INSTITUTE FOR CANCER RESEARCH

Annual Report 2020

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.

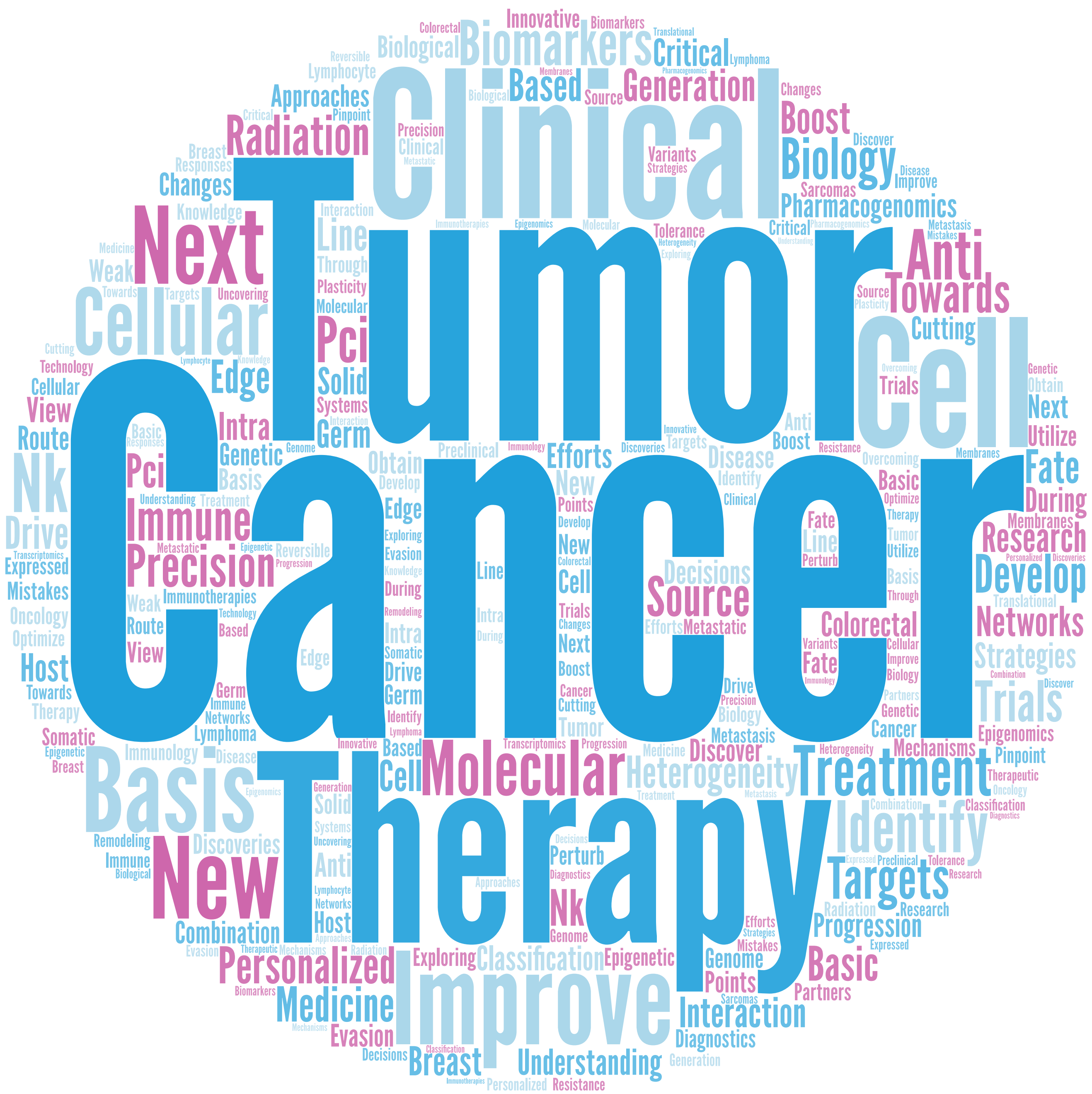
FRONT PAGE:
Hunting for a cure: testing sensitivity to novel breast cancer drugs at Dept. of Tumor Biology.
- Cancer drug sensitivity screening of cell lines, primary cancer cells, patient-derived organoids and in patient-derived xenograft-models are new cutting-edge technologies paving they away into future diagnostics in precision medicine.

PAPER: 150/300 Profimatt
CIRCULATION: 800

Contents

THE ICR IN ESSENCE

- WHO WE ARE AND WHAT WE DO



WHO WE ARE

1954 RESEARCH – INNOVATION – EDUCATION **2021**

LEGACY IN RESEARCH, INNOVATION AND EDUCATION

The Institute for Cancer Research (ICR) was founded in **1954** representing **66** years of continuous advances in cancer research. Through the years, our work has significantly contributed to better understanding 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. There is also a proud history of translational research and innovation, with multiple spin-out companies and with numerous other past and present translational and innovation projects at the ICR in various stages of development. 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

390 RESEARCH STAFF

Approximately 390 research staff in 25 research groups, 6 core facilities and 1 admin unit
(organization see pages 8-9)

PAST 5 YEARS (2016-2020)

ICR researchers have raised almost 1.1 billion NOK extramural funding (of total 1.6 billion accounted)

1.10 BILLION NOK

1700 WORKING YEARS

Put in almost 1700 working years (1690 FTEs)

150 EDUCATED PhDs and MScs

Educated more than 150 PhDs (61) and MScs (90) that have graduated

1100 PUBLICATIONS

Leading to production of more than 1100 (1116) publications (mean IF > 6, median IF 4.7)

(for 2020 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 lead in developing new OUH and national strategies for advanced molecular cancer diagnostics, cancer precision medicine and experimental cell therapy

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 a new SAB for the ICR
5. Increase internationalisation and technology development

Introduction by the Director

I am very happy to present our Annual Report for 2020. You can read about all our exciting research under presentation of Departments and Groups (pages 18-61) and under Centre of Excellence, KG Jebsen Centres and Oslo University Hospital (OUH) Strategic Research Areas (pages 62-73). As a little teaser on research topics, see the word cloud generated from key quotes from all units (page 4). The ICR in 2020 had 391 employees plus students organised in 25 research groups complemented with cutting-edge core facilities and excellent administrative support (pages 8-11, 58-61, 80). At the ICR, we also have 29 project groups led by senior scientists and affiliated with the research groups (see pages 18-61). More than one third of the ICR staff is international and comes from 34 different countries outside Norway (page 12-13) and we have staff at all educational levels training and developing their careers (page 76).

The Covid-19 pandemic has in 2020-21 had major impacts world-wide, on the Norwegian society at large as well as on OUH and University of Oslo (UiO) research activity. At the ICR, as part of the hospital, with good support from the leadership at all levels and strong efforts from all our employees, we have kept the institute open throughout. This in recognition of the importance of the science we do (including Covid-19 related research) and how it is intimately connected with hospital operations. With appropriate risk assessments, precautions and personal protection measures, reduced density at work and somewhat reduced activity, this has gone well. I want to thank all our staff for putting in hard work under these difficult circumstances! So far, we have maintained scientific output and the numbers of PhD and MSc students that have defended their degrees are up (pages 5 and 10-11), and I am truly proud of that.

As part of our strategy for 2019-20 (see aims and goals, page 5), we have worked to strengthen translational research, improve coordination and collaboration with clinicians and diagnostic staff in the Oslo University Hospital Comprehensive Cancer Centre (OUH-CCC) and beyond, and to build further excellence in research where we would like to see originality, depth, quality, and international value. Furthermore, the ICR is a key driving force in the new and developing strategies for precision medicine and for cell therapy in the Division for Cancer Medicine and the OUH-CCC. In 2020 we have developed the **InPreD-IMPRESS-INSIGHT-CONNECT national project cluster** and public-private partnership for precision cancer medicine and raised more than 175 MNOK for these activities together with our partners across Norway (see page 16). We are truly grateful for all the support from regional health authorities, the ministry and other key public stakeholders, private partners, the Cancer Society and the Radium Hospital Foundation in this respect. It is great that cancer patients with advanced disease can now get molecular diagnostics through the InPreD-Norway Infrastructure, that our national molecular tumor board (piloted at OUH this spring) will now be operative and that the IMPRESS-Norway trial opens April 1 (page 16). To advance cell therapy and open opportunities for gene transfer we have worked together at ICR and with the Section for Cell Therapy, Department of Oncology to launch an **Advanced Cell and Gene Therapy Centre**, ACT. This is made possible through a generous donation of 50 MNOK from a private donor consortium with Svanhild and Arne Must's Fund, RADFORSK and the Cancer Society; it all came together in the fall of 2020 and we will open ACT from April 2021 (page 17).

In line with our goals for 2019-20, we have established the ICR **Translational Research and Innovation Committee** (TRIC), that meets monthly to discuss projects, support innovators and mobilize internal competencies (page 77-78). We also recruited a new **Scientific Advisory Board** (SAB) of six highly distinguished international colleagues who had their first meeting in January 2021 to review the ICR's activity and provided valuable advice that that we will integrate as we plan forward (page 14).

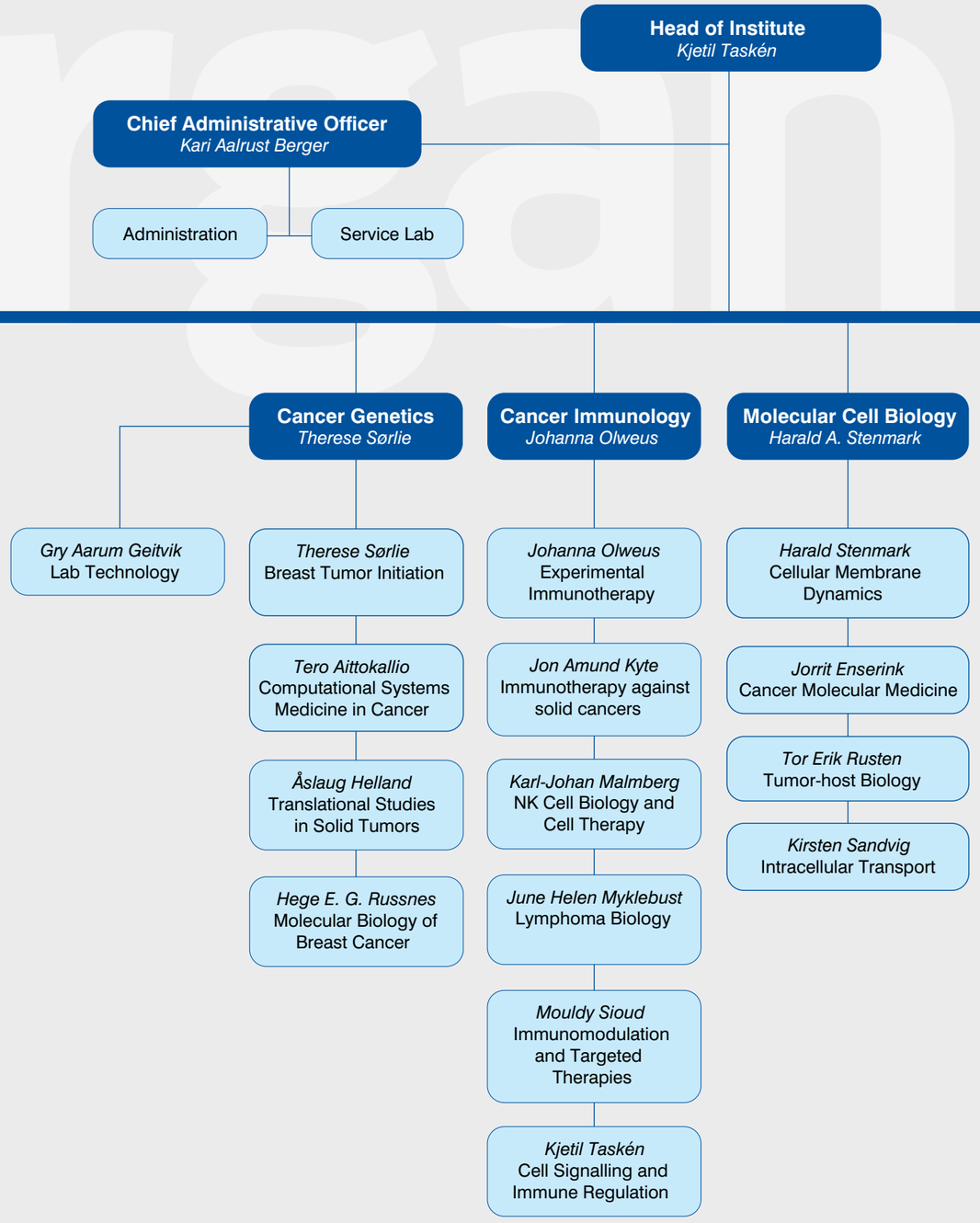
Since the new SAB could not visit the ICR at this time, we took the opportunity to make a **movie about the institute** and what we do. The full-length movie (https://www.youtube.com/watch?v=-p8DlY6ykfc) as well as a shorter introduction to the ICR (https://www.youtube.com/watch?v=MtcgDwqB_6Q) are now published on YouTube and linked from our web-pages (https://www.ous-research.no/institute/).

We celebrate our victories at the ICR, and in 2020 we have marked the start of the ERC Consolidator project OUTSOURCE by Johanna Olweus, the funding of EU projects PanCAIM and CLL-CLUE, and that ICR scientists have been able to obtain substantial new funding and secured major new grants from the RCN, Cancer Society, the Regional Health Authority for South-Eastern Norway and other sources. OUH-CCC and the ICR also received very significant grants for new instrumentation from OUH and UiO and jointly from the Radium Hospital Foundation and Cancer Society for a NovaSeq for research and diagnostics (see page 15). We celebrated internally the award of the Ragnar Mørk's Prize to Theodossis Theodossiou and the award of the ICR Researcher-of-the-year and Employee-of-the-year Prizes to Anita Sveen and Gry Aarum Geitvik (see page 81). Furthermore, OUH awarded prizes for best papers to ICR researchers Mantas Grigalavicius et al (May 2020) and Marina Vietri et al (Nov 2020). I would also like to honor Group Leader Einar Rofstad who retired end 2020 after almost 45 years of service at the Department of Radiation Biology. His continuous research has led to more than 280 publications.

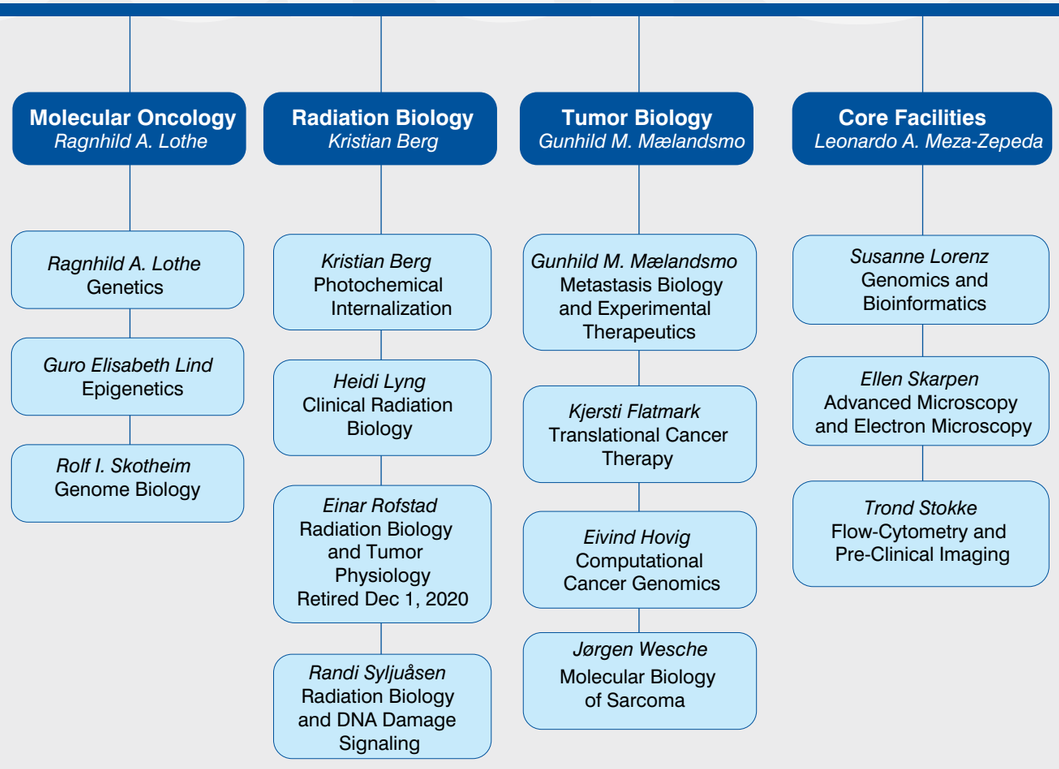
In line with our vision and values (page 5), the ICR sets out to maintain the excellent science and outstanding production and to further build excellence by organising more collaborative efforts at all levels to handle the grand challenges in cancer medicine and to position the ICR in national and international alliances and consortia. We aim to be a significant partner for the clinical activities in OUH-CCC. We continue feeding results into a translational research path and to have **patient benefit** in mind in all aspects of research and innovation.

March, 2021
Kjetil Taskén, Head of the ICR

Organisation



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.

