INSTITUTE FOR CANCER RESEARCH

ANNUAL REPORT 2017

Oslo University Hospital

HELSE SØR-ØST

UiO : University of Oslo

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The photographic theme of this year's Annual Report is people at work.

FRONT PAGE:
New group leader Tor Erik Rusten had great success in 2017 with papers in Nature and Nature Cell Biology on autophagy and cell signalling in tumour progression.

MICROSCOPY IMAGES OF CELLS
Microscopy images of cells by Vigdis Sørensen, Advanced Light Microscopy Core Facility

PAPER: 150/300 Profimatt
CIRCULATION: 600

CONTENTS

INTRODUCTION BY THE ACTING DIRECTOR

In 2017, Institute for Cancer Research (ICR) has continued its progress as one of Europe's strongest cancer research institutions. The accreditation of the Division of Cancer Medicine as a Comprehensive Cancer Centre (CCC), as highlighted in this report, is a new boost for research at ICR and is also a quality mark of ICR as the major contributor of research in the Division of Cancer Medicine.

Among research highlights, the newly established research group on tumour-host biology, headed by Tor Erik Rusten, published a particularly remarkable finding in 2017. This group showed that tumours turn on cellular self-eating, autophagy, in their microenvironment, and that this generates amino acids that fuel further tumour growth. The group's finding that genetic or pharmacological inhibition of autophagy in the tumour microenvironment causes tumours to shrink opens up novel therapeutic strategies. This paper, which was published in *Nature*, attracted considerable attention, including commentary articles in three major international research journals and coverage by national TV news. In addition to this finding, several other research discoveries made at ICR represented major scientific advances and represent good news for future cancer patients, as exemplified elsewhere in this report.

About 2/3 of ICR's funding comes from external grants, and ICR scientists have been able to obtain substantial new funding. Both Karl-Henrik Malmberg and Tor Erik Rusten obtained the very prestigious 5-year "Toppforsk" grant from the Research Council and the University of Oslo, which will profoundly stimulate their research on cell-based immunotherapy and tumour-host interactions, respectively. ICR scientists also secured major grants from the Norwegian Cancer Society, the Research Council of Norway, and the South-Eastern Norway Regional Health Authority. Although ICR researchers have also succeeded in obtaining international grants, ICR still has great potential for improvement, and hopefully the new CCC status will facilitate participation in Horizon-2020 and other large international projects.

After Anne-Lise Børresen retired as head of Department of Cancer Genetics, Gry Aarum Geitvik has done a very good job as acting head of department. It was nevertheless important to hire a permanent head of this department, which has a central role in ICR's translational research programme. With Therese Sørlie as new head of department, the Department of Cancer Genetics has got a leader with strong research background in breast cancer genetics and considerable experience with research leadership. In the Department of Tumour Biology, Jørgen Wesche has been hired as leader of the group on Molecular Biology of Sarcomas. Jørgen, with experience in studies of fibroblast growth factor signalling, will benefit from the strong sarcoma research programme that has already been established at this department.

ICR's strong standing in Norwegian research is illustrated by the fact that the institute has been host for a Centre of Excellence (CoE) and two K.G.Jebsen Centres in 2017. The CoE, Centre for Cancer Biomedicine (CCB), closed in August 2017 after a 10-year run as one of Norway's most successful CoEs. However, the director of CCB, Harald Stenmark, will lead a new CoE, Centre for Cancer Cell Reprogramming (CanCell), with three ICR group leaders joining as principal investigators - Jorrit Enserink, Tor Erik Rusten, and Jørgen Wesche. In addition, two other ICR group leaders, Eivind Hovig and Åslaug Helland, are associate members of the new CoE. Both the two K.G. Jebsen centres, the one for Cancer Immunotherapy (led by Johanna Olweus) and the one for Colorectal Cancer Research (led by Ragnhild A. Lothe) have been granted prolongation. In addition, a new K.G. Jebsen Centre for B Cell Malignancies has strong participation from ICR, including June Myklebust (deputy centre director), Erlend B. Smeland and Kjetil Taskén. This means that, in 2018, ICR will host as many as 3 KG Jebsen centres in addition to a CoE, which is exeptional among Norwegian research institutes.

A new permanent director of ICR has been appointed from January 2018, Kjetil Taskén. With administrative experience as director of the Biotechnology Centre of Oslo and the Norwegian Centre for Molecular Medicine, and scientific background as one of Norway's leading cancer researchers, Kjetil is very well qualified for directing ICR. As acting director of ICR for the last year, I wish Kjetil good luck with his vision of developing ICR further as a world-leading cancer research institute.

Harald Stenmark

CANCER RESEARCH OF INTERNATIONAL EXCELLENCE

THE INSTITUTE FOR CANCER RESEARCH
– FORWARD-LOOKING STATEMENT

It is with a great deal of humility and respect that I come to the position as Head and Director of the Institute of Cancer Research (ICR) at Oslo University Hospital (OUH) from January 2018.

The ICR is an institution with more than 300 employees and some 25 research groups as well as a complement of cutting-edge core facilities. The ICR is the foremost institution in basic and translational cancer research on a national arena and a well-renowned institution on an international arena. Its research production is truly excellent both in volume and quality of the output. The ICR also has a strong prior track record in translational research and innovation.

Leading the ICR is, in my view, going to be about maintaining the excellent science and outstanding production while at the same time facilitating further building of excellence and organising more collaborative efforts both inside the institute, across the hospital and university and regionally, nationally and internationally to deal with grand challenges in cancer medicine and to position the ICR in national and international alliances and consortia. The ICR should be a key element in building the OUH Comprehensive Cancer Centre (CCC), feed results into a translational research path and continue to have **patient benefit** in mind in all aspects of research and innovation. As the foremost national institution in cancer research the ICR should, to meet the needs of its owners and take national responsibility, have research and expertise on all major cancers and explore current and cutting-edge strategies for diagnosing and treating cancer.

The most important part of ICR is by far its human resources. Making the ICR continue to succeed is also about maintaining the competence and excellence represented by its current staff, developing and training excellent researchers at all levels and to provide good and predictable career development programs for younger researchers in order to secure internal recruitment. At the same time, the ICR should, in my view, aim also to have international recruitment programs at all levels including PI positions and develop a truly international environment in order to attract top talent also on an international arena.

With respect to the leadership strategy looking forward I envision that a truly open, conductive and interactive milieu should be the future hallmark of ICR. ***Open*** in the sense that it should encourage influx of new ideas, new methodology, new approaches; ***Conductive*** in the sense that the atmosphere should be welcoming, friendly and helpful; ***Interactive*** in the sense that collaborations are encouraged, experts from different fields meet and discuss on a regular basis and true inter-disciplinary collaborations are formed, national and international resources are used, international networks are established, and interactions with pharmaceutical companies are ongoing. These are activities that I would want to encourage and establish.

The values I have come to cherish as part of my leadership philosophy are: ***courage*** to strive to become excellent, ***joy*** of working together and with ***generosity*** to share. I have during my past tenure and service as a research director over the past 20 years aimed to establish an atmosphere where these values are held forward and have experienced that to work.

On this background, ambitions and a forward plan for both continued operation and development of the ICR should, in my view, include the following elements:

- Maintain and develop excellence.
- Continue to develop competitive edge and international standing as well as visibility.
- Increase translational activities.
- Increase collaboration inside OUH-CCC and to UiO, nationally and internationally in transdisciplinary activities.
- Develop strategies to continuously maintain and increase funding base.

