- Characterize breast cancer subtype-specific progression pathways
- Explore the role of LGR5-expressing cells in the mammary tumorigenesis
- Investigate the role of Hedgehog/GLI1 signaling in breast cancer progression
- Investigate the role of FOXA1 and FGFR1 in endocrine resistant breast cancer
- Genomic and functional analysis of therapeutic targets

RECENT ACHIEVEMENTS

8 publications by group members in 2019. One Master of Science completed.

Computational Systems Medicine in Cancer

Group leader: Tero Aittokallio

“A systems view of disease networks to pinpoint critical targets and their interaction partners”

ABOUT

The group was launched in September 2019 when Tero Aittokallio moved from Finland (FIMM, University of Helsinki and University of Turku). Our group has expertise in integrating multi-omics profiling and clinical information from cancer patients using mathematical and statistical approaches, such as machine learning and network modeling. We carry out multidisciplinary projects in collaboration with other researchers from the institute and as part of international projects, where we develop, test and implement novel practices of how to use artificial intelligence (AI) and machine learning (ML) models in translational and clinical studies. We believe that combining functional, molecular and genomic profiling information is critical for next-generation precision medicine applications, where integrative modeling and clever use of patient-level big data will pinpoint effective and selective targets for personalized therapies.

AIMS

The modeling aim is to develop novel supervised learning approaches to identify multi-omic features predictive of clinical outcomes for individual patients by means of efficient AI/ML models that maximize the accuracy of outcome predictions using minimal panels of biomarkers. The medical aim is to optimize treatment outcomes for individual patients using the maximally predictive models and minimal biomarker signatures that enable real-time and cost-effective diagnostics and prognosis.

PROJECTS

- Multi-omics prediction of clinical outcomes for precision oncology applications
- AI-guided treatment optimization by means of cost-effective biomarker panels
- Decision support systems for real-time patient monitoring and adaptive trials

RECENT ACHIEVEMENTS

In 2019, the group published 11 articles in peer-review journals and 2 book chapters. We are partnering in several international translational projects, including ERA-PerMed project JAK/STAT TARGET, EU-H2020 project HERCULES, and the UK Breast Cancer Now Catalyst Programme for predictive markers for TNBC drug responses. In 2019, the group received 3-year open-project grant from South-Eastern Norway Regional Health Authority for AI-guided treatment optimization by means of multi-omics biomarker panels.

Department of Cancer Genetics

Translational Studies in Solid Tumors

Group leader: Åslaug Helland

”With starting point in clinical studies and clinical questions, we do molecular analyses aiming at improving outcome for cancer patients”

ABOUT

Our group focuses on translational studies on solid tumours, with a special interest in pancreatic, lung and colorectal cancers. By increasing the understanding of the underlying biology of tumour development, we will improve precision medicine in cancer care. Several of our projects include material from patients included in clinical studies, and we have detailed clinical data from all patients. Predictive biomarkers and mechanisms of resistance is in focus.

We are organized into three project groups, headed by Elin H. Kure (Professor USN), Odd Terje Brustugun and Åslaug Helland (Professor UIO) , with a total of 17 members. Seven of these are MDs. We are three researchers, three postdocs, seven PhD-students, one study nurse and three engineers.

AIMS

The ultimate goal is to increase our ability to offer personalised cancer treatment, and thereby improve prognosis.

Sub aims are:

- Identification of biomarkers in blood samples, for diagnostics, follow-up and prognostication
- Identification of tumour biomarkers for prediction of therapy response and for prognostication

PROJECTS

- Molecular characterization (-omics) of pancreatic- and lung cancers
- Proteogenomic analysis of pancreatic tumors and characterization of circulating biomarkers in free plasma and exosomes
- Identification of circulating plasma biomarkers in colorectal cancers (the Nordic VII clinical trial)
- Protein (TMA) analyses in lung cancers
- Serum predictive markers for therapy response
- Elucidate mechanisms for therapy resistance
- Expand biomarker identification material to stool (microbiome) and urine
- Investigate combination of radiotherapy and immunotherapy
- Gender differences in side effects on immunotherapy

RECENT ACHIEVEMENTS

In 2019, the group published 18 papers in peer-reviewed journals. We have had several talks at national and international meetings, and are PIs on >20 translational and clinical studies. An ERA-network we are part of received funding (Gender-net). We are partners in several South-Eastern Norway Regional Health Authority networks (NORSMAN, ReMics, NIRO), and received approximately 36.2 mill NOK in research funding (Elin Kure 1.2 mill, Odd Terje Brustugun 2 mill, Åslaug Helland 33 mill).

Cancer Genome Variation

Group leader: Vessela Kristensen

“Germ-line and somatic genetic and epigenetic variants in cancer and pharmacogenomics”

ABOUT

The Kristensen group with 2 senior scientists, 3 postdocs, 2 PhD students, 1 MSc and 2 research technologists moved Q3-2019 to Institute for Medical Genetics (IMG) at OUH. The group will continue to work towards intensive and fruitful collaboration between ICR and IMG and with the Institute for Clinical Medicine, University of Oslo. Group members work closely together and in collaboration with breast clinicians, pathologists and oncologists. A remaining project group at ICR consists of 1 senior scientist and 3 PhD students. This project group is headed by Thomas Fleischer (Epigenomics of Breast Cancer) and works to characterize epigenetic alterations in breast cancer, and assess the implications for breast cancer pathogenesis and utilization for precision medicine (http://ous-research.no/fleischer).

AIMS

The Cancer Genome Variation group is working to understand how genetic variation affects occurrence of somatic alterations, gene expression patterns and genome wide copy number alterations in human tumours (http://ous-research.no/kristensen/)

PROJECTS

Together with our collaborative network we received several major grants in 2019: from EU Horizon 2020 (RESCUER: 63 mill NOK), EU EraCoSysMed (PI, 3 mill NOK), South-Eastern Norway Regional Health Authority (Open Project, 9 mill NOK; PhD student, 3 mill NOK). Projects include:

- **Genome variation:** In the breast cancer association consortium we identified 160 new breast cancer risk loci (published in *Nature Genetics*) and contributed to the fine-mapping of these loci (credible causal variants CCV).
- **Epigenomics of Breast Cancer:** Identification of epigenetically regulated cancer-driving pathways in breast cancer, and functional validation using CRISPR epigenetic engineering.
- **MicroRNAs in breast cancer:** Alterations in miRNA expression caused by neo-adjuvant treatment with chemotherapy and bevacizumab is associated with proliferation and response to therapy (published in *Molecular Oncology*). Identification of miRNAs as potential master regulators of the methylome in breast cancer.
- **Non-canonical transcriptomes**: Characterization of alternate exon usage and long non-coding RNA expression in breast cancer and connection to epigenetic profiles and patient outcomes.
- **Immune signaling:** Identification of patient groups based on immune signaling identifies a bad prognosis immune infiltration type independently of PAM50 classification and other known clinicopathological features (published in *Nature Communications*)

RECENT ACHIEVEMENTS

Publication activity. 22 publications in 2019, popular at https://radiumlegat.no/Prosjekter/Vessela-Kristensen,

Department of Cancer Genetics

Molecular Biology of Breast Cancer

Group Leader: Hege G. Russnes

"Exploring inter- and intra-tumor heterogeneity to improve molecular classification of breast cancer"

ABOUT

The group was founded January 2018 and have a total of 2 scientists, 1 postdoc, 1 research engineer, 1 nurse/MSc, 1 MD-PhD student and 1 MD student. In addition, 1 prof. emerita (A-L Børresen-Dale, UiO), 1 researcher (group leader A. Mathelié̇r, NCMM), 1 oncologist (L. Ottestad) and 1 professor in bioinformatics (O. C. Lingjærde, UiO) are associated with the group (part-time).

Focus of the group is to reach a more fundamental understanding of the biological dynamics of breast cancer through high-throughput molecular analyses of DNA, mRNA, miRNA and protein, both at diagnosis and during disease progression.

As co-PI/partners in several clinic trials we perform "state of the art" analyses of patient material, both on bulk tumors, single cells and liquid biopsies, at various stages of the disease. The group is active in the IMI/EU funded project CancerID aiming at standardizing liquid biopsies for cancer diagnostics. Hege G. Russnes is also senior consultant at Dept. of Pathology, OUH where she is Head of "Section for experimental pathology and research support", a lab developing and performing molecular diagnostics for clinical trials. She is also appointed "Young Associated Investigator" at NCMM (Centre for Molecular Medicine Norway).

AIMS

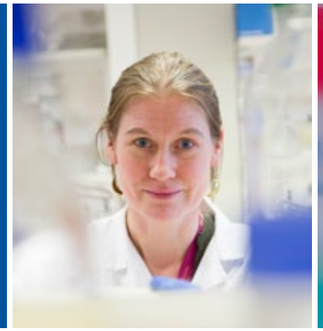
Our group aims at defining, refining and implementing molecular classification and biomarker analyses to improve stratification of cancer patients into treatment relevant groups. We are addressing the impact of inter- and intra-tumor heterogeneity as well as host response on disease progression, response to therapy and patient outcome.

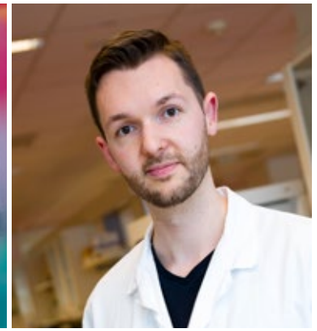
PROJECTS

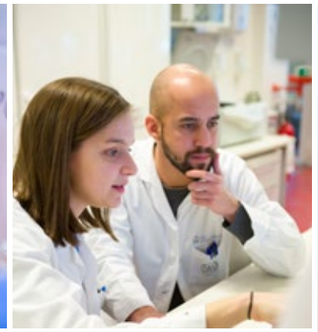
- LATE: Characterizing in time and space the metastatic process of hormone receptor positive breast cancer
- TREAC: Towards personalized treatment for patients with aggressive breast cancer
- Somatic Genetics of Breast Cancer, from single genes to whole genome sequencing
- SN - Sentinel Lymph Node in Breast Cancer- revealing the interaction between tumor subtypes and host immune response.
- CANCAN: CANcer specific Copynumber alteration Analysis
- CARMA: Copy Aberration Regional Mapping Analysis
- Liquid biopsies – optimizing methodologies for nucleic acid and single cell detection, capture and analysis

RECENT ACHIEVEMENTS

In 2019 we published 9 articles in peer-reviewed journals (in addition to 19 publications by our affiliated members). The LATE project received major funding from South-Eastern Norway Regional Health Authority (open project support) and from the Wellcome Sanger Institute (coll. MD/PhD Lucy Yates). The TREAC project, a collaboration with Elin Mortensen (University of Northern Norway), received a generous grant from Jeanette and Søren Bothners legat. In addition to being active partners in several clinical trials (ICON, ALICE, OPTIMA, I-BCT) we are coordinating the EMIT trial (A. Langerød). The EU/IMI collaboration CancerID finished December 2019, and we are active partners in the initiation of The European Liquid Biopsy Society (ELBS).



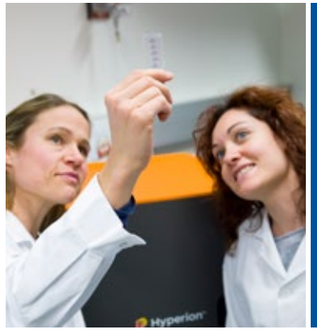


"Our goal is to improve cancer diagnostics and therapy through cutting edge research on tumor immunology and lymphocyte biology"







Department of

Cancer Immunology

Headed by Johanna Olweus

ABOUT

The Department of Cancer Immunology (DCI) consists of five research groups (Olweus, Taskén, Sioud, Myklebust, Malmberg) and one project group (Kyte). Four DCI members are full professors at the University of Oslo. Groups at the DCI are partners in two K.G. Jebsen Centers (Cancer Immunotherapy and B-cell malignancies) and several EU-funded research programs in cancer immunotherapy. The groups provide complementary expertise in molecular and cellular immunology, including a broad experimental tool-box for antigen discovery and studies of immune cells at the single cell level. The aim is to decipher the molecular regulation of key cellular components of the innate and adaptive immune system, including dendritic cells (DC), B cells, T cells, regulatory T cells (Treg) and NK cells. The key driving force is to develop better tools for cancer diagnostics and new therapeutic strategies. The latter include investigator-initiated clinical trials to alleviate immune suppression and improve the use of check-point inhibition, and the design of gene-edited T- and NK cells for adoptive cell therapy.

PROJECTS

- Lymphocyte biology, by deciphering
  - ontogeny and function of B, T and NK cells
  - tumor heterogeneity (signaling and mutanome)
  - immune cell recognition elements (antigen discovery)
- Biomarkers, by profiling of
  - lymphocyte repertoires
  - the tumor and its microenvironment
  - T-cell receptors and humoral immunity
- Therapeutics, by
  - genetically engineered T and NK cells
  - immune priming with siRNA and antigen-targeting to DC
  - genetically engineered human antibodies and lytic peptides
  - cell therapy across HLA barriers to overcome immune tolerance
  - clinical trials using experimental immunotherapy
  - small molecules

RECENT ACHIEVEMENTS (2019)

- 27 publications; 70% with first/last authors from DCI (mean/median IF 10.1/6.4), including first and/or senior authorships in high-impact journals like Nature Communications, Nature Protocols, Cell Reports, Leukemia and Haematologica
- Awarded ERC Consolidator Grant (2 mill Euro) to Olweus for the project "Outsourcing Cancer Immunity to healthy donors" (only scientist in Life Science category in Norway)
- Launched Strat-Cell, a strategic research program (5 years) in cell therapy at Oslo University Hospital (Malmberg Director, Olweus/Kyte co-Directors)
- Filed four new DOFIs, three patent applications filed and two granted.
- 1 graduated Msc

CLINICAL TRIALS:

- Recruited first 300 patients to the ASAC trial that examines the effect of reversing prostaglandin E2-mediated inhibition of tumor immunity in patients with metastatic colorectal cancer by the end of 2019 (www.asac.no)

Department of Cancer Immunology

Experimental Immunotherapy

Group leader: Johanna Olweus

"Overcoming tolerance by T-cell based cancer immunotherapies"

ABOUT
The group counts 16 members (F/M 70/30); 1 full professor (JO), 6 postdocs, 5 PhD students and 3.5 engineers, and two associated clinicians. Four members have MD background. 13 members are recruited from abroad. The group is partner in K.G. Jebsen Center for Cancer Immunotherapy (2013-); (JCIT). Olweus is Director of JCIT, which was awarded maximal prolongation in 2016 (two years), till 2020

AIMS
To find new immunotherapeutic T-cell based strategies that overcome the major challenge of self-tolerance in cancer, and couple clinical trials with penetrating mechanistic analyses. Two principally distinct approaches are pursued in an interdisciplinary and translational program:
Strategy 1: Use of T cell-based alloreactivity to target self-antigens.
Strategy 2: Identification and targeting of cancer-specific neo-antigens.

PROJECTS
Strategy 1
- Identification of novel TCRs targeting self-antigens and epitope discovery

Strategy 2
- Identification of novel TCRs targeting neoantigens and epitope discovery
- Characterization of anti-tumor reactive T cells in biobanked material from patients responding to immunotherapy

RECENT ACHIEVEMENTS
Olweus was awarded an ERC Consolidator Grant (2 mill Euro over 5 yrs), as the only Norwegian scientist in the Life Science category. The group described a technology for identification of neoantigen specific T cells from healthy donors (Ali/Foldvari/Giannakopoulou et al, Nature Protocols, 2019), and wrote an invited perspectives article for Blood (Olweus and Lund-Johansen, 2019). The group continued their research collaboration with biotech company Kite Pharma (acquired by Gilead) on development of T-cell receptors to target cancer. Olweus was elected member of the Executive Board of CIMT, organizing the largest and most influential annual cancer immunotherapy meeting in Europe. She was invited speaker at numerous international conferences in 2019, including the CIMT Winter School in immunology (Innsbruck), Synthetic Systems Immunology (Ascona), MDS Symposium (Copenhagen), Cancer Research UK Symposium (London).

NK Cell Biology and Cell Therapy

Group leader: Karl-Johan Malmberg

"Towards the next generation NK cell therapy"

ABOUT
The Malmberg Lab in Oslo counts 18 members (F/M: 10/8); 1 full professor (KJM), 2 scientists, 1 project manager, 7 postdocs, 5 PhD students, 3 engineers. Malmberg is a visiting Professor at the Karolinska Institute (KI) and a partner in the K.G. Jebsen Center for Cancer Immunotherapy. Affiliated to the group is the Kyte Project group in Translational Cancer Immunotherapy led by Dr. Jon Amund Kyte, with 10 members: Project group leader (JAK), 3 researchers, two postdocs, 1 MD PhD student, 3 technicians. Dr. Kyte is also a senior consultant in oncology and Head of Dept. Clinical Cancer Research and is appointed Group Leader at DCI from 2020.