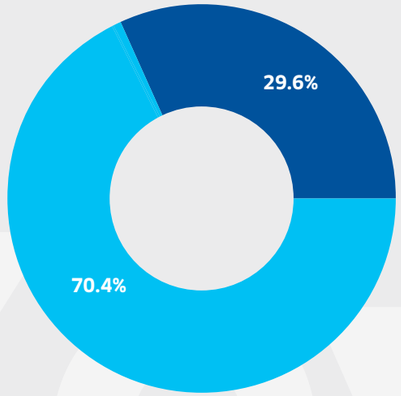


Key Figures 2020

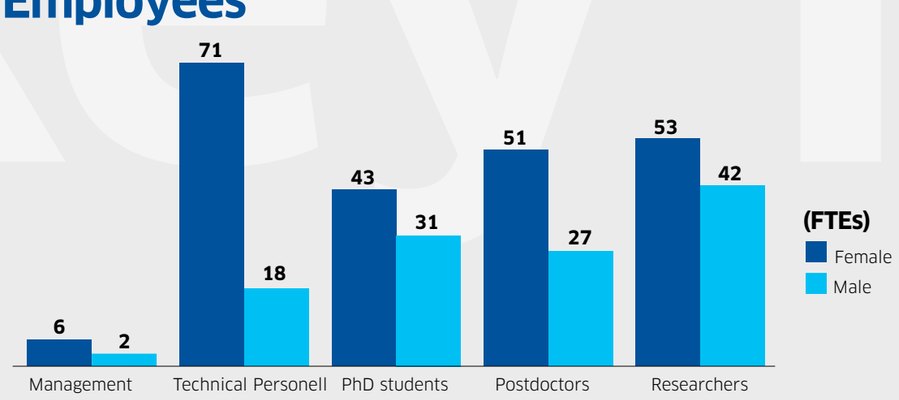
Funding

Percent

Actual Institute expenditure for 2020
by internal and external funding sources
(total 337,9 MNOK = approx. 34,5 M€)

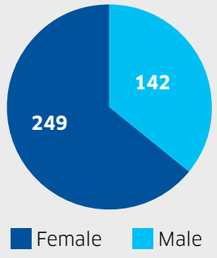


Employees



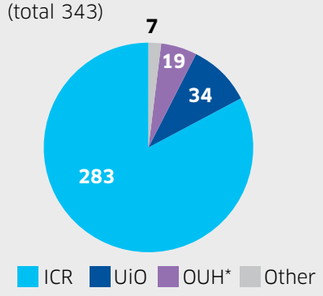
Employees by Gender

(total 391)



FTEs by Employer

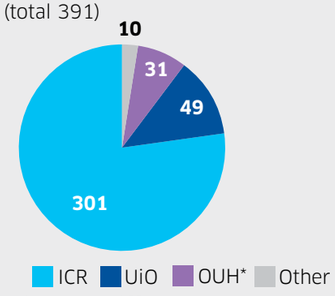
(total 343)



*other than ICR

Employed by

(total 391)

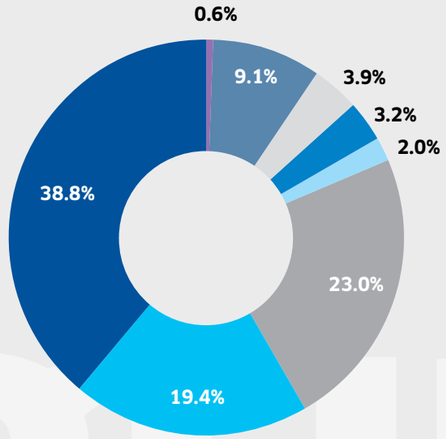


*other than ICR

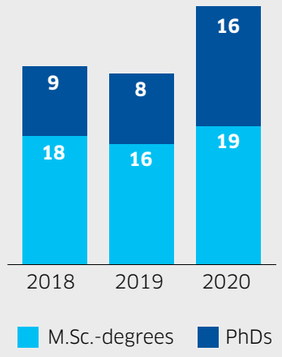
External funding by source

Percent

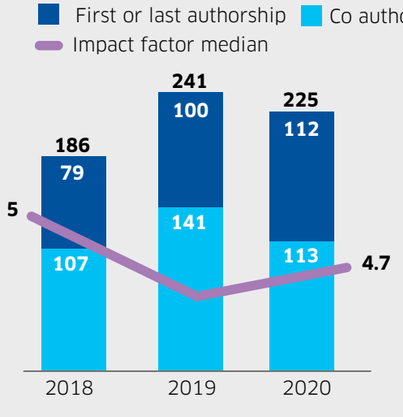
Sources of external competitive funding for
2020, based on actual expenditure (total
237,7 MNOK= approx. 24,2 M€)



Completed PhDs and M.Sc.-degrees



Articles published

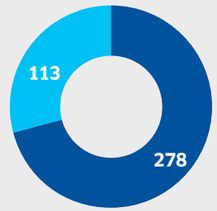


IMPACT FACTOR

	2018	2019	2020
Mean	6.5	6.1	6.3
Median	5	4.5	4.7

International Staff Distribution

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



■ Norwegian: **278 (71%)***
■ International: **113 (29%)**
*Including naturalised foreigners

01

Countries represented by one person
Brazil
Chile
Colombia
Croatia
Czech Republic
Denmark
Ecuador
Estonia
Lebanon
Macedonia
Russia
Serbia
Singapore
Slovakia
Switzerland

02
People
Finland
Japan
The Netherlands
Portugal

03
People
France
USA
Great Britain

04
People
Iran
Poland
Austria

05
People
Italy
Lithuania
Hungary

06
People
Greece

07
People
Spain
Sweden

11
People
Germany

13
People
India
China

The new Scientific Advisory Board for the Institute for Cancer Research meets

The Institute for Cancer Research in 2020 renewed and rotated its Scientific Advisory Board (SAB) that provides regular reviews of scientific output, quality and performance and gives advice on research strategy. The SAB consist of six highly distinguished scientists recruited from different institutions in Sweden, Denmark, Great Britain, The Netherlands and Austria. They represent a variety of different scientific backgrounds in basic, translational and clinical cancer research, collectively have a great set of complementary competences and a long track record of scientific and strategic leadership experience. They are thus very well equipped for evaluating the scientific activity at the institute.

SAB review January 2021

The SAB in January 2021 finished a review of the scientific activity of the Institute of Cancer Research. The review was performed on zoom due to the current pandemic (see picture) and since we could not show the new SAB our lab space and facilities, the SAB was presented with a video presenting the institute to give an impression of working conditions in our buildings and that you can watch here:

https://www.youtube.com/watch?v=PDq9DYRfPqQ&feature=youtu.be

The SAB was also beforehand presented with written material that included an overview of the overall research strategy of the institute, strategic projects in progress, development and work to address earlier SAB comments and material from all the sections and research groups at the institute. During the review the SAB received a presentation from each department and each of its research groups and had the opportunity to ask individual group leaders questions regarding the scientific strategy and output.

The SAB has also presented the institute with written feedback that will be used in our continuing work to develop and improve. Evaluation of the scientific activity of the institute is an important way to improve the quality and output of science produced ensuring that the institute continues to deliver cutting-edge research and stays abreast with strategic and scientific development internationally.

Scientific Advisory Board members

Professor Carl-Henrik Heldin
Department of Medical Biochemistry and Microbiology, Uppsala University, SAB Chair
https://katalog.uu.se/profile/?id=N96-1274

Professor Carl Figdor
Head, Dept of Tumor Immunology, Institute for Molecular Life Sciences, Radboud UMC, The Netherlands
https://www.radboudumc.nl/en/people/carl-figdor

Professor Margaret C. Frame
FRSE, FmedSci, OBE, Professor of Cancer Research and Director, MRC Institute of Genetics and Molecular Medicine, University of Edinburgh, Edinburgh, UK
https://www.ed.ac.uk/profile/margaret-frame

Professor Ruth Palmer
Institute of Biomedicine, University of Gothenburg
https://ruthpalmerlab.se

Professor Karen-Lise Garm Spindler
Department of Experimental Clinical Oncology, University of Aarhus; Consultant Oncologist, Aarhus University Hospital
https://pure.au.dk/portal/en/persons/karenlise-garm-spindler(44550b92-1db9-45d9-97ed-e0dfc3d89e50).html

Professor Giulio Superti-Furga
Scientific Director, Research Center for Molecular Medicine (CeMM) of the Austrian Academy of Sciences, and Professor for Medical Systems Biology, Center for Physiology and Pharmacology Medical University of Vienna.
https://cemm.at/research/groups/giulio-superti-furga-group/

Oslo University Hospital Comprehensive Cancer Centre

Oslo University Hospital, a OECI-accredited Comprehensive Cancer Centre since 2017, aims to be a leading cancer centre in Europe. The accreditation is based on high quality in both clinical practice, research and teaching. The cancer research performed by the Institute for Cancer Research (ICR) is a corner stone in our OECI accredited Comprehensive Cancer Centre (CCC), with several world leading research groups and environments.

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. The Cancer Registry of Norway is also located in the same area, encouraging collaboration and synergies between the different environments.

More patients into clinical trials is an expressed aim for the 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. The tight connection between research groups at ICR and clinical research groups in Oslo University Hospital is an important factor to improve the clinical trials, by including high quality translational research connected to the investigator initiated clinical trials. 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 (RCN CoE, KG Jebsen Centres) 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 centre 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, CCC Research Committee

- December 2020: OUH-CCC and its Division of Cancer Medicine is receiving a new top-line sequencing instrument to be placed in the Genomics Core, Dept of Core Facilities, ICR and to be used for precision medicine research and diagnostics in InPreD to stratify patients into clinical trials such as IMPRESS.

From left: Jan Vincents Johannessen, Radiumhospitalets Legater, Susanne Lorenz and Leonardo Meza-Zepeda, ICR Dept of Core Facilities, Sigbjørn Smeland, Hege Russnes and Bodil Bjerkhagen, InPreD and Dept, of Pathology, Ingrid Stenstadvold Ross, Norwegian Cancer Society.

See video at
https://radiumlegat.no/Prosjekter/2020/KF_og_RL_bidrag

"The donation of a NovaSeq from The Norwegian Cancer Society and Radiumhospitalets Legater is like receiving a red Ferrari for Christmas!"

- Sigbjørn Smeland

Oslo University Hospital
Comprehensive Cancer Centre

OECI COMPREHENSIVE Cancer Centre

Precision Cancer Medicine at OUH Comprehensive Cancer Centre

In 2020 we have built on the recommendation from the OUH project group for precision medicine from 2019 to establish a national cluster of strategic projects in response to the suggested actions:

1. Patients where advanced molecular cancer diagnostics will be instrumental for selection of treatment should be offered such diagnostics (Fig 1.)
2. Cancer patients should have opportunity to receive individualised treatment (Fig 2).
3. OUH will learn and build competence in advanced molecular cancer diagnostics and individualised treatment and contribute to development and production and dissemination of new knowledge (Fig. 3)

FIG 1: A national Infrastructure for Precision Diagnostics (InPreD) headed by H. Russnes (Head Exp. Pathology/Group Leader ICR) was established in 2020. At OUH InPreD is organized as a collaboration between the Division for Laboratory Medicine and the Section for Core Facilities at ICR. The aim of InPreD is to offer patients advanced molecular diagnostics needed for inclusion into clinical trials e.g. tumor sequencing with extended gene-panels and/or whole genome sequencing. The logistics for extended gene panels was piloted in 2020 and the national molecular tumor board is up and running spring 2021.

FIG 3: Implementation of precision medicine requires regulatory changes and a project called INSIGHT (headed by E. Aas, UiO) has been initiated to explore the possibilities for using the Norwegian registry data to develop synthetic control groups for IMPRESS (non-randomized, small number of patients) for evaluating the efficacy and cost-effectiveness of the treatment offered in the trial. The project will also address the ethical and juridical challenges that need to be overcome for implementation of precision medicine. The project is a collaboration between ICR, OCBE and UiO (Faculty of Medicine and Faculty of Law).
ICR has also been instrumental in establishment of the public-private partnership CONNECT for driving the implementation of precision cancer medicine by jointly addressing key obstacles and piloting novel solutions to transform the current practice. CONNECT will be operationalized via Working Groups (ICR represented in several) engaging public and private partners as well as regulators and payors and is an arena for all relevant stakeholders to jointly address important issues. The Consortium contract was signed by 22 founding partners at end of 2020 (6 University hospitals, NIPH, Cancer Society, Oslo Cancer Cluster, Pharma Association, 10 pharma companies, 2 IT/biotech companies).

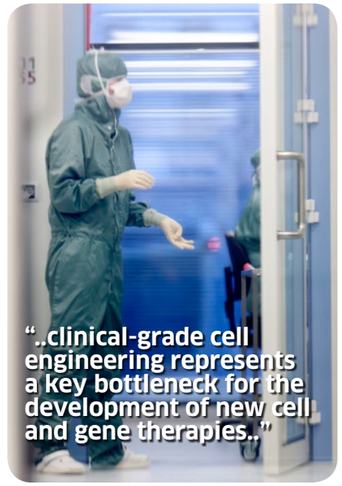

Medisin

Presisjonsmedisin: Nytt offentlig-privat samarbeid

FIG 2: A national Precision Cancer Medicine Trial (IMPRESS-Norway) headed by Å. Helland (Oncologist and Group Leader ICR) has been initiated. The trial is modelled on the DRUP trial in the Netherlands with combined umbrella and basket design and using a Simon two-stage model of expanding cohorts. EMA or FDA approved drugs will be tested against new indications in cohorts defined by cancer diagnosis, mutational profile and drug. All hospitals treating cancer patients in Norway are participating (17 hospitals). A Trial Management committee consisting of members from OUH, HUS, St.Olav and UNN has had regular meetings in 2020 for planning the trial. IMPRESS-Norway has secured funding from the national clinical trials program KLINBEFORSK (50 mNOK), 16 mNOK from the Norwegian Cancer Society and from Roche with more pharma companies expecting to join spring 2021. IMPRESS-Norway will start inclusion of patients April 2021.
Read more at: impressnorway.com


Nytt initiativ for innføring av personlilpasset kreftbehandling

New Centre for Advanced Cell Therapy hosted by Division of Cancer Medicine, OUH

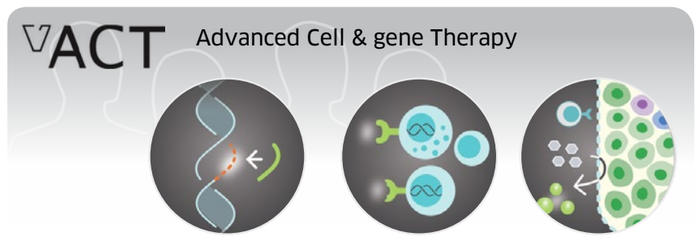


Cell and gene therapy form two of the most dynamic research areas world-wide and provide fundamentally new therapies for diseases without available treatment. Advanced Therapy Medicinal Products (ATMPs) typically target the underlying biology of the disease rather than the symptoms and therefore offer the possibility of cure. The development of new cell and gene therapies is spearheaded by the unprecedented clinical success of cancer immunotherapy, such as chimeric antigen receptor (CAR)-T cell therapy for B cell malignancies. In parallel, new advances in stem cell biology, including the possibility for differentiation of mesenchymal stem cells (MSCs), and of induced pluripotent stem cells (iPSC) reprogrammed from somatic cells, open up new possibilities to regenerate cells and tissues for the treatment of chronic diseases such as diabetes as well as various organ failures, including liver diseases. However, clinical-grade cell engineering and manufacturing represents a key bottleneck for the development of new cell and gene therapies.

The academic leadership at ICR and the Department of Cancer Immunology has, together with the leadership at the OUH-CCC and the Department of Oncology and Section for Cell Therapy, outlined a path to restructure the cell therapy unit at OUH to meet the demands of the future and ensure that Norway stays at the international forefront in the development of cell and gene therapies. This effort has moreover been strengthened by the formation of a strategic research area in cell therapy at OUH (StratCell).

CRITICAL CONTRIBUTION FROM A PRIVATE DONOR CONSORTIUM

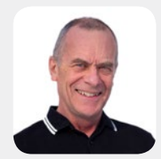
A donor consortium consisting of Svanhild and Arne Must´s Fund for Medical Research (lead donor), RADFORSK oncology research fund and the Norwegian Cancer Society, has committed 50 MNOK to form a Centre for Advanced Cell therapy (ACT Centre) located in clean room facilities at the OUH. The investment is dedicated to the establishment of a center that will provide a new national service for the manufacturing of genetically engineered cells for therapy, under full-scale good manufacturing practices (GMP). The center will moreover include existing local competence in cell differentiation and manufacturing for production of other ATMPs to OUH.



DAG JOSEFSEN
HEAD OF THE SECTION OF CELL THERAPY:
"The formation of a dedicated core facility for cell and gene therapy to tackle challenges in this rapidly developing field is a milestone for the Department of Cell Therapy and we are committed to make sure this unit can provide services at the international forefront."

KARL-JOHAN MALMBERG
SCIENTIFIC DIRECTOR, ACT CENTRE:
"With the launch of the ACT centre, we outline a path to acquire and establish new competence and equipment in existing GMP facilities to serve as a national infrastructure for ATMP manufacturing to make advanced therapies available to Norwegian patients, and to create a fundament for innovation and industrial collaborations."

JOHANNA OLWEUS
HEAD OF THE DEPARTMENT OF CANCER IMMUNOLOGY:
"This donation brings a lot of excitement as it removes the biggest hurdle for translation of novel concepts in cell and gene therapies generated in Norway all the way to patients."

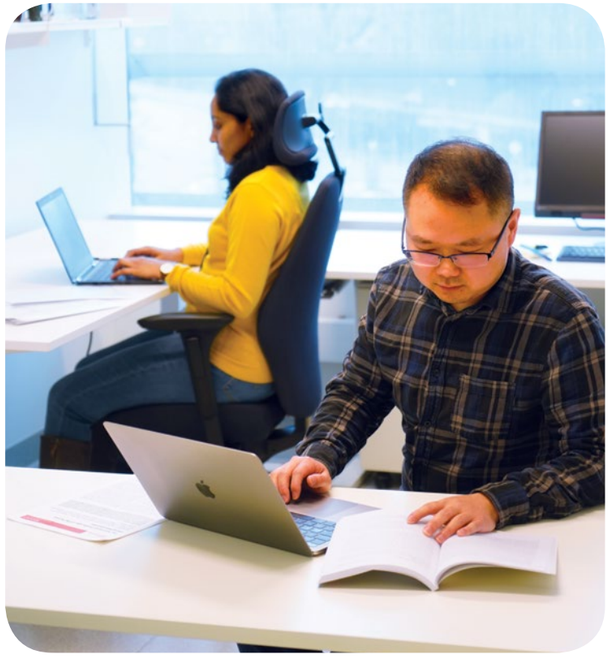


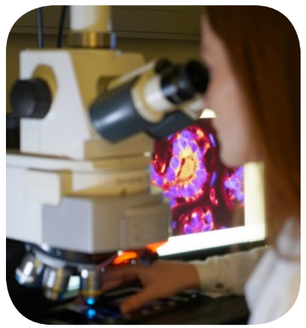
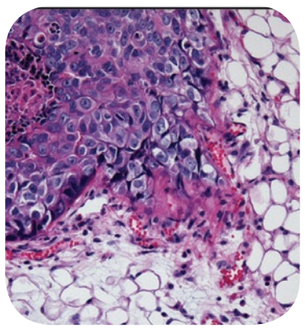
HANS PETER BØHN
SVANHILD OG ARNE MUST´S FUND FOR MEDICAL RESEARCH
The group of donors is very happy to help Norwegian scientists in the promising field of Advanced Cell Therapies prepare their projects for clinical testing in patients who desperately need a new lease of life.

Departments and research groups







"Our mission is to improve the lives of cancer patients through scientific advances in precision oncology"

Headed by **Therese Sørlie**

Department of

Cancer Genetics

Our aim is to improve risk estimation, achieve earlier diagnosis and improve prediction of treatment responses and other clinical outcomes for patients with both solid tumors and hematologic malignancies. Our translational research strategy includes functional studies, molecular classification, data integration, artificial intelligence, and pan-cancer analyses. We work towards facilitating the implementation of discoveries into clinical use and are the leading part in several clinical trials. 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 45 researchers including medical doctors, molecular biologists, computational biologists and highly specialized engineers organized into four research groups, two project groups and one lab-technology unit. Two of the group leaders hold part-time clinical positions and three have affiliated professor positions. The lab technology unit reinforces the department's expertise in state of the art technology, and allows seamless 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. Our translational studies take advantage of our established pipeline for high-quality biobanking and secure data handling of patient cohorts with long-term follow-up that enables omics-level analysis of tumors down to the single cell. Our clinical database consists of > 3000 subjects from consecutive studies and trials with high quality clinical information. We are involved in the following clinical studies:

- IMPRESS-Norway – Implementing Precision cancer medicine in Norway
- DART – Durvalumab after chemo-radiotherapy for NSCLC (multinational phase II trial)
- IBCT - Improved Breast Cancer Therapy in the neoadjuvant and metastatic setting
- EMIT - Establishment of Molecular profiling for Individual Treatment decisions in Early BC (observational national study)
- OPTIMA-optimal personalized treatment of early breast cancer using multi-parameter analysis (international prospective RCT)
- ComIT - evaluation of the benefit of radiation in combination with immune therapy for lung cancer
- NorPACT-1/2 - Neo-adjuvant chemotherapy for pancreatic cancer
- NIPU – Nivolumab and ipilimumab +/- UV1 vaccine in second line treatment of mesotheliomas
- ICON - A randomized phase IIb study evaluating immunogenic chemotherapy combined with ipilimumab and nivolumab in luminal B breast cancer
- ALICE - atezolizumab combined with immunogenic chemotherapy in metastatic triple-negative breast cancer
- Oslo2 - observational study with comprehensive biobanking

We are partnering or leading several networks and consortia; including the Oslo Breast Cancer Consortium; the Norwegian Cancer Society Expert Groups on Lung and Pancreatic Cancer; Personalized Cancer Treatment and Metaflammation; Regional Network in Radiation Oncology; the Regional Research Network on Microbiome Research; the Norwegian Network of Symptom Management (NORSMAN); Personalized Cancer Therapy (PERCATHE); International Cancer Genome Consortium (ICGC); EuroPDX; and the EU projects Cancer-ID, Gender Net Plus, HERCULES, PANCAIM and RESCUER. The total number of publications in 2020 was 61.