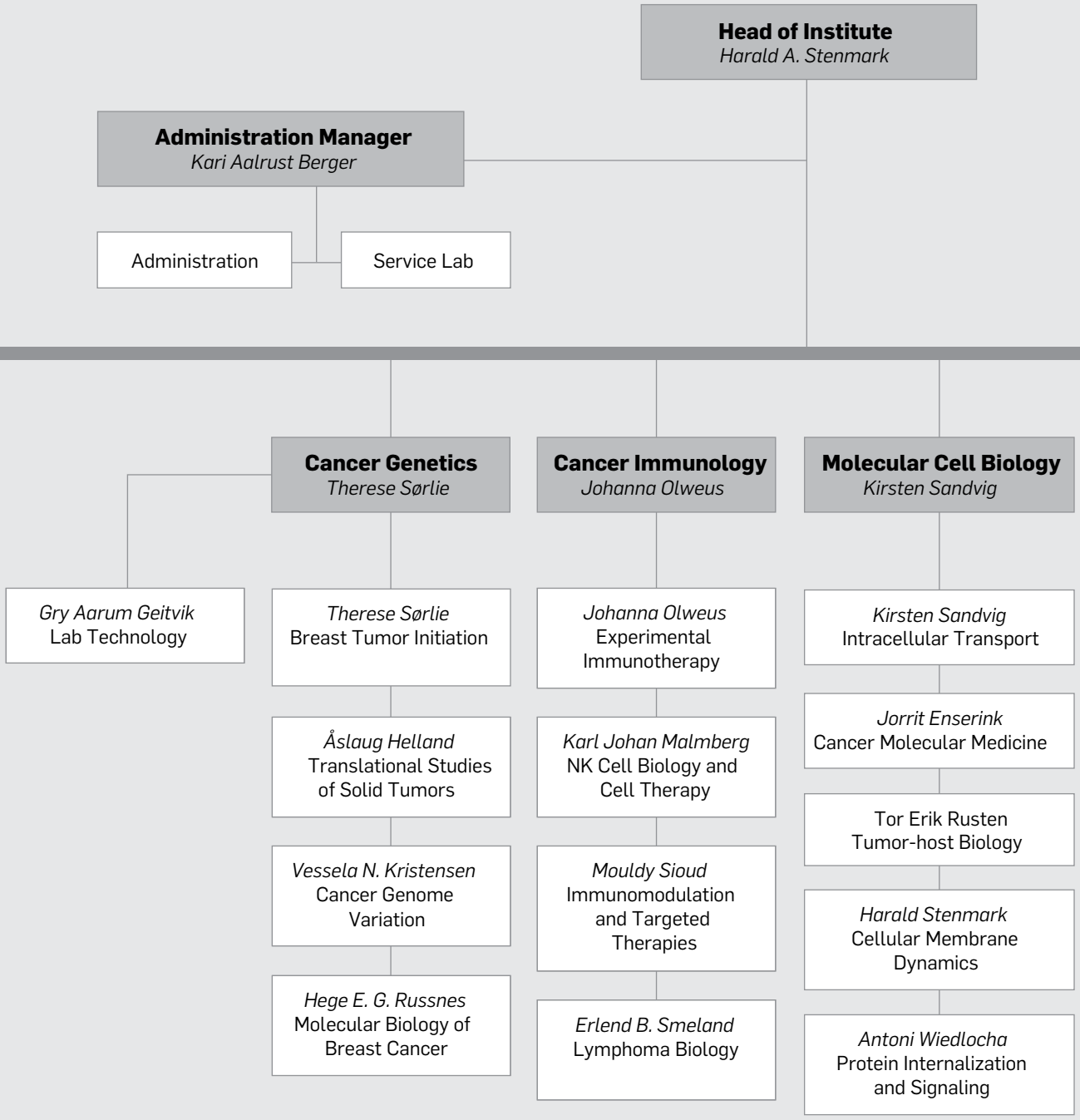
To be able to succeed with such a strategy, I think the ICR needs to work interactively to form a matrix organisation with disease working groups, focus on developing complementarity, collaboration and cohesion, establish good training and career paths as well as good methods for benchmarking, internally, through the SAB and on competitive arenas. Furthermore, the implications of the ICR being the foremost institution in basic and translational cancer research in Norway is, in my view, that not only should the ICR excel in research, but it should also excel in innovation, education and training, career development, research ethics, compliance with legislation and regulations, health, environment and safety, dissemination and visibility and in setting standards. Moreover, the ICR as a premier institution on a national and international arena, should be a source of new strategies in cancer research, take lead on a national arena, and take its rightful place in all strategic processes in Norway and internationally on a European area and beyond. And the ICR should take its rightful proportion of research grants on a national and international arena.

The ICR will only achieve its goals if everybody on board joins forces. I look forward to working with all the ICR staff and with the wider environment of outstanding collaborators to reach for the vision and goals of the ICR and OUH.

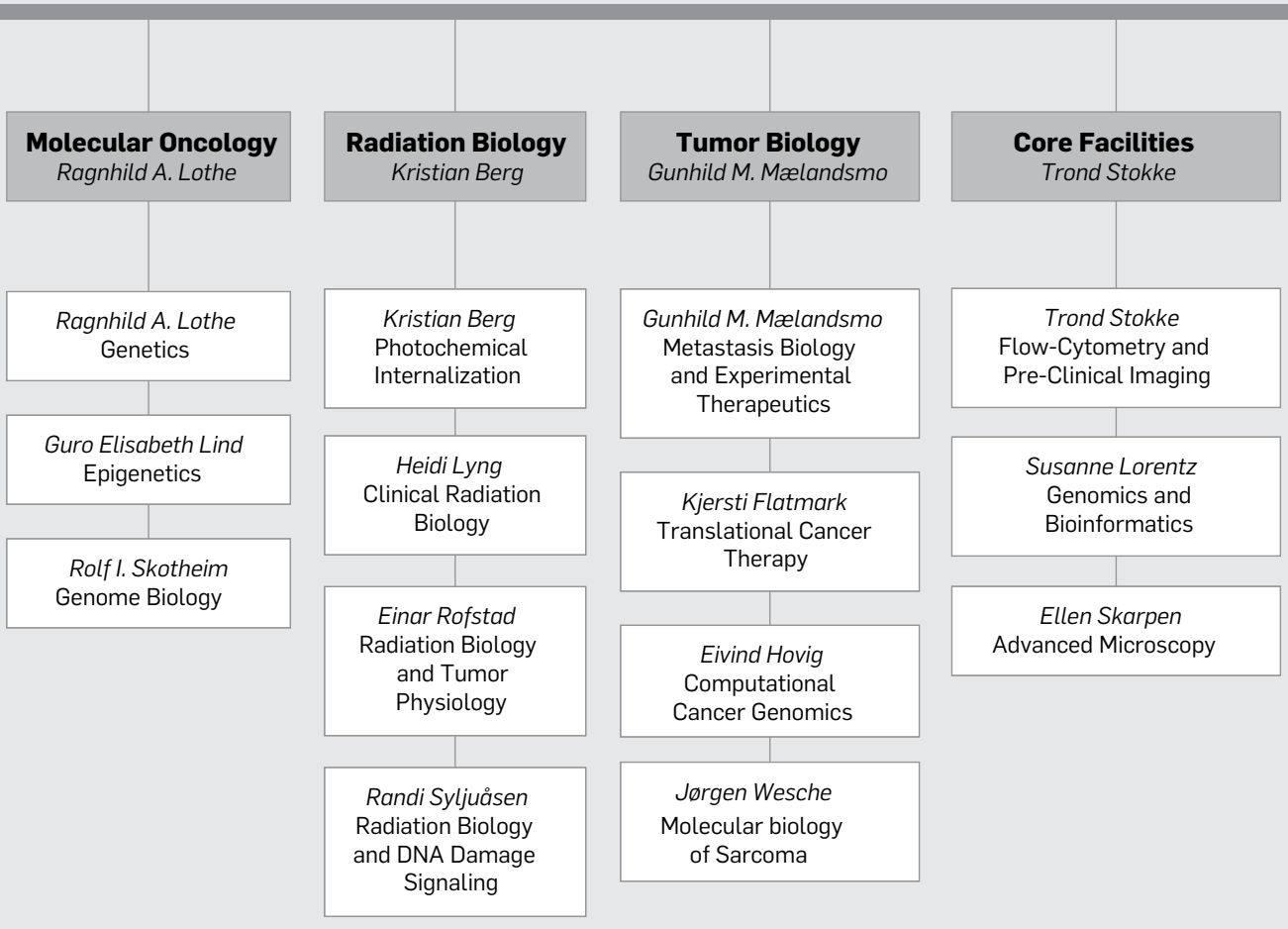
March, 2018,
Kjetil Taskén, incoming Head of the ICR