AIMS
The Malmberg group seeks to develop new strategies for cell-based immunotherapy based on insights into the functional regulation of natural killer (NK) cells. A combination of single-cell assays, including live cell imaging, high-dimensional immune profiling by mass cytometry, flow cytometry and RNA-seq is used to decipher the cellular and molecular mechanisms involved in calibration of effector functions in human NK cells. The Kyte group aims to develop improved cancer treatment based on two strategies for immunotherapy: 1) Development of cell therapy by use of novel tumor-targeting chimeric antigen receptors (CARs) and concepts for countering tumor tolerance 2) Development of optimized regimes for combining checkpoint inhibitors with chemotherapy or radiotherapy. The Kyte group has from 2017 started three clinical trials, in breast cancer (ALICE, ICON) and head and neck cancer (REPORT).

PROJECTS
1) Functional Diversification of human NK cell repertoires
2) Cell therapy with iPSC-derived NK cells

RECENT ACHIEVEMENTS
- Gained new insights into the functional regulation of human NK cells *(Goodridge et al, Nature Communications 2019)*
- Deciphered molecular pathways involved in NK cell homeostasis *(Jacobs et al., J Immunology 2019, Pfefferle et al., Cell Reports 2019)*
- Completed a one-year research sabbatical at UCSD resulting in new collaborations with world leading iPSC environments *(Sætersmoen et al., Seminars in Immunopathology 2019).*
- Launched Strat-Cell, a strategies research program (5 years) in cell therapy at Oslo University Hospital.
- Innovation: Initiated a 2-year collaborative agreement with EMD-Serrono to develop functional modulators of NK cells in vivo.

Department of Cancer Immunology

Lymphoma Biology

Group leader: June Helen Myklebust

“Understanding B-cell lymphoma biology to identify new therapeutic targets and treatment strategies”

ABOUT
The group counts 13 members with research background in medicine, biology and biotechnology, and includes 1 professor, 1 associate professor, 1 scientist, 7 postdocs (including visiting postdoc at MGH/Broad Institute, Boston), 2 PhD students and 1 technician. Five members have MD background and four members are recruited from abroad. The group is part of the KG Jebsen Centre for B-cell malignancies.

AIMS:
The group performs translational studies in B-cell lymphoma to define tumor clonal evolution, cancer driver genes, actionable targets and new targets for immunotherapy.

PROJECTS
We use single-cell technologies to characterize tumor cells and intratumor immune cells in patient biopsies. This includes high-dimensional flow cytometry, mass cytometry and mass cytometry imaging (Hyperion), and single-cell RNA sequencing. We also use CRISPR/Cas9 genomic editing combined with immunological assays to characterize potential cancer driver genes, and have established patient-derived xenograft (PDX) mouse models for pre-clinical drug testing. Ongoing projects are:

- Clonal evolution and recurrent mutations associated with therapy relapse
- Functional characterization of recurrent driver mutations
- Novel targets for immune checkpoint blockade
- Cancer sensitivity drug screen and preclinical testing
- Clinical register studies

RECENT ACHIEVEMENTS
The group published 7 original papers, 1 commentary and 1 news&views (Nature) in 2019: Our in-depth analysis of the tumor microenvironment identified TIGIT and PD-1 as relevant targets for co-checkpoint blockade in B-cell lymphoma (Josefsson, Cancer Immunol Res). Our collaborative effort with Cell therapy has led to preclinical development of CD37 CAR T cell therapy (Köksal, Blood Adv and patent filed). We developed the clinical-genetic prognostic tool BTK-FLIPI to identify follicular lymphoma at high risk for adverse disease (Steen, Haematologica), and contributed to convergence of risk prediction models (Silva, Haematologica). Several members had oral presentations at international meetings; the most prestigious being our collaborative project with lymphoma clinicians, the Hovig group and Genomics core facility to map tumor clonal evolution in follicular lymphoma, selected for oral presentation at the American Society of Hematology (Bai, ASH 2019).

Immunomodulation and Targeted Therapies

Group leader: Mouldy Sioud

“Innovative approaches for cancer therapy”

ABOUT
The group has 8 members, including 1 postdoc, 2 research engineers, 1 PhD student, 3 master students, and the group leader (DEA Pharm, PhD) with formal research experience in immunology, molecular and cell biology, microbiology, and medicine. Sioud is a visiting professor at University of Tunis. To date, the group has published **197** peer-reviewed original articles (mean IF = **5.865**) and reviews, with 1st and/or last authorship on 85% of the papers.

Traditional cancer treatments like radiation and chemotherapy have major side effects because they not only affect the tumors, but also the healthy parts of the body. Hence, there is a need for improvement. The group is mainly focused on the development of therapeutic antibodies, lytic peptides, and small RNA modulators to target and kill cancer cells or counteract immune suppression. With respect to clinical translation, we developed the first RNA interference-modified dendritic cell cancer vaccine that is now available to patients under compassionate use (Sioud 2019, *Cancers*, IF 6.2).

AIMS
The principal aim is to develop antibodies, antibody derivatives (e.g., antibody-photosensitizer conjugates, chimeric antigen receptors, bispecific antibodies), and lytic peptides for use in cancer immunotherapy.

PROJECTS
- Profiling the cell surface proteome using high-throughput phage display technologies
- Development of therapeutic human antibodies and lytic peptides
- Fingerprinting immune responses in cancer patients
- RNA interference and CRISPR technologies as immune modulators

RECENT ACHIEVEMENTS
- Reported the first lytic peptide targeting tumor macrophages and leukemia cells (Sioud et al. *Cancers* 2019)
- Developed new antibody-photosensitizer conjugates to target and kill cancer cells (Gebretensaie et al. manuscript in preparation)
- Developed new human antibodies to modulate immune cell functions
- Described a new mechanism of action of extracorporeal photopheresis immunotherapy involving IDO+ tolerogenic dentritic cells (Sagar et al. *Cancers* 2020).
- Three publications
- Sioud edited a new book on RNA interference and CRISPR technologies (Springer-Nature: https://www.springer.com/gp/book/9781071602898).
- The group obtained funding from South-Eastern Norway Regional Health Authority and Radforsk

Department of Cancer Immunology

Cell Signalling and Immune Regulation

Group leader: Kjetil Taskén

«We want to perturb tumor immune evasion mechanisms to boost anti-tumor immunity»

ABOUT

In 2019 the group counted 18 members (F/M: 10/8), 1 full professor (KT), 1 senior consultant, 2 researchers, 8 postdocs, 1 PhD student, 1 MD/PhD student, 2 technicians and 2 M.Sc. students. The group is part of K.G. Jebsen Centres for Immunotherapy and B Cell Malignancies.

AIMS

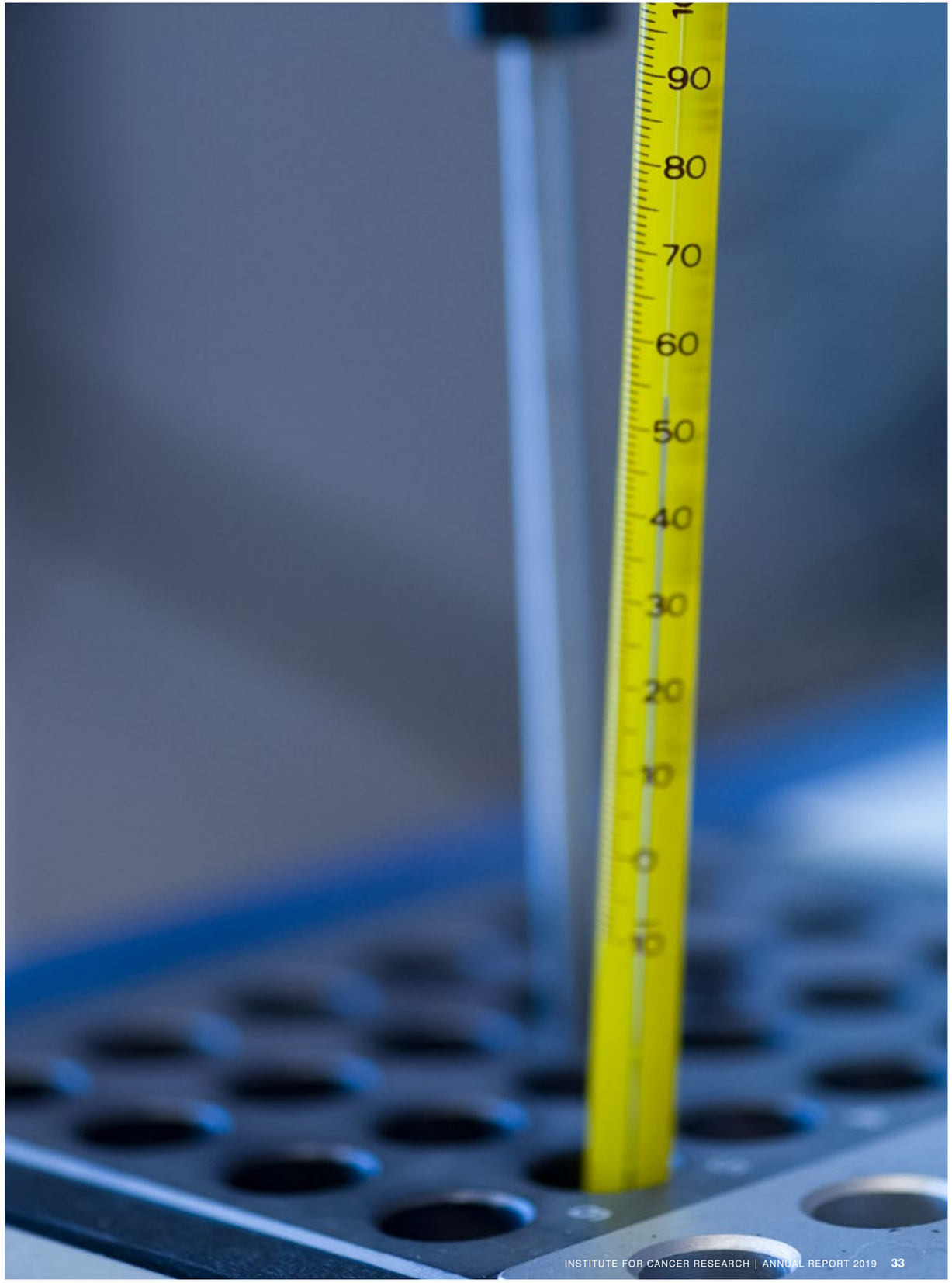
The Taskén group aims to understand intracellular signalling networks, the anchoring and localization of signaling complexes through scaffold proteins, how these signalling networks mediate physiological and pathophysiological processes and can be perturbed using drug-like small molecules. We aim to understand tumor immune evasion mechanisms, and how we can interfere to boost anti-tumor immunity. We proceed with cancer drug sensitivity screening (CDSS) to explore individual drug responsiveness and resistance patterns in patient cancer cells and aiming to develop models to assist individualised clinical decisions in precision medicine in oncology and haematology.

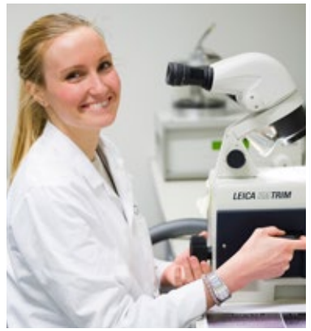
PROJECTS

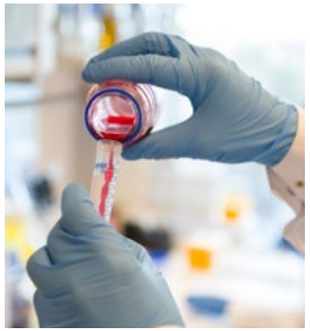
- T cell function in cancer and immune-related diseases
- Identification of regulatory T cell targets that can be perturbed to reverse tumor immune suppression
- Role of Prostaglandin E2, cAMP and AKAPs in signaling and regulation of T cell function
- Targeting the cAMP signalling pathway for cancer immunotherapy
- CDSS in chronic lymphocytic leukemia and multiple myeloma, understanding drug synergies and predicting effective drug combinations in individual patients (RCN-Digital Life PINpOINT project)
- Acetyl salicylic acid clinical intervention study in metastatic colorectal cancer (ASAC)

RECENT ACHIEVEMENTS

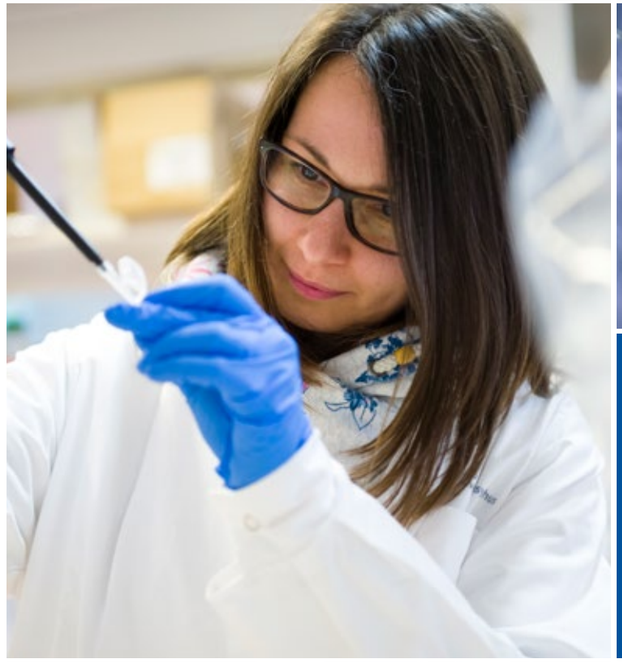
Publication highlights include studies on CLL patients in our precision medicine programme where we predict clinical dosing of combinatorial treatments based on biomarker studies (Leukemia), on regulatory T cells and tumor immune suppression by idelalisib (J. Immunol.) and on signalling complexes orchestrated by CD28 and CD2 (J. Immunol.). Furthermore, in co-authored papers we have contributed to understanding metabolic regulatory programmes for aerobic glycolysis in T cells (Nature) and TLR8 signaling in T cells (Nature Commun., in press). 1 DOFI was submitted, 1 patent was filed and 1 granted. One M.Sc. student graduated.

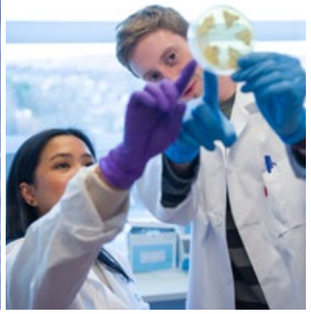


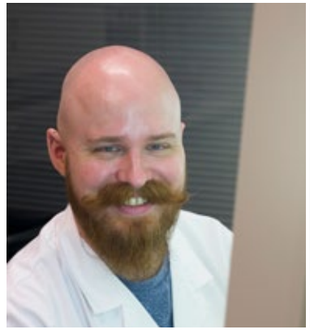
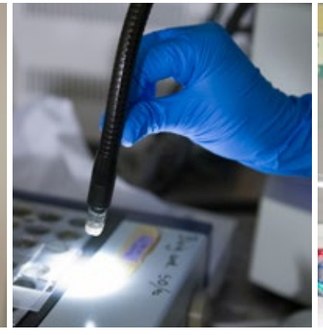


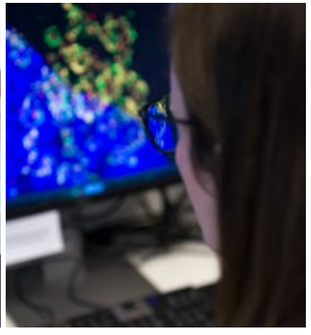


"Uncovering the cellular basis of cancer development"





Department of

Molecular Cell Biology

Headed by Harald Stenmark

The department has a staff of 80 (including 11 MSc students and trainees) of 23 nationalities and hosts 4 research groups (Enserink, Rusten, Sandvig and Stenmark), 9 project groups, and a departmental service unit. Research in the department comprises various aspects of cancer relevant cell biology, including membrane traffic, cell signaling, cell metabolism and cell division. In addition, the department carries out biotechnological research on nanoparticles and translational research on leukemia drug sensitivity, cancer-related fungal infections, and cancer derived exosome biomarkers.

A common goal for researchers in the department is to uncover novel molecular mechanisms that control cellular functions related to cancer. The department's research strategy is to combine molecular cell biology with biochemistry, genetics, drug screening and advanced imaging in order to address relevant scientific questions. Recent key achievements from the department's scientists include studies on autophagy and tumour growth, growth factor signalling and intracellular transport, molecular mechanisms of cell division, exosome secretion and biomarkers for prostate cancer. In general, the department's groups have been successful in obtaining national and international external funding.