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 the transition from ductal carcinoma (DCIS) in situ to invasive breast cancer. We have broad expertise in laboratory technologies including high-throughput genomics, in vivo lineage tracing, 2D and 3D in vitro culture techniques, in situ hybridization and confocal microscopy. We use patient cohorts and mouse models (transgenic and patient derived xenografts – PDXs, including the mouse intraductal (MIND) method) in our studies. We also have competence in bioinformatics and statistical modeling. The group counts 8 members, including the group leader and professor (TS), four postdocs, one PhD student, two engineers as well as an affiliated scientist in 10% position and an affiliated breast surgeon. One member is MD and one is DVM.

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 mammary tumorigenesis
- Investigate the role of HER2 in transition from DCIS to invasive breast cancer
- Investigate the role of FGFR1 in progression of luminal breast cancer

RECENT ACHIEVEMENTS
In 2020, the group published 9 peer-reviewed articles. Two members completed their PhD degrees and we had one master student exam. We obtained funding from the Pink Ribbon campaign through the Breast Cancer Society and the Norwegian Cancer Society. Two group members were interviewed in the Norwegian radio program Ekko.

Computational Systems Medicine in Cancer

Group leader:
Tero Aittokallio

"A systems view of disease networks to pinpoint selective therapeutic targets"

ABOUT
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 believe that combining functional, genetic and epigenetic profiles is critical for the 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.

The project group, headed by Thomas Fleischer, uses whole-genome epigenetic profiling and advanced imaging combined with experimental approaches such as CRISPR epigenetic editing to characterize cancer-driving epigenetic alterations and to assess the potential of novel biomarkers and treatment strategies. Together, we develop integrated computational-experimental approaches to map systems-level networks to identify targeted means to selectively inhibit disease progression.

AIMS
The modeling aim is to develop systematic approaches to identify combinations of molecular and clinical features most predictive of individual medical outcomes, such as differences in disease risk or treatment responses, which may eventually provide predictive biomarkers for clinical translation. The medical aim is to optimize treatment outcomes for individual patients using maximally predictive models and minimal biomarker signatures that enable real-time and cost-effective diagnostics and prognosis. Learn more about the group's aims (video): https://youtu.be/KrqcAAbctds

PROJECTS
The group is carrying out multidisciplinary projects in close collaboration with other researchers at the institute and as part of international projects, where we develop, test and implement novel ways of how to use artificial intelligence (AI) and machine learning (ML) models in translational and clinical studies. These projects make use of large scale 'omics' profiling to identify cancer-promoting alterations and novel therapeutic targets for both solid tumors and hematologic malignancies. Specific projects include:

- Multi-omics prediction of clinical outcomes for precision oncology applications
- Identification of synthetic lethal interactions and anticancer drug combinations
- AI-guided treatment optimization by means of cost-effective biomarker panels
- Decision support systems for real-time patient monitoring and adaptive trials
- Epigenomics and radiomics for refined classification of breast cancer patients

RECENT ACHIEVEMENTS
In 2020, the group published 23 articles in peer-review scientific journals. We are partnering in several international translational projects, including three ERA-PerMed projects (HEURECA, JAK/STAT TARGET and CLL-CLUE), three EU-H2020 projects (RESCUER, HERCULES and PANCAIM), and the UK Breast Cancer Now Catalyst Programme for predictive markers for TNBC drug responses. As for national funding, the group received in 2019 3-year open-project grant from South-Eastern Norway Regional Health Authority for AI-guided treatment optimization by means of multi-omics biomarker panels. In 2020, the group received grant from the Norwegian Cancer Society for high-resolution identification and isolation of therapy-resistant cancer cell subpopulations for phenotypic profiling, and a European-level H2020 grant for pancreatic cancer AI for genomics and personalized medicine. These grants will enable further implementation of the computational-experimental approaches at OUH and internationally.

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 tumors, with a special interest in pancreatic, lung and colorectal cancers. By increasing the understanding of the underlying biology of tumor development, we will improve precision medicine in cancer care. Several of our projects include material from patients participating in clinical studies, and we have detailed clinical data from all patients. Predictive biomarkers and mechanisms of resistance are in focus. The group is headed by Åslaug Helland (Professor UiO), and we have one project group headed by Elin H. Kure (Professor USN). The group counts 21 members and eleven of these are MDs. We are four researchers, three postdocs, ten PhD-students, one coordinator and three engineers.

AIMS
The ultimate goal is to increase our ability to offer personalized cancer treatment, and thereby improve prognosis. Sub aims are:
• Identification of biomarkers in blood samples, for diagnostics, follow-up and prognostication
• Identification of tumor 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
- 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
The national clinical precision medicine study IMPRESS-Norway (ÅH PI) has been planned, and received >50 million NOK in funding. One master and one PhD degree were completed.
In 2020, the group published 20 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 70 mill NOK in research funding: Vilde Haakensen, HSØ open call 8.5 mill; Elin Kure 11.5 mill NOK (EU/H2020 - PANCAIM Pancreatic cancer AI for genomics and personalized Medicine (2021-2024, 9 European partners, >88M NOK), our part >10M NOK); Kure and Aittokallio, Norwegian Cancer Society 2020 – 2025 (15M NOK): The Norwegian Group of Expertise on Pancreatic Cancer: New insight in disease mechanisms, better diagnosis, and improved treatment and care (KNEP), our part 1.5M NOK; Åslaug Helland, KlinBeForsk, 50 million NOK.

Cancer Genome Variation

Group leader:
Hege G. Russnes

“Exploring inter- and intra-tumor heterogeneity to improve molecular classification of cancer”

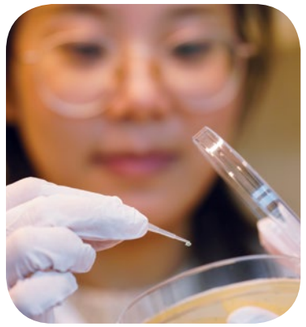
ABOUT
Our group fosters trans-disciplinary interaction to reach a more fundamental understanding of the biological dynamics of breast cancer through high-throughput molecular analyses of DNA, mRNA, miRNA and protein, both at diagnosis and during disease progression. We use multiple types of methodology on a variety of biological material (including bulk tumor and single cell -omics, liquid biopsies and in situ analyses) combined with tailored bioinformatic analyses. The group has a special focus on breast cancer but is also exploring molecular features across tumor types.

As co-PI/partners in several clinic trials we perform “state of the art” analyses of large numbers of patient samples at various stages of the disease. 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. In 2020 this section has coordinated “Infrastructure for Precision Diagnostics, cancer (inPreD)” at the national level. She is also appointed “Associated Investigator” at NCMM (Centre for Molecular Medicine Norway). Our group has a total of 8 members (2 scientists, one postdoc, one research engineer, one nurse/MSc, two PhD students and one MSc student) in addition to 3 associated members (prof. emerita A-L Børresen-Dale, oncologist L. Ottestad and professor O. C. Lingjærde).

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
- TREAT-ABC: Towards personalized treatment for patients with aggressive breast cancer
- SN - Sentinel Lymph Node in Breast Cancer- revealing the interaction between tumor subtype and host immune response.
- CANCAN: CANcer specific Copy number 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 2020 we published 9 articles in peer-reviewed journals. 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).



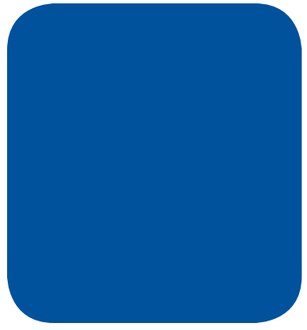







“Our goal is to improve cancer diagnostics and therapy through cutting edge research on tumor immunology and lymphocyte biology”





Headed by **Johanna Olweus**

Department of

Cancer Immunology

ABOUT

The Department of Cancer Immunology (DCI) consists of six research groups. The groups of Olweus (Head), Taskén, Sioud, Myklebust and Malmberg were in 2020 complemented by the group of Kyte and a new project group leader, Skånland (Tasken group). Total approx. 70 staff. Four DCI members are professors at the University of Oslo. Groups at the DCI are partners in the K.G. Jebsen Center for B-cell malignancies and several EU- and NIH-funded research programs in cancer immunotherapy, a newly formed competence center in NK cell biology (co-director), and have co-led several national initiatives to implement precision medicine (InPred, IMPRESS and CONNECT). 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

- Decipher normal and cancerous lymphocyte biology
- Identify novel biomarkers and immunotherapy targets
- Develop novel therapeutic strategies, and translate them into the clinic
- Conduct clinical trials testing out existing drugs in novel combinations or in new indications

RECENT ACHIEVEMENTS

- 37 publications, including 21 original papers with mean/median IF of 11.5/6.4 (17 with IF>5), including senior/first authorships in journals like Leukemia, and co-authorships in journals like Nature, Nature Communications, Science Transl Med, Cell, Science Immunology (x2), PNAS, and Blood
- Department groups won two Open Call grants from the Research Council of Norway, two Open Call grants from the Norwegian Cancer Society and three Open Call grants from South Eastern Norway Regional Health Authority (HSE) (total of 67mNOK)
- Secured funding through a major private donation (50 mNOK) to a National Center for Advanced Cell Therapy (ACT) at OUH to provide services for manufacturing of gene-modified cells (Malmberg Scientific Director)
- ERC Consolidator Grant (2 mill Euro) to Olweus for the project “Outsourcing Cancer Immunity to healthy donors” launched in September
- ERA PerMed Grant to Sigrid Skånland (coordinator, 6 international PIs)
- 4 graduated Msc

CLINICAL TRIALS

- Completed patient enrolment in the randomised phase IIb trial ICON, combining immune checkpoint inhibitors with chemotherapy (breast cancer)
- Recruited 56/75 patients in the randomised phase IIb trial ALICE, combining immune checkpoint inhibitors with chemotherapy (breast cancer)
- Completed patient enrolment in the clinical trial REPORT (Jan 21), evaluating PD1-blockade combined with radiotherapy (head and neck squamous cell carcinoma).

Experimental Immunotherapy

Group leader:
Johanna Olweus

“Overcoming tolerance by T-cell based cancer immunotherapies”

ABOUT

The group counts 15 members (F/M 9/6); 1 full professor (JO), 5 postdocs, 6 PhD students and 3.5 engineers, and two affiliated clinicians. Four members have MD background.

AIMS AND CORRESPONDING PROJECTS

1. To develop novel immunotherapeutic T-cell based strategies that overcome the major challenge of self-tolerance in cancer, by outsourcing of cancer immunity to donor-derived T-cell receptors (TCRs). Identify novel TCRs with therapeutic potential for future use in cancer immunotherapy using donor T cells that
   - selectively kill defined cell types by recognition of cell-type specific molecules presented on mismatched HLA, or
   - recognize antigens encoded by shared mutations presented on matched (self) HLA.
2. To identify new targets of immunotherapy
3. To identify mechanisms of action of successful experimental cancer immunotherapy
4. Translate TCRs developed by the group into clinical trials

RECENT ACHIEVEMENTS

- Olweus ERC Consolidator Grant project (2 mill Euro over 5 yrs) started in September 2020
- Achieved open call funding from the Research Council of Norway, The Norwegian Cancer Society and the Regional Health Authorities South-Eastern Norway
- The group demonstrated that translational mistakes made by cancer cells (melanoma) can be specifically targeted by healthy donor T cells, opening possibilities for new immunotherapy, recently published as a full article in Nature. Four members of Olweus group were co-authors, including postdoc Maarja Laos as second author. The article was the focus of an article (highlight) in Nature Reviews Cancer and received considerable media attention.
- The group continued their research collaboration with biotech company Kite/Gilead.
- Olweus had a central role in securing funding through a major private donation to a National Center for Advanced Cell Therapy (ACT) at OUH to provide services for manufacturing of gene-modified cells, to be established 2021.

Immunotherapy against solid cancers

Group leader:
Jon Amund Kyte

“Developing immunotherapy for resistant cancer”

ABOUT

The Kyte Group includes 13 members (group leader JAK, 2 researchers, 4 postdocs, 2 MD PhD students, 4 technicians) and three associated clinicians. JAK is also a senior consultant in oncology and Head of Section for Experimental Cancer Therapy at Dept of Oncology.

AIMS

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.

PROJECTS

1. Development of CARs targeting solid cancers
2. Development of constructs making CAR T cells resistant to immune suppression in solid tumors
3. Development of optimized regimes for combining immune checkpoint inhibitors with chemotherapy or radiotherapy
4. Identification of biomarkers for use in personalised cancer immunotherapy

RECENT ACHIEVEMENTS

- Preclinical development of a novel CAR for T cell therapies targeting prostate cancer
- Preclinical development of a novel CAR for T cell therapies targeting breast cancer
- Initiated the randomised phase IIb trial ICON, combining immune checkpoint inhibitors with chemotherapy against metastatic hormone receptor positive breast cancer (JA Kyte et al J Transl Med. 2020). Patient enrollment completed November 2020.
- Initiated the randomised phase IIb trial ALICE, combining immune checkpoint inhibitors with chemotherapy against metastatic triple negative breast cancer (JA Kyte et al J Transl Med. 2020). Recruited 56/75 patients.
- Initiated the clinical trial REPORT, evaluating PD1-blockade combined with radiotherapy against head and neck squamous cell carcinoma. Patient enrollment completed January 2021.

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 17 members (F/M: 9/8); 1 full professor (KJM), 1 project manager, 1 scientist, 4 postdocs, 8 PhD students and 3 engineers. Malmberg is a visiting Scientist and leads a translational NK cell team of 6 at the Karolinska Institute (KI).

AIMS
Research in the Malmberg Lab aims at understanding the cellular and molecular mechanism underlying the formation and diversification of human NK cell repertories. A central aspect of these studies is to examine the dynamic tuning of NK cell function by killer cell immunoglobulin-like receptors (KIR) during NK cell differentiation and education. We develop and use a wide range of single cell technologies, advanced imaging and computational tools to study the regulatory gene circuits involved in shaping the interior of the NK cell with a primary focus on lysosomal signalling. In more translational efforts, we seek to implement new insights into NK cell biology in clinical trials for patients with advanced cancer.

PROJECTS
1. INSIDE-NK: Role of inter-organelle communication for effector function
2. DIVERSIFY-NK: Functional diversification of human NK cell repertoires
3. SYNTHETIC KILLER: Genetic engineering of iPSC-derived NK cells for off-the-shelf cell therapy

RECENT ACHIEVEMENTS
- Collaborated with Prof Dan Kaufman (UCSD) during Sabbatical to develop novel engineered iPSC-derived CAR-NK cells (Zhu et al. Cell Stem Cells 2020).
- Entered into a new academic-industry collaboration with Merck to develop new NK cell engagers (2020-2023).
- Defined a systemic protein deviation score to predict outcome in DLBCL. Paper published by Eivind Heggernes Ask in Med (online December 2020). Patent filed December 2020. 70082-19110 ER
- New position (20%) as Scientific Director of the Centre for Advanced Cell Therapy (ACT).
- Contributed to the COVID19 cell atlas project https://covid19cellatlas.com/#/ with co-authorships in Cell, Science Immunology x2 and PNAS.
- Full partner in a NIH PO1 grant to support the transatlantic NK cell trial based on adaptive NK cells.

Lymphoma Biology

Group leader:
June Helen Myklebust

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

ABOUT
The group counts 9 members in full time positions and 3 members part time, with research background in medicine, biology, biotechnology and bioinformatics, and includes 1 professor, 1 associate professor, 4 scientists, 4 postdocs, 1 PhD student and 1 head engineer. Three members are MDs and four members recruited from abroad. We are part of the KG Jebsen Centre for B-cell malignancies.

AIMS
We focus on translational studies in B-cell lymphoma to define tumor clonal evolution and early cancer driver genes, and to identify immunosuppressive mechanisms in the tumor microenvironment.

PROJECTS
We use advanced single-cell technologies and high-dimensional imaging analysis to characterize tumor cells and intratumor immune cells in patient biopsies.

Ongoing projects are:
- Clonal evolution and identification of early genetic changes in lymphomagenesis
- Explore B-cell antigen receptor as a therapeutic target for B-cell lymphoma
- Spatial high-dimensional characterization of the tumor microenvironment and correlation to tumor genotypes
- Characterize intratumor regulatory T cells and explore how these can be targeted
- Clinical register studies

RECENT ACHIEVEMENTS
The group published five original papers and one methodological paper in 2020. By utilizing whole exome sequencing of tumor samples from a unique cohort of DLBCL patients enriched for patients who relapse after standard of care, we identified mutations and loss of the antigen presentation molecule HLA-A to be associated with higher risk of relapse (Wise et al, Blood Adv 2020). We have implemented imaging mass cytometry, a technology facilitating imaging analysis of tissues with subcellular resolution of more than 30 different markers simultaneously. This will provide new insight into tumor microenvironment architecture and cellular interaction patterns (Blaker and Huse et al). We participated in a study led by researchers at Stanford University, demonstrating that anti-CD19 CAR T cells are less efficient in targeting tumor cells with low CD19 expression (Majzner et al, Cancer Disc 2020).

Immunomodulation and Targeted Therapies

Group leader:
Mouldy Sioud

“Innovative approaches for cancer therapy”

ABOUT

The group has 6 members, including 1 PhD student, 1 postdoc, 1 research engineer, 2 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 198 peer-reviewed original articles (mean IF = 5.44) and reviews, with 1st and/or last authorship on 85% of the papers.

AIMS

The first objective of the group is to develop novel antibodies and peptides to membrane proteins and convert these into cancer killers or immunomodulators. The second objective is to modulate immune cell function using our in-house developed antibodies and siRNA formulations.

PROJECTS

1. To develop high-affinity antibodies and peptides to membrane proteins
Membrane proteins are attractive as targets for diagnostic and therapeutic applications. By use of our phage display platform we have developed several promising peptides and scFv antibodies that recognize surface receptors specifically expressed on tumor cells or immune cells. The best candidates are being pursued to demonstrate therapeutic efficacy in vitro and in animal models for cancer.

2. To develop antibody- and peptide-targeted photodynamic therapy to kill cancer
This project seeks to improve the specificity and efficacy of photodynamic therapy by coupling photosensitizers to our developed human antibodies or peptides that recognize surface antigens expressed on cancer cells.