WITH PATIENT BENEFIT IN MIND IN ALL ASPECTS OF RESEARCH AND INNOVATION

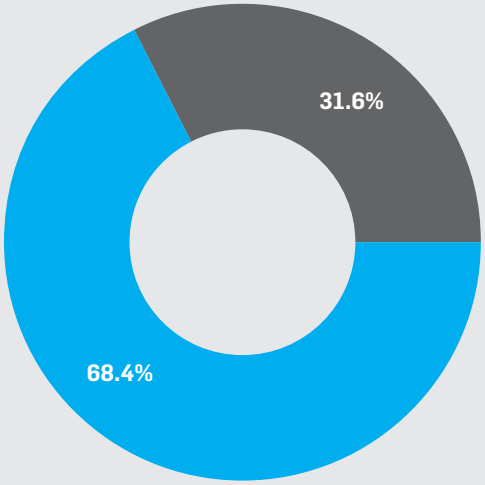
ORGANISATION



THE INSTITUTE FOR CANCER RESEARCH
Institute for Cancer Research is organized in 6 research departments with 24 research groups, and one Department of Core Facilities.



KEY FIGURES 2017



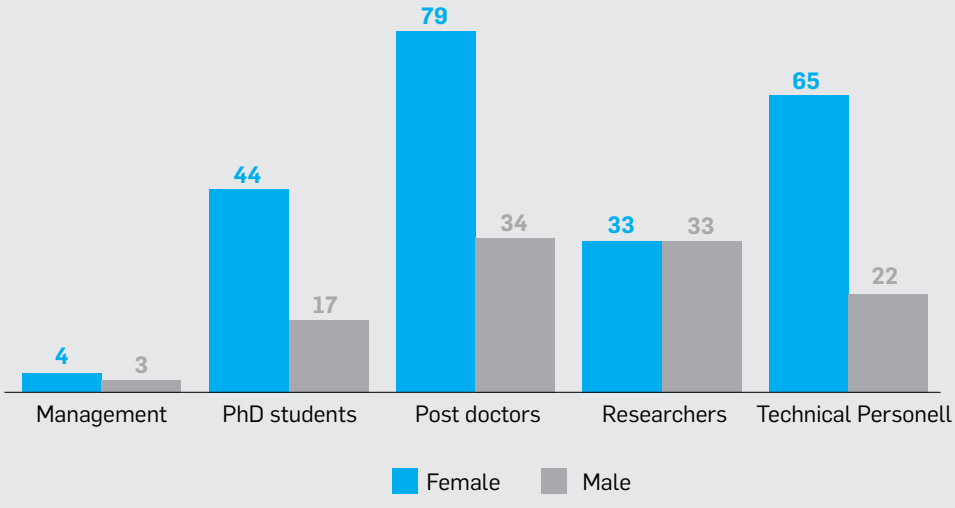
FUNDING

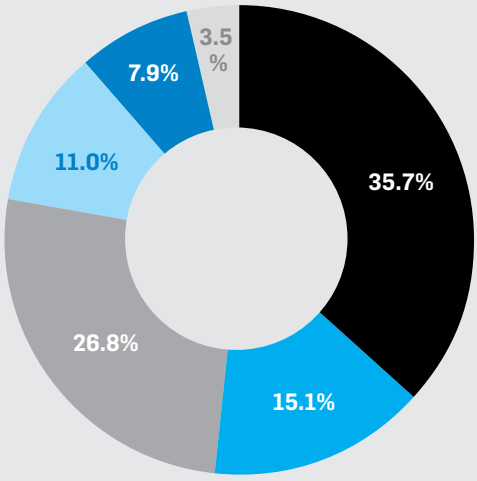
Percent

Actual Institute expenditure for 2017 by internal and external funding sources (total 301,1 MNOK = approx. 31,1 M€)

Internal funding
External funding

EMPLOYEES





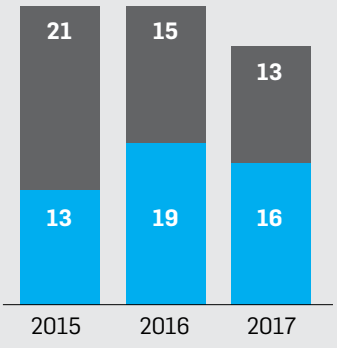
EXTERNAL FUNDING BY SOURCE

Percent

Sources of external competitive funding for 2017, based on actual expenditure (total 206 MNOK= approx. 21,3 M€)

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

COMPLETED PHDS AND MASTER DEGREES



ARTICLES PUBLISHED

IMPACT FACTOR

Mean	5.6	6.3	6
Median	4.4	5	4.3

OSLO UNIVERSITY HOSPITAL COMPREHENSIVE CANCER CENTRE

In April of 2017 the Oslo University Hospital (OUH) Cancer Centre was designated by the Organisation of European Cancer Institutes (OECI) as a European-level Comprehensive Cancer Centre (CCC). The accreditation is based on documented high volume and quality in clinical cancer care, with integration of high level cancer research and innovation and following a rigorous review and audit of both cancer care, the cancer care organisation and cancer research at OUH.

The accreditation means that the OECI considers that the OUH CCC performs at a level with premier national institutions across Europe in the cancer field. In this process OUH has made necessary adjustments to both its clinical and research organisations, with the aim of integrating all cancer-related activities in a common cancer centre structure. The process included the elaboration of an institutional cancer strategy with an incorporated research strategy.

The Board of the OUH CCC encompasses the Division for Cancer Medicine with its Departments of Oncology, Hematology, Gynecological Cancer and the Institute of Cancer Research, The Division for Surgergy, Inflammation and Transplantation with its Departments of Gastrosurgery and Urology, The Division for Radiology and Nuclear Medicine and the Division for Laboratory Medicine with the Department of Pathology and more. The CCC board is set up to reinforce the Divisional Directors and Department Heads' executive power across the organisation and OUH localities to forge coordination and collaboration with operations and strategy for diagnostics and treatment, care, follow-up and research.

OUH and its Division for Cancer Medicine are truly proud of the OECI-CCC accreditation and will continue to develop the OUH CCC as a premier cancer centre on a European arena.