The groups of Harald Stenmark, Jorrit Enserink and Tor Erik Rusten are members of a Norwegian Centre of Excellence, CanCell, headed by Harald Stenmark. Harald Stenmark also heads the Norwegian Advanced Light Microscopy Infrastructure Network, NALMIN, and the Chinese-Norwegian Partnership for Education and Research in Cancer Cell Biology, ChiNoCell. Stenmark's group is member of a Convergence Environment under UiO Life Science, called "Programmable cell-like compartments". Jorrit Enserink participates in a project under Norwegian Centre for Digital Life, "Pipeline for individually tailoring new treatments in hematological cancers". Enserink's group also participates in the EU Horizon 2020 project, RESCUER.

Department of Molecular Cell Biology

Cellular Membrane Dynamics

Group leader: Harald Stenmark

"Understanding how remodelling of cellular membranes contributes to cancer"

ABOUT
The group studies the dynamics of cellular membranes with the aim of understanding their relevance to cancer. Cellular membrane dynamics processes studied by the group include endocytosis, autophagy, and cell division. The group has 34 members from 12 nations and is headed by Harald Stenmark (group leader) and Camilla Raiborg (assistant group leader). Its 5 project groups are led by Andreas Brech, Kaisa Haglund, Camilla Raiborg, Kay O. Schink, and Antoni Wiedlocha.

AIMS
The principal aim of the group is to understand how membrane dynamics contribute to tumour suppression and how their dysfunction may promote cancer development.

PROJECTS
- Phosphoinositides in regulation of membrane dynamics
- Mechanisms of autophagy and lipid droplet biogenesis, and their role in cell metabolism
- Centrosome dynamics in cancer
- Cytokinesis in development and carcinogenesis
- The β-catenin destruction complex in physiology and cancer
- Membrane dynamics in promotion of genome integrity
- Mechanisms of cancer cell invasion

RECENT ACHIEVEMENTS
- New mechanism of tumour suppression – intracellular retention of matrix metalloproteinases (Sneeggen et al., Nature Communications 2019). Awarded publication prize from Oslo University Hospital.
- ESCRT proteins promote autophagy by mediating sealing of newly formed autophagosomes (Zhen et al., Autophagy, 2019).
- Novel mechanism for recruitment of the abscission machinery to the midbody during cytokinesis – (Lie-Jensen et al., Current Biology, 2019). Dedicated a commentary article in Current Biology.
- Comprehensive review on ESCRT proteins in sealing and scission of cellular membranes (Vietri et al., Nature Reviews Molecular Cell Biology, 2019).
- Major grants in 2019 to Kay O. Schink, Harald Stenmark, and Viola Nähse.
- Marte Sneeggen obtained her PhD in November 2019.
- Harald Stenmark was invited speaker at international conferences in Okinawa, Paris, Trondheim, Glasgow, Beijing, Edinburgh, Essen and Strasbourg in 2019.
- Nina Marie Pedersen and Lene Malerød were selected for oral presentations at the international conference on "Cell Signaling and Intracellular Trafficking in Cancer Biology" in Turin, and Yan Zhen and Andreas Brech received prizes for best posters at the 9th International Symposium on Autophagy in Taipei.
- New collaboration on cancer cell invasion, InvaCell, with the group of Philippe Chavrier at the Curie Institute, Paris. InvaCell is generously sponsored by Trond Paulsen.
- Members of the group published 13 original papers and 3 reviews in 2019.

Cancer Molecular Medicine

Group leader Jorrit Enserink

"Identifying weak points in the molecular networks that drive cancer"

ABOUT
The group currently consists of one group leader, two project group leaders, seven post-docs, one clinician in a 20% post-doc position, two PhD students, four MSc students and one Erasmus student. A large fraction of the group consists of scientists from abroad , including the Netherlands, Austria, Spain, Colombia and the UK. The group is mainly focused on basic cancer biology and personalized medicine, using a wide range of models such as budding yeast and fruit flies, human and mouse cell lines, and primary human cancer samples.

AIMS
Research is aimed at understanding cancer cell biology, with the ultimate goal of developing precise cancer treatments. A major focus is on hematopoietic cancers, including –but not limited to– Acute Myeloid Leukemia (AML). A second research theme is to better understand cellular responses to sudden environmental changes.

PROJECTS
- High-throughput drug combination screens to identify drug synergies and to reveal correlations between driver mutations and drug sensitivity profiles
- Development of novel immune therapy for AML
- Modeling of leukemia in fruit flies to better understand the genetic networks that drive AML
- Genome-wide CRISPR-Cas9 screens in leukemic cells to identify novel mechanisms of resistance to tyrosine kinase inhibitors
- Cellular responses to nutrient stress; particularly the identification of the upstream pathways that control the dynamics of autophagy

ACHIEVEMENTS
- Five MSc degrees were completed and the group published three articles.

- Funding obtained: A research grant from The Norwegian Cancer Society to Jorrit Enserink and a Young Research Talent grant from The Research Council of Norway to Dr. Helene Knævelsrud.

- The group is also part of the RESCUER project headed by Dr. Vessela Kristensen, which was awarded by the EU Horizon 2020 scheme in 2019.

Tumor-host Biology

Group leader Tor Erik Rusten

"Tumor-host interactions during cancer progression"

ABOUT

The research group counts 12 members representing 7 nationalities in 2019 (Australia, India, Iran, Hungary, France, Spain and Norway): 1 group leader, 1 scientist, 5 postdocs and 1 PhD student, 1 technician and 1 master students and 2 Erasmus exchange students.
Cancer can be regarded as organ development derailed. Our overarching interest is to understand the mechanisms by which tumor and host cells mutually engage each other in reciprocal interactions that promote cancer progression. These interactions occur locally in the tumor microenvironment, but also systemically causing organ dysfunction such as in cancer cachexia - the catastrophic wasting of muscle and adipose tissue. We believe that studying these processes can uncover new ways to intercept carcinogenesis. To mechanistically probe 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 will allow us to selectively and independently manipulate tumor and either tumor microenvironment or somatic organs in vivo. We investigate the molecular genetic mechanisms and cell biology of genetically defined experimental tumor-host interactions using a mix of human cell culture and the fruit fly Drosophila melanogaster, as an animal model system. In this work we employ a wide array of techniques and collaborate with experts in cell biology, genetics, imaging, electron microscopy, tumor biology, metabolism, bioinformatics and clinical cancer cachexia in order to survey, measure and mechanistically understand these complex aspects of cancer biology.

AIMS

The principal aim of the group is to understand tumor-host interactions that facilitate cancer progression in order to uncover novel ways to intercept cancer.

PROJECTS

- Oncogene-induced epithelial disintegration and invasion.
- Tumor-microenvironment interactions and growth support.
- Mechanisms of cancer cachexia.
- Roles of autophagy in metabolic reprogramming, nutrient mobilization and breakdown of muscle and adipose tissue during cancer cachexia.

RECENT ACHIEVEMENTS

- EMBO long-term postdoctoral fellowship was awarded to Dr. Swarupa Panda to work on "Mechanisms of non-autonomous support of tumor cell growth"
- Tor Erik Rusten was invited at 5 international research conferences (including a Gordon Research Conference) in Heidelberg, Lisbon, Utrecht, Barcelona and Santa Fe in 2019, one of these as keynote speaker
- In 2019 one MSc was completed and the group published one review, one preview and contributed to two original research articles

Intracellular Transport

Group leader: Kirsten Sandvig

"All the way from basic research to translation"

ABOUT

Sandvig's group, counting 15 members, is interested in the mechanisms of endocytosis, intracellular transport and secretion. Uptake of receptors and ligands and correct intracellular sorting of endocytosed molecules are crucial for maintenance of a normal differentiated phenotype.
In some studies we are using protein toxins such as ricin and Shiga toxin, which are well established as markers for studies of membrane traffic, and which can be used as agents in cancer diagnosis and therapy. Our expertise is also applied to investigate uptake of nanoparticles for drug delivery, and since 2013 we have had a large grant from the Norwegian Research Council to build national competence in nanomedicine. This project, "Biodegradable nanoparticles in cancer diagnosis and therapy", headed by Sandvig, involved collaboration with ten other Norwegian groups working in academia, research institutes, hospitals and industry, and was running until March 2019. The Sandvig group has also been involved in an INNO INDIGO granted project, which started April 2016 and ended September 15th, 2019. INNO INDIGO is an innovation-driven initiative for the development and integration of Indian and European research. Our nanoparticle research has, based on results from these projects, obtained further support from the Norwegian Cancer Society for 2020-2023. We also characterize exosomes from prostate cancer cells and patients with the goal of detecting lipid, RNA and protein biomarkers. Our research spans all the way from basic to translational medicine, including innovation. The work published by the Sandvig group is well cited, and Sandvig's H-index is now 73 (~340 publications). The group has extensive national and international collaborations.

AIMS

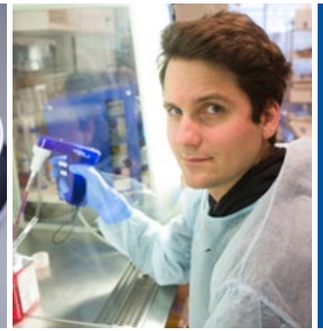
The projects aim at increasing our knowledge about intracellular transport, nanoparticles for drug delivery, and exosomal biomarkers in order to provide a rational basis for diagnosis, treatment and prevention of cancer.

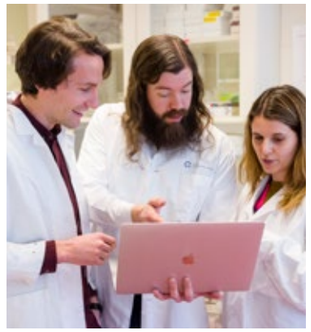
PROJECTS

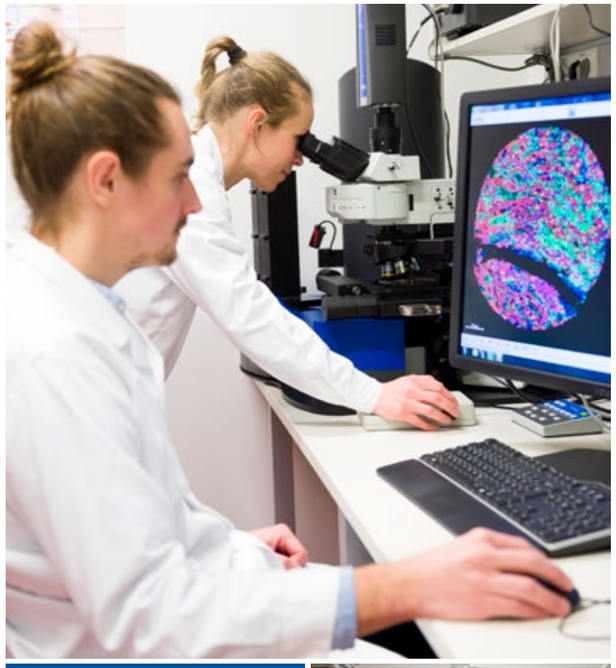
- Characterization of intracellular transport
- Biodegradable nanoparticles in cancer diagnosis and therapy
- Exosomes and prostate cancer

RECENT ACHIEVEMENTS

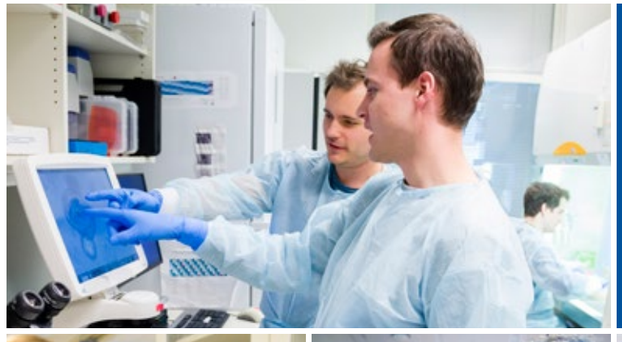
- Mechanistic studies of different types of endocytosis and intracellular transport. Our competence concerning cellular membranes and lipid species made us publish a perspective article (Skotland et al., Nature Communications, 2019) about the role of specific lipid species and what should be done in the future to increase our understanding of cellular membranes.
- We have performed further studies of exosome biogenesis and release, as well as of biomarkers for prostate cancer. Investigations of cytotoxic effects of different types of nanoparticles with and without drugs were performed both in vitro and in vivo.
- In 2019 the group published on the different topics; 10 articles in different journals.
- Kirsten Sandvig obtained a research grant of 8 MNOK from the Norwegian Cancer Society on a project that will investigate the efficacy of drug-containing nanoparticles in breast and colorectal cancers.

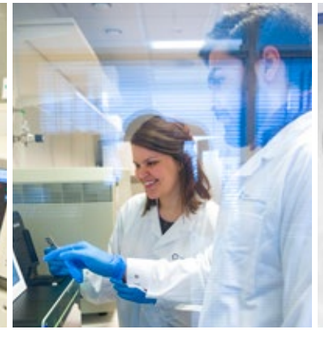



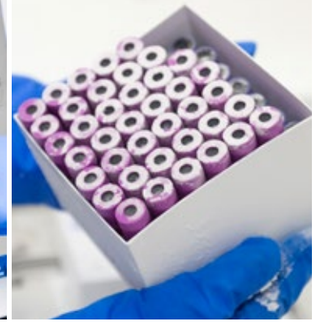





”Biological discoveries for improved precision cancer medicine”





Department of

Molecular Oncology

Headed by Ragnhild A. Lothe

Our main research programs are devoted to colorectal cancer and prostate cancer, but with a longstanding project portfolio also on other solid tumor types. Our expertise in biomedical research spans across several disciplines, and we have a broad range of advanced technologies and analytical tools established in the lab. The department hosts three research groups and three project leaders, in total ~10 % of the total staff at the Institute (full time equivalent). Six of the senior scientists are affiliated with the University of Oslo as professors (three), associate professor, or lecturers (two). We are devoted to teaching and supervision, and six academic degrees (4 MSc and 2 PhD) with main supervisors from our Department were successfully completed last year.

Our research groups are current partners of the K. G. Jebsen Colorectal Cancer Research Centre, an OUH Strategic Research Area, and several national and international scientific networks. The latter includes national multicenter studies on colorectal cancer and bladder cancer, European cooperation studies on colorectal cancer (COST action), a European multicenter study on the rare tumor type malignant peripheral nerve sheet tumor, the European network for study on cholangiocarcinoma, and the Global Testicular Cancer Consortium.

A few selected results from last year:
We showed that multifocal primary prostate cancers have an exceptional degree of intra-patient genomic heterogeneity (Løvf et al., Eur Urol), and this challenges the usefulness of known molecular classifiers (Carm et al., Sci Rep). Furthermore, we published a comprehensive review on biomarker-guided therapy for colorectal cancer (Sveen et al., Nature Rev Clin Oncol), and demonstrated the clinical impact of tumor microenvironment markers relative to cancer genomic markers in patients with colorectal cancer (Dienstmann et al., Ann Oncol; Berg et al., Oncogene).
A national multicentre study and innovation project to monitor bladder cancer patients with cancer-specific epigenetic markers in urine samples documented strong discovery and validation results (unpublished), and externally financed by major grants from the Norwegian Research Council and National Health Regions (KLINBEFORSK)

Our main research goals for the next three to five years are three-fold, (i) to decipher spatio-temporal tumor heterogeneity and its clinical relevance in colorectal cancer and prostate cancer, (ii) to monitor minimal residual disease, early recurrence and clonal evolution by analyses of repeated liquid biopsies and tumor samples, and (iii) to predict treatment responses by combined molecular profiling and ex vivo drug screening of patient-derived organoids in clinical trials and translational studies.

Department of Molecular Oncology

Genetics

Group leader: Ragnhild A. Lothe

“Molecular tumor heterogeneity and personalized pharmacogenomics - the basis for next generation clinical trials”

ABOUT

Our main research program involves translational studies of primary and metastatic colorectal cancers (CRC), using genomics, drug screening, digital pathology and functional analyses. The group has 23 members and includes two project groups in Cell signaling and Computational oncology.

AIM

Our overarching goal is to translate novel biomedical knowledge into improved patient stratification and treatment of CRC.