3. To develop therapies to kill tumour-associated macrophages (TAMs)
Given the association between high macrophage infiltration into tumors and poor survival in the majority of cancer patients, macrophages represent an attractive therapeutic target. This project seeks to develop new targeted lytic peptides to kill monocytes and/or their progeny TAMs.

RECENT ACHIEVEMENTS

- Developed new antibody-photosensitizer conjugates
- Developed new human antibodies against plasma cell malignancies
- Nine publications
- One DOFI-21012
- Two master theses
- Obtained funding from Radforsk

Cell Signalling and Immune Regulation

Group leader:
Kjetil Taskén

“We want to perturb tumor immune evasion mechanisms to boost anti-tumor immunity”

ABOUT

In 2020 the group counted 18 members (F/M: 13/5), 1 PI, 1 researcher/lab leader, 1 senior consultant, 7 postdocs incl one senior consultant/postdoc, 1 PhD student, 1 M.D./Ph.D. student, 4 MSc students, and 2 technicians. The group is part of K.G. Jebsen Centre for B Cell Malignancies.

AIMS

The Taskén group aims to understand tumor immune evasion mechanisms, and how we can interfere to boost anti-tumor immunity. We want to define future precision immune oncology strategies.
We proceed with cancer drug sensitivity screening (CDSS) to explore individual drug responsiveness and resistance patterns in patient cancer cells. We aim to develop models to assist individualised clinical decisions in precision cancer medicine (PCM) in oncology and haematology.
We aim 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.

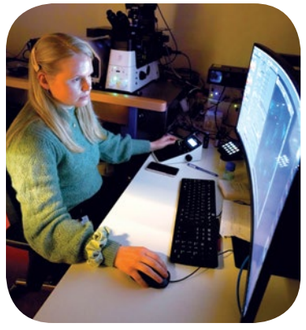
PROJECTS

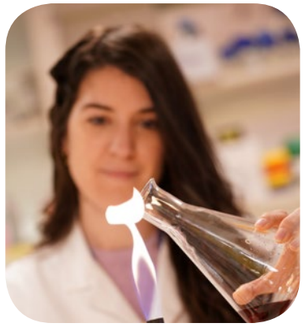
- Tumor immune evasion mechanisms, T cell function in cancer and immune-related diseases
- Identification of regulatory T cell targets that can be perturbed to reverse tumor immune suppression
- CDSS in chronic lymphocytic leukemia (CLL) and multiple myeloma, understanding drug synergies and predicting effective drug combinations in individual patients
- Functional PCM approaches in solid tumors, hereunder CDSS on pancreatic cancer, breast cancer and ovarian cancer
- IMPRESS-Norway national PCM clinical implementation trial (trial management)
- Acetyl salicylic acid clinical intervention study in metastatic colorectal cancer (ASAC)

RECENT ACHIEVEMENTS

Publication highlights include PCM approaches to predict clinical dosing of combinatorial treatments in CLL patients based on biomarker studies (Leukemia 2020), Furthermore, in co-authored papers we have contributed to understanding TLR8 signaling in T cells (Nature Commun., 2020), role of OPA1 regulating DNA metylation (iScience, 2020), Covid-19 outcomes in CLL patients (Blood, 2020) and reported a CD100 germline mutation giving primary sclerosing cholangitis (Science Transl. Med., in press).
In 2020 we won major new grants from 2021 from the Cancer Society, Research Council of Norway and HSE (PI Tasken) as well as an ERA PerMed grant (CLL-CLUE) on PCM in CLL (coordinator Sigrid Skånland, 6 PIs). Sigrid Skånland was promoted project leader at the DCI from 2021, and two MSc students graduated.

“Uncovering the cellular basis of cancer development”





Headed by **Harald Stenmark**

Department of

Molecular Cell Biology

The department has a staff of 79 (including 8 MSc students and trainees) of 24 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 melanoma and leukemia drug sensitivity, 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. Kirsten Sandvig´s group participates in the EU ITN project ITN projecet DIRNANO, Direct the immune response through designed nanomaterials.In addition, the department´s groups participate in three EEA projects.

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 6 project groups are led by Andreas Brech, Kaisa Haglund, Camilla Raiborg, Kay O. Schink, Maria Torgersen 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 and functions of selective autophagy in cancer
- Centrosome dynamics in cancer
- Cytokinesis in development and carcinogenesis
- Membrane dynamics in promotion of genome integrity
- Mechanisms of cancer cell invasion
- Mechanisms and biomedical importance of lysosome repair
- Mechanisms and functions of macropinocytosis in cancer cell feeding

RECENT ACHIEVEMENTS

- Characterization of Protrudin-dependent mechanism for formation of invadopodia –cellular protrusions that promote cancer cell invasion (Pedersen et al, Journal of Cell Biology, 2020). Dedicated commentary article in Journal of Cell Biology.
- Demonstration that unrestrained accumulation of ESCRT-III on ruptured micronuclei drives micronuclear catastrophe and chromosome fragmentation (Vietri et al., Nature Cell Biology, 2020). Dedicated “Highlight” in Nature Reviews Molecular Cell Biology. Awarded Article Prize of Oslo University Hospital.
- In collaboration with Andreas Carlson’s group at Department of Mathematics, demonstration that protein crowding mediates ESCRT-induced formation of intraluminal vesicles in endosomes (Liese, Wenzel et al., PNAS, 2020).
- Demonstration that ESCRT proteins promote autophagy by mediating sealing of newly formed autophagosomes (Zhen et al., Autophagy, 2020).
- Comprehensive review on ESCRT proteins in sealing and scission of cellular membranes (Vietri et al., Nature Reviews Molecular Cell Biology, 2020).
- Major grants in 2020 to Kay O. Schink, Marina Vietri, Antoni Wiedlocha and Harald Stenmark.
- Patrycja Szybowska and Anette Lie-Jensen successfully defended their PhDs in 2020.”
- Members of the group published 14 original papers, one review and one commentary article in 2020. Of these, 11 were published in journals with IF > 9.

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, one project group leader, one researcher, nine post-docs, three PhD students, two research assistants, two medical students and three MSc students. A large fraction of the group consists of scientists from abroad, including Spain, Chile, Lebanon, Colombia, The Netherlands and Austria. 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 the identification of synergizing drug combinations. 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

RECENT ACHIEVEMENTS

The Covid-19 pandemic has had a profound negative impact on overall progress. Nonetheless, three PhD degrees and two MSc degrees were completed and the group submitted one DofI and published two articles. Funding obtained: A research grant from The Norwegian Research Council and three Scientia fellowships. One of the group members (Helene Knævelsrud) became a junior associated member of NCMM, and one of the former group members became an assistant professor at UiO (Pierre Chymkowitch). The group leader was an invited speaker at the 2020 FASEB conference SRC on Cell Signaling in Cancer: From Mechanisms to Therapy.

Tumor-host Biology

Group leader:
Tor Erik Rusten

“Tumor-host interactions during cancer progression”

ABOUT
The research group counted 10 members representing 7 nationalities in 2019 (Australia, India, Iran, Hungary, Germany, Spain and Norway): 1 group leader, 1 scientist, 4 postdocs and 1 PhD student, 1 technician and 1 master student and 1 Erasmus exchange student.
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 and utilize 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
- Tumor-microenvironment interactions and growth support.
- Mechanisms of cancer cachexia.
- Uncovering nutrient vulnerabilities to stall tumor growth in vivo.
- Roles of autophagy in metabolic reprogramming, nutrient mobilization and breakdown of muscle and adipose tissue during cancer cachexia.

RECENT ACHIEVEMENTS
- New 3-year research project funded by the Regional Health Authority, “Uncovering Nutrient Vulnerabilities to stall Tumor Growth in vivo”
- In 2020 Rojyar Khezri completed her PhD and Eduardo Martin Quintana finished his ERASMUS stay

*The group participated in 3 original research articles and 1 commentary article in 2020

Intracellular Transport

Group leader:
Kirsten Sandvig

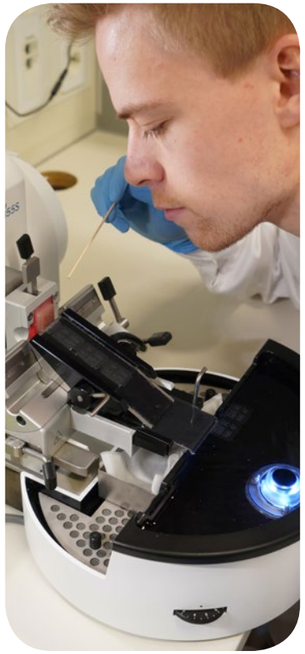
“All the way from basic research to translation”

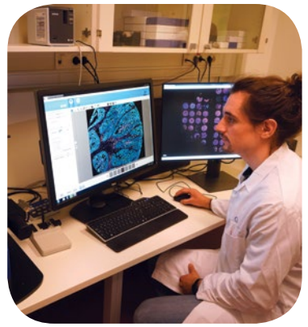
ABOUT
Sandvig’s group, counting around 10 members during 2020, is interested in the mechanisms of endocytosis, intracellular transport and secretion. Uptake of receptors and ligands and correct intracellular sorting of endocytosed molecules are crucial for maintenance of a normal differentiated phenotype. In some studies we use protein toxins such as ricin and Shiga toxin, which are well established 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 in 2013 we obtained a 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, lasted to 2019 and involved collaboration with ten other Norwegian groups working in academia, research institutes, hospitals and industry. This project formed the basis for further grants from EU (InnoIndigo), the Norwegian Cancer Society and a Romania-Norway EEA grant. Tore Geir Iversen is a project leader focusing on nanoparticles. The group also studies release of exosomes from cells and characterizes exosomes from prostate cancer cells and patients with the goal of detecting biomarkers; project leader is Alicia Llorente, who in 2020 obtained a new grant from the Norwegian Cancer Society to continue this work. 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 76 (~345 publications). The group has extensive national and international collaboration, and group members are involved in three COST-networks.

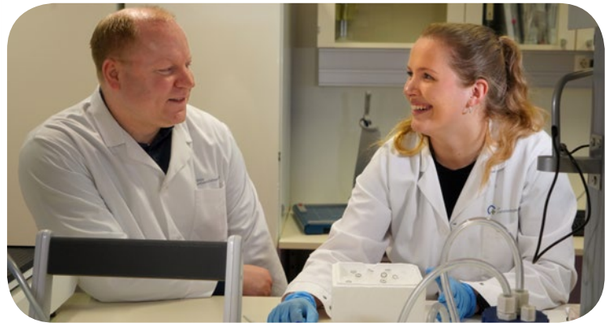
AIMS
The projects aim at increasing our knowledge about intracellular transport, nanoparticles for drug delivery, and exosomal biomarkers in order to provide a rational basis for diagnosis, treatment and prevention of cancer.

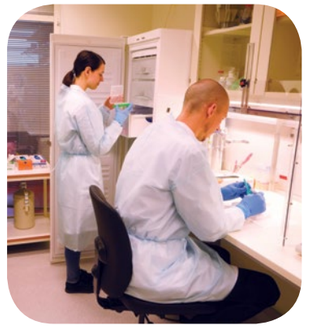
PROJECTS:
- Characterization of intracellular transport
- Biodegradable nanoparticles in cancer diagnosis and therapy
- Exosomes and prostate cancer

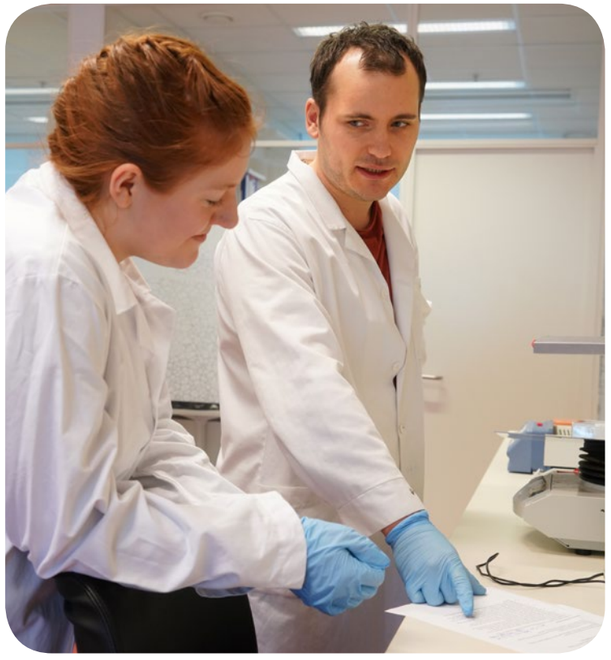
RECENT ACHIEVEMENTS:
- Our competence concerning cellular membranes, intracellular transport, nanoparticles and exosomes resulted in 13 publications in high quality journals in 2020. Group members were both first and last authors on articles in the following journals with impact above 6:, Adv. Drug Delivery Rev., Cancer Metastasis Rev., Nano Today, Cell Mol. Life Sci. and J. Nanobiotechnology.
- In 2020 a M.Sc. degree from Dept. Biosciences, UIO, was awarded to Silvana Romero, who is now a Ph.D. student in the group.
- The group was awarded new grants both for nanoparticle and extracellular vesicle research. Alicia Llorente was awarded NOK 5.4 mill from the Norwegian Cancer Society and Kirsten Sandvig/ Tore Geir Iversen obtained an EEA grant, Norway-Romania of NOK 4.7 mill NOK, as well as support from Radforsk. Group members obtained an ITN project (DIRNANO: Direct the immune response through designed nanomaterials).



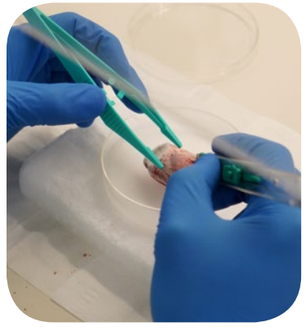








“Biological discoveries for improved precision cancer medicine”



Headed by **Ragnhild A. Lothe**

Department of

Molecular Oncology

Our main research programs are devoted to colorectal cancer and prostate cancer, but we also have longstanding project portfolios on other solid tumor types. The department hosts three research groups and four project leaders, and our expertise in biomedical research spans across several disciplines. In a year of home office and reduced lab activity due to COVID-19 restrictions, our labs have managed to keep up with our main activities. We published 16 research articles registered in PubMed in 2020, of which 94% had department members as 1st and/or last authors. We are pleased to see a continuation in the upward trajectory of citations, h-index and impact factor of the journals in which we publish.

ACHIEVEMENTS 2020

In the largest published study so far of ex vivo functional profiling in the context of tumor heterogeneity, we showed that the degree of intra-patient pharmacotranscriptomic heterogeneity among patient-derived organoids of metastatic colorectal cancer is modest (Bruun et al., Clin Cancer Res 2020). For clinical translation of this ex vivo drug screening platform, and to investigate its potential to guide experimental therapies for patients with metastatic colorectal cancer, we reached a milestone by getting national approvals for the intervention trial EVIDENT. The study will start patient inclusion in 2021.

We also started patient inclusion in the national bladder cancer study (BLADMETRIX) at all participating hospitals, to evaluate the clinical utility of an epigenetic biomarker-based urine test for patient surveillance.
Milestones in development of research resources for prostate cancer were reached with the completion of a heterogeneity-TMA consisting of more than 3000 lesions from 571 prostatectomies, and collection of >18 700 diagnostic PSA measurements from ten-year follow-up of the same patient cohort.

We published three review articles, including a comprehensive summary of biomarker-guided therapy in colorectal cancer (Sveen et al., Nat Rev Clin Oncol 2020). Five academic degrees (3 MSc and 2 PhD) with supervisors from our Department were successfully completed last year.

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

Genetics

Group leader:
Ragnhild A. Lothe

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

ABOUT
Our main research program is translational studies of primary and metastatic colorectal cancers (CRC). We conduct genomics, drug screening, digital pathology and functional analyses. We are also the core lab of a European multicenter study on the orphan disease malignant peripheral nerve sheath tumor (MPNST). The research group has 22 members and includes two project groups in Cell signaling (Leithe) and Computational oncology (Sveen).

AIMS
Our main objective is to translate novel biomedical knowledge into improved prognostic stratification and treatment of patients with CRC and MPNST.

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

RECENT ACHIEVEMENTS
We published 10 research articles in 2020, with central authorship positions. Two MDs, Tuva H Brunsell and Jørgen Smeby, defended their PhDs in molecular biology at the Faculty of Medicine, U of Oslo. Anita Sveen received the "Researcher of the Year" prize at the Institute of Cancer Research and the Radium Hospital Foundation.

We published the largest study of PDOs from metastatic CRCs in a tumor heterogeneity setting (Bruun et al., Clin Cancer Res). Our "living biobank" currently includes 130 PDO lineages established from 60 patients and screened for sensitivity to 47 anti-cancer agents or combinations (unpublished). This will serve as reference data in the EVIDENT study (see below).
Pre-clinical investigation showed a rationale for repurposing of PARP inhibitors to a small subgroup of CRCs. Sensitivity to PARP inhibition was dependent on wild-type TP53 activity, and TP53-mediated suppression of RAD51 was identified as a possible mechanism of action for synthetic lethality between homologous recombination deficiency and PARP inhibition (Smeby et al., EBioMed).
We established a platform and published four papers on multiplex fluorescence-based immunohistochemistry and digital image analyses of biomarkers in tumor tissue. Prognostic value of RCC2 was validated in non-metastatic CRCs, and we also proposed low RCC2 expression as a biomarker of benefit from chemotherapy (Bergsland et al., ESMO Open). Clinically relevant biomarkers in CRC were reviewed (Sveen et al., Nat Rev Clin Oncol).

CLINICAL TRIALS
A protocol for an intervention study of metastatic CRCs with experimental therapy based on personalized ex vivo pharmacogenomics (EVIDENT) was approved by the regional ethics committee and the Norwegian Medicines Agency. Patient inclusion will start in 2021.
A phase II study of pembrolizumab in MPNST was supported by Merck, and the pre-specified criterion of at least one responder among the first 7 patients was met.
An project on "Adoption of an orphan-MPNST", funded by an open call grant from the Health Region South Eastern Authorities started in 2020. We have identified novel molecular subtypes with new treatment potentials for this disease (unpublished).

Epigenetics

Group leader:
Guro E. Lind

"Epigenetics - a source for improved cancer management"

ABOUT
We are studying DNA methylation alterations in various cancer types, with a main focus on gastrointestinal and urological cancer. In 2020 the group counted ten members: a researcher, postdoc, study nurse, and PhD student, four engineers (including two PhDs, and bioinformaticians) and the project group- and group-leader. Two additional MD PhD students are supervised from the group.

AIMS
1) Conquer hurdles of liquid biopsy analyses in cancer by establishing a standardized roadmap, from biobanking, through biomarker discovery and to clinical implementation.
2) Establish liquid biopsy-based tests for (i) early detection and monitoring of bladder cancer and (ii) early detection of rare gastrointestinal cancers with high mortality, among high risk patients.
3) Explore the inter- and intra-tumor diversity of epigenetic aberrations in cancer, and effect on patient outcome.