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

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

Oslo University Hospital
Comprehensive Cancer Centre

OECI COMPREHENSIVE Cancer Centre

DEPARTMENTS AND RESEARCH GROUPS

OUR MISSION IS TO IMPROVE THE LIVES OF CANCER PATIENTS WITH SOLID TUMORS BY PERFORMING TRANSLATIONAL RESEARCH

DEPARTMENT OF

CANCER GENETICS

HEADED BY: **THERESE SØRLIE**
ACTING HEAD IN 2017: **GRY AARUM GEITVIK**

OUR GOALS ARE:

- improve risk estimation
- achieve earlier diagnosis
- improved prediction of treatment response, and improve prognosis for patients with early and advanced stages of breast, lung, pancreatic and ovarian cancer.

Our research focus is on molecular classification, data integration, pan-cancer analyses and translation to clinic. A common theme across groups is to achieve deeper molecular understanding of inter- and intra-tumor heterogeneity and tumor evolution using human tumor cohorts and mouse models. We are an interdisciplinary team of 54 members with MDs, molecular biologists, bioinformaticians and highly educated engineers organized in 4 research groups and one lab-technology unit. The lab technology unit enhances the department's skills of "state of the art" technology and improves exchange of knowledge across research groups and cancer types. This is a key asset leading to increased quality of the department's laboratory work and project management.

We have established a pipeline for high-quality biobanking (>200 000 vials) and data handling of patient cohorts with long-term follow-up and perform multilevel molecular characterization of tumors down to single cell levels. Our database consists of > 3000 patients with analyses at 2-6 molecular levels, and includes samples from, among others, the following trials:

- MetAction - Actionable targets in cancer metastasis.
- NeoAva - Neoadjuvant chemotherapy in breast cancer with/without bevacizumab.
- IBCT - Improved Breast Cancer Therapy in the neoadjuvant and metastatic setting
- EMIT -Establishment of Molecular profiling for Individual Treatment decisions in Early BC; three-phase study including randomized and observational clinical trials.
- TREM – Lung cancer patients with EGFR mutations and primary TKI-resistance
- ThoRaT - Lung cancer patients receiving radiotherapy
- NorPACT-1 and 2 - Neo-adjuvant chemotherapy for pancreatic cancer

We have extensive institutional, national and international collaborations and are partners in several networks and consortia; the Regional Network for Breast Cancer Research, the Regional Research Network on Extracellular Vesicles (RRNEV), Personalized Cancer Treatment and Metaflammation, International Cancer Genome Consortium (ICGC), EuroPDX, the Breast Cancer Association Consortium (BCAC); EU funded projects (EpiMark, Cancer-ID). We host The National Competence Center for Lung Cancer. The total number of peer reviewed publications in 2017 was 72.

DEPARTMENT OF CANCER GENETICS

BREAST TUMOR INITIATION

GROUP LEADER:
THERESE SØRLIE

UNDERSTANDING CELL FATE DECISIONS IN TUMOR PROGRESSION

ABOUT

The group counts 12 members (two men, 10 women) including the group leader (TS), one senior researcher and project leader, Silje Nord, one scientist, four postdocs, two PhD students, one MD-PhD student, one master student and two engineers. Two members are MD and one is DVM. Sørlie is head of Department since 1. Oct 2017, professor at University of Oslo, Medical Faculty and adjunct professor at CCBIO, University of Bergen. Our group studies molecular aspects of breast tumor initiation and progression including the functional effect of known risk variants, cell of origin of molecular subtypes and the specific pathways and processes that are deregulated and lead to invasion. We have a broad expertise in laboratory technologies which include high-throughput genomic technologies, in vivo lineage-tracing, 2D and 3D in vitro culture techniques, in situ hybridization, confocal microscopy, and FACS analysis. We use patient cohorts and mouse models (transgenic and patient derived xenograft - PDX) in our studies. We also have expertise in bioinformatic and statistical methods and modeling.

AIMS

Our aim is to identify the cellular origins of breast tumors and the mechanisms behind 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 the functional effect of breast cancer risk variants
- Characterize subtype-specific progression pathways of pre-invasive lesions in the breast
- Investigate the role of Hedgehog/GLI1 signaling in breast cancer progression
- Explore the tumorigenic potential of LGR5 expressing cells in the mammary gland
- Drivers of the BRCAness phenotype in basal-like tumors
- Investigate the role of FOXA1 in endocrine resistant breast cancer

RECENT ACHIEVEMENTS

- 9 publications in 2017
- One completed Master thesis
- OUS award for excellent publication
- Sørlie researcher of the month, December, Helse Sør-Øst

TRANSLATIONAL STUDIES IN SOLID TUMOURS

GROUP LEADER:
ÅSLAUG HELLAND

> **WITH STARTING POINT IN CLINICAL STUDIES AND CLINICAL QUESTIONS, WE DO MOLECULAR ANALYSES AIMING AT IMPROVING OUTCOME FOR CANCER PATIENTS**

ABOUT

Our group focuses on translational studies on solid tumours, with a special interest in pancreatic, lung, ovary and colorectal cancers. We do whole genome analyses on patient material, aiming at identifying predictive and prognostic biomarkers. We are analysing mRNA, miRNA, DNA, methylation, glycosylation, mutations and proteins. By increasing the understanding of the underlying biology of tumour development, we aim at improving cancer patient care. We also study therapy resistance. Several of our projects include material from patients included in clinical studies, and we have clinical and follow-up data from all patients. The group has two project groups (headed by Elin Kure and Odd Terje Brustugun), with a total of 18 members (12 women). Nine of these 18 are MDs, and India and Great Britain are represented in addition to Norway. We are three researchers, three postdocs, eight PhD-students, one master student, one study nurse and two engineers.

AIMS

The ultimate goal is to personalise cancer treatment, and improve prognosis. We aim for:

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

PROJECTS

- Molecular characterisation of lung squamous cell carcinomas
- Molecular characterisation of pancreatic cancers
- MiRNA in ovarian cancer
- Improving radiotherapy in lung cancer
- Identification of biomarkers in colorectal cancers
- Protein (TMA) analyses in lung cancers
- Genome-wide detection of diagnostic plasma miRNAs in pancreatic cancer
- Exosome profiles of proteins and miRNAs in plasma of pancreatic cancer patients
- Serum N-glycans as prognostics markers in pancreatic and colorectal cancers
- Serum predictive markers for therapy response
- Elucidate mechanisms for therapy resistance

RECENT ACHIEVEMENTS

In 2017, the group was involved in several EU-applications and published 18 papers in peer-review journals. We have had several talks at national and international meetings, and are PIs on >20 translational and clinical studies. We received approximately 22 mill NOK in research funding (Elin Kure 9 mill, Odd Terje Brustugun 5 mill, Åslaug Helland 8 mill).

DEPARTMENT OF CANCER GENETICS

CANCER GENOME VARIATION

GROUP LEADER:
VESSELA N. KRISTENSEN

GERM-LINE AND SOMATIC GENETIC AND EPIGENETIC VARIANTS IN CANCER AND PHARMACOGENOMICS

ABOUT

The group at ICR consists of 4 postdocs, 1 PhD student, 1 MSc student, 2 research technologists and 1 ERASMUS student in 2017. Two other postdocs are shared with other groups at the Department and Institute. Vessela Kristensen is a professor I at the Faculty of Medicine, UiO, and works towards intensive and fruitful collaboration between ICR and University of Oslo, where she also leads a group of 3 postdocs, 2 PhD students, 1 MSc and 1 research technologist. Group members work closely together and in collaboration with breast clinicians, pathologists and oncologists.