PROJECTS

- Prognostic and predictive biomarkers
- Modeling tumor heterogeneity and clonal evolution
- Pharmacogenomics of solid tumors using patient-derived organoids (PDO)
- E3 ubiquitin ligases in intercellular communication and carcinogenesis

RECENT ACHIEVEMENTS

In 2019 we published 20 papers, including in Ann Oncol (2), Oncogene (2), PNAS, and Nature Rev Clin Oncol. Kaja Christine Graue Berg defended her PhD at the Faculty of Medicine, U of Oslo. Two early career scientists were rewarded for their excellence, Anita Sveen received “Early Career Award” from OUH, and a major grant from the Norwegian Cancer Society; Peter W. Eide received the “Young researcher award” from Onkologisk Forum (Annual National Oncology meeting).

We published a comprehensive review on biomarker-guided therapy for CRC (Sveen et al., Nature Rev Clin Oncol 2019), showed that splice variants of KRAS has prognostic relevance beyond its mutation status (Eilertsen et al., Int J Ca 2019) and we concluded that the long noncoding RNA MIR31HG is a bona fide prognostic marker in CRC (Eide et al., Int J Ca 2019). We showed that TP53 mutations may modulate the immune microenvironment in a particularly immunogenic subgroup of CRCs, inferring a poor patient survival (Smeby et al., ESMO Open 2019). In multicentre studies we confirm that tumor microenvironment markers are key determinants for risk of relapse in early-stage CRC (Dienstmann et al., Ann Oncol, 2019; Glaire et al., Brit J Ca 2019).

Much effort is put into the pharmacogenomics project: multiple ex vivo cultures from CRC liver metastases have been successful established as PDOs, and screened for sensitivity to 40 anticancer agents. Intra-patient inter-metastatic pharmacological heterogeneity is not pronounced and variation in drug sensitivities is reflected at the transcriptomic level, suggesting great potential to develop gene expression-based predictive signatures to guide experimental therapies (paper in revision). A protocol for a clinical trial implementing such personalized pharmacological models is currently in development.

Epigenetics

Group leader: Guro E. Lind

“Epigenomics – reversible changes in cancer and a source for clinical biomarkers”

ABOUT

In the group of Epigenetics we are studying DNA methylation alterations by integrating genome wide methylation profiling (sequencing and arrays), with detailed candidate gene characterization. The research is performed across cancer types, with a main focus on gastrointestinal and urological cancer. In 2019 the group counted eleven members: 3 postdocs/scientists, 2 PhD students, 3 engineers, one study nurse, one MSc student and the group leader, and includes a project group.

AIMS

1) To identify and develop epigenetic biomarkers with clinical impact, including markers for early detection and monitoring of cancer.
2) To explore the inter- and intra-tumor diversity of epigenetic aberrations in cancer, and effect on patient outcome.

PROJECTS

- Epigenetic subclassification and prognostic markers for colorectal cancer
- Methylome-based early detection and monitoring of bladder and gastrointestinal cancer
- Epigenetic heterogeneity in gastrointestinal cancers

RECENT ACHIEVEMENTS

During 2019, the group has continued the development of a urine-based test for monitoring of bladder cancer patients. A set of biomarkers, identified in-house using methylome sequencing, demonstrated high accuracy in a test series and was recently validated using a blinded prospective international patient series (manuscript). A cohort of 50 post-surgery individuals is being followed at Aker for two years, in order to compare the urine test to the current gold standard method (cystoscopy). Full follow up time will be reached in 2020. Preliminary data indicate that the urine test enables earlier detection of bladder cancer recurrence.

The data have laid the foundations of a national multi-center study aiming at demonstrating the clinical utility of the urine test. Hospitals from all health regions are participating, and the first patient was recruited in December. All together 500 patients will be followed for a two-year period. The study is funded through “klinisk behandlingsforskning” and received additional funding from the Research council in 2019.

In 2019 Marine Jeanmougin was appointed leader of a project group with expertise in biostatistics.
One PhD degree (Heidi Pharo) and one MSc degree (Ida Marie Børresen) were completed from the group in 2019.

Department of Molecular Oncology

Genome Biology

Group leader: Rolf I. Skotheim

“Molecular heterogeneity of prostate cancer - Improved precision diagnostics”

ABOUT

The research group studies how genomes and transcriptomes are altered in cancer cells by using both computational and wet-lab based approaches. Mutation analyses in cancer benefit from knowing which genes and variants that are expressed, and the group has specialized in RNA-level analyses. Further, most projects focus on prostate cancer. An interdisciplinary set of expertise is beneficial for genome-scale cancer research, and the personnel have their education across the disciplines biology, informatics, and medicine. Through 2019, the group consisted of twelve members.

AIM

To improve the diagnosis and management of cancer by utilizing genome technologies.

PROJECTS

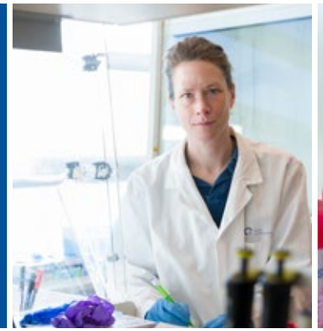
- Interfocal heterogeneity of prostate cancer
- RNA variation caused by aberrant splicing and as a source of cancer biomarkers
- Fusion gene identification and characterization

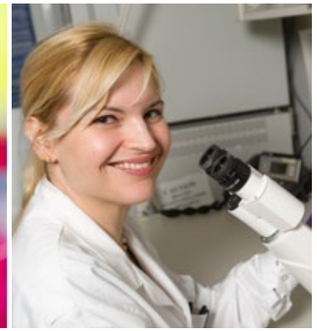
RECENT ACHIEVEMENTS

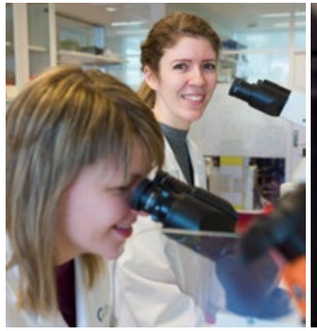
During 2019, the group continued the development of a large prostate cancer research program. The first large in-depth genomic heterogeneity analysis of primary prostate cancer was reported (Løvf et al., Eur. Urol, 2019). Here, whole-exome sequencing of 89 tumor foci from 41 patients revealed that different tumor foci within the same patient only exceptionally share any somatic mutations. A follow-up study pointed out that existing molecular signatures are useless in the clinic if inter-focal heterogeneity is not considered (Carm et al., Sci. Rep., 2019). This is important for how genetics can inform on treatment decisions as information from all tumor foci is necessary to conclude about the cancer. The group continued to develop bioinformatics pipelines for high-throughput sequencing of DNA and RNA. A paper in press describes a tool for sensitive fusion gene detection and with biomedical data from testicular cancer (Zhao et al., NAR Genomics and Bioinformatics). In addition to these three articles, the group contributed to four publications from internal and external collaborations.

In 2019, three MSc degrees were achieved. Karina Borlaug got her degree at Dept. Informatics, whereas Susanne Kidd and Linn Olsen got theirs from Dept. Molecular Biosciences.

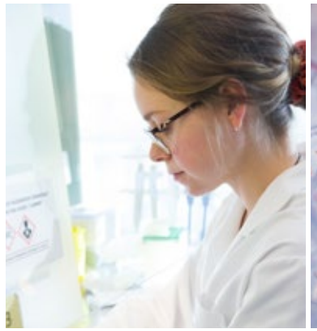
Important research funding was obtained from the Norwegian Cancer Society and South-Eastern Norway Regional Health Authority.










"Our goal is to develop new predictive methods and treatment strategies for improved radiation therapy"

Department of

Radiation Biology

Headed by Kristian Berg

The Department has more than 60 employees organized in 4 research groups and 6 project groups. The research at the department is focused on the biological responses to ionizing and non-ionizing radiation, including γ-radiation, radiation from radionuclides, ultraviolet radiation, visible light as well as proton therapy. Our department is actively engaged in revealing the mechanisms involved in DNA repair, cell-cycle regulation, genomic instability and immune responses after radiation, the impact of hypoxia on the radiation response and predictive markers for the outcome of radiotherapy of cancer patients. The department is also involved in delivering radionuclides to cancer tissue. Another research area is the use of visible light to activate photosensitive compounds, thereby generating reactive oxygen species, which are used for cancer detection and therapy. In that respect a technology has been developed, photochemical internalization (PCI), which enables site-directed intracellular delivery of anticancer therapeutics.

OUR GOALS ARE

- To understand the molecular and physiological mechanisms behind tumour response to radiation, and to develop predictive methods and treatment strategies;
- To utilize acquired knowledge to establish new radiation-based treatment regimens with improved specificity and efficacy towards cancer cells;
- To develop treatment strategies utilizing non-ionizing radiation combined with photosensitizing agents, either to induce tumour cell kill directly or via internalization of therapeutic or sensitizing agents.

KEY ACHIEVEMENTS THE LAST 3-4 YEARS INCLUDE

- Pancreatic carcinoma xenografts treated with sunitinib show less abnormal microvessels but larger hypoxic regions after treatment than before treatment;
- Cervical cancer patients with tumors showing high hypoxic fraction in combination with high interstitial fluid pressure have particularly poor prognosis with a 5-year survival rate of only 13 %;
- A novel mechanism of activation of the DNA damage kinase;ATR (Ataxia Telangiectasia and Rad3-related) was identified;
- PCI has been found to efficiently enhance antigen presentation during anti-cancer vaccination.;
- A production unit for biomolecular therapeutics has been established. Several new recombinant targeted protein toxins have been developed and are under preclinical evaluation;
- Documented for the first time that protons can activate photosensitizers used in photodynamic therapy (PDT) to mimic responses as in PDT;
- A new method to image hypoxia in prostate cancer based on integration of images reflecting oxygen consumption and supply has been developed;
- We gained important new knowledge about the regulation of translation in response to cellular stress as well as about the function of the stress-response kinase GCN2 in human cells;
- Combinatorial drug partners were identified that overcome resistance to CD37-targeted radioimmunotherapy in B cell lymphoma;
- Described a key mechanism required for formation of Hh-signaling competent cilia that is potentially exploitable as treatment target for Hh-dependent cancers.

Photochemical Internalization

Group leader: Kristian Berg

"Our goal is to develop and optimize the PCI technology for treatment of solid cancers"

ABOUT
Group members: 21, including 5 researchers, 5 postdocs, 3 PhD students, 6 technical positions and 2 MSc students, including the project groups of Asta Juzeniene, Pål Kristian Selbo, Anette Weyergang and Theodossis Theodossiou.

Project *Photochemical Internalization (group leader Berg, project leaders Selbo, Weyergang and Theodossiou):* Endocytic entrapment is a hurdle for therapeutic utilization of macromolecular therapeutics with intracellular targets. Photochemical internalisation (PCI) is a technology for cytosolic release of therapeutic macromolecules subjected to endocytosis. PCI is invented and developed in our research group and is currently evaluated in clinical trials.

Project *Targeted alpha therapy (project leader Juzeniene):* Metastases are the primary cause of death in cancer patients. Targeted alpha-particle therapy is a promising treatment for eradicating *micrometastases.*

AIMS
Project Photochemical internalization:
The main aim of our group is to develop and optimize the PCI technology for treatment of solid cancers with a curative endpoint.

Project Radionuclide therapy:
The main goal is to develop a novel technology with potentially broad therapeutic applications for cancer micrometastases by means of dual targeted alpha particle radiation.

PROJECTS
- Design and development of recombinant immunotoxins for activation by PCI
- Light-controlled delivery of cancer immunotherapeutics including PCI of 1) immunotoxins targeting cancer stem cells (CSCs) and 2) CSC-derived vaccines.
- Utilize new vehicles for targeted delivery of small molecular drugs to endocytic vesicles for activation by PCI
- Evaluation of the vasculature as a target for PCI and further utilize these effects to reach a curative endpoint
- Using mitochondria-powered chemiluminescence to non-invasively treat inaccessible tumours
- Utilizing other radiation sources to induce PCI effects
- Targeted alpha radionuclide therapy for bone and visceral metastases of osteosarcoma, prostate and breast cancer

RECENT ACHIEVEMENTS
- Documented for the first time that protons can activate photosensitizers used in photodynamic therapy (PDT) to mimic responses as in PDT;Published in *Nature Comm.*
- The new FET-OPEN project FRINGE (Co-ordinator: Theodossiou) was launched in 2019,
- New grants in 2019: PhD stipend from HSE (Selbo); Project grant from Radforsk (Weyergang)
- Theodossis A. Theodossiou awarded the prize researcher of the year at the Institute for Cancer Research
- The EU Innovative Science 2019 awarded to the Lumiblast project (Theodossiou and Berg)
- No. of papers in 2019: 8
- MSc thesis: 2

Clinical Radiation Biology

Group leader: Heidi Lyng

"Our goal is to discover biomarkers and molecular targets for combination therapies with radiation"

ABOUT
Group members: 10, including one researcher, four postdocs, three PhD students, and two technicians.

The focus is to develop molecular biomarkers that can identify patients at risk of radiotherapy failure and to find targets for therapeutic intervention in a combined radiotherapy regimen. The research projects are run in close collaboration with medical doctors and physicists at the hospital.

The work is based on tumor biopsies and blood samples collected at diagnosis or during therapy.
Whole genome methodology is used, including microarray and sequencing techniques, which provides new insight into the disease and enables identification of novel biomarkers and drug targets. We also explore whether functional tumor images (MRI/PET) can aid the translation of the molecular findings into radiotherapy practice.

AIMS
- Understand molecular mechanisms behind radioresistance of cervical and prostate cancer
- Develop biomarkers and find drug targets for personalized radiotherapy of patients with these diseases

PROJECTS
- Genetic alterations and chemo-radioresistance in cervical cancer
- Molecular hypoxia biomarkers in cervical and prostate cancer
- Combined molecular and imaging biomarkers in cervical and prostate cancer

RECENT ACHIEVEMENTS
In 2019, the group published 4 articles. Major findings were:
- Discovery of a miRNA candidate biomarker for hypoxia related treatment resistance in cervical.
- Identification and exploration of an aggressive cervical phenotype with elevated oxidative phosphorylation and proliferation activity.

Radiation Biology and Tumor Physiology

Group leader: Einar K. Rofstad

"Our goal is to identify strategies for personalized radiation therapy of cancer"

ABOUT
Group members: 7, including 2 researchers, 4 postdocs, 2 PhD students, and 1 technician.

The focus of the group is to improve the outcome of radiation therapy of cancer. Poor outcome is a consequence of radiation resistance and elevated metastatic propensity of the primary tumor, and our research is based on the hypothesis that poor outcome is caused primarily by an abnormal physicochemical tumor microenvironment. Xenografts of human cervical carcinoma, pancreatic carcinoma, and malignant melanoma are used as preclinical tumor models. In addition to standard molecular biology methods, important methods include intravital microscopy, MRI, and probe measurements of physicochemical parameters.

AIMS
To reach the primary goal, our research is divided into two arms with the following aims:
- To develop MRI-based methods that can provide information on the physicochemical microenvironment, metastatic propensity, and radiocurability of tumors
- To develop treatment strategies for normalizing the physicochemical microenvironment, decreasing the metastatic propensity, and enhancing the radiocurability of tumors

PROJECTS
- Clinical and preclinical MRI of the physicochemical microenvironment of tumors
- Treatment strategies targeting the physicochemical microenvironment of tumors

RECENT ACHIEVEMENTS
Anette Hauge defended her Doctor Philosophiae (Dr Philos) thesis at the Faculty of Mathematics and Natural Sciences, University of Oslo in 2019. The thesis (The Tumor Microenvironment and Its Assessment with DCE-MRI and DW-MRI) consists of 4 first-author and 3 second-author papers.

Our group developed novel MRI methods for characterizing the physicochemical microenvironment of tumors in 2019.

Important scientific findings in 2019:
- Highly elevated tumor interstitial fluid pressure is a stronger biomarker of the outcome of locally advanced carcinoma of the uterine cervix than high fraction of hypoxic tumor tissue.
- Antiangiogenic treatment of cervical carcinoma with bevacizumab may cause increased tumor hypoxia, owing to treatment-induced vessel pruning.

Radiation Biology and DNA Damage Signaling

Group leader: Randi Syljuåsen

"Our goal is to obtain new knowledge about cellular responses to radiation and utilize it to improve cancer therapy"

ABOUT
Group members
14.3 including 5 researchers, 1 postdoc ,5 PhD students and 3.3 technicians.