PROJECTS
- Methylome-based early detection and monitoring of bladder and gastrointestinal cancer
- Epigenetic heterogeneity in gastrointestinal cancers

RECENT ACHIEVEMENTS
From blinded analyses of a prospective series, comprising ~300 patients with gross hematuria, our epigenetic biomarker-based urine test achieved an accuracy well above 90% (Pharo & Jeanmougin et al., submitted). In parallel, we completed patient inclusion in a surveillance study, where 700 urine samples have been collected at Aker from >50 bladder cancer patients who have been followed for >2 years. We reached an important milestone by starting patient inclusion in our national bladder cancer study at all contributing hospitals, to evaluate the clinical utility of the urine test for patient surveillance. All together 500 patients will be followed for a two-year period.

We have demonstrated that the epigenetic phenotype CIMP is consistent within multiregional colorectal cancers, likely representing a clonal phenotype (Flatin et al., Int J Cancer). We have developed and shared a shiny app tool for ddPCR data analysis. By combining molecular subtyping with gene expression measures of tumor infiltration, we have contributed with improving prognostic models in glioblastoma (Jeanmougin et al, Mol Oncol).

Lind is co-manager and responsible for the translational research in the newly granted Norwegian Esophageal Cancer Consortium, aiming at bringing together a multidisciplinary expert group to develop cutting edge translational research and patient management. We are grateful to the Cancer Society for granting us open project support.

Genome Biology

Group leader:
Rolf I. Skotheim

“Transcriptomics – the expressed genome mistakes and a source for clinical biomarkers”

ABOUT
The Genome Biology group studies how genomes and transcriptomes are altered in cancer cells by using both computational biology and wet-lab based approaches. The group has particularly specialized in RNA-level analyses, and translational projects focus on prostate cancer, but also include testicular, colorectal, and ovarian cancers. The research group is interdisciplinary and the personnel have their basic education across biology, informatics, and medicine. Through 2020, the group had eleven members, including two researchers, one engineer, one postdoc, three PhD students, two MSc students, a study nurse and the group leader.

AIMS
The research group aims to improve the diagnosis and management of cancer by utilizing genome technologies. This includes identification and characterization of genes that are critical for development of cancer.

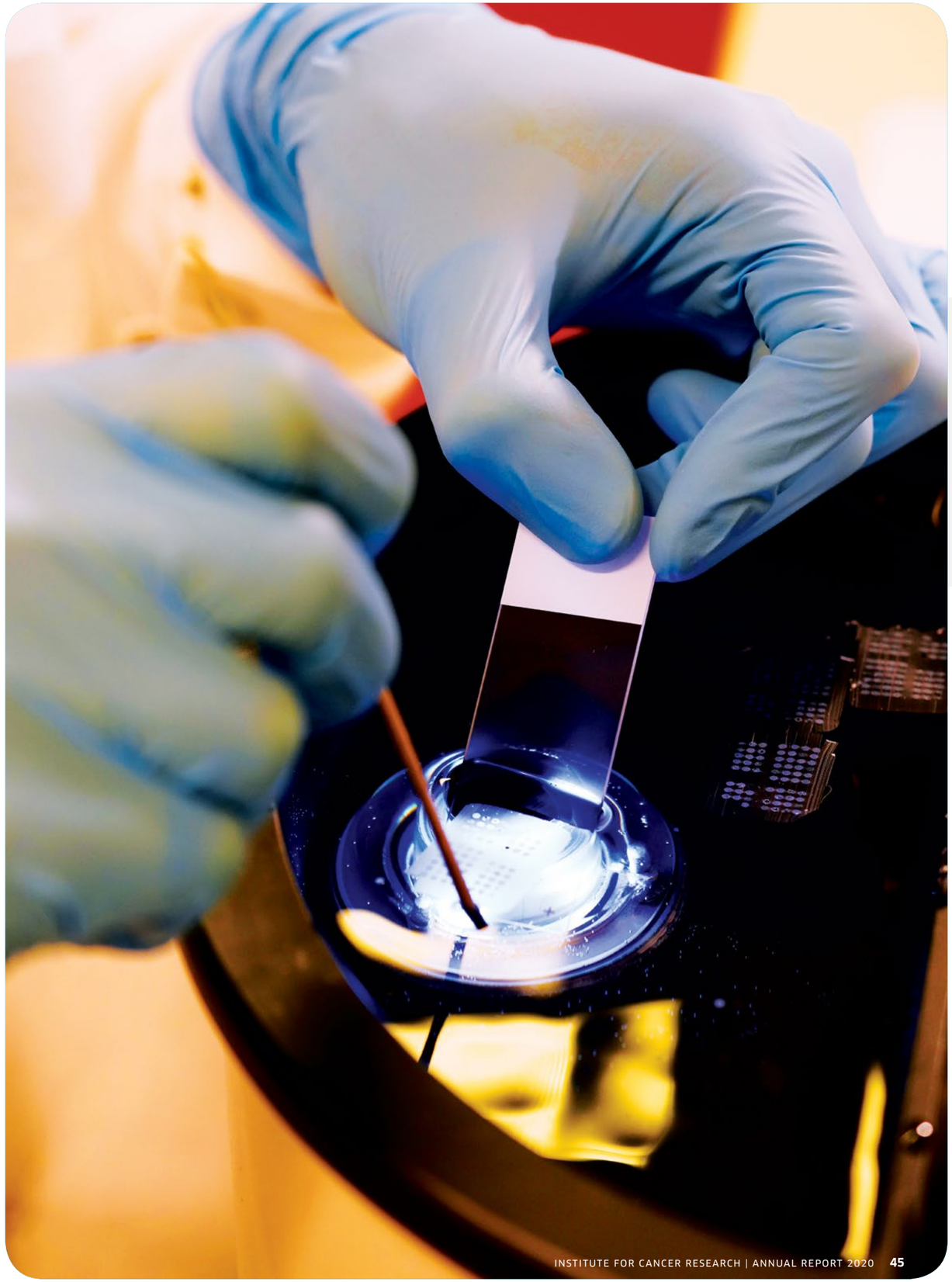
PROJECTS
- Genomics-based precision management of prostate cancer
- RNA variation caused by aberrant splicing and as a source of cancer biomarkers
- Fusion gene identification and characterisation

RECENT ACHIEVEMENTS
The group continued the development of its prostate cancer research program, primarily utilising a biobank resource with multiple frozen tissue cores from multifocal primary prostate cancer. Following the initial study where exceptional molecular heterogeneity among primary lesions was identified, the group has now showed that several biomarker genes are heterogeneously expressed among lesions. This has important implications for implementation of gene-based testing in prostate cancer management as information from all tumor foci is necessary to draw valid conclusions about the cancer. Milestones in research resource-development were reached with the establishments of genomics protocols from liquid biopsies, completion of a heterogeneity-TMA consisting of 3000 lesions from 571 prostatectomies, and collection of almost 20000 PSA measurements from the follow-up period after the prostatectomies.

On testicular cancer, articles on DNA copy number changes (Hoff et al., Endocr. Relat. Cancer) and fusion genes were published, and new software for particularly sensitive detection of their transcripts from RNA-sequencing data were made available (Zhao et al., NAR Genomics & Bioinformatics).

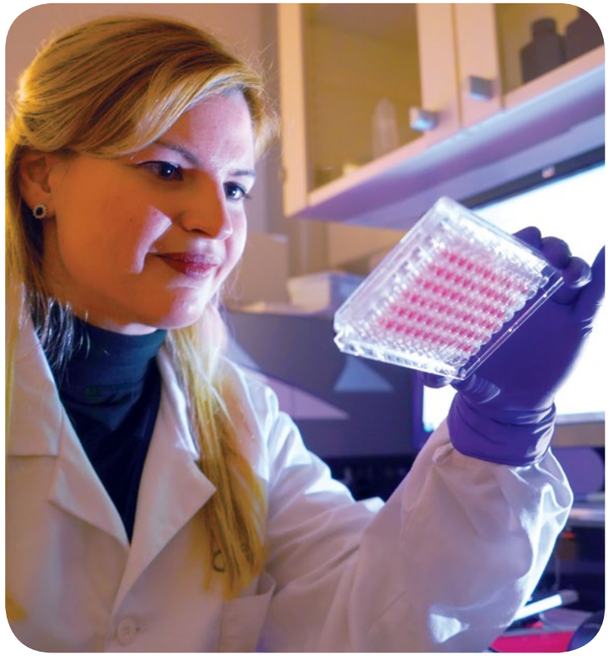
The group continues to develop bioinformatics pipelines for genomics data. In 2020, the Cancer informatics project group was established, led by Bjarne Johannessen. Johannessen is also responsible for cross-group cancer informatics within the Department of Molecular Oncology.

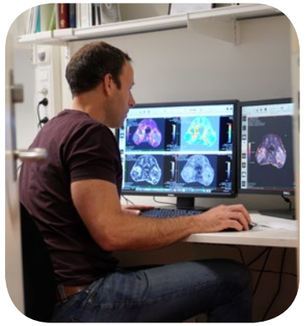
Mikael Ravndal completed his MSc degree at Department of Informatics, University of Oslo. Two large projects with grants from the Norwegian Cancer Society and South-Eastern Norway Regional Health Authority were started during 2020.



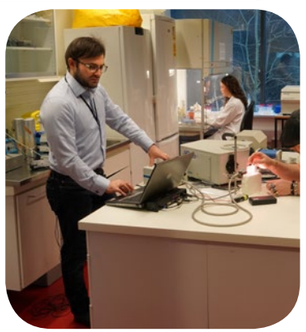


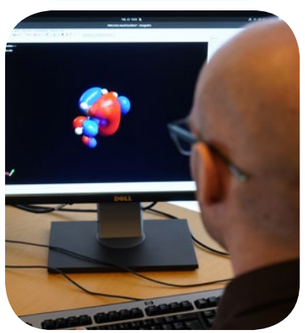




"Our goal is to develop new predictive methods and treatment strategies for improved radiation therapy"




Headed by **Kristian Berg**

Department of
Radiation Biology

The Department has more than 60 employees organized in 4 research groups and 7 project groups. Our research is focused on biological responses to ionizing radiation (gamma-rays, X-rays and alpha, beta, neutron, proton particles) and non-ionizing radiation (ultraviolet radiation and visible light). Our department is engaged in revealing the mechanisms of DNA repair, cell-cycle regulation, genomic instability and immune responses after radiation, the impact of tumour metabolism on the radiation response and predictive markers for the outcome of radiotherapy of cancer patients. The department is also involved in targeted delivery of radionuclides to cancer tissue. Another research area is the use of visible light to activate photosensitive compounds, thereby generating reactive oxygen species, to induce site-directed intracellular delivery of anticancer therapeutics, a technology named photochemical internalization (PCI). Furthermore, a new research area has emerged, the use of chemi- and bio-luminescence to elicit photodynamic therapy (PDT) effects on cancer cells.

OUR GOALS ARE

- To understand the mechanisms behind tumour response to radiation, and develop predictive methods and treatment strategies
- To establish new radiation-based treatment regimens with improved specificity and efficacy towards cancer cells
- To utilizing non-ionizing radiation combined with photosensitizing agents, to induce cellular internalization of therapeutics

KEY ACHIEVEMENTS THE LAST 3-4 YEARS INCLUDE

- DCE-MRI shown excellent for monitoring alterations in tumor oxygenation induced by antiangiogenic treatment;
- Cervical cancer patients with tumors showing high hypoxic fraction in combination with high interstitial fluid pressure have particularly poor prognosis;
- A novel mechanism of activation of the DNA damage kinase;ATR (Ataxia Telangiectasia and Rad3-related) identified;
- PCI found to efficiently enhance antigen presentation during anti-cancer vaccination in humans;
- A production unit for biomolecular therapeutics established.
- Documented that protons can activate photosensitizers to mimic responses as in photodynamic therapy (PDT) ;
- A new method to image hypoxia levels in cervix tumors gained novel molecular insight into treatment resistance mechanisms;
- New insight into the regulation of translation and the function of the stress-response kinase GCN2 in response to cellular stress;
- Combinatorial drug partners identified that over-come resistance to CD37-targeted radioimmunotherapy in B cell lymphoma;
- Discovered a key mechanism required for formation of Hh-signaling competent cilia, a potential treatment target for Hh-dependent cancers;
- Documented novel chemiluminescence compounds to activate photosensitisers with outstanding cytotoxic outcomes;

Photochemical Internalization

Group leader:
Kristian Berg

"Our goal is to develop and implement PCI into clinical practice for treatment of solid cancers"

ABOUT
Group members: 27, including 5 researchers, 6 postdocs, 5 PhD students, 6 technical positions and 4 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):* Targeted alpha-particle therapy (TAT) is a promising treatment for eradicating cancer micrometastases.

AIMS
Project Photochemical internalization:
Our projects involve the development of drugs for PCI enhancement, evaluation of PCI as an adjuvant to established therapy, studies on predictive markers for PCI response, evaluation of novel light and radiation sources for activation of photosensitizers.

Project Radionuclide therapy:
The main goal is to develop a novel therapy for disseminated cancer by dual targeted alpha particle radiation.

PROJECTS
- Recombinant immunotoxins and diabodies for activation by PCI
- PCI of immunotoxins targeting cancer stem cells and therapeutic cancer vaccines
- PCI as an enhancer of immune checkpoint inhibitors
- Biomarkers for targeted therapeutics with intracellular mechanism of action
- New vehicles for targeted delivery of small molecular drugs to endocytic vesicles
- The vasculature as a target for PCI
- Mitochondria-powered chemiluminescence to non-invasively treat inaccessible tumours
- Utilizing other radiation sources to induce PCI effects
- TAT for disseminated cancer
- Proton and neutron irradiation to activate photosensitizers towards PDT/PCI effects.

RECENT ACHIEVEMENTS
- First-in-human demonstration of PCI-enhanced HPV peptide-based vaccination in healthy volunteers (Selbo & PCI Biotech)
- Technology transfer of recombinant production of anti-cancer biologics (Weyergang)
- First time *in vivo* documentation of PCI to enhance small molecular inhibitors (Weyergang)
- Novel biomarker for ADC documented in clinical verification cohort (Weyergang)
- Production procedure for EGFR-targeted toxin for PCI-mediated delivery (Weyergang)
- PCI enhancement of checkpoint inhibitors, finalization of *in vivo* study (Weyergang)
- Proof of concept PCI of diabody-based therapeutics (Weyergang)
- Comprehensive review of the PCI technology published in J.Clin.Med.
- New grants in 2020: Euronanomed (Berg)
- Theodossiou awarded the Dr. Ragnar Mørk's prize for excellent researcher
- *In vitro* proof of concept of Lumiblast effects.
- First Lumiblast patent published and now entering national phase
- Protonic was selected to be showcased in the 2020 HSØ national projects report
- Two patents entered national phase (Weyergang/ Berg;Theodossiou/Berg)
- No. of papers in 2020: 22
- 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: 9, including four researchers, one postdoc, three PhD students, and one technician.

We work 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. Our focus is metabolic stress, including hypoxia and lactic acidosis, and its interaction with cancer cells, immune cells and stroma in the tumor microenvironment.
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 2020, the group published 2 articles; one in Cancer Research and one in EBioMedicine.

Major findings were:
- Development of a MR based medical imaging approach to visualize hypoxia levels in patient tumors
- Utilized the imaging approach to gain novel molecular insight into hypoxia related treatment resistance in cervical cancer
- Showed improvement in prediction of chemoradiotherapy failure in cervical cancer by combining imaging and gene based hypoxia biomarkers

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: 4, including 2 researchers, 1 PhD student, and 1 technician.
Einar K. Rofstad retired Dec 1, 2020.

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
The group published 4 papers in 2020.
Important recent findings include:
- Cervical carcinomas and pancreatic carcinomas show significant intratumor heterogeneity in interstitial fluid pressure (IFP), and the highest IFP level correlates with tumor metastatic propensity.
- Highly elevated tumor IFP is a stronger predictive biomarker of treatment failure in cervical carcinoma than high fraction of hypoxic tumor tissue.
- The intertumor heterogeneity in response to antiangiogenic treatment with bevacizumab is significant in cervical carcinoma and pancreatic carcinoma. Some tumors may show decreased hypoxia after treatment whereas others may show increased hypoxia. DCE-MRI is an excellent imaging modality for monitoring bevacizumab-induced alterations in tumor oxygenation status.

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
13.5 including 5.5 researchers, 3 postdoc ,3 PhD students and 2 technicians.

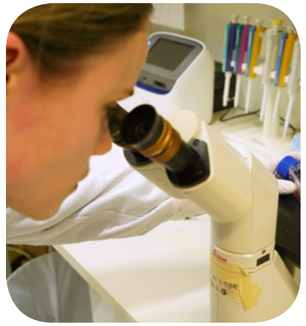
Theme
In radiotherapy ionizing radiation is used to cause DNA damage in cancer cells. The DNA damage is rapidly sensed and a network of intracellular DNA damage signaling cascades is activated. These signaling cascades influence whether the cells die or survive, through regulation of DNA repair, cell cycle checkpoint and cell death pathways. Our group works on 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. The group includes three project groups, headed by Beata Grallert, Trond Stokke and Sebastian Patzke.

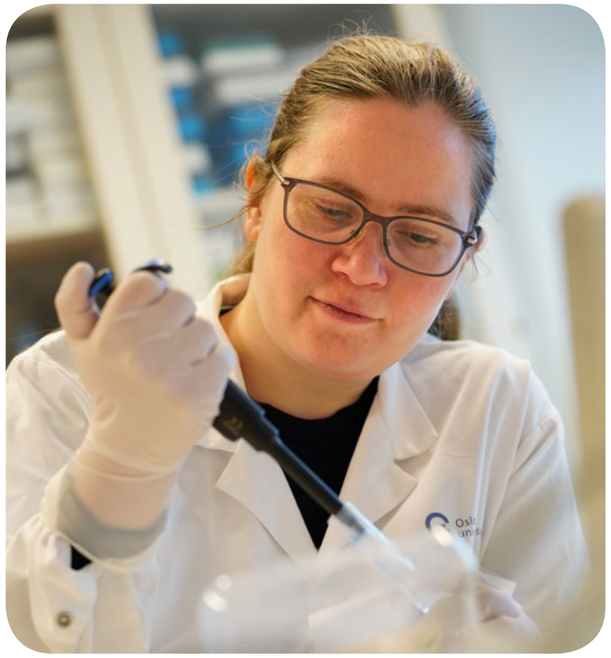
AIMS
- Obtain new knowledge about cellular responses to radiation, with focus on cell cycle checkpoints, DNA damage signaling and repair, and explore how such knowledge can be used to improve radiotherapy.

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
- Connections between DNA damage signaling and anti-tumor immune effects
- 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 2020, a total of 8 articles were published. Members of the group were senior/first authors on 2 of these, published in Cell Reports and Cytometry. Two Ph.D. degrees and one M.Sc. degree were completed. New funding was obtained from EEA Norway-Romania grants.








“Preclinical and clinical efforts towards precision oncology”

Headed by
Gunhild M. Mælandsmo

Department of
Tumor Biology

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 also 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 several national and regional collaborative projects in precision cancer medicine
- Project leader responsibilities for clinical trials in sarcoma, breast-and colorectal cancer
- All research groups have during the period received major funding (Norwegian Cancer Society, EU Horizon2020, South Eastern Regional Health Authority)
- The department has published 48 papers, with 24 as first or last author, and educated three PhDs and three MSc in 2020

Metastasis Biology and Experimental Therapeutics

Group leader:
Gunhild M. Mælandsmo

"Cellular plasticity - the route to resistance and metastasis"

ABOUT
Employees: The group has 18 members with multidisciplinary background and expertise (cell- and molecular biologists, medical doctors, laboratory- and animal technicians), including two MDs in shared clinical positions.