AIMS

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

PROJECTS

Together with our collaborative network we received several grants in 2017: from the Norwegian Cancer Society (The genetic make-up of breast cancer), Pink Ribbon (Hereditary breast cancer), Convergence grant from UiO-Life Science (Personalised Patient Care, PerCaThe) and we are member of the TRANSCAN EpiMark EU network. Projects include:

- **Genome variation:** In the breast cancer association consortium we identified 65 new breast cancer risk loci (published in *Nature*) and ten variants - with risk of ER-negative breast cancer (*Nature Genetics*) as highlighted in CNN and other media world-wide.
- **DNA methylation** at enhancers was identified in distinct breast cancer lineages (Published in *Nature communications*) and distinct subgroups of luminal A (published in *Oncotarget.*)
- **Data integration:** Integrative clustering revealed a novel split in the luminal A subtype of breast cancer with impact on outcome (published in *Breast Cancer Res*)
- **Non-canonical transcriptomes:** Wide-spread alternative exon usage was identified in clinically distinct subtypes of BC (published in *Scientific Reports*)
- **Immune signaling:** Bioinformatic approaches to profile the tumor microenvironment in association with disease progression, ER activity, genomic complexity and age (Publications in *OncoImmunology, highlight in New England J Medicine* and others).

RECENT ACHIEVEMENTS

Publication activity. 17 publications in 2017, 2 book chapters.

MOLECULAR BIOLOGY OF BREAST CANCER

GROUP LEADER:
HEGE G. RUSSNES

EXPLORING INTER- AND INTRA-TUMOR HETEROGENEITY AT VARIOUS MOLECULAR LEVELS AND PERFORMING INTEGRATED ANALYSES TO DEVELOP PROGNOSTIC AND PREDICTIVE SIGNATURES FOR BREAST CANCER

ABOUT

The group is organized into three project groups (headed by Anita Langerød, Kristine Kleivi Sahlberg and Hege Russnes) with a total of 4 scientists, 5 postdocs, 2 research engineers and one MD-PhD student in 2017. In addition, 1 oncologist, 1 study nurse and 1 professor in bioinformatics (UiO) are associated with the group (part-time).

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

As partners in several clinic trials we perform "state of the art" analyses of patient material, both on bulk tumors, single cells and liquid biopsies, at various stages of the disease. In July 2016 the former group leader, Prof. emerita Anne- Lise Børresen-Dale retired and project group leader Hege G. Russnes has been acting as Head of the group thereafter. Hege G. Russnes is in addition senior consultant in Pathology at Dept. of Pathology, OUS and is also appointed as "Young Associated Investigator" at NCMM (Centre for Molecular Medicine Norway).

AIMS

Our group aims at defining, refining and implementing molecular classification and biomarker analyses to improve stratification of breast 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

- Somatic Genetics of Breast Cancer, from single genes to whole genome sequencing
- Single-level and multi-level data analyses of DNA/RNA/protein/metabolic alterations of primary tumors and metastases at various stages of the disease to improve classification of breast cancer
- Intra tumor heterogeneity
- Cell-free tumor DNA in blood
- Genomic and functional analysis of therapeutic targets in breast cancer
- Functional screens elucidating the role of miRNA's
- Glycans and miRNA as serum biomarkers

RECENT ACHIEVEMENTS

- 28 original publications in 2017
- Prof. emerita Anne-Lise Børresen-Dale received several honours in 2017:
  - Appointed Commander of the Royal Norwegian St. Olav's Order
  - Recipient of the AACR-Women in Cancer Research Charlotte Friend Memorial Lectureship in 2017

OUR GOAL IS TO IMPROVE CANCER DIAGNOSTICS AND THERAPY THROUGH CUTTING EDGE RESEARCH ON TUMOR IMMUNOLOGY AND LYMPHOCYTE BIOLOGY

DEPARTMENT OF

CANCER IMMUNOLOGY

HEADED BY: **JOHANNA OLWEUS**

ABOUT:

The Department of Cancer Immunology (DCI) consists of five research groups (Olweus, Myklebust/Smeland, Sioud, Malmberg and Taskén (joined in 2018)) and one project group (Kyte). Four of the group leaders are full professors at the University of Oslo. Groups at the DCI are partners of three K.G. Jebsen Centers (Cancer Immunotherapy, Inflammation Research and B-cell malignancies) and several EU-funded research programs in cancer immunotherapy. The groups provide complementary and cross-fertilizing expertize in molecular and cellular immunology, including a broad experimental tool-box for antigen discovery and studies of immune cells at the single cell level. Research at the department aims at deciphering the molecular regulation of key cellular components of the innate and adaptive immune system, including dendritic cells (DC), B cells, T cells, regulatory T cells (Treg) and NK cells. The key driving force in all these efforts is to develop better tools for cancer diagnostics and new therapeutic strategies. The latter include investigator-initiated clinical trials to alleviate immune suppression and improve the use of check-point inhibition, and the design of gene-edited T- and NK cells for adoptive cell therapy.

PROJECTS:

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

RECENT ACHIEVEMENTS (2017)

- In 2017, 15 publications were published, of which 10 with first/last authors from DCI, with mean IF of 10.3.
- Two DOFIs and two patent applications were filed.
- Three PhD degrees.
- Signed a license agreement and entered into a 2-year research agreement with Fate Therapeutics Inc. concerning the development of a universal iPS-derived NK cell platform for cancer immunotherapy.
- Signed a 2-year research agreement with Kite Pharma to use in-house developed technology for identification of therapeutic T-cell receptors
- Launched a clinical trial Lymvac II as co-PI (Arne Kolstad main PI) in collaboration with Merck.
- Awarded Mørks Legat´s research prize.

DEPARTMENT OF CANCER IMMUNOLOGY

EXPERIMENTAL IMMUNOTHERAPY

GROUP LEADER:
JOHANNA OLWEUS

OUR FOCUS IS TO DEVELOP NEW STRATEGIES FOR T-CELL BASED IMMUNOTHERAPY

ABOUT:
The group counts 13 members (67% women); 1 full professor (JO), 5 postdocs, 4 PhD students and 2.5 engineers, and two associated clinicians. Three members have MD background. Ten members are recruited from abroad. The group is partner of two K.G. Jebsen Centers (2013-); "Cancer Immunotherapy (JCIT)" and "Inflammation Research (JIRC)", respectively. Olweus is Director of JCIT, which was awarded maximal prolongation in 2016 (two years), till 2020.

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

PROJECTS
Strategy 1
- Identify cell-type specific T-cell epitopes from self-antigens and T-cell receptors reactive with such epitopes for future genetic transfer in adoptive cellular therapy (*Nat Biotechnol 2017*)

Strategy 2
- Target neo-antigens neglected by patients *(Front Immunol 2017)*
- Profile T-cell receptors as a tool to identify T-cell reactivities *(J Hepatol 2017)*
- Identify neo-antigens and reactive T cells in biobanked material from patients responding to immunotherapy *(Lymvac I and II trials)*
- Identify auto-antibody targets by protein arrays and T cell biology in autoimmune disease (CVID) *(J Autoimmun 2017, Clin Immunol 2017)*

RECENT ACHIEVEMENTS
(2017-): The group published 5 articles and two PhD students graduated. Olweus and Inven2 signed a research agreement with biotech company Kite Pharma (acquired by Gilead for 12bUSD) on development of T-cell receptors to target cancer. Olweus was invited speaker at a large number of international conferences, including Keystone Symposium "Lymphocytes and their roles in cancer".

NK CELL BIOLOGY AND CELL THERAPY

GROUP LEADER:
KARL-JOHAN MALMBERG

TOWARDS THE NEXT GENERATION NK CELL THERAPY

ABOUT

The Malmberg Lab counts 16 members (F/M: 6/10); 1 full professor (KJM), 2 scientists, 1 project manager, 3 postdocs, 7 PhD students, 2 engineers. Malmberg is a visiting Professor at the Karolinska Institutet (KI) and a partner in the K.G. Jebsen Center for Cancer Immunotherapy. Affiliated to the group is a Project group in translational cancer immunotherapy led by Jon-Amund Kyte.