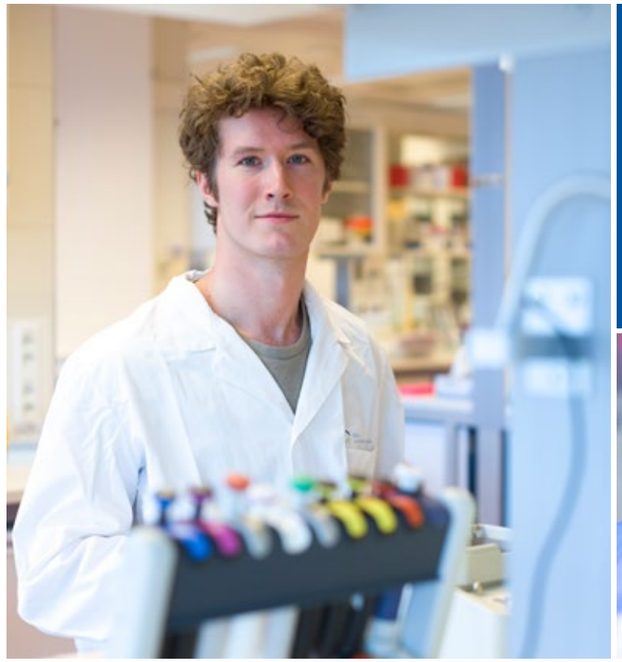
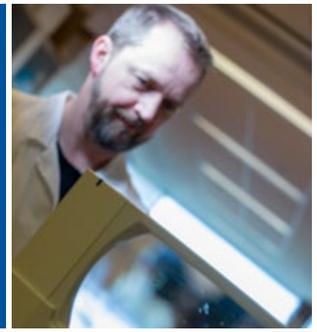
Theme
In radiotherapy ionizing radiation is used to cause DNA damage in cancer cells. The DNA damage is rapidly sensed and a network of intracellular DNA damage signaling cascades is activated. These signaling cascades influence whether the cells die or survive, through regulation of DNA repair, cell cycle checkpoint and cell death pathways. Our group works at the border between basic and translational radiation research. We conduct basic projects to identify novel mechanisms of DNA damage signaling, in addition to more applied projects to understand how inhibitors of DNA repair and checkpoints can be used in an optimized manner for cancer treatment. Three project groups, headed by Beata Grallert Trond Stokke and Sebastian Patzke, are members of our group.

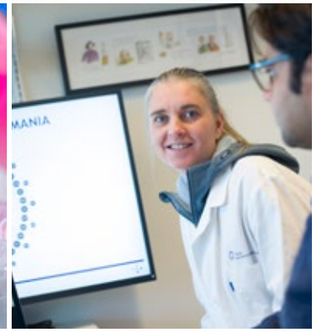
AIMS
- Obtain new knowledge about cellular responses to radiation, with focus on cell cycle checkpoints, DNA damage signaling and repair, and explore how such knowledge can be used to improve radiotherapy.

PROJECTS
- Pre-clinical exploration of the effects of checkpoint kinase (CHK1, WEE1, ATR) and PARP inhibitors
- Functional roles of Protein phosphatase 1 (PP1) targeting subunits in DNA damage signaling
- Identification of drugs that inhibit DNA repair after radiation, through flow cytometry-based compound screens
- Centrosomal and ciliary proteins in cell cycle regulation and genome integrity- roles and targets in cancer etiology, diagnostics and treatment
- The role of GCN2 and translational regulation in the cell cycle and cellular stress

RECENT ACHIEVEMENTS:
In 2019, a total of 10 articles were published. Members of the group were senior/first authors on 6 of these, published in Nucleic Acids Research, Cell Reports, Frontiers in Oncology, Cell Cycle, Current Genetics and Bioessays. One new grant was obtained from the Norwegian Research Council.





"Preclinical and clinical efforts towards precision oncology".





Department of

Tumor Biology

Headed by Gunhild M. Mælandsmo

The department has four research groups and 54 employees with a common vision to improve treatment of metastatic cancer. Our strategy is, through basic and translational research in the areas of cancer biology and computational science, to advance systems understanding and identify novel intervention strategies. We emphasize multidisciplinary competence and collaboration between researchers, clinicians and patients to stimulate the necessary synergy for improved cancer care.

We are performing basic, translational and clinical research, and our scientific goal is to provide knowledge for clinical translation of precision cancer medicine. We will do so by contributing with expertise in genomics and bioinformatics and by utilizing patient samples as model systems for investigation of therapeutic efficacy. We have a large collection of patient-derived cell lines and xenografts from different types of human cancer. The models are utilized for mechanistic studies of disease progression and treatment responses, and for preclinical evaluation of novel drugs and drug combinations. Together with patient samples, collected in consecutive, longitudinal or study-specific biobanks, the patient-derived models serve as resources to identify novel targets and biomarkers.

To foster a strong link between translational and clinical research we have several researchers holding part-time clinical positions. An ambition for the department is to participate in design and conduct of clinical trials, and to provide molecular and bioinformatics competences in multidisciplinary tumor boards in the area of precision cancer medicine.

Key achievements over the last 3-4 years include:

- Project leader responsibilities in collaborative projects in precision cancer medicine:
  NCGC - The Norwegian Cancer Genomics Consortium, NoSarc - Norwegian Sarcoma Consortium, MetAction - Actionable targets in cancer metastasis, MOVEMBER - The Norwegian Prostate Cancer Biomarker Consortium, The EuroPMP Cost Action, Biobank Norway 2 – multicenter biobanking of prostate cancer tissue in Norway
- Project leader responsibilities for clinical trials:
  NeoAva: Bevacizumab in combination with neoadjuvant chemotherapy in breast cancer
  I-BCT: DNA targeted chemotherapy to breast cancer patients with an aggressive phenotype
  ImmunoPeCa: Immunotoxin in Peritoneal Carcinomatosis
- Co-PI responsibilities in the METIMMOX multicenter trial which will investigate the combination of oxaliplatin and checkpoint inhibition (nivolumab) in microsatellite stable metastatic CRC

- All research groups have during the period received major funding (Norwegian Cancer Society, H2020, South-Eastern Norway Regional Health Authority)
- The department has published 66 papers, with 28 as first or last author, and educated three PhDs and one M.Sc. in 2019

Department of Tumor Biology

Metastasis Biology and Experimental Therapeutics

Group leader: Gunhild M. Mælandsmo

"Cellular plasticity - the route to resistance and metastasis"

ABOUT

Employees: The group has 20 members with multidisciplinary background and expertise (cell- and molecular biologists, medical doctors, laboratory- and animal technicians), including two MDs in shared clinical positions. Several of the technicians are trained in specialized technologies and compose resources for all groups in the department.

Research focus: Investigations on mechanisms of resistance and metastasis for improved cancer treatment.

Methodology: Molecular and functional analyses utilizing clinical samples, human cell cultures and patient-derived models (ex vivo, in vitro and in vivo).

AIMS

Metastatic progression is the major clinical challenge and the principal cause of death in cancer patients. To combat metastatic cancer our goal is to understand the underlying biological mechanisms causing therapy resistance, invasion and re-growth. Knowledge on these processes is vital for identification of molecules that can be utilized as prognostic and predictive biomarkers or as targets for therapy. We are working with malignant melanoma, breast cancer and prostate cancer.

PROJECTS

1. Basic research revealing mechanisms causing treatment resistance and metastasis
   - Molecular and cellular determinants regulating cancer cells plasticity, with special emphasis on the role of tumor-stroma interactions
2. Preclinical research investigating novel drugs and drug combinations
   - Mechanistic studies and assessment of treatment efficacy in patient-derived models in vivo and ex vivo
   - Biomarker discovery by molecular and functional techniques
   - Response evaluation of experimental drugs (often in collaboration with commercial partners, eg.: Lytix Biopharma and Arctic Pharma)
3. Clinical trials in precision medicine – clinical and translational efforts towards biomarker discovery
   - NeoAva: bevacizumab in combination with neoadjuvant chemotherapy for patients with locally advanced breast cancer
   - I-BCT: extended DNA-targeted chemotherapy to breast cancer patients with an aggressive phenotype

RECENT ACHIEVEMENTS

- The group was credited with 20 publications in 2019, of which nine with group members as first and/or last author; two PhD degrees completed
- One clinical intervention trial in breast cancer open for inclusion (I-BCT)
- Successful establishment of a user board for melanoma research
- Funding: Two innovation grants from the South-Eastern Norway Regional Health Authority, one researcher grant for biomarker stratification in breast cancer and two partnerships in new H2020-projects
- One patent approved

Translational Cancer Therapy

Group leader: Kjersti Flatmark

"New treatment for metastatic colorectal cancer"

ABOUT

In 2019, the Translational Cancer Therapy group comprised 16 members (including part-time employees and students) with a broad variety of expertise, including basic biologists, translational scientists, and clinician-scientists. Our approach to research is translational, encompassing methods from biochemistry and cell biology, preclinical drug testing in animal models, biomarker studies in clinical cohorts and interventional clinical trials. Extensive collaboration has been established within the Institute, with clinical departments, nationally and internationally.

AIMS

Our long-term aim is to make new, efficacious treatment(s) available to patients with colorectal cancer (CRC). This will be accomplished by bringing the clinic and lab together in translational research projects utilizing 1) preclinical models for efficacy and mechanistic studies 2) clinical cohort studies to understand CRC biology and identify biomarkers and therapeutic targets 3) clinical intervention trials to test new drugs and therapeutic concepts in patients.

PROJECTS

- Peritoneal metastasis – molecular targets and new therapies
  - Personalizing CRC therapy – identification of biomarkers and therapeutic targets in locally advanced and metastatic CRC, involving generation and use of our extensive biobanks, molecular and bioinformatics analyses (subprojects include: genomics, microRNA, mRNA, and immune cell analysis, participation in the BigMed project)
  - Novel drugs and therapeutic concepts in models of peritoneal and liver metastases
- Translational studies within the METIMMOX multicenter trial (Colorectal Cancer Metastasis – Shaping Anti-Tumor Immunity by Oxaliplatin), which will investigate the combination of oxaliplatin and checkpoint inhibition (nivolumab) in microsatellite stable CRC
- Commercial development of MOC31PE and BM7PE immunotoxins for cancer therapy

RECENT ACHIEVEMENTS

- Group members were credited with 25 publications in 2019
- The multicenter METIMMOX trial has included almost half of the planned number of patients, and interesting responses have been registered
- Our COST Action, EuroPMP, European Research Network on rare cancer pseudomyxoma peritonei currently comprises >80 members from 21 European countries.
- Two patent applications filed

Department of Tumor Biology

Computational Cancer Genomics

Group leader: Eivind Hovig

“Enabling the transition to clinical utility”

ABOUT

The 10-member group has strong interest in the development of computational approaches in cancer genomics, with focus on melanoma systems biology, and prostate cancer functional genomics. Further activity is centered on computational aspects of deep sequencing for cancer, with downstream analysis. The group facilitates moving precision cancer medicine towards the clinic, leveraging participation in the BigMed RCN-financed ICT lighthouse project.

The group collaborates with deCODE, Iceland, on the characterization of a familial cancer biobank, with 16000 genotyped samples, and where 2000 Norwegians have been whole genome sequenced. We pursue both the heritable cancer information from this effort, as well as a characterization of the ethnic Norwegian population genetics as a communal resource for Norway.

AIMS

- to develop and apply novel methodologies for computational studies of cancer-related processes, including statistical genomics, drug prediction algorithms, and mutational processes
- to contribute insight on heritable cancer-predisposing DNA-variation in the Norwegian population
- to characterize geographical stratification aspects of the Norwegian population
- to develop solutions for precision cancer medicine towards the clinic
- to understand signaling and epigenetic processes in melanoma and prostate cancer

PROJECTS

- Development of solutions for integrative cancer sequencing towards diagnostic utility, for patient stratification, and prediction of treatment response
- Participation in national and international efforts for standardization and development of best practice methods, including the 1 Million genomes community effort, partner of the BigMed project, and participating in the Center of innovation Big Insight for the knowledge economy.
- Melanoma signaling perturbations for systems understanding, including MITF, BRAF and CDKN2A aberrations
- Biomarkers in prostate cancer epigenomics
- Identification of familial cancer predisposing variants in Norwegian families with overrepresentation of cancer
- Clinical implications of Lynch syndrome genetics in Europe and Latin America

RECENT ACHIEVEMENTS

- Group members were credited with 15 publications in 2019, with 8 as first or last author
- Cancer society research funding for prostate cancer to Alfonso Urbanucci

Molecular Biology of Sarcomas

Group leader: Jørgen Wesche

“Towards precision medicine to improve treatment of sarcomas”

ABOUT

The 14-member group has a long standing interest in the biology of mesenchymal tumors (sarcomas). The current focus is on precision medicine for sarcomas. To achieve this, the group has broad expertise in basic cell biology, genomics and translational research and, in addition, one MD in a shared clinical position. The group is part of a Centre of Excellence (CanCell).

AIMS

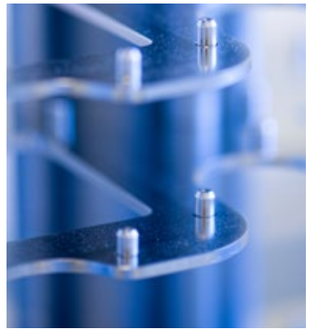
The group aims to improve the treatment of sarcoma patients by investigating how genetic changes (mutations) affect signalling in sarcoma cells, and how tumors evolve and become resistant. We combine extensive genomic characterization of clinical cohorts with preclinical investigation in sarcoma cell lines and xenografts to better understand the biology of sarcomas. Sarcomas are rare cancers with poor treatment options, and we aim to use our biological knowledge to identify new treatments opportunities by repurposing approved drugs for other cancers types.

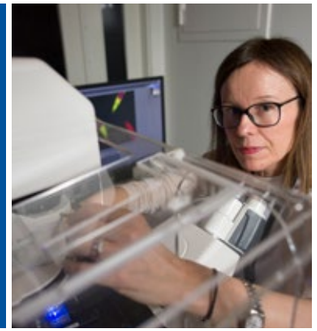
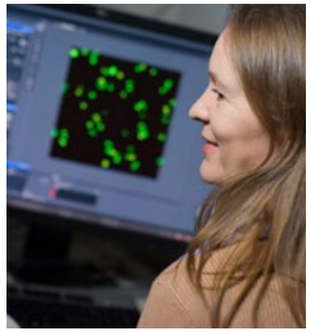
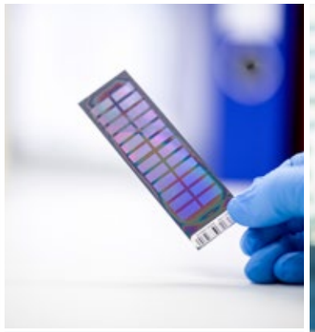
PROJECTS

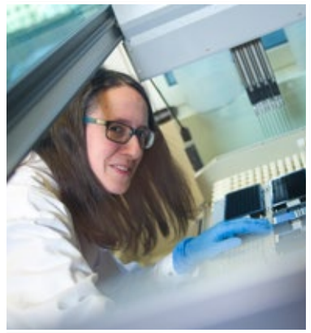
- Sarcoma cell biology – Gaining understanding of the development and progression of rhabdomyosarcoma, liposarcoma and osteosarcoma, which will lead to the identification of biomarkers and novel drug targets. A main focus is the study of the role of fibroblast growth fact receptors (FGFRs).
- Norwegian Sarcoma Consortium (NoSarC) – Biobanking and genomic characterization of patient material of 3-4 national cohorts of sarcomas (~500 samples).
- Exploration of “liquid biopsies”, as a non-invasive methods for detection of tumor-derived DNA in blood, to monitor disease progression, treatment response and tumor evolution.
- Dissecting drug resistance in gastrointestinal stromal tumors - Revealing the underlying mechanisms of early drug resistance in light of the complexity of the tumor to identify novel treatment modalities.

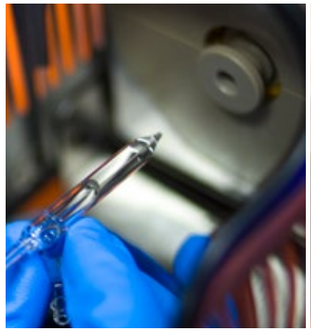
RECENT ACHIEVEMENTS

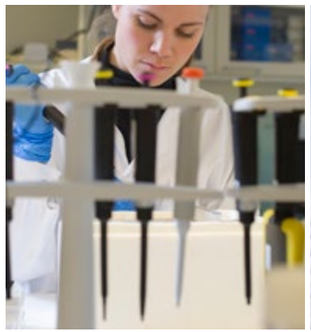
- 10 publications in 2019
- The group obtained a grant from the South-Eastern Norway Regional Health Authority (PhD project).
- Group visit to Vall d’Hebron, Barcelona, resulted in a new important collaboration
- 1 Master degree was completed








Department of

Core Facilities

Headed by Leonardo A. Meza-Zepeda

The Department of Core Facilities runs six regional and national technology platforms financed by the South-Eastern Norway Regional Health Authority and the Research Council of Norway, providing advanced competence, infrastructure, and services to regional, national and international users. The Department aims to deliver easy access to cutting-edge advanced technologies and competence, and to improve research quality through an optimal choice of technology, ultimately increasing the scientific competitiveness of our users. The Department of Core Facilities is organized in three units; Advanced Microscopy, Genomics and Bioinformatics, and Flow Cytometry and Pre-Clinical Imaging, with a total of 20 employees. More information at www.ous- research.no/corefacilities.