Research focus: Investigation of mechanisms involved in 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).

Project groups:
- Urological molecular biology, headed by Kristin Austlid Taskén
- Tumor-microenvironment interactions, headed by Lina Prasmickaite
- Molecular precision medicine in breast cancer, headed by Mads Haugland Haugen

AIMS
Metastatic progression is a 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 tumor-stroma interactions, EMT and neuronal differentiation
2. Preclinical research investigating novel drugs and drug combinations
   - Assessment of treatment efficacy and downstream mechanistic studies in patient-derived models
   - Biomarker discovery by molecular and functional techniques
3. Clinical trials in precision medicine – clinical and translational efforts for improved therapeutic efficacy and 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 13 publications in 2020 of which five with group members as first and/or last author; one PhD degree completed
- One clinical intervention trial in breast cancer open for inclusion (I-BCT)
- Funding: One postdoctoral grant from HSØ and one partnership in a H2020-ITN project

Translational Cancer Therapy

Group leader:
Kjersti Flatmark

"New treatment for locally advanced and metastatic colorectal cancer and pseudomyxoma peritonei"

ABOUT
In 2020, 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) and pseudomyxoma peritonei (PMP). 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 the 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
- Pseudovax - a novel vaccine-based treatment for GNAS-mutated pseudomyxoma peritonei
- New treatment strategies in locally advanced and recurrent rectal cancer
- Translational studies within the METIMMOX I and II multicenter trials investigating the combination of oxaliplatin and checkpoint inhibition in microsatellite stable metastatic CRC
- Commercial development of MOC31PE and BM7PE immunotoxins for cancer therapy
- Targeted alpha therapy in colorectal liver metastases (collaboration with Bayer)

RECENT ACHIEVEMENTS
- Group members were credited with 17 publications in 2020
- The BM7PE phase I clinical trial in metastatic CRC started accrual
- The NAVI-LARRC clinical trial (Computer NAVIgation assisted surgery in Locally Advanced and Recurrent Rectal Cancer) started accrual
- The EuroPMP COST Action, European Research Network on the rare cancer PMP, currently comprises >90 members from 21 European countries.
- Pseudovax vaccine concept ready for filing of patent

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 emphasis on prostate, melanoma and heritable cancer functional genomics. Further activity is centered on computational aspects of deep sequencing for cancer, including downstream analysis. The group also facilitates moving precision cancer medicine towards the clinic, leveraging participation in the BigMed RCN-financed ICT lighthouse project. The group collaborates with deCODE Genetics, Iceland, on the characterization of a familial cancer biobank, with 16,000 genotyped samples, and where 2000 Norwegians have been whole genome sequenced.

Project groups:
- Translational Prostate Cancer Genomics, headed by Alfonso Urbanucci
- Autophagy in cancer, headed by Nikolai Engedal

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
- To examine autophagy in 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, 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
- Autophagy in prostate cancer
- 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 26 publications in 2020, with 9 as first or last author
- Regional health research funding (9MNOK) for autophagy in prostate cancer to Nikolai Engedal

Molecular Biology of Sarcomas

Group leader:
Jørgen Wesche

"Towards precision medicine to improve treatment of sarcomas"

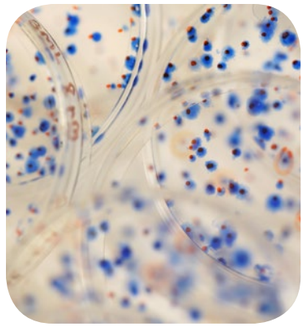
ABOUT
The 12-member group has a long-standing interest in the biology of sarcomas, malignant tumors of mesenchymal origin. The current focus is on precision medicine for sarcomas. To achieve this, the group has broad expertise in cell biology, genomics and translational research and, in addition, one associated MD (Kjetil Boye) is in a shared clinical position. The group is part of a Centre of Excellence (CanCell).

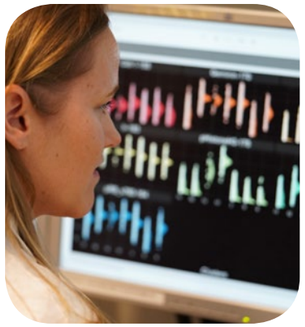
Project group:
Translational Genomics Leonardo A. Meza-Zepeda

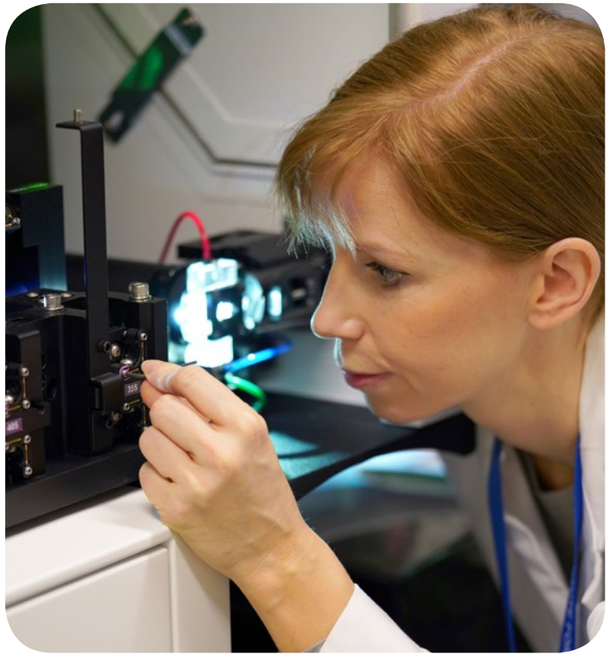
AIMS
The group aims to improve the treatment of sarcoma patients by investigating how genetic changes (mutations) affect signalling in sarcoma cells, and how tumors evolve and become resistant. We combine extensive genomic characterization of clinical cohorts with preclinical investigation in sarcoma 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.

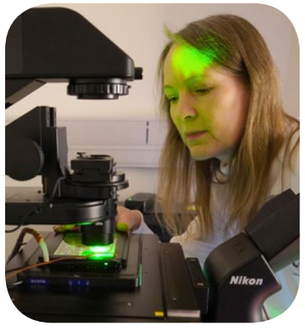
PROJECTS
- Sarcoma cell biology – Gaining understanding of the development and progression of rhabdomyosarcoma, gastrointestinal stromal tumors, liposarcoma and osteosarcoma, which will lead to the identification of biomarkers and novel drug targets. A main focus is the study of the role of fibroblast growth factor receptors (FGFRs) and KIT tyrosine kinase receptor.
- Norwegian Sarcoma Consortium (NoSarC) – Biobanking and genomic characterization of patient material of 3-4 annual cohorts of sarcomas (~500 samples).
- Exploration of "liquid biopsies", as a non-invasive method 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.

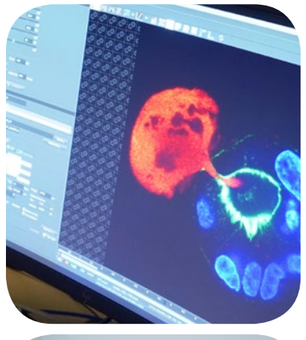
RECENT ACHIEVEMENTS
- 7 publications in 2020
- Kjetil Boye obtained a grant from the South-Eastern Norway Regional Health Authority (Postdoc project)
- Jørgen Wesche is part of a consortium that obtained a Norway-Czech Republic EEA grant to develop targeted radiotherapy.



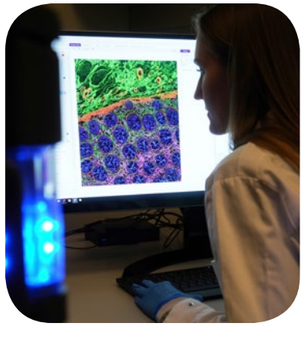


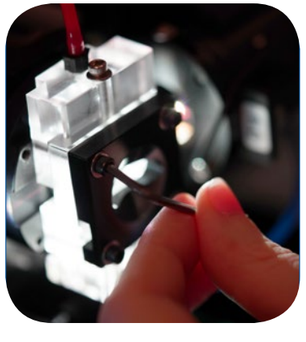






"Providing cutting-edge-technology and competence to excel research"





Headed by
Leonardo A. Meza-Zepeda

Department of
Core Facilities

The Department of Core Facilities runs six regional and national technology platforms financed by the South-Eastern Norway Regional Health Authority and/or the Research Council of Norway, providing easy access to advanced competence, infrastructure, and services. The Department aims to provide state-of-the-art services in advanced technologies, and thus contribute to the international competitiveness of research groups by optimal choice and use of technology. The Department of Core Facilities with its six technology platforms is organized into 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 super-resolution microscopy. Current instruments include a Zeiss LSM 880 FAST Airyscan microscope, a Zeiss LSM 710 confocal microscope, an OMX Blaze microscope for super-resolution imaging (structured illumination, STORM, and TIRF), as well as live-cell microscopy, and a Nikon spinning disk system enabling high content imaging and fast confocal live-cell imaging. 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 part of the national infrastructure NALMIN and 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 services 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 electron 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 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 NALMIN 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 the 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 the development of the new Infrastructure for precision diagnostics (InPreD), including the development of analysis and reporting pipelines. 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 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 genome-wide level. Our single-cell analysis platform provides transcriptome analysis, T & B cell receptor sequencing, as well as scATAC-Seq and feature barcoding to study protein expression. Our experienced personnel deliver advanced competence to basic, translational, and clinical research projects, supporting experimental design, choice of technology, and basic data analysis. Together with the Department of Pathology, we have established the infrastructure for precision diagnostics (InPreD) to deliver advanced molecular testing for the stratification of cancer patients into clinical studies. 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 cooperates 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. Our state-of-the-art analyser (BD Symphony) with 5 lasers can 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 SH800 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 using flow cytometry. We also have a “mass-spec cytometer” (Helios). This instrument can measure up to 60 parameters simultaneously at single-cell resolution. We have further equipped the Helios with an add-on for imaging (Hyperion), which allows 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 Department of Comparative Medicine 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 have developed a protocol for synchronization of images obtained by MRI, IVIS, and X-ray imaging, as well as a method for imaging of hypoxia levels by MRI. 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 and OUH strategic research areas

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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 B Cell Malignancies) or Oslo University Hospital (KG Jebsen Colorectal Cancer Research Centre).

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OUH strategic research areas
Oslo University Hospital selects Strategic Research Areas, three at a time, each for six years and with 7.2 mNOK funding. These should be cross-disciplinary and involve new collaborations across divisions for patient benefit. Rotating calls every three years are published by the OUH Research Committee, applications evaluated the OUH SAB and the top-ranked Strategic Research Areas formally approved by the CEO. For the period 2019-2024 two OUH Strategic Research Areas, TEAM-ACT and STRATCELL, are led from the ICR.

"Reprogramming of cancer"

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, of which 4 are based at Institute for Cancer Research (Harald Stenmark, Jorrit Enserink, Tor Erik Rusten and Jørgen Wesche) and two at Institute of Basic Medical Sciences (Anne Simonsen and Ragnhild Eskeland). The centre 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 2020, CanCell had 114 members (including students and trainees) of 33 nationalities. The payrolls correspond to 84 full-time equivalents. CanCell promotes equality in research and has established its own Equality Forum. The centre supports CanCell Young Scientists, a forum for career development, scientific exchange and social activities among the centre's junior researchers.

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
- Cancer molecular medicine
- Tumour-host interactions
- Molecular biology of sarcomas
- Mechanisms of epigenetic regulation in cancer

RECENT ACHIEVEMENTS

- CanCell scientists published 36 papers in 2020, many of these in leading journals such as *Nature Cell Biology, Nature Communications, Nature Immunology, Nature Reviews Molecular Cell Biology, EMBO Journal, PNAS, Current Biology and Journal of Cell Biology.*

- In 2020, CanCell organized for the first time its own MSc/PhD course, "Molecular cancer medicine" under the Faculty of Medicine with strong participation by the centre's junior scientists as teachers.

- Six PhD students (Patrycja Szybowska, Anette Lie-Jensen, Dagim Tadele, Aurélie Nguéa, Laure Piechaczyk and Rojyar Khezri) successfully defended their theses in 2020. Nine MSc students were graduated.

- In 2020, major grants were obtained by Tor Erik Rusten, Harald Stenmark, Anne Simonsen, Jørgen Wesche, Marina Vietri, Kjetil Boye, Kay O. Schink and Antoni Wiedlocha. Three of the grants were international (EEA grants) and one was a career fellowship.

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

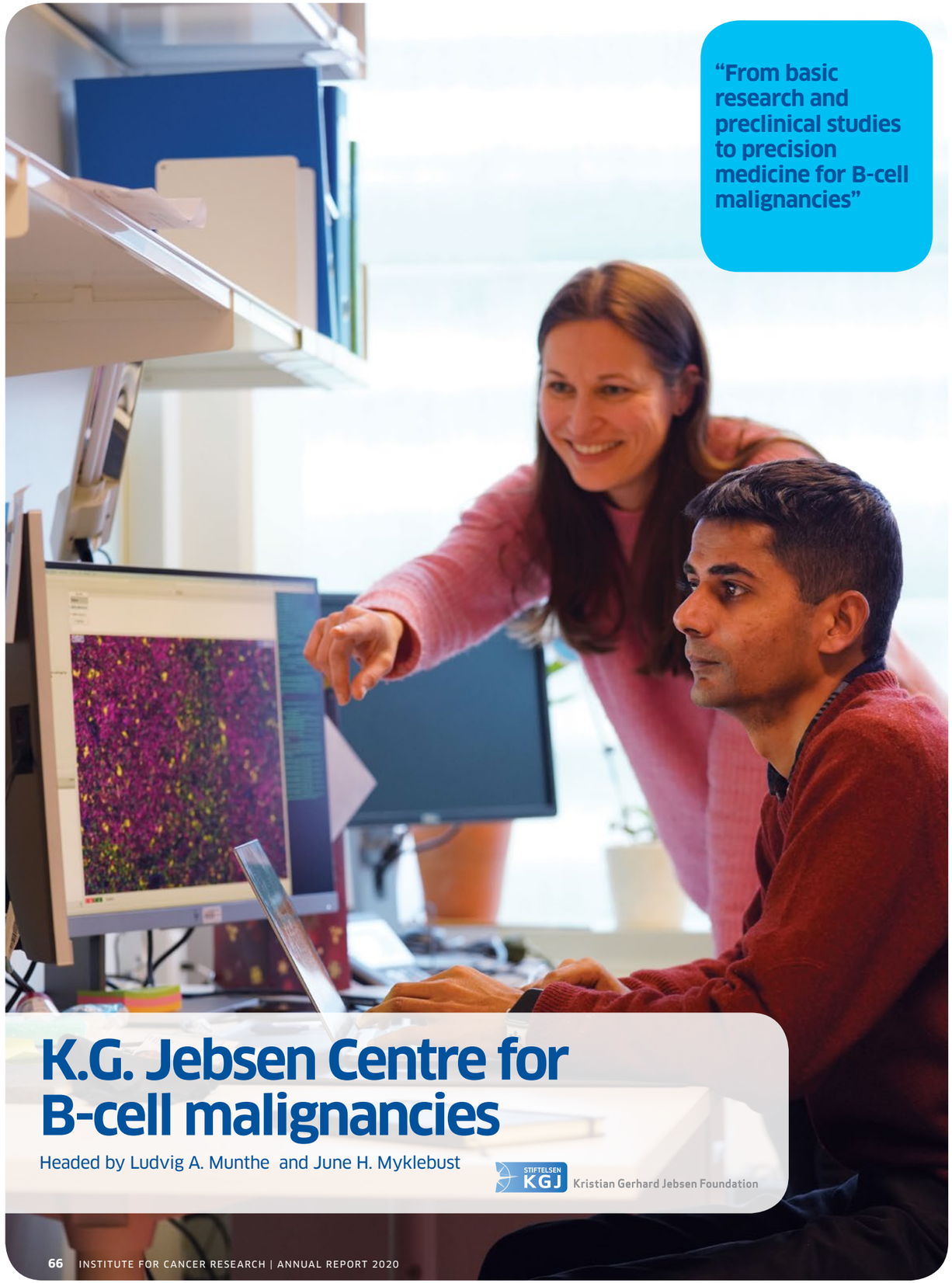
Jorrit Enserink, Institute for Cancer Research, OUS, and Department of Biosciences, UiO

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 Clinical Medicine, UiO

Anders Øverbye, administrative coordinator, CanCell



"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 currently holds 59 members and 7 associated members. The Centre bridges three translational research groups with three clinical groups, creating unique opportunities for translating preclinical results into clinical trials in B-cell lymphoma, B-cell leukemia and multiple myeloma. Collectively, the Centre represents multi-disciplinary integration of life science research with preclinical development of personalized medicine, cancer drug discovery and cell-based immunotherapy, and clinical trials with 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 Centre has 63 trials at different phases, 25 trials currently enrolling patients and 6 in start-up. The majority of the trials are researcher initiated. Key achievements in 2020:

- Established new diagnostic criteria and treatment guidelines for idiopathic multicentric Castleman disease *(Fajgenbaum, Am J Hematol. 2020).*
- PET interim analysis was used to develop new response criteria for relapsed/ progressive Hodgkin lymphoma *(Kluge, J Nucl Med 2020).*
- Patients with high-risk diffuse large B-cell lymphoma (DLBCL) benefit from dose-dense immunochemotherapy combined with early systemic CNS prophylaxis. *(Leppä, Blood Adv 2020)*
- CD37-directed radioimmunotherapy represents an alternative treatment approach in relapsed/refractory non-Hodgkin lymphoma *(Kolstad, Blood Adv 2020)*
- ICARIA-MM study revealed that Isatuximab plus pomalidomide and dexamethasone is effective in elderly patients with relapsed/refractory multiple myeloma (Schjesvold, Haematologica 2020).
- *Ixazomib* maintenance versus placebo post autologous stem cell transplant led to improved progression-free survival in multiple myeloma patients *(Kaiser, Ann Hematol 2020).*
- An international observatory study evaluated the outcome of various treatment regimens in patients with cold agglutinin disease (Berentsen, Blood 2020)
- A multicentre experience revealed that CLL patients admitted at hospital with COVID-19 had high risk of death, regardless of disease phase or treatment status *(Mato, Blood 2020).*

TRANSLATIONAL RESEARCH ACHIEVEMENTS:

- By utilizing whole exome sequencing in a DLBCL cohort enriched for patients who relapse after standard of care, we identified mutations and loss of the antigen presentation molecule HLA-A to be associated with higher risk of relapse *(Wise, Blood Adv 2020).*
- DLBCL tumors with higher abundance of anti-inflammatory macrophages and regulatory T cells are associated with inferior outcome *(Autio, Haematologica 2020)*
- A simplified follicular lymphoma PRIMA-prognostic index had improved risk stratification compared to FLIPI in follicular lymphoma patients treated with rituximab *(Kimby, Br J Haematol 2020).*
- Cold agglutinin-associated B-cell lymphoproliferative disease has frequent copy number gains of chromosome 3 and 12 or 18 *(Małecka, Blood Adv 2020).*
- We developed a functional precision medicine assay in CLL by ex vivo screening of cancer drugs for inhibition of signaling pathways. Studying drug synergies revealed that combination of ibrutinib and venetoclax exerted synergistic inhibitory effects, and dosages of these drugs could be lowered without loss of efficacy *(Skånland, Leukemia 2020).*
- Stromal cell PKC-beta inhibition enhances chemosensitivity in B-cell malignancies and overcomes drug resistance *(Park, Sci Transl Med 2020).*
- Tumor resident macrophages can be powerful mediators of tumor cell killing as demonstrated in a murine myeloma model, where bone marrow–residing tumor-specific CD4+ T cells elicit antitumor responses through interaction with macrophages *(Haabeth, Blood Adv 2020).*

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
Kjetil Taskén (MD, PhD)2,3

1 Dept. of Immunology, Div. for Laboratory Medicine, Oslo University Hospital (OUH)
2 Institute for Clinical Medicine, University of Oslo
3 Dept. of Cancer Immunology and Institute for Cancer Research, OUH
4 Dept. of Haematology, Div for Cancer Medicine, OUH
5 Dept. of Oncology, Div. for Cancer Medicine, OUH
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

"High quality translational research to the benefit of colorectal cancer patients"

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 new stratified treatment strategies and patient monitoring. The Centre is hosted by the Clinic for Cancer Medicine, Oslo University Hospital (OUH), and was renewed to the maximum duration of 6 years (2014-2020). Home page: www.colorectalcancer.no

GROUP LEADERS/STEERING COMMITTEE

- Professor Ragnhild A. Lothe (MSc, PhD, Centre leader), Dept. Molecular Oncology, Inst. Cancer Research, OUH and Inst. Clinical Medicine, University of Oslo (UiO)
- Professor Arild Nesbakken (MD, PhD, deputy Centre leader), Dept. Gastrointestinal Surgery, OUH and Inst. Clinical Medicine, UiO
- Professor Rolf I. Skotheim (MSc, PhD), Dept. Molecular Oncology, Inst. Cancer Research, OUH, and Dept. Informatics, UiO.
- Senior Consultant Marianne G. Guren (MD, PhD), Dept. Oncology, OUH
- From 2018/06: Professor Guro E. Lind (MSc, PhD), Dept. Molecular Oncology, Inst. Cancer Research, OUH and Dept. BioSciences, UiO
- 2017/06-2018/06 Associate Professor Mette Kalager (MD, PhD), Inst. Health and Society, UiO, and Dept. Epidemiology, Harvard T.H.Chan School of Public Health, USA
- 2014-2017/06: Professor Michael Bretthauer (MD. PhD), Inst. Health and Society, UiO

Our Centre had an active Patient Advisory Board. This was established in 2016 and continues its activities in the CRC research program beyond the Centre period.