AIMS

The group seeks to develop new strategies for cell-based immunotherapy based on insights into the functional regulation of natural killer (NK) cells. We use a combination of single-cell assays, including live cell imaging, high-dimensional immune profiling by mass cytometry, flow cytometry and RNA Seq to decipher the cellular and molecular mechanisms involved in calibration of effector function in human NK cells. The Kyte group aims to develop new combinations of check point inhibition and CAR-engineering.

PROJECTS

1) Functional plasticity and diversification of human NK cell repertoires in health and disease
2) Programming a synthetic killer cell
3) Towards iPS-derived NK cells for off-the-shelf cancer immunotherapy

RECENT ACHIEVEMENTS

- Reported the first Phase I/II clinical trial based on transfer of allogeneic NK cells to patients with high-risk AML and MDS. (Björklund et al., Clinical Cancer Research 2018).
- Defined a method for selective expansion of adaptive NK cells and showed their efficacy against acute leukemia and as a platform for CAR engineering. (Cancer Immunology Research 2017 and 2018).
- Innovation: Main inventor of a pending patent concerning a method for selective expansion of educated NK cells. Licensed to Fate Therapeutics Inc. January 2018. “Modulation of function of immune effector cells”. A PCT application describing the use of agents to altered signalling from secretory granules was filed 25 September 2017.
- Signed a 2-year collaborative agreement with Fate Therapeutics to develop “adaptive” NK cell therapy.

DEPARTMENT OF CANCER IMMUNOLOGY

IMMUNO-MODULATION AND TARGETED THERAPIES

GROUP LEADER:
MOULDY SIOUD

OUR GOAL IS TO DEVELOP BIOLOGICAL PHARMACEUTICALS AND BIOMARKERS THAT IMPROVE CANCER TREATMENT

ABOUT

Currently the group consists of 7 members (66% women), including 1.5 postdocs, 2 research assistants, 1 visiting scientist, 1 master student and the group leader (DEA Pharm, PhD) with formal research experience in immunology, molecular/cell biology, pharmacology and medicine. Sioud is a visiting professor at University of Tunis since 1997. The group is a part of the OUS-focus area cancer immunotherapy and H2020 NANO-D-SIRE consortium. Research is mainly focused on probing surface changes in cancer cells and patient serum antibodies using phage display technologies as well as the development of targeted dendritic cell cancer vaccines.

Notably, some of our previous studies have shed light on the underlying mechanisms regulating RNA sensing by the immune system, hematopoietic stem cell sensing of microbial products and gene regulation by endogenous antisense transcripts [e.g., Sioud & Sørensen *Nature Biotech* 1998; Røsok & Sioud 2004 *Nature Biotech*; Sioud 2006 *Nature Biotech* (IF=41); Sioud 2004 *Trends Pharmacol Sci* (IF= 11.8); Sioud 2006 *Trends Mol. Med* (IF=10.1)].

AIMS

Our primary aim is to develop new cancer therapeutic agents (e.g. antibodies, lytic peptides, vaccine formulations) and to probe the immune responses in patients treated with checkpoint inhibitors.

PROJECTS

- Engineering new therapeutic human antibodies and lytic peptides
- Probing immune responses in breast cancer patients treated with checkpoint inhibitors
- Developing super-active checkpoint blocking siRNAs
- Uncovering the mechanisms by which dendritic cells suppress immunity during extracorporeal photopheresis

RECENT ACHIEVEMENTS

- 4 publications
- One patent application (Inven-35426/US-1/PRO).
- Secured funding for 2017-2020 from the Norwegian Cancer Society
- One master thesis

So far the group has published 184 peer-reviewed original articles (mean impact factor = 5.875) and reviews, with 1st and/or last authorship on 86% of the published papers. The work on cancer therapeutic antibodies resulted in 2017 in one patent application (Inven-35426/US-1/PRO) and a DOFI (in preparation).

LYMPHOMA BIOLOGY

GROUP LEADER:
ERLEND BREMERTUN SMELAND/JUNE MYKLEBUST

DEVELOPING PROGNOSTIC AND PREDICTIVE MOLECULAR SIGNATURES FOR B-CELL LYMPHOMA.

ABOUT

The group consists of 13 members with research background in medicine, biology, biochemistry and biotechnology, and includes 1 professor (EBS), 1 associate professor (JHM), 1 senior scientist (50% position), 5 postdocs, 4 PhD students and 1 technician. Three of the members are recruited from abroad (USA, China, Sweden). The group is part of the new KG Jebsen Centre for B-cell malignancies. The research focus is translational studies in B-cell lymphoma, with strong institutional and international collaboration. We use next generation sequencing technologies, high-dimensional flow cytometry and mass cytometry to characterize tumor cells and intratumor immune cells from patient biopsies.

AIMS

Identify prognostic and predictive signatures and identify actionable targets/pathways in B-cell lymphoma. Study clonal evolution of B-cell lymphoma and characterize impact of novel driver mutations. Identify patient specific changes in normal infiltrating immune cell subsets to guide choice of immunotherapy.

PROJECTS

- Next generation sequencing of lymphoma serial biopsies to study clonal evolution and to identify recurrent mutations associated with progression and therapy relapse
- Transcriptomics and proteomics characterization of tumor cells and infiltrating immune cells
- Characterize recurrent driver mutations – biological function and potential immunogenicity
- Cancer sensitivity drug screen and in vivo testing of novel drugs

RECENT ACHIEVEMENTS

Awarded excellent article, OUH, for comprehensive characterization of signaling pathways in B-cell lymphoma (Myklebust, Blood 2017). Discovery of TIGIT as a new target for checkpoint inhibition in FL (Josefsson, Clin Cancer Res 2017). Contributed to development of new molecular prognostic test for mantle cell lymphoma (Scott, J. Clin Oncol 2017). Patent application for CD37 CAR to target lymphoma cells (2017). Mørk Legacy Research prize to June Myklebust.

UNCOVERING THE CELLULAR BASIS OF CANCER DEVELOPMENT

DEPARTMENT OF

MOLECULAR CELL BIOLOGY

ACTING HEAD: **KIRSTEN SANDVIG**

The department has a staff of about 75 and hosts 5 research groups (Enserink, Rusten, Sandvig, Stenmark, and Wiedlocha), 9 project groups, and a departmental service unit. Research in the department comprises various aspects of cancer relevant cell biology, including membrane traffic, receptor signaling and cell division. Also primary human cancer samples are studied.

Translational research on cancer cell-derived exosomes is a relatively recent development in the department. 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 and advanced imaging in order to address relevant scientific questions. Recent key achievements from the department's scientists include studies on autophagy and tumor growth, growth factor signaling and intracellular transport, 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 Stenmark, Sandvig, Wiedlocha and Rusten have been associated with a Centre of Excellence, Centre for Cancer Biomedicine, which ended in August 2017. In addition, Kirsten Sandvig heads a national project on Biodegradable Nanoparticles in Cancer Diagnosis and Therapy, and Harald Stenmark heads the Norwegian Advanced Light Microscopy Infrastructure Network.