ADVANCED LIGHT MICROSCOPY

Unit Leader: Ellen Skarpen
Scientifically responsible: Harald Stenmark
Facility staff: 2

The Core Facility for Advanced Light Microscopy (ALM) offers services in various types of ALM, including confocal microscopy, live-cell microscopy and superresolution microscopy. Current instruments include a Zeiss LSM 880 FAST airyscan microscope, a Zeiss LSM 710 confocal microscope, and an OMX Blaze microscope for structured illumination and STORM super-resolution imaging, as well as live-cell microscopy. The core facility cooperates with nodes at the Rikshospitalet and Ullevål campuses of OUH, as well as the light microscopy core facility at the Institute for Biosciences, University of Oslo. The core facility for ALM is a Eurobioimaging node, providing state-of-the-art technologies in the fields of biological and medical imaging. Services include training, courses, access to microscopes and microscopy performed by competent core facility personnel.

ADVANCED ELECTRON MICROSCOPY

Unit Leader: Ellen Skarpen
Scientifically responsible: Andreas Brech
Facility staff: 1

The Core Facility for Advanced Electron Microscopy (AEM) includes nodes at the Radium Hospital and Rikshospitalet, and provides service, training, and access to microscopes for ultrastructural studies. Available techniques at the facility include conventional plastic embedding, immune EM, correlative light/electron microscopy (CLEM), high-pressure freezing, electron tomography, cryo-EM and STEM. The facility staff is actively developing new methods in order to offer state-of-the-art microscopy solutions for researchers.
We cooperate with the imaging platform at the Institute for Biosciences, University of Oslo and are part of the Norwegian Advanced Light Microscopy node within EuroBioImaging.

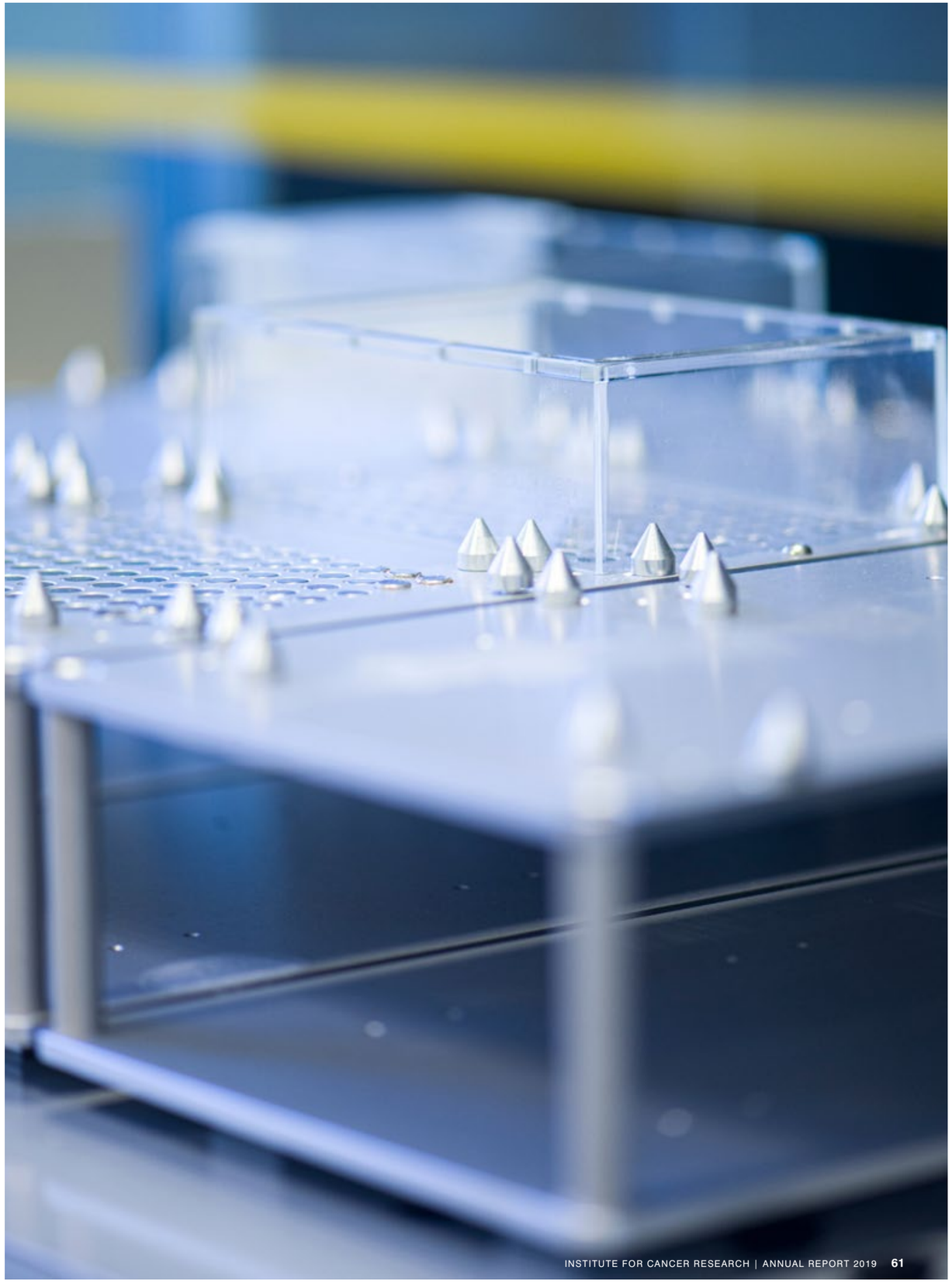
Department of Core Facilities

BIOINFORMATICS
Unit Leader: Susanne Lorenz
Scientifically responsible: Eivind Hovig
Facility staff: 5
The Bioinformatics Core Facility (BCF) provides service, support and advice in the field of bioinformatics. By combining biology with computer science, statistics and mathematical modelling, we offer support for analysis and interpretation of biological data for basic and translational research.
The BCF has a specific focus on developing and providing solutions for precision medicine and cancer-related projects. Through dedicated support from the South-Eastern Norway Regional Health Authority, we are actively assisting in developing the infrastructure for precision diagnostics at the hospital. Our service also includes support with data handling and storage by providing approved solutions for sensitive data. The operation of the BCF is aligned with the national and local Elixir bioinformatics infrastructure project, and also interacts with USIT, University of Oslo.

HIGH-THROUGHPUT SEQUENCING (GENOMICS)
Unit Leader: Susanne Lorenz
Scientifically responsible: Leonardo A. Meza-Zepeda
Facility staff: 5
The Genomics Core Facility (GCF) provides state-of-the-art high-throughput genomic services to the scientific community. The GCF offers advanced technologies and competence to study genome structure, dynamics and function using high-throughput sequencing, nanoString, and microarray technologies. Our services include solutions to study the transcriptome, genome, and epigenome from multi-gene analysis to a genome-wide level. Highly experienced service personnel provide advanced support to clinical, translational and basic research projects. We have extended our services for single-cell transcriptome analysis to the single-cell analysis of T & B cell receptors, scATAC-Seq, and feature barcoding to study protein expression. In addition, we have established a collaboration with the Department of Pathology at OUH to develop the infrastructure for advanced precision diagnostics towards clinical studies with dedicated support from the South-Eastern Norway Regional Health Authority. The GCF is a member of the Norwegian Consortium for Sequencing and Personalised Medicine (NorSeq) running the National platform for sequencing technology. The core facility collaborates with the sequencing node at the Ullevål campus for sequencing services.

FLOW CYTOMETRY
Unit Leader: Trond Stokke
Scientifically responsible: Trond Stokke
Facility staff: 4
The Flow Cytometry Core Facility (FCCF) provides analysis and sorting services for users within the South-Eastern Health Region of Norway. We have recently installed a state-of-the-art analyser (BD Symphony) with 5 lasers that may measure up to 28 fluorescence parameters simultaneously. In total, the core facility provides services using 3 analysers and two sorting instruments. Flow cytometry analysis is performed by the users themselves. Sorting experiments are either performed by core facility personnel (in the BD Aria), or by the users in the Sony SH100 sorter. The FCCF has possibilities for high throughput screening, processing and staining of cells in 96- or 384-well plates, followed by an automated analysis. We also have a “mass-spec flow cytometer” (Helios). This instrument can measure up to 60 parameters simultaneously at single-cell resolution. We have recently installed an add-on to the Helios, Hyperion, which allows for imaging of sections labelled with up to 60 heavy metal-tagged antibodies. The FCCF collaborates with facility nodes at the Rikshospitalet and Ullevål campuses of OUH.

PRECLINICAL IMAGING FACILITY
Unit Leader: Trond Stokke
Scientifically responsible: Tord Hompland
Facility staff: 2
The Preclinical Imaging Facility provides access to state-of-the-art non-invasive imaging equipment for mice and rats. The equipment is situated within the animal facility and consists of a 7T Bruker MRI, IVIS spectrum and Zeiss Stereo Macroscope for optical imaging, and a Multirad 225 small animal irradiator capable of doing x-ray imaging. The facility also provides all the necessary equipment for in vivo research on small animals or tissue/organ samples from larger animals or humans. A comprehensive library of standard off-the-shelf imaging protocols are available, and custom-protocols can be developed upon user request. We are at present developing a protocol for synchronization of images obtained by MRI, IVIS and X-ray imaging. The service offered by the core facility includes design, development and running of the imaging experiment, as well as post-processing of the data in addition to instrument-specific training. The core facility collaborates with the Preclinical MRI node at the Ullevål campus.



Research centres

64

Centre of Excellence

The Centres of Excellence (CoE) scheme is a national programme under the auspices of the Research Council of Norway. The granted CoE (CanCell) is funded for 5 + 5 years (if recommended following a mid-term evaluation). The total basic funding is ~167 million NOK.

66

K. G. Jebsen Centres

The K.G.Jebsen Foundation supports Centres for Medical Research of high international quality as part of its program for translational medicine. The centres are selected in collaboration with the Norwegian Medical Faculties and University Hospitals for a period of 4 years with the possibility of a 2-year extension. The selected Centres receive 16-18 million NOK in basic funding over the first four years from the Foundation and support from the host institutions, University of Oslo (KG Jebsen Centre for Cancer Immunotherapy, KG Jebsen Centre for B Cell Malignancies) or Oslo University Hospital (KG Jebsen Colorectal Cancer Research Centre).

Centre for Cancer Cell Reprogramming (CanCell)

Headed by Harald Stenmark

ABOUT

Centre for Cancer Cell Reprogramming (CanCell) is a Norwegian Centre of Excellence (CoE) which opened 01.01.2018 and has a planned CoE funding period of 10 years. CanCell is led by Harald Stenmark at Institute for Cancer Research, whereas Anne Simonsen at Institute of Basic Medical Sciences is co-director. The centre consists of 6 research groups and has 7 associate members (Eivind Hovig, Åslaug Helland, Yngvar Fløisand, Philippe Collas, Arnoldo Frigessi, Emmet McCormack, and Terje Johansen) and 4 international visiting professors (Kristian Helin, Ivan Dikic, Eileen White, and Eyal Gottlieb). By the end of 2019, CanCell had 100 members of 34 (!) nationalities.

AIMS

CanCell's vision is to identify novel vulnerabilities of cancer cells that can be targeted for cancer cell reprogramming. The centre's founding hypothesis is that pathway intersections between chromatin regulation, membrane dynamics, cell signaling and metabolism during cancer progression represent potential "Achilles' heels" of cancer cells. These will be identified through close cooperations between specialists within these four cellular processes, and will be targeted by genetic and pharmacological regimens to achieve reprogramming of cancer cells into harmless (or dying) cells.

PROJECTS:

- Membrane dynamics in cancer
- Autophagy in immunity and cancer
- Molecular medicine of leukemia
- Tumour-host interactions
- Molecular biology of sarcomas
- Mechanisms of epigenetic regulation in cancer

RECENT ACHIEVEMENTS

- Demonstration of distinct functions of ATG16L1 isoforms in membrane binding and LC3B lipidation in autophagy-related processes (Lystad et al., *Nature Cell Biology*, 2019).
- Identification of NIPSNAP proteins as "eat-me" signals for autophagic degradation of damaged mitochondria (Abudu et al., *Developmental Cell*, 2019). This was a collaboration between Anne Simonsen's group and the group of CanCell associate member Terje Johansen.
- Demonstration that ESCRT proteins seal the autophagosome during starvation-induced autophagy and autophagy of damaged mitochondria (Zhen et al., *Autophagy*, 2019). This was a collaboration between the CanCell groups of Harald Stenmark and Anne Simonsen.
- Identification of a new mechanism of tumour suppression – intracellular retention of matrix metalloproteinases (Sneeggen et al., *Nature Communications*, 2019).
- Demonstration that Centralspindlin recruits ALIX to the midbody during cytokinetic abscission in fruit flies via a mechanism analogous to virus budding (Lie-Jensen et al., *Current Biology*, 2019).
- Demonstration that desumoylation of RNA Polymerase III lies at the core of the Sumo stress response (Nguéa et al., *Journal of Biological Chemistry*, 2019).
- Demonstration that cancer mutations in fibroblast growth factor receptor 2 prevent a negative feedback loop mediated by the ERK1/2 pathway (Szybowska et al., *Cells*, 2019).
- CanCell scientists published 41 papers in 2019, many of these in leading journals. Two PhD students, Marte Sneeggen and Ignacio Cuervo, successfully defended their theses. Eight MSc students were graduated.
- In 2019, major grants were obtained by Jorrit Enserink, Leonardo Meza-Zepeda, Anne Simonsen, Harald Stenmark, Kay O. Schink, Swarupa Panda, Helene Knævelsrud and Viola Nähse. Two of these were international grants – EMBO long-term fellowship to Swarupa Panda and Horizon-2020 Initial Training Network grant to Anne Simonsen.

GROUP LEADERS/STEERING COMMITTEE

CanCell was established by the following 6 group leaders, who also serve as CanCell´s steering committee:

Harald Stenmark, Institute for Cancer Research, OUS, and Institute of Clinical Medicine, UiO

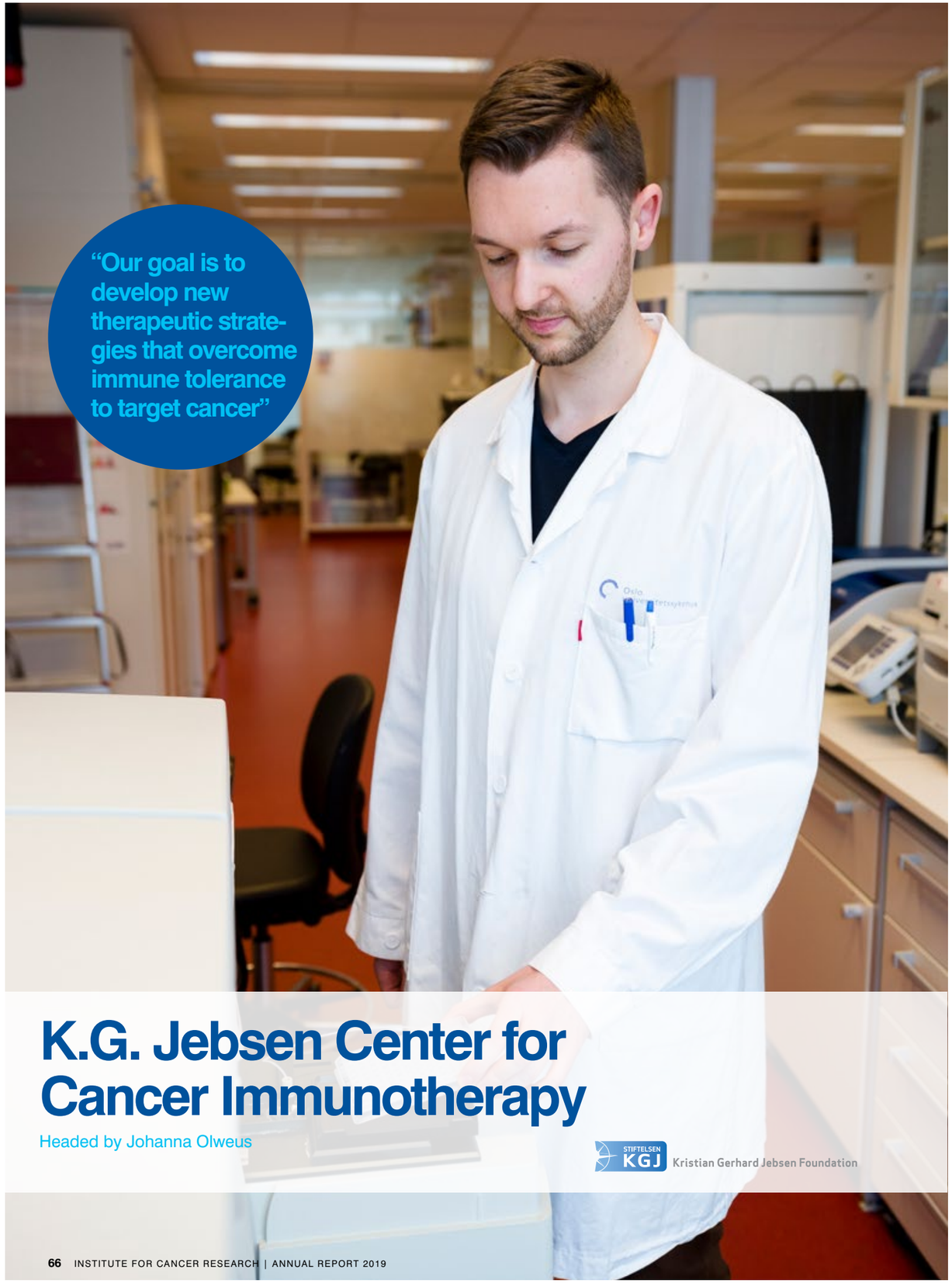
Anne Simonsen, Institute of Basic Medical Sciences, UiO, and Institute for Cancer Research, OUS