AIM

The primary objective of the Centre was to translate new biomedical knowledge into improved stratified medicine for patients with CRC in the context of tumor heterogeneity.

PROJECTS, ACHIEVEMENTS AND CLINICAL TRANSLATION

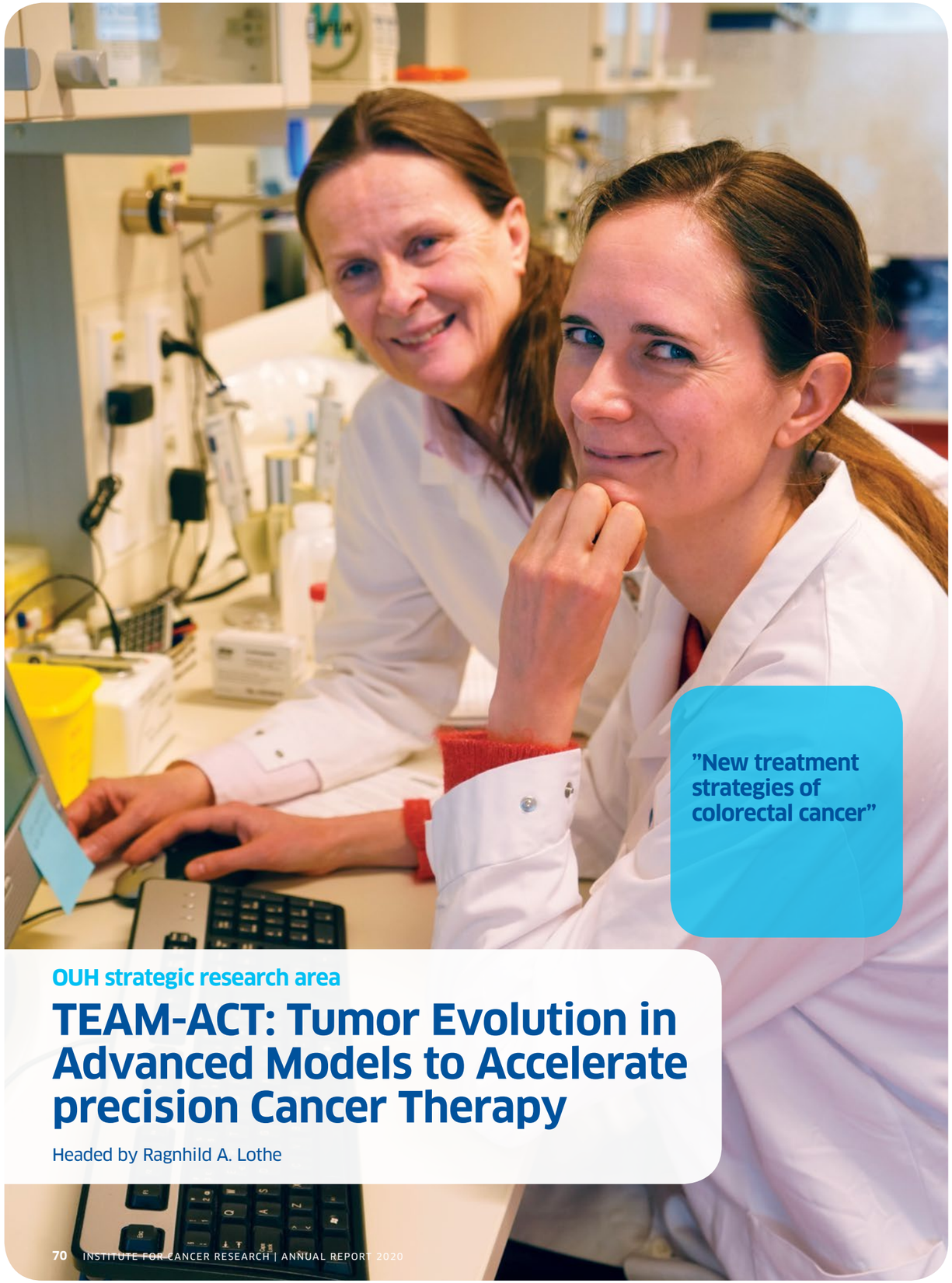
The foundation for the success of this Centre is the multidisciplinary competence and infrastructure build within the Centre. Our multifaceted translational project portfolio includes: (a) development of prognostic and predictive biomarkers for patient outcome and treatment benefit, (b) delineation of molecular tumor heterogeneity and its clinical relevance in the primary and metastatic settings by multiple sampling and "multi-omic" analyses, (c) establishment of a pre-clinical drug screening platform, including a "living biobank" of three-dimensional, patient-derived models of colorectal tumors, (d) establishment of an immunohistochemistry platform for multiplex tumor biomarker analysis using fluorescence and digital image analyses, (e) new clinical trials representing the next generation of precision oncology studies, and (e) initiated a nation-wide population-based biomarker study of 5000 stage I-III CRCs (BIOMAN). Multiple studies have been conducted and published in each project cluster

Main research output from the Centre:

- 164 scientific articles published in peer-review journals (credited to Stiftelsen K.G. Jebsen), 25% of which were published in highly ranked journals (impact factor>10), including Ann Intern Med (2), Ann Oncol (6), Ann Surg, BMJ, Clin Cancer Res (4), Gastroenterol, Genome Med, GUT (6), Hepatology, JAMA, JCO, JNCI, Lancet, Lancet Gastroenterol & Hepatol (3), Lancet Oncol (2), Mol Cancer, Nat Rev Clin Oncol, NEJM (2). About 60% have Centre scientists in central authorship positions.
- 20 candidates (10 MD and 10 MSc; 11 females and 9 males) have completed their PhDs
- 20 post docs worked in the Centre
- 7 international research stays (up to 1 year) for young investigators
- 9 Young investigator awards
- 117 mill NOK in major research grants beyond Centre financing
- 28 articles for public outreach in newspapers, journals and social media

CRC screening trials and prevention studies: major results from Bretthauer/ Kalager group have been published, and recruitment has started in the European multi-centre (30 countries) EPoS polyp surveillance project (PI Bretthauer).
Investigator initiated oncology trials: ACE - adjuvant chemotherapy of elderly patients with stage III CRC (PI M.G.Guren), and EVIDENT – *ex vivo* drug sensitivity testing of the patients' own tumors to guide treatment selection (PI T.K. Guren).

The Centre has contributed to consolidation of the translational CRC research program at OUH beyond the Centre period. Its funding has also enabled development of new research data and infrastructure for which the full potential has not yet been realized. We consider us as former Centre participants to be very well positioned to contribute to the development of the next generation of treatment concepts for CRC.



"New treatment strategies of colorectal cancer"

OUH strategic research area

TEAM-ACT: Tumor Evolution in Advanced Models to Accelerate precision Cancer Therapy

Headed by Ragnhild A. Lothe

ABOUT

This network addresses current challenges in the treatment of colorectal cancer (CRC) by a multifaceted strategy to integrate early intervention and personal therapy modeling in the context of tumor heterogeneity and the gut microenvironment. We aim to develop new prototype concepts for cancer treatment with transfer value also to other GI-malignancies. Furthermore, we will improve the molecular pre-screening of patients for inclusion in clinical trials.

MANAGEMENT GROUP

TEAM-ACT is granted for the period 2019-24 and is led by Ragnhild A. Lothe (PI) and Anita Sveen (co-PI). The management group includes Kristoffer Lassen, Sheraz Yaqub, and Pål Dag Line at Dept. Surgery, Division of Surgery, Inflammatory Medicine and Transplantation; Tormod K Guren and Morten Brændengen at Dept. Oncology, Division of Cancer Medicine; and Atle Bjørnerud at the Computational Radiology and Artificial Intelligence group, Division of Radiology and Nuclear Medicine.

AIMS

- Intercept the clinical consequences of tumor heterogeneity in metastatic CRC and identify more effective personalized treatment strategies.
- Expand the clinical benefit of immunotherapy by identification of resistance mechanisms in hypermutated tumors and pharmacological "immune conversion" of immunologically cold cancers.
- Improved outcome after surgery of metastatic CRC by new surgical procedures and neo-adjuvant treatments.
- Improved prediction of patient survival and response to standard therapies using artificial intelligence on genomics data and digital images.

PROJECTS

- Multi-level molecular modeling of tumor heterogeneity and clonal evolution under treatment pressure
- Clinical translation of personal *ex vivo* drug sensitivity models
- Drug synergy modeling by pre-clinical pharmacogenomics
- Resistance mechanisms and combination therapies with immune checkpoint inhibitors in patient-derived organoids of CRCs co-cultured with tumor-infiltrating immune cells.
- Molecular profiles and biomarkers of high and low risk metastatic CRC in liver transplantation oncology
- Radiogenomics of neoadjuvant therapy in metastatic CRC

RECENT ACHIEVEMENTS

Professor Pål Dag Line and senior consultant Svein Dueland published the SECA-II trial, documenting long-term survival after liver transplantation of patients with non-resectable CRC liver metastases (Dueland et al., Ann Surg 2020). Improved selection criteria of cancer patients (Dueland et al., Am J Transplant 2020) resulted in similar survival outcomes to patients with other indications for liver transplantation. The authors also reviewed current knowledge on the difficult balance between survival and recurrence after transplantation for secondary liver tumors (Line & Dueland, J Hepatol 2020).

Two studies were published from our pre-clinical drug sensitivity testing platform. Screening of organoids of multi-metastatic lesions in the liver showed that intra-patient inter-metastatic heterogeneity in drug sensitivity was not pronounced (Bruun, Kryeziu et al., Clin Cancer Res 2020;). Potential for repurposing of PARP inhibitors to CRCs with wild-type TP53 was demonstrated in our cell line panel (Smeby et al., EBioMed 2020;).
The protocol for the EVIDENT phase II study was recently approved by all regulatory authorities. This trial will test therapies guided by a combination of biomarkers and personal *ex vivo* drug sensitivity models of metastatic CRC after progression on standard chemotherapy.

RAS/*TP53* co-mutations and genomic heterogeneity of multi-metastatic CRCs provided improved patient prognostication (Berg et al., Mol Oncol 2020). RCC2 protein expression was identified as a potential biomarker of benefit from adjuvant chemotherapy for stage III CRC (Bergsland et al., ESMO Open 2020).

Surgeon Sheraz Yaqub was appointed Assoc. Professor at the Faculty of Medicine, University of Oslo, and Assoc. Professor Anita Sveen received the Researcher-of the-year Prize from the Inst. Cancer Research and the Radium Hospital Foundation.

Clin3ical Translation

Several investigator initiated intervention trials with translational sub-studies are ongoing/starting patient inclusion:

- EVIDENT – ex vivo drug sensitivity testing of metastatic CRC (PI: Tormod K Guren)
- SYLMET – simultaneous versus staged surgery of synchronous CRC liver metastases; (PI: Sheraz Yaqub)
- SECA-III – liver transplantation for non-resectable CRC liver metastases; (PI: Pål Dag Line)
- EXCALIBUR –liver transplantation, liver resection, or hepatic artery infusion of chemotherapy for patients with high-load of CRC liver metastases (PI: Kristoffer Lassen)

OUH strategic research area

Strategic Research Area in Cell Therapy – StratCell

Headed by Karl-Johan Malmberg

"Bringing best in class cell therapy to Norwegian patients"

ABOUT
StratCell (2019-2023) is a strategic research area in cell therapy supporting the development of new cell therapies by PIs at OUH and industrial partners to the benefit of Norwegian patients.

AIMS
The overall objective of the Strategic Research Area in Cell Therapy (StratCell) is to address key logistic and scientific bottlenecks for the clinical implementation of advanced cell- and gene therapy against cancer. Tasks include establishment of a pre-GMP unit to serve as a dynamic hub between innovative experimental approaches and clinical implementation of armed biological cell therapy drugs. The initiative is intended to operate at the interface between academia and industry and support a clinical pipe-line of investigator-initiated trials. Together the scientists and physicians brought together in StratCell have a broad expertise in cancer immunology and immunotherapy and we anticipate synergies in terms of sharing of methodological platforms.

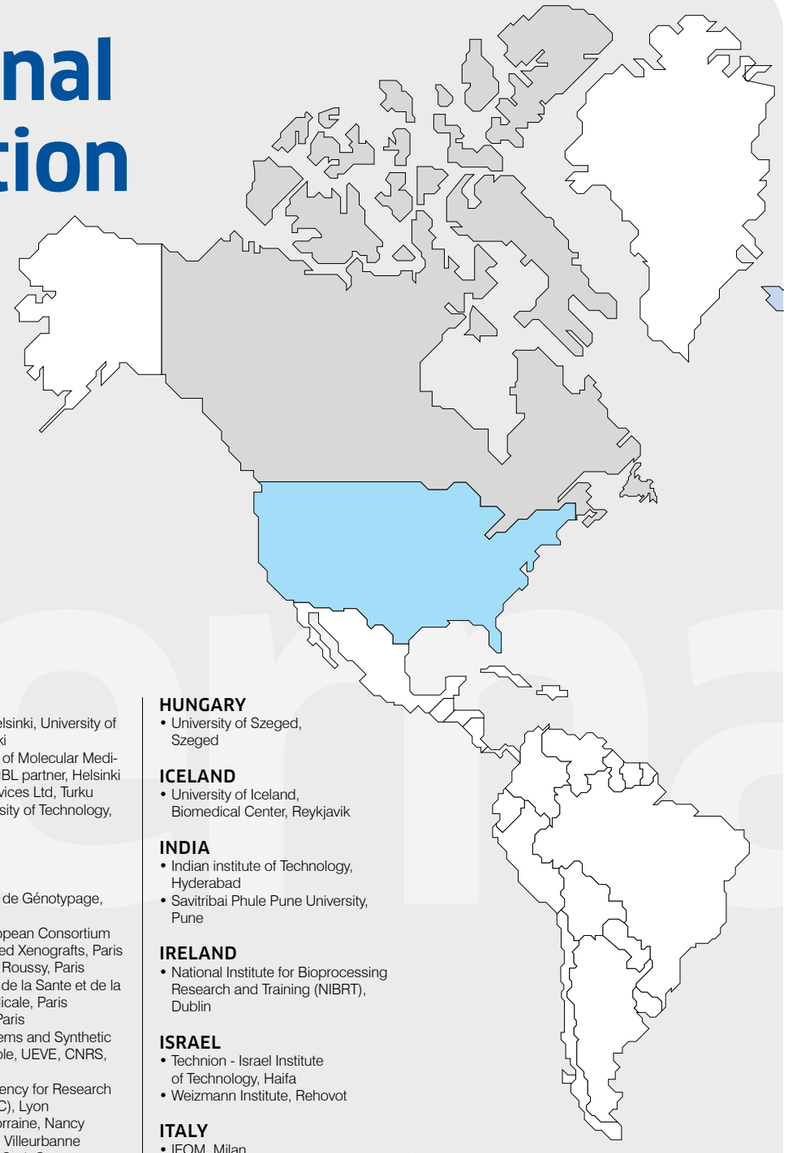
PROJECTS / CLINICAL TRANSLATION
- Establish a protocol for clinical-grade genetic engineering for a minimum of one cell type
- Develop novel strategies for off-the-shelf NK and T cell therapy from allogeneic sources and of Macrophages, DC, T and NK cells.
- GMP transfer: In-house developed first-in-man clinical trial with selectively expanded allogeneic NK cells for high-risk MDS (pending)
- GMP transfer: First-in-man clinical trial with a TCR targeting T-ALL and relapsed B-ALL (pending)
- GMP transfer: First-in-man clinical trial with in-house developed CAR targeting prostate cancer (pending)
- Launch Adapt-NK: A multicenter, transatlantic clinical trial against acute myeloid leukemia (AML), based on selectively expanded NK cells. Grant application covering this trial will be filed in the US (NIH), Norway (HSØ, RCN and Norwegian Cancer Society), and Sweden (Swedish Cancer Society).
- Support the first iPSC-derived CAR-NK cell therapy trial in Europe (pending)

RECENT ACHIEVEMENTS
- StratCell co-director Johanna Olweus awarded ERC consolidator grant for her Therapeutic TCR strategy.
- Collaborated with Prof Dan Kaufman (UCSD) during Sabbatical to develop novel engineered iPSC-derived CAR-NK cells (Zhu et al. Cell Stem Cells 2020).
- Contributed to the formation of a new Centre for Advanced Cell Therapy (ACT) with the goal of advancing new cell and gene therapies at OUH and in Norway. The launch of the ACT centre is supported by a 50MNOK donation by a private donor consortium consisting of Svanhild and Arne Must´s Foundation for Medical Research (lead donor), RADFORSK oncology research fund and the Norwegian Cancer Society. The donation will cover personnel, training and equipment to establish a service for GMP viral gene transfer and GMP viral production for gene delivery for academic and industrial customers. The ACT centre has appointed a Scientific Director (Malmberg), a Research and protocol board (access committee), and a Steering board. A center leader will be recruited and an international scientific advisory board will be appointed. During 2020, StratCell hired Helene Midttun (PhD) as a dedicated engineer at the Department of Cell Therapy to acquire competence in gene editing under full GMP.
- StratCell PI Malmberg joined as a full partner in a NIH PO1 grant to support a transatlantic NK cell trial based on adaptive NK cells with genetically modified feeder cells (Master cell bank under production at the Department of Cell Therapy.
- StratCell is on Twitter: @StratCell and at: https://www.ous-research.no/strat-cell

GROUP LEADERS AND KEY CLINICAL PARTNERS
Oslo University Hospital (OUH): Karl-Johan Malmberg (Leader), Johanna Olweus (co-leader), Jon-Amund Kyte (co-leader), Arne Kolstad, Dag Josefsen, Geir Tjønnfjord, Tobias Gedde-Dahl, Jochen Büchner, Anders Tveita, and Ludvig Munthe. Bjørn Naume (Breast), Åslaug Helland (Lung), Kjetil Boye (Sarcoma), Harald Holte (Lymphoma), Iver Langmoen (Neuro) and Kristine Engen Andreassen (Urology).