DEPARTMENT OF MOLECULAR CELL BIOLOGY

INTRACELLULAR TRANSPORT

GROUP LEADER:
KIRSTEN SANDVIG

ALL THE WAY FROM BASIC RESEARCH TO TRANSLATION

ABOUT

Sandvig's group, counting 17 members, is interested in the mechanisms of endocytosis, intracellular transport and secretion. Uptake of receptors and ligands and correct intracellular sorting of endocytosed molecules are crucial for maintenance of a normal differentiated phenotype. In some studies we are using protein toxins such as ricin and Shiga toxin, which are well established as markers for studies of membrane traffic, and which can be used as agents in cancer diagnosis and therapy. Our expertise is also applied to investigate uptake of nanoparticles, and in 2013 we obtained a five year grant from the Norwegian Research Council to build national competence in nanomedicine. This project, "Biodegradable nanoparticles in cancer diagnosis and therapy", headed by Sandvig, involves collaboration with ten other Norwegian groups working in academia, research institutes, hospitals and industry. The Sandvig group is also involved in an INNO INDIGO granted project, which started April 2016. INNO INDIGO is an innovation-driven initiative for the development and integration of Indian and European research. We also characterize exosomes from prostate cancer cells and patients with the goal of detecting lipid, RNA and protein biomarkers. Our research spans all the way from basic to translational medicine, including innovation. The work published by the Sandvig group is well cited, and Sandvig's H-index is now 72 (~330 publications). The group has extensive national and international collaborations. It has four project groups, led by Alicia Llorente, Tore-Geir Iversen, Tore Skotland and Sascha Pust.

AIMS

The projects aim at increasing our knowledge about intracellular transport, nanoparticles, and 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

Modulation of endocytic mechanisms by lipids and studies of retrograde transport in cells, further studies of exosome biogenesis and release, as well as biomarkers for prostate cancer, and cytotoxic effects of different types of nanoparticles. In 2017 the group published 19 articles, and one Ph.D. student finished her degree. Concerning innovations, see separate paragraph.

CANCER MOLECULAR MEDICINE

GROUP LEADER:
JORRIT ENSERINK

IDENTIFYING WEAK POINTS IN THE MOLECULAR NETWORKS THAT DRIVE CANCER

ABOUT

The group, which started recently at the Institute for Cancer Research (November 2016), currently consists of one adjunct professor, two externally funded senior scientists, seven post-docs, one clinician in a 20% post-doc position, three PhD students, two MSc students and two Erasmus students. All but two of the group members are recruited from abroad, i.e. Ethiopia, France, the Netherlands, Austria, Spain and the UK. The group is mainly focused on basic cancer biology and personalized medicine, using a wide range of models such as budding yeast, fruit flies and zebrafish, 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. The main focus is on hematopoietic cancers, including –but not limited to– Acute Myeloid Leukemia (AML).

PROJECTS

- High-throughput drug screens on primary AML blast cells to identify correlations between driver mutations and drug sensitivity profiles
- Development of a novel small-molecule immune checkpoint inhibitor
- Modeling of leukemia in fruit flies to better understand the genetic networks that drive AML
- Genome-wide CRISPR-Cas9 screens in CML cells to identify novel mechanisms of resistance to tyrosine kinase inhibitors
- Cellular responses to nutrient stress; particularly the role of Sumo in promoting cell proliferation, and identification of the upstream pathways that control the dynamics of autophagy

ACHIEVEMENTS

Four Erasmus-sponsored MSc degrees were completed. The group is a founding member of the Norwegian Center of Excellence “CanCell”, which was awarded in 2017. Funding obtained: a grant from The South-Eastern Health Authorities. The group published seven articles.

DEPARTMENT OF MOLECULAR CELL BIOLOGY

TUMOR-HOST BIOLOGY

GROUP LEADER:
TOR ERIK RUSTEN

TUMOR-HOST INTERACTIONS DURING CANCER PROGRESSION

ABOUT

The research group counts 6 members representing 6 nationalities in 2017 (Iran, Finland, Switzerland, India, Ireland and Norway): 1 group leader, 1 scientist, 2 post docs and 2 PhD students.

Cancer can be viewed as animal development derailed. Our overarching interest is to understand the mechanisms by which tumor and host cells mutually engage each other in reciprocal interactions to facilitate carcinogenesis. These interactions occur locally in the tumor microenvironment, but also systemically causing organ dysfunction such as in cancer cachexia - the catastrophic wasting of muscle and adipose tissue. We believe that studying these processes can uncover new ways to intercept carcinogenesis.

To this end, 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 animal model system, the fruit fly Drosophila melanogaster. We collaborate with national and international experts in cell biology, electron microscopy, genetics, transcriptomics and metabolism to reach our goals.

AIMS

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

PROJECTS

- Oncogene-induced epithelial disintegration and invasion.
- Tumor-microenvironment interactions and growth support.
- Mechanisms of cancer cachexia.

RECENT ACHIEVEMENTS

Discovery that malignant tumors induce a stress response in the tumor microenvironment that supports tumor growth through nutrient-generating autophagy (Katheder, N.S., et al, Nature 2017). The tumor suppressor LKB1,responsible for the Peutz-Jegher cancer syndrome, is controlled by endocytic vesicle trafficking and its derailment contributes to tumor growth (O´Farrell, F. et al Nature Cell Biology, 2017).

CELLULAR MEMBRANE DYNAMICS

GROUP LEADER:
HARALD STENMARK

DIVING INTO CELLULAR MEMBRANES TO FIND THE KEYS OF CANCER

ABOUT

The group studies the dynamics of cellular membranes and tries to understand their relevance to cancer. Cellular membrane dynamics processes studied by the group include endocytosis, autophagy, and cell division. The group employs advanced molecular biology methods in combination with biochemistry and advanced light and electron microscopy technologies. As model systems the group uses cell cultures, organoid models, fruit flies and zebrafish.

The group is headed by Harald Stenmark (group leader) and Camilla Raiborg (assistant group leader). Its 5 project groups are led by Andreas Brech, Kaisa Haglund, Camilla Raiborg, Kay O. Schink and Eva Wenzel. The staff consists of 1 group leader, 5 project leaders, 2 researchers, 10 postdocs, 4 PhD students, 4 technicians, 1 laboratory assistant and 2 visiting students.

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

- Interplay between membrane dynamics and cell signalling in carcinogenesis
- Phosphoinositides in regulation of membrane dynamics
- Centrosome dynamics in cancer
- Cytokinesis in development and carcinogenesis
- The β-catenin destruction complex in physiology and cancer
- Membrane dynamics in promotion of genome integrity

RECENT ACHIEVEMENTS

- In a recent study we showed that the PI3P-binding proteins Protrudin and FYCO1 cooperate to mediate translocation of late endosomes towards the plasma membrane for stimulation of protrusion outgrowth (Raiborg et al., Nature 2015). We have now found that PI3P acts upstream of growth-promoting TOR signalling through mediating lysosome translocation close to the plasma membrane (in the proximity to signalling receptors), thus providing a new concept in control of metabolic signalling (Hong et al., J. Cell Biol. 2017).
- Together with peers at Oslo University Hospital and University of Oslo, we have succeeded in obtaining funding from the Research Council for a new Centre of Excellence, Centre for Cancer Cell Reprogramming (CanCell).
- One PhD student was graduated in 2017 (Liliane Christ), and 19 papers were published by group members.