Jorrit Enserink, Institute for Cancer Research, OUS, and Department of Biosciences, UiO

Ragnhild Eskeland, Institute of Basic Medical Sciences, UiO

Tor Erik Rusten, Institute of Clinical Medicine, UiO, and Institute for Cancer Research, OUS

Jørgen Wesche, Institute for Cancer Research, OUS, and Institute of Basic Medical Sciences, UiO



K.G. Jebsen Center for Cancer Immunotherapy

Headed by Johanna Olweus

Kristian Gerhard Jebsen Foundation

ABOUT

In the K.G. Jebsen Center for Cancer Immunotherapy (JCIT) hosted by the University of Oslo, five Norwegian and one Dutch research group have come together to find new immunotherapeutic strategies that overcome the major challenge of self-tolerance in cancer. JCIT was granted prolongation following the first 4-year period, throughout 2019. The partnering groups of JCIT span complementary competencies ranging from basic proteomics, cell signaling and T-cell receptor engineering to expertise in experimental clinical immunotherapy trials. This places the center in a unique position to pursue novel therapeutic opportunities, and the strong focus on translating therapeutic opportunities is a fundamental characteristic of JCIT. Results from basic research are pursued through the necessary translational steps to testing in patients, and in-depth mechanistic studies of patient material obtained in experimental clinical trials are performed with the aim of improved designs of immunotherapeutic strategies.

AIMS

Three principally distinct approaches are pursued in an interdisciplinary and translational program: 1. Use of T-cell and NK-cell based alloreactivity to overcome self-tolerance. 2. Identification and targeting of cancer-specific neo-antigens. 3. Enhancement of effector T-cell function by counteracting inhibitory mechanisms.

PROJECTS

- Epitope discovery to identify targets for immunotherapy
- Identify immune cells expressing immune receptors that recognize and kill cells that express the identified targets
- Molecular cloning, genetic transfer and profiling of immune receptors
- Enhance cytotoxic lymphocyte function by overcoming inhibitory mechanisms
- In vivo evaluation of immune modulating therapies

RECENT ACHIEVEMENTS

- Deciphered molecular mechanisms of NK cell homeostasis, education and differentiation *(Goodridge et al, Nature Communications, 2019, Jacobs et al., J. Immunology 2019 and Pfefferle et al., Cell Reports 2019).*
- Described a technology for identification of neoantigen specific T cells from healthy donors (Ali et al, *Nature Protocols, 2019)*
- Olweus was awarded an ERC Consolidator Grant (2 mill Euro over 5 yrs) for an application based on results generated within the center – “Outsourcing cancer immunity”.
- Reported low and variable tumor reactivity of the intratumoral TCR repertoire in human cancers *(Scheper et al, Nat. Med. 2019)*
- Included 10 patients in Lymvac-2, an experimental immunotherapy trial combining intratumoral immunotherapy with anti-PD1 for treatment of patients with follicular lymphoma, in collaboration with Merck (Kolstad PI).
- Started GMP virus production for first clinical trial in Norway using an in-house generated immune receptor (JCIT TCR) for cancer immunotherapy.
- Recruited first 300 patients to the ASAC trial that examines the effect of reversing prostaglandin E2-mediated inhibition of tumor immunity in patients with metastatic colorectal cancer by the end of 2019 (www.asac.no).
- Malmberg completed a research sabbatical at UCSD resulting in new collaborative efforts with leading iPSC-NK/T cell environments, including Kaufman Lab at UCSD, and Sadelain Lab at MSKCC *(Sætersmoen et al, Seminars in Immunopathology 2019, Hong et al., Journal of Clinical Investigation in press).*
- Demonstrated that idelalisib preferentially inhibits human regulatory T cells, enhancing anti-tumor immunity *(Chelappa et al, J Immunol., 2019)* and characterized the CD28 and CD2 interactomes in T cells *(Skånland and Taskén, J. Immunol. 2019)*
- Characterized how metabolic regulation through the FoxK1/2 master switch affects T cell function *(Sukonina et al, Nature, 2019)* and contributed to understanding TLR8 signaling in T cells *(Meås et al., Nature Commun., in press 2020).*
- Obtained funding for proteomics infrastructure from The Norwegian Research Council (total 50M NOK, Lund-Johansen partner in NAPI consortium) and funding from the Norwegian Cancer Society for identification of HLA_bound peptides from tumor-associated antigens.
- Obtained funding from UiO for production of antibodies to peptides in the ImmunoLingo convergence consortium (total 11.5 mill NOK, Lund-Johansen partner).

HOME PAGE

http://www.med.uio.no/klinmed/english/research/centres/kgj-cancer-immunotherapy/

GROUP LEADERS/ STEERING COMMITTEE

Johanna Olweus (MD, PhD, Director), Dept of Cancer Immunology, Institute for Cancer Research, Oslo University Hospital (OUH)-Radiumhospitalet and University of Oslo (UiO)

Karl-Johan Malmberg (MD, PhD, deputy Director), Dept of Cancer Immunology, Institute for Cancer Research, OUH-Radiumhospitalet and UiO

Arne Kolstad (MD, PhD), Dept of Oncology, OUH-Radiumhospitalet

Kjetil Taskén (MD, PhD), Dept of Cancer Immunology, Institute for Cancer Research, OUH-Radiumhospitalet and UiO

Fridtjof Lund-Johansen (MD, PhD), Dept of Immunology, OUH-Rikshospitalet

Ton Schumacher (PhD), The Netherlands Cancer Institute, Amsterdam

"From basic research and preclinical studies to precision medicine for B-cell malignancies"

K.G. Jebsen Centre for B-cell malignancies

Headed by Ludvig A. Munthe and June H. Myklebust

STIFTELSEN KGJ Kristian Gerhard Jebsen Foundation

ABOUT

The K.G. Jebsen Centre for B-cell malignancies was established in June 2018, and bridges 4 translational research groups with 3 clinical groups; placing us in a unique position to translate pre-clinical results into clinical trials in lymphoma, B-cell leukemia and multiple myeloma (MM). The centre utilizes "cutting edge" technologies for deep profiling of patient samples, cancer drug sensitivity screens for precision medicine, and development of novel approaches for immunotherapy. Collectively, the Centre represents a multidisciplinary integration of life science research with preclinical development of personalized medicine, drug discovery and cell-based immunotherapy, as well as clinical trials and establishment of best practice on how to treat B-cell malignancies.

AIMS

The centre aims to identify, develop and test new therapeutic options for patients with B-cell malignancies.

PROJECTS

- Identify molecular biomarkers to guide precision medicine and to identify high risk patients
- Deciphering signal integration and interactions with the tumor microenvironment to reveal actionable targets
- Develop novel therapeutics: identify antigens for vaccination, T-cell epitope discovery, and CAR T cell design
- Preclinical testing: immunotherapy and personalized medicine
- Translating results into clinical initiatives – from bench to bedside and back

RECENT ACHIEVEMENTS/CLINICAL TRANSLATION

- The clinical portfolio includes 58 clinical trials at different stages, majority are researcher initiated.
- Enrolled most MM patients in clinical trials
- Ixazomib improved progression-free survival (PFS) after autologous stem cell transplantation in MM (Dimopolous, Lancet 2019).
- The addition of isatuximab to pomalidomide-dexamethasone or pomalidomide to bortezomib-dexamethasone improved PFS in refractory/relapsed MM *(Attal, Lancet 2019; Richardson, Lancet Oncol 2019).*
- Consensus recommendations on imaging in monoclonal plasma cell disorders *(Hillengass, Lancet Oncol. 2019).*
- Phase II trial testing CD19 CAR T-cell therapy in Diffuse Large B-Cell Lymphoma demonstrated 52% overall response rate *(Schuster, NEJM 2019).*
- Chemotherapy can be reduced in aggressive Non-Hodgkin's Lymphoma with favorable prognosis *(Poeschel, Lancet 2019)*
- Established B-cell directed therapy as treatment of-choice in chronic cold agglutinin disease *(Berentsen, J Blood Med 2019)*
- Relapse risk and loss of lifetime after modern combined modality treatment of young patients with Hodgkin Lymphoma *(Biccler, J Clin Oncol 2019).*
- Investigated inheritance of susceptibility to malignant blood disorders *(Jønsson, Sci Rep. 2019).*
- Stromal cell PKC-beta inhibition enhances chemosensitivity in B-cell malignancies and overcomes drug resistance *(Park, Sci Transl Med, in press 2019).*
- Developed in vitro phospho-flow cytometry assay for biomarker discovery and dose prediction in CLL *(Skånland, Leukemia, in press 2019).*
- Distinct subtypes of diffuse large B-cell lymphoma can be defined by hypermutated genes *(Alkodsi, Leukemia 2019).*
- Developed the prognostic predictor BTK-FLIPI to identify follicular lymphoma patients at high risk for adverse disease *(Steen, Haematologica 2019)*, and contributed to convergence of risk prediction models *(Silva, Haematologica 2019).*
- Identified TIGIT and PD-1 as relevant targets for co-checkpoint blockade in B-cell lymphoma *(Josefsson, Cancer Immunol Res 2019).*
- Identified tumor-reactive T cells in B-ALL patients *(Bürgler, Oncogene 2019).*
- Bone marrow Th1 T cells induce activation and proliferation of leukemic cells from B-ALL patients *(Traxel, Oncogene 2019).*
- Preclinical development of CD37 CAR T-cell therapy *(Köksal, Blood Adv 2019; patent filed).*
- The PI3Kδ inhibitor idelalisib enhances anti-tumor immunity preferentially through inhibition of regulatory T cells *(Chellappa, J Immunol, 2019)*, and CSK binds CD28 upon activation and mutes downstream signaling *(Skånland, J Immunol 2019).*
- B-cell receptor ligation induces display of V-region immunoglobulin peptides on MHC class II molecules to T cells *(Hutszky, PNAS 2019)*
- FOXK1 and FOXK2 regulate aerobic glycolysis *(Sukonia, Nature 2019).*

HOME PAGE

https://www.med.uio.no/klinmed/english/research/centres/kgj-b-cell-malignancies/

GROUP LEADERS/STEERING COMMITTEE

Ludvig A. Munthe (MD, PhD, Centre Director)[1,2]
June H. Myklebust (PhD, Assistant Director)[2,3]
Geir E. Tjønnfjord (MD, PhD)[2,4]
Harald Holte (MD, PhD)[5]
Hilde Schjerven (PhD)[1,6]
Erlend B. Smeland (MD, PhD)[2,3]
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2 Institute for Clinical Medicine, University of Oslo
3 Dept of Cancer Immunology, Institute for Cancer Research, OUH
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6 Dept. of Laboratory Medicine, University of California, San Francisco.

K.G. Jebsen Colorectal Cancer Research Centre

Headed by Ragnhild A. Lothe

Kristian Gerhard Jebsen Foundation

ABOUT

Colorectal cancer (CRC) is a major global health burden, and the focus of our Centre is to meet the current challenges in disease management by improved patient monitoring and stratified treatment. The Centre is hosted by the Clinic for Cancer Medicine, Oslo University Hospital (OUH). The Centre PIs are also partners in the recently appointed OUH Strategic Research Area TEAM-ACT (2019-24).
Home page: www.colorectalcancer.no

GROUP LEADERS/STEERING COMMITTEE

- **Professor Ragnhild A. Lothe** (MSc, PhD, Centre leader), Dept. of Molecular Oncology, Institute for Cancer Research, OUH and Institute for Clinical Medicine, University of Oslo (UiO)
- **Professor Arild Nesbakken** (MD, PhD, deputy Centre leader), Dept. of Gastrointestinal Surgery, OUH and Institute for Clinical Medicine, UiO
- **Professor Rolf I. Skotheim** (MSc, PhD), Dept. of Molecular Oncology, Institute for Cancer Research, OUH, and Dept. of Informatics, UiO.
- **Senior Consultant Marianne G. Guren** (MD, PhD), Dept. of Oncology, OUH
- **Professor Guro E. Lind** (MSc, PhD), Dept. Molecular Oncology, Institute for Cancer Research, OUH and Dept. of BioSciences, UiO

Our Centre has an active Patient Advisory Board, established in 2016.

AIM

Translate biomedical knowledge in the context of tumor heterogeneity into improved stratified medicine of CRC.

PROJECTS

- Clinical and molecular biomarkers for improved risk stratification of patients
- Model tumor heterogeneity and clonal evolution to monitor early relapse and treatment failure
- Pharmacogenomic profiling of organoid models derived from the patients’ own tumor cells to guide therapy selection, identify biomarkers for response prediction, and develop synergistic drug combinations

RECENT ACHIEVEMENTS AND CLINICAL TRANSLATION

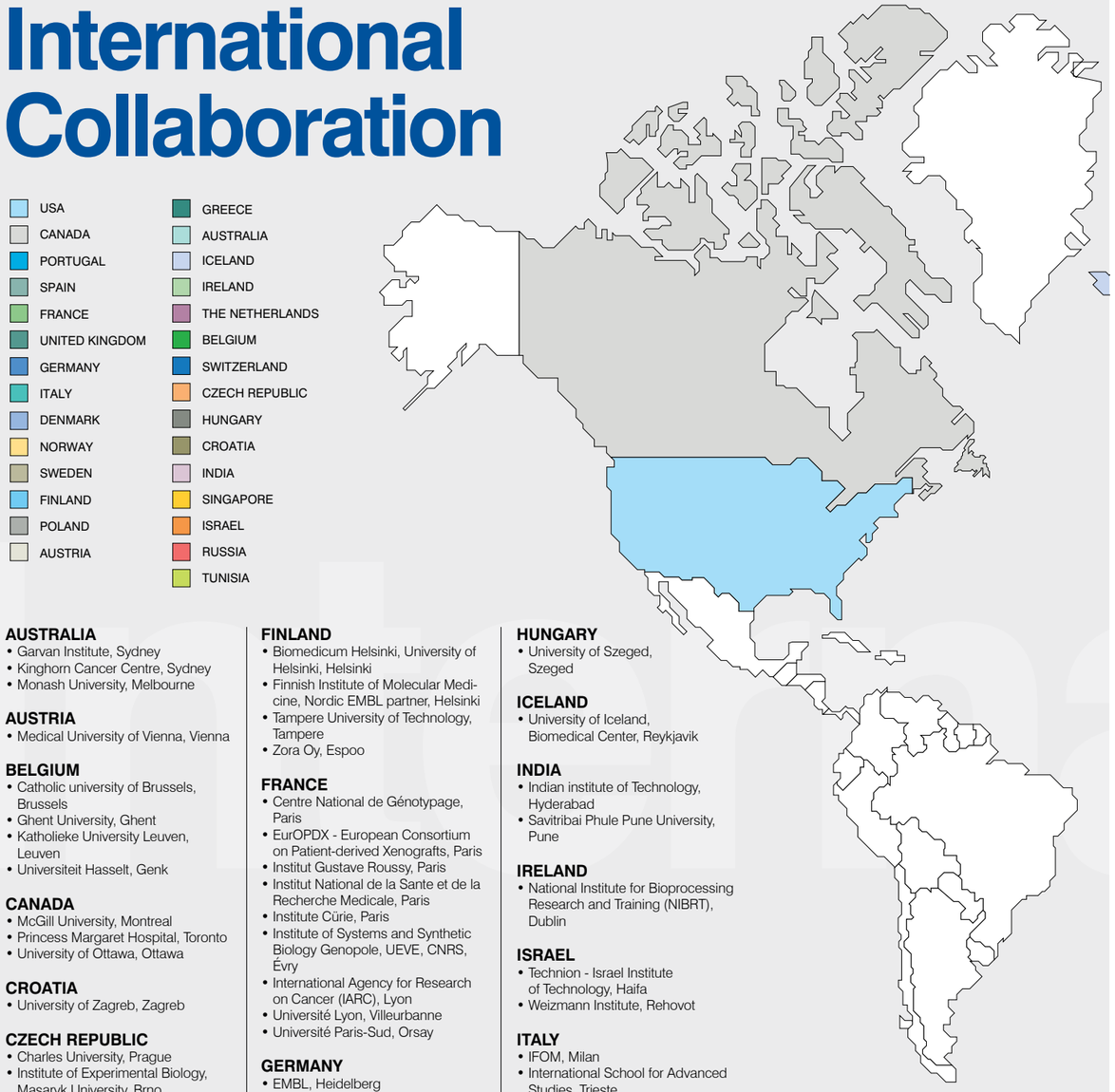
In 2019, we were granted a 6-year strategic research area from OUH (TEAM-ACT) to continue the translational and clinical research program on primary and metastatic CRC established in the K.G. Jebsen Centre. TEAM-ACT is led by professor R. A. Lothe and associate professor Anita Sveen. Sveen also received a major grant from the Norwegian Cancer Society to further develop the platform for pre-clinical pharmacogenomics of patient-derived models to enable testing and optimization of immunotherapy. Peter Wold Eide received the Young Researcher Award from the national annual meeting in oncology (“Onkologisk Forum”) for his studies in CRC genomics, and Sveen received the Early Career Award from OUH. Heidi Pharo and Kaja Christine Graue Berg defended their PhDs at the UiO.