KEY INTERNATIONAL PARTNERS
Karolinska Institute (KI): Hans-Gustaf Ljunggren, Eva Hellström-Lindberg and Stefan Mielke. The Netherlands Cancer Institute: Ton Schumacher (TS). University of California SD (UCSD), Dan Kaufman, University of Minnesota, Jeff Miller. MSKCC: Michel Sadelain and Isabelle Rivière,

International Collaboration



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- BELGIUM
- SWITZERLAND
- CZECH REPUBLIC
- HUNGARY
- CROATIA
- INDIA
- SINGAPORE
- ISRAEL
- RUSSIA
- TUNISIA

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

AUSTRIA
- Institute of Pathophysiology Biocenter, Innsbruck Medical University, Innsbruck
- 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
- 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
- Pharmatest Services Ltd, Turku
- 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 de Lorraine, Nancy
- Université Lyon, Villeurbanne
- Université Paris-Sud, Orsay

GERMANY
- EMBL, Heidelberg
- 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
- University of Stuttgart, Stuttgart

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

POLAND
- Faculty of Biotechnology, University of Wroclaw, Wroclaw
- Jagiellonian University, Kraków
- University of Gdansk, Gdansk

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

ROMANIA
- Horia Hulubei National Institute for Physics and Nuclear Engineering Bucharest - Magurele

RUSSIA
- Institute of Cytology and Genetics, Novosibirsk

SINGAPORE
- Cancer Science Institute of Singapore, Singapore

SPAIN
- Biocruces Bizkaia Health Research Institute, Barakaldo
- 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
- Utrecht University, Utrecht
- VU Medical Center, Amsterdam

TUNISIA
- University of Tunis, Tunis

UNITED KINGDOM
- Cambridge Cancer Institute, Cambridge
- Hampshire Hospitals/Southampton University, Southampton
- Institute of Cancer and Genomic Sciences, University of Birmingham, Birmingham
- London Research Institute,The Francis Crick Institute, London
- Newcastle University, Newcastle upon Tyne
- 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
- MedKoo Biosciences, Morrisville, North Carolina
- 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

Career Development and Mentorship

The ICR has people at different academic levels and at all stages of development of their careers. Training and mentoring are important to us, and in 2020, we employed almost 75 PhD students and more than 75 postdocs at the ICR. In addition, we have around 20 MSc-students as well as other types of students that train with us. Our more permanent staff includes 95 researchers and 89 technical personnel, encompassing Group Leaders, Project Group Leaders, Senior Scientists, Research Scientists, Head Engineers, Engineers, Technicians and Lab Managers, who collectively gathers a broad spectrum of important competencies and supervises students and postdocs. Many of the younger scientists and technical staff are also on a career track and will take on more leadership in the future. We aim to stimulate our junior staff to reach independence through mentorship and by promoting their visibility. Also, more than 60% of our staff and leaders are female reflecting our commitment to obtaining gender balance at all levels.

Our PhD and MD/PhD-track students benefit from formal training in the UiO Faculty of Medicine or UiO Faculty of Mathematics and Natural Science PhD programmes. Our Postdocs benefit from the UiO Faculty of Medicine Postdoc Career Development Programme and the Scientia Fellows Programme. The School of Health Innovation, jointly by UiO, NTNU, University of Copenhagen, Karolinska Institutet (KI) as well as the UiO-Life Science SPARK programme offer great possibilities to learn more about translation, innovation and commercialization. Together, UiO and OUH offer a range of training opportunities to build competence and preparing our staff for future jobs.

The Postdoc-forum

The goal of the Postdoc-forum is to serve as a meeting place for postdocs at the institute to increase the knowledge of what others are doing and enable the postdocs to form contacts and collaborations. In addition, we aim to provide knowledge and insight which can benefit the career of the postdocs independent of whether they will continue within academia or outside. The Postdoc-forum arranges approximately five seminars a year for postdocs and researchers at the institute. We have two different formats for these seminars, project seminars and non-research topics. In the project seminars normally two postdocs present their project with focus on a question they need help to discuss. We invite external speakers to inspire and teach the postdocs on various subjects such as writing grant applications, fraud in research, career development, both within research and outside of academia. We have also arranged speed dating (pre-covid) where postdocs spent a few minutes one-on-one to talk about their projects. This was a great success and new collaborations were established.

Catherine Sem Wegner, Thea Kristin Våtsveen og Simona Kavaliauskiene.
Postdoc-forum Board

The PhD-forum

The PhD-forum is organized by and for PhD candidates at the Radium Hospital. We aim to create a space where PhD candidates from the different departments can meet and exchange their experiences, learn new skills and make new connections.

We have planned a variety of workshops and seminars relating to the whole PhD experience - from writing and publishing scientific articles, on how to present your research in a compelling way and inspirations for finding and shaping a career after your PhD. In order to support the PhD candidates on their way to finding their career path we organized a site visit at Thermo Fisher, invited ICR alumni now working at different companies in and around Oslo, had inspirational talks by senior scientists from Oslo and abroad and got firsthand accounts what it takes to start your own start-up. But it was not all just work, before Covid19 we organized regular PhD lunches and Christmas gatherings to create opportunities for meeting and socializing with fellow PhD candidates from other departments.

Jeanne G. Corrales, José Teles Reis og Hélène Spangenberg
PhD-forum Board

ICR TRIC Committee and Clinical Research Collaborations

The Translational Research and Innovation Committee (TRIC) was established in late 2019 to focus on translational research and innovation at ICR in line with the ICR Objective #1 to strengthen translational research. The first aim of TRIC was to gain an overview over relevant projects at ICR, and 118 projects were identified split between clinical trials, innovation projects and translational projects (Fig. 1a). The translational and innovation projects covered a wide range of different applied developments including new treatment strategies, algorithms, drugs and biomarkers (Fig. 1b). The projects differed significantly in their maturity as seen when describing the stage of the IPR-process for the approx. 25% of the projects where this is relevant (Fig. 1c).

To further stimulate and encourage translation and innovation, a permanent meeting series of monthly meetings with the TRIC-board was initiated in autumn of 2020 (somewhat delayed due to the pandemics) where 2-3 projects are presented each month. The TRIC consists of all the Department Heads and invited ad hoc members and the aim of the meeting series is to inform the TRIC, focus on translation and innovation, stimulate collaboration and address potential hurdles.

In the meetings the project leader and project team (including clinical collaborators) presents the project for approximately 15 minutes followed by approx 15 minutes discussion and feedback.

The projects presented varied significantly in degree of maturity, but the overall conclusion is that the TRIC-presentations are valuable both for dissemination between the departments at the institute and to solve concrete hurdles for the individual projects. Based on the projects presented we see a clear need to develop specific innovation strategies for biomarker-based projects and a translational pipeline for projects with high public, low commercial interest.

The overview of ongoing translational and innovation projects shows that ICR collaborates with almost all of the clinical divisions at hospital as well as with diagnostic environments, with the majority of collaborations within the Division for Cancer Medicine. The TRIC will continue to review projects on a monthly basis on 2021. In addition the ICR Leadership aims to organise monthly meetings with clinical and diagnostic environments at OUH to further foster collaboration (ICR Objective #2).

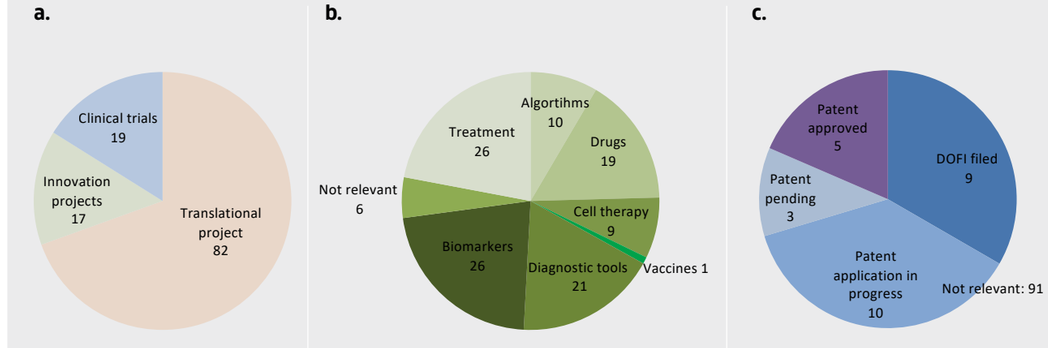


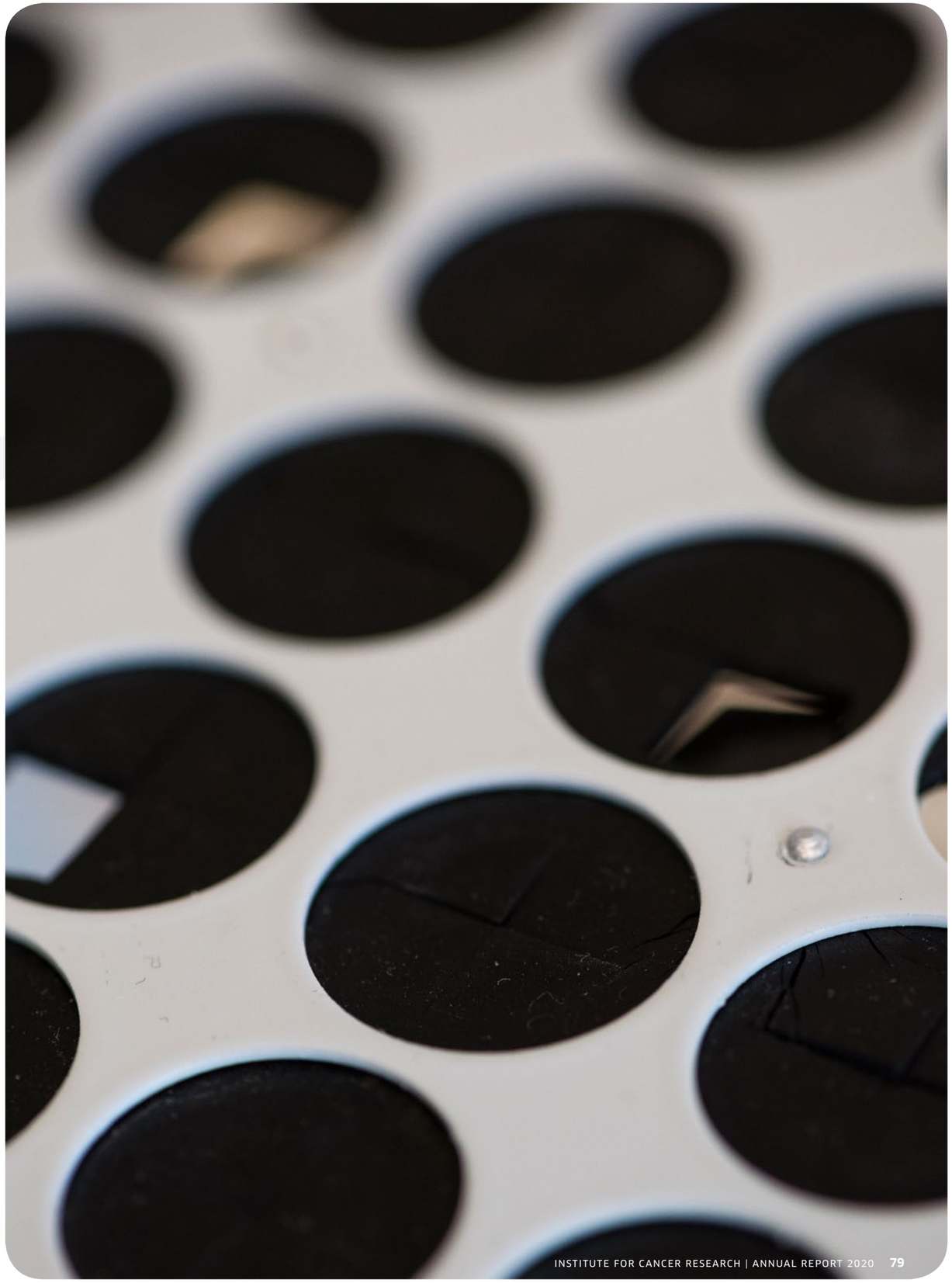
Figure 1: Overview over identified translational and innovation projects ongoing at the institute of cancer research. a. The projects split into categories of projects b. type of innovations c. IPR situation.

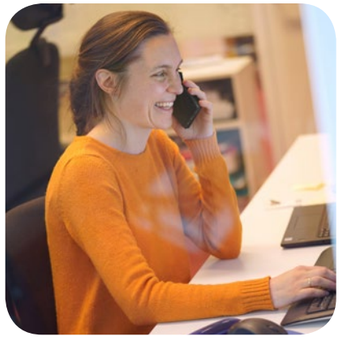
Recent Innovations

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

Research group (inventor)	Department	DOFI #
Ragnhild A. Lothe	Molecular Oncology	20154
Kjetil Taskén	Cancer Immunology	20139
Jon Amund Kyte	Cancer Immunology	20097
Kjetil Taskén	Cancer Immunology	20047
Kristian Berg	Radiation Biology	20021
Jorrit Enserink (Carmen Herrera)	Molecular Cell Biology	20020
Kjersti Flatmark	Tumor Biology	20010

Application type or granted patent	Research group(s) (inventor)	Department	DOFI #
Priority Application	Jon Amund Kyte	Cancer Immunology	18126
Priority Application	Karl-Johan Malmberg	Cancer Immunology	19110
Priority Application	Hege Russnes (O.C. Lingjærde)	Cancer Genetics	18053
US (National) Application	Guro E. Lind	Molecular Oncology	17135
US (National) Application	Kjersti Flatmark	Tumor Biology	15189
EP (Regional) Application	Kjersti Flatmark	Tumor Biology	15189
US (National) Application	Kjersti Flatmark	Tumor Biology	18153
Granted US patent (US10598663B2)	Ragnhild A. Lothe	Molecular Oncology	14030





ICR Administrative Unit

The Institute for Cancer Research has seven departments, 30 groups and units and more than 350 employees. In order to perform excellent research and keep focus on the scientific tasks, our leaders at all levels are supported by ICR administrative staff to help out with the daily management of the institute and its many units. Under the leadership of Kari Aalrust Berger, the ICR administrative unit of nine people (6.65 FTEs) provided support on a wide range of tasks. The unit is responsible for budgeting, keeping track of expenses and accounting for around 400 projects. ICR admin staff support application processes, both with budgeting and grant writing (ICR strategy and research advisor), and reporting to internal and external funding sources. On a daily basis ICR admin staff perform HR-tasks, take part in recruitment processes, make sure everyone gets a salary every month, renew work contracts, keep track of absences and vacation and in the challenging year of 2020, supported implementation of Covid regulations, kept track of people in Covid-quarantine and followed up infected cases. The ICR admin staff is also involved in property management and matters regarding Health Safety and Environment, as well as public relations and keeping our web sites up to date. In essence, the ICR admin staff is vital for the day-to-day business and operation of the institute as a whole.

"Serving to let our scientists excel at the ICR"

The institute is also, on behalf of the OUH Hospital Services Division, running a conference center, consisting of several smaller meeting rooms, a couple of seminar rooms with a combined capacity of 80 people, and an auditorium that can house 150 people, all with state-of-the-art equipment. The meeting rooms are used for our weekly seminars and group meetings, but we also rent the rooms out to external users and groups. However, in 2020 most of these meeting were done virtually, via Zoom or Skype.

Researcher- and Employee of the year

Anita Sveen awarded the ICR Researcher-of-the-Year Prize for 2020

Anita Sveen (39) – senior researcher and project group leader at Institute for Cancer Research – was December 16 awarded the prize Researcher-of-the-Year from the leadership at ICR for her outstanding scientific contributions. The award of 100 000 NOK is financed by the Radium Hospital Foundation (Radiumhospitalets legater) and is a personal scholarship for stimulating further excellence in research.

Sveen is a project leader in computational oncology in Ragnhild Lothe's group at the Department of Molecular Oncology. Her research focuses on new treatment concepts for patients with colorectal cancer. She has built strong interdisciplinary competence in molecular oncology and computational approaches to treatment prediction. She works in a translational research program that includes surgeons and oncologists, cancer biologists and bioinformaticians that come together in the OUH TEAM-ACT strategic research area. She is key in planning of a next generation precision medicine trial for metastatic colorectal cancer. The trial will open for inclusion in 2021 and will combine molecular analyses with *ex vivo* drug sensitivity testing of the patients' own cancer cells to select the optimal treatment for the individual cancer patient.

Sveen has won several other early career prizes and received an RCN Young Research Talent Grant, a Cancer Society Open Call grant and funding from HSE. The committee describes Sveen as a very accomplished and promising young researcher publishing in high impact journals and with a steep upward trajectory. The leadership at the Institute for Cancer Research is looking forward to see more excellent research from Dr. Sveen in 2021.

Employee-of-the-year 2020 - Gry Aarum Geitvik

Gry Aarum Geitvik – biomedical laboratory scientist at the Institute for Cancer Research - was awarded the price as Employee-of-the-year 2020 from the leadership group at the Institute for Cancer Research. Geitvik has worked in the Department for Cancer Genetics since 1982 and is currently Head of the lab technology unit. Her responsibilities include management of laboratory activities and biobanks, as well as budgeting and HR for large international projects in the department.

The Employee-of-the-year award goes to a person that has contributed to the ICR research community and promoted the ICR vision, values and objectives. Gry Aarum Geitvik has over many years been involved in implementing cutting-edge techniques in molecular cancer research and important biobanking activities. She was involved in the planning and move to the new ICR building, served as an employee representative on the Radium Hospital Board and DNR Foundation Board, and she has broad organizational knowledge and competence. She currently serves on the Cancer Biobank Steering Committee and OUH Biobank and Register Committee as well as the Oslo Breast Cancer Consortium Board. She is truly a good citizen in wider research community

The committee describes Gry Aarum Geitvik as essential for the Institute's handling of the Covid-19 situation in 2020. She has ensured that critical activities, such as biobanking of patient material from clinical studies, have been maintained throughout the whole period. She has developed the contingency plan for transfer of key personnel to the hospital and managed the day-to-day laboratory activities at the Department of Cancer Genetics. Her positive and problem-solving attitude combined with high work capacity has been essential for the Institute in this challenging year. She is a very worthy recipient of the Employee-of-the-year award.

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