DEPARTMENT OF MOLECULAR CELL BIOLOGY

PROTEIN INTERNALIZATION AND SIGNALING

GROUP LEADER:
ANTONI WIEDLOCHA

SEARCHING FOR MOLECULAR TARGETS IN FGF-RELATED MALIGNANCIES

ABOUT

The group is composed of 6 members from 3 nationalities (1 group leader, 1 researcher, 3 postdocs, 1 Ph.D. student; 3 men, 3 women). Maintenance of tissue homeostasis depends on complex intercellular growth factor/ growth factor receptors- mediated signaling networks that control basic cell functions. The fibroblast growth factor (FGF) signaling system represents one of the fundamental tools of such cell-to-cell communication. The signaling system exerts a powerful combination of biological effects during development and in maintaining a malignant phenotype. FGF/FGFR signaling is strongly oncogenic once the tight regulation on its physiological function is lost; it is enabled to be a central driver of tumor progression. FGFs as well as their receptors are frequently and abundantly expressed in various cancers and recognized as mediators of the epithelial-mesenchymal transition, tumor cell survival, migration/ metastasis and neoangiogenesis, Therefore, the interest of FGF-induced signaling as a promising target for cancer therapy has systematically been increasing.

AIMS

The main goal of the research group is to elucidate differences in mechanisms of signaling induced by the FGF/FGFR axis in normal tissue and in progression of tumors.

PROJECTS

- Activation and downregulation of FGF/FGFR induced signaling
- Endocytosis, sorting and intracellular transport of FGF1 and FGFRs
- Mechanisms of FGF-induced malignant phenotype
- Targeted therapy for FGFR-expressing cancer – experimental approach

RECENT ACHIEVEMENTS

Using proteomic approaches, we found that FGFR4 uses clathrin-mediated endocytosis for internalization and that FGFR4 can recycle back to surface also through the trans-Golgi network (Haugsten E.M., et. al., J. Proteome Res., 2016). We have also elucidated that PTPRG, a membrane bound tyrosine phosphatase, is an important modulator of FGFR tyrosine kinase activity, by dephosphorylation of the activated FGFR1. Since PTPRG depletion elevated cell growth and negatively affected the efficacy of FGFR1 kinase inhibitors, the phosphatase may have future clinical relevance by being a predictor of outcome after FGFR inhibitor treatment (Kostas M., et al. under review).

BIOLOGICAL DISCOVERIES FOR PRECISION CANCER MEDICINE

DEPARTMENT OF

MOLECULAR ONCOLOGY

HEADED BY: **RAGNHILD A. LOTHE**

As a research department within the Oslo University Hospital (OUH) Comprehensive Cancer Centre, it is our responsibility and goal to accomplish high quality and interdisciplinary biomedical research for improved precision medicine and management of cancer patients. Our main research programs are devoted to colorectal cancer and prostate cancer, and we have a longstanding project portfolio also on other solid tumor types. Our expertise in biomedical research spans several disciplines from cell biology to translational research, including also active partnerships in clinical studies, and we have a broad range of advanced technologies and analytical tools established in-lab. The department scientists are inventors of several biomedical patents and active innovation projects.

All three group leaders are adjunct professors at the University of Oslo and are affiliated with the Institute for Clinical Medicine, the Institute for Biosciences and the Institute for Informatics. The scientists in the department are devoted to teaching and supervision, and a minimum of three academic degrees are completed annually; 53 MSc/PhD degrees have successfully been completed since the inauguration of the department in 2006.

The research groups are partners of the K. G. Jebsen Colorectal Cancer Research Centre, the OUH priority area for colorectal cancer (both led by Prof. Lothe), the Norwegian Cancer Genomics Consortium, and several international networks including the European network for study on Cholangiocarcinoma, the Global Testicular Cancer Consortium, and Cooperation Studies on Colorectal Cancer (COST action).

During the past 3-years, we have published 55 scientific papers, with 1st and/or last authorships on 58% and with a mean IF of 6.1. Six PhD and 8 MSc students with supervisors from the department received their academic degrees.

Our main research focus for the next three to five years is three-fold, (i) to explore spatio-temporal tumor heterogeneity in colorectal cancer and prostate cancer, (ii) to monitor minimal residual disease and tumor evolution by parallel analyses of repeated liquid biopsies and tumor samples, and (iii) combine genomics with ex vivo drug screening of tumor cell-derived organoid cultures to predict treatment response in translational studies and within clinical trials.

DEPARTMENT OF MOLECULAR ONCOLOGY

GENETICS

GROUP LEADER:
RAGNHILD A. LOTHE

GENOMICS – IRREVERSIBLE MISTAKES IN CANCER AND A SOURCE FOR CLINICAL BIOMARKERS

ABOUT

Our main research program is translational studies of primary and metastatic colorectal cancer (CRC). The group has 24 employees (9 postdocs/scientists, 9 PhD students, 6 research assistants/engineers) and 1 current MSc student, and includes two project groups in Cell signaling (Edward Leithe) and Computational oncology (Anita Sveen).

AIMS

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

PROJECTS

- Prognostic and predictive biomarkers (CRC and malignant peripheral nerve sheet tumors, MPNST)
- Modeling tumor heterogeneity and clonal evolution in primary and metastatic CRC
- Pharmacogenomics of preclinical models
- Ex vivo drug screening of tumor organoids derived from metastatic CRC
- E3 ubiquitin ligases in intercellular communication and CRC pathogenesis

RECENT ACHIEVEMENTS

Most resources were put into the genomics and pharmacogenomics projects, and two international collaborative papers with clinical implications were published from our lab last year. In a multi-omics study focused on microsatellite instable CRC, we discovered a large degree of tumor heterogeneity with potential implications for response to immunotherapy and prognostic assessment (Sveen et al., Genome Med 2017). Pharmacogenomic analyses combining gene expression subtyping and drug screening of cell lines and patient-derived xenografts identified HSP90 inhibitors as potent drugs to overcome chemoresistance in patients with an aggressive subtype of CRC. (Sveen*, Bruun* et al. Clin Cancer Res 2017). In addition we successfully established a protocol for tumor-organoid cell culturing from resected liver metastases followed by drug screening (to be published).

A recent project studying E3 ubiquitin ligases in cancer development found NEDD4 to act oncogenic by reducing cell communication (Totland et al., J Cell Science 2017).

Three papers were published for the purpose of data sharing in the scientific community (Berg et al., Mol Cancer 2017; Sveen et al., CCR 2017; Eide et al., Scientific Rep 2017).

A US patent was granted for a prognostic gene signature for stage III CRC, Anita Sveen received the YI prize at the National Annual Meeting for Oncologists, and Tone Fykerud defended her PhD and Marthe N Thorsen completed her MSc.

EPIGENETICS

GROUP LEADER:
GURO E. LIND

EPIGENOMICS – REVERSIBLE CHANGES IN CANCER AND A SOURCE FOR CLINICAL BIOMARKERS

ABOUT

In the group of Epigenetics we are studying DNA methylation alterations by integrating methylome sequencing with detailed candidate gene characterization. The research is performed across cancer types, with a main focus on colorectal and urological cancer. In 2017 the group counted ten members, including three postdocs, one PhD student, two engineers, three MSc students and the group leader.

AIMS

1) To identify epigenetic biomarkers with clinical impact, including markers for early detection and monitoring of cancer.
2) To analyze and understand the underlying biology of these aberrations and how they affect the cancer development.

PROJECTS

- Epigenetic subclassification and prognostic markers for colorectal cancer
- Mechanisms of the DNA methylation machinery
- Methylome-based early detection and monitoring of urological cancers
- Identification of epigenetic drivers of tumor development

RECENT ACHIEVEMENTS

The digital PCR technology allows absolute quantification of nucleic acids, and has great potential for DNA methylation analyses of liquid biopsies. However, lack of standardization has so far limited the use of this method (see Editorial in Epigenomics, Lind GE and van Engeland M, 2017). We have developed a robust internal control and an accompanying scoring algorithm that solves the challenges