2019 was a successful year for the Centre with respect to scientific production. Together with collaborator Scott Kopetz at The MD Anderson Cancer Centre, USA, a practice changing clinical trial of targeted combination therapy in metastatic CRC was published in NEJM (Kopetz et al., 2019), in addition to a comprehensive review on biomarker-guided therapy for CRC (Sveen et al., Nature Rev Clin Oncol 2019). Totally 31 peer-reviewed papers were published within a broad range of topics. Epidemiological research demonstrated a rising incidence of CRC among young people (Araghi M et al., Lancet Gastroenterol Hepatol 2019), and compared survival after surgery for CRC in Norway to other high-income countries (Benitez Majano S et al., Lancet Oncol, 2019). Molecular studies were published of circulating biomarkers for management of CRC (Hamfjord J et al., Ann Oncol 2019), the strong influence of tumor microenvironment features on patient prognosis (Dienstmann et al., Ann Oncol, 2019; Glaire et al., Brit J Ca 2019), tumor heterogeneity and multi-level genomics (Berg et al., Oncogene 2019; Brunsell et al., Eur J Surg Oncol; Smeby et al., ESMO Open 2019), as well as advanced technologies (Eilertsen et al., Cancer Letters 2019; Lopes et al., Lab Invest 2019).

Unpublished results of drug screening and molecular profiling of organoids derived from 30 patients with multiple CRC liver metastases, gene expression-based classification in a tumor heterogeneity context, and identification of new high-level amplifications in CRC were recently presented at the Keystone Symposium on “Cancer Evolution and Combinatorial Cancer Therapies” in Banff, Canada.

Key opinions:
Centre members published several editorials and reviews related to a variety of challenges in CRC: “The complexity of biomarkers” (Sveen et al., Nat Rev Clin Oncol); “The global challenge of CRC” (Guren MG, Lancet Gastorenterol Hepatol); “Gene expression-based modelling of targeted therapies” (Sveen et al., Ann Oncol 2019); “Combination therapies with HSP90 inhibitors” (Kryeziu et al., BBA Rev Cancer); “Circulation biomarkers for early detection and management” (Marcuello et al., Mol Aspects of Medicine). Also modelling costs and survival of several treatment strategies of CRC was published (Joranger et al., EurJ Health Econ).

International Collaboration



AUSTRALIA
- Garvan Institute, Sydney
- Kinghorn Cancer Centre, Sydney
- Monash University, Melbourne

AUSTRIA
- Medical University of Vienna, Vienna

BELGIUM
- Catholic university of Brussels, Brussels
- Ghent University, Ghent
- Katholieke University Leuven, Leuven
- Universiteit Hasselt, Genk

CANADA
- McGill University, Montreal
- Princess Margaret Hospital, Toronto
- University of Ottawa, Ottawa

CROATIA
- University of Zagreb, Zagreb

CZECH REPUBLIC
- Charles University, Prague
- Institute of Experimental Biology, Masaryk University, Brno
- Institute of Molecular Genetics, Academy of Sciences of the Czech Republic, Prague
- National Institute of Public Health, Prague

DENMARK
- Aalborg University Hospital, Aalborg
- Aarhus University Hospital, Aarhus
- Copenhagen University Hospital, Copenhagen
- University of Copenhagen, Copenhagen
- University of Southern Denmark, Odense

FINLAND
- Biomedicum Helsinki, University of Helsinki, Helsinki
- Finnish Institute of Molecular Medicine, Nordic EMBL partner, Helsinki
- Tampere University of Technology, Tampere
- Zora Oy, Espoo

FRANCE
- Centre National de Génotypage, Paris
- EurOPDX - European Consortium on Patient-derived Xenografts, Paris
- Institut Gustave Roussy, Paris
- Institut National de la Sante et de la Recherche Medicale, Paris
- Institute Cürie, Paris
- Institute of Systems and Synthetic Biology Genopole, UEVE, CNRS, Évry
- International Agency for Research on Cancer (IARC), Lyon
- Université Lyon, Villeurbanne
- Université Paris-Sud, Orsay

GERMANY
- EMBL, Heidelberg
- Institut für Biochemie, University of Stuttgart, Stuttgart
- Jacobs University, Bremen
- University of Bayreuth, Bayreuth
- University of Bochum, Bochum
- University of Cologne, Cologne
- University of Freiburg, Freiburg
- University of Heidelberg, Heidelberg
- University of Mainz, Mainz
- University of Marburg, Marburg

GREECE
- National and Kapodistrian University of Athens, Athens
- National Centre for Scientific Research "Demokritos", Athens
- University of Ioannina, Ioannina

HUNGARY
- University of Szeged, Szeged

ICELAND
- University of Iceland, Biomedical Center, Reykjavik

INDIA
- Indian institute of Technology, Hyderabad
- Savitribai Phule Pune University, Pune

IRELAND
- National Institute for Bioprocessing Research and Training (NIBRT), Dublin

ISRAEL
- Technion - Israel Institute of Technology, Haifa
- Weizmann Institute, Rehovot

ITALY
- IFOM, Milan
- International School for Advanced Studies, Trieste
- Istituto Nationale di Tumori, Milano
- The Rizzoli Institute, Bologna
- University of Bologna, Bologna
- University of Padova, Padova
- University of Salento, Lecce

NORWAY
- Cancer Registry of Norway, Oslo
- Haukeland University Hospital, Bergen
- Norwegian University of Life Sciences, Ås.
- Norwegian University of Science and Technology, Trondheim
- Stavanger University Hospital, Stavanger
- Trondheim University Hospital-St. Olavs Hospital, Trondheim
- University hospital of North Norway, Tromsø
- University of Bergen, Bergen
- University of Oslo, Oslo

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- Jagiellonian University, Kraków
- University of Gdansk, Gdansk

PORTUGAL
- Institute of Molecular Pathology and Immunology, University of Porto
- Portuguese Oncology Institute, Porto

RUSSIA
- Institute of Cytology and Genetics, Novosibirsk

SINGAPORE
- Cancer Science Institute of Singapore, Singapore

SPAIN
- CABIMER, University of Sevilla, Sevilla
- Centre for Biological Studies, Madrid
- Fundacion Instituto Valenciano de Oncologica (FIVO), Valencia
- ICGC, Technical validation group and Ivo Gut, Barcelona
- University of Lleida, Lleida
- University of Valencia, Valencia
- Universitat Politècnica de València, Valencia
- Vall d'Hebron Institute of Oncology, Barcelona

SWEDEN
- Karolinska Institutet and University of Stockholm, Stockholm
- Lund University, Lund
- The Sahlgrenska Academy at the University of Gothenburg, Gothenburg
- Uppsala University Hospital, Uppsala

SWITZERLAND
- University Hospital Zurich, Zurich

THE NETHERLANDS
- Leiden University, Leiden
- Netherlands Cancer Institute (NKI), Amsterdam
- Radboud University Nijmegen, Nijmegen
- The Netherlands Proteomics Centre, Utrecht
- University Medical Center, Groningen
- VU Medical Center, Amsterdam

TUNISIA
- University of Tunis, Tunis

UNITED KINGDOM
- Cambridge Cancer Institute, Cambridge
- Hampshire Hospitals/Southampton University, Southampton
- London Research Institute,The Francis Crick Institute, London
- Royal National Orthopaedic Hospital, Stanmore, Middlesex
- The Beatson Institute for Cancer Research, Glasgow
- The European Bioinformatics Institute (EMBL-EBI), Hinxton
- University College London Medical School, UCL, London
- University of Cambridge, Cambridge
- University of Liverpool, Liverpool
- University of Oxford, Oxford
- Wellcome Sanger Institute, Hinxton

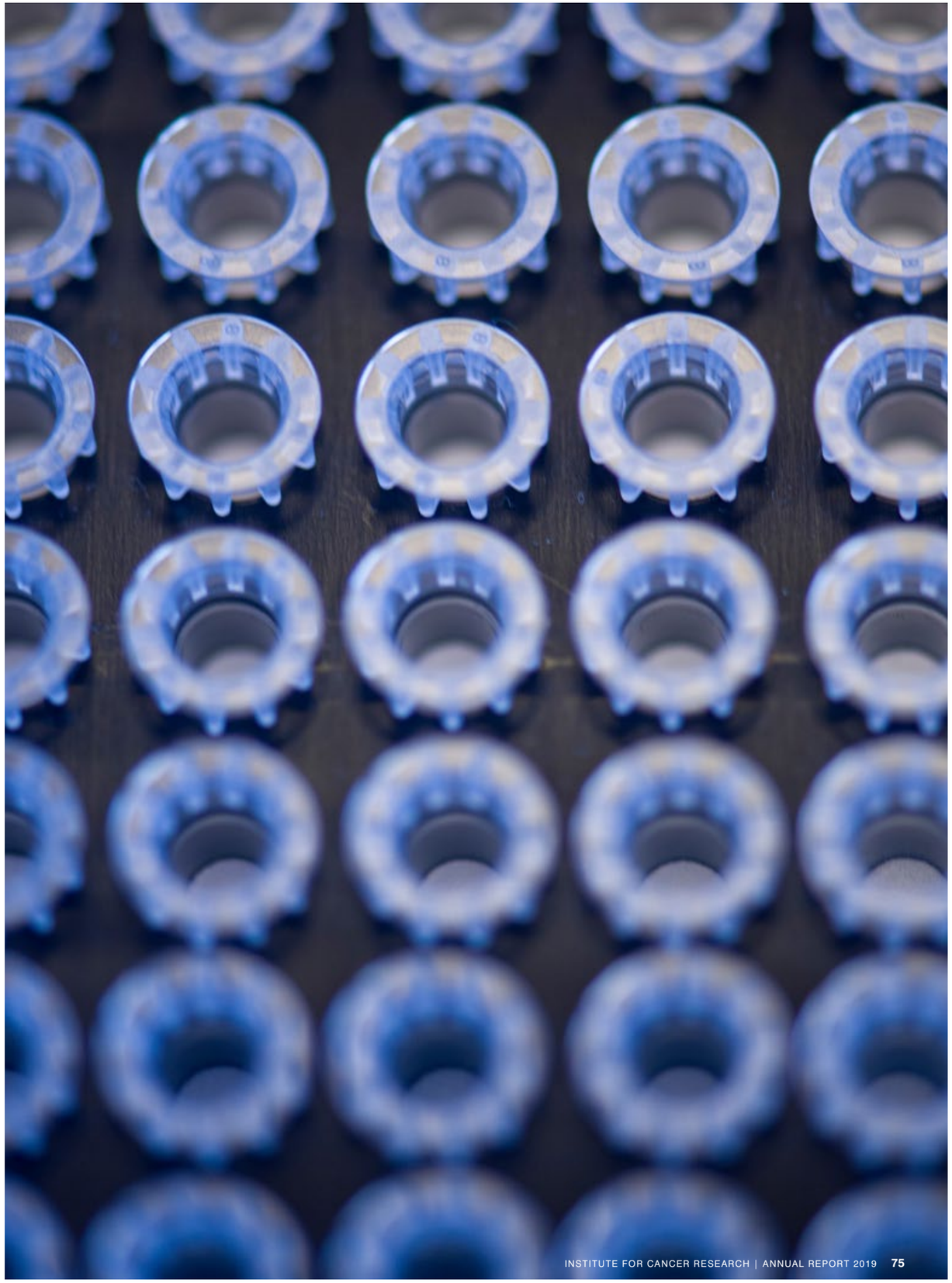
USA
- Buck Institute for Research on Aging, Novato, California
- Dana Farber Cancer Institute, Boston, Massachusetts
- Dartmouth College, Hanover, New Hampshire
- Duke University Medical Center, Durham, North Carolina
- Fred Hutchinson Cancer Research Center, Seattle, Washington
- Georgetown University, Washington DC
- Harvard University, Boston, Massachusetts
- Johns Hopkins Medicine, Baltimore, Maryland
- Lawrence Berkeley National Laboratory, Berkeley, California
- Lineberger Comprehensive Cancer Center, Chapel Hill, North Carolina
- Masonic Cancer Center and University of Minnesota, Minneapolis
- Massachusetts General Hospital, Boston, Massachusetts
- MD Anderson Comprehensive Cancer Center, Houston, Texas
- National Institutes of Health (NIH), Bethesda, Maryland
- Oregon State University, Corvallis, Oregon
- Princeton University, New Jersey
- Rutgers Cancer Institute of New Jersey
- Stanford University, California
- The Mount Sinai Hospital, New York
- The University of Kansas Hospital, Kansas
- Tisch Cancer Institute, New York
- UCSF, Helen Diller Family Cancer Centre, San Francisco, California
- University of Albany, New York
- University of California, Berkeley, California
- University of Chicago, Illinois
- University of Colorado, Denver, Colorado
- University of Illinois, Champaign, Illinois
- University of Washington, Seattle, Washington
- Washington University, St Louis, Missouri
- Weill Medical College of Cornell University, New York

Recent Innovations

Registered Disclosures of Invention (DOFIs), Patent Applications and Granted Patents

Research group (inventor)	Department	DOFI #
Karl-Johan Malmberg	Cancer Immunology	19110
Kristian Berg	Radiation Biology	19075
Vessela Kristensen	Cancer Genetics	19074
Karl-Johan Malmberg	Cancer Immunology	19055
Kjersti Flatmark	Tumor Biology	19054
Therese Sørlie (Jens Henrik Norum)	Cancer Genetics	19050
Kjetil Taskén	Cancer Immunology	19038
Kristian Berg (Anette Weyergang)	Radiation Biology	19035
June Myklebust	Cancer Immunology	19021
Kjersti Flatmark	Tumor Biology	19033

Application type or granted patent	Research group(s)	Department	DOFI #
Priority Application	Kjetil Taskén	Cancer Immunology	19038
Priority Application	Kjersti Flatmark	Tumor Biology	17179
PCT Application	G. M. Mælandsmo, K. Flatmark, K. Sandvig	Tumor Biology, Molecular Cell Biology	18030
US (National) Application	Guro E. Lind	Molecular Oncology	17135
US (National) Application	Karl-Johan Malmberg	Cancer Immunology	16132
EP (Regional) Application	Karl-Johan Malmberg	Cancer Immunology	16132
US (National) Application	Kjersti Flatmark	Tumor Biology	18153
Granted EP patent (EP 3,069,138)	Johanna Olweus	Cancer Immunology	13003
Granted US patent (US 10,308,980)	Lothe R. A., Ågesen T.H., Sveen A., Lind G.E., Nesbakken A., Skotheim R.I.	Molecular Oncology	11057
Granted EP patent (EP 2,630,261)	Guro E. Lind	Molecular Oncology	53212
Granted EP patent (EP 3,243,077)	Kristin Austlid Taskén, Ingrid Jenny Guldvik	Tumor Biology	14040 15004
Granted EP patent (EP 2,861,568)	Kjetil Taskén	Cancer Immunology	12047



Publications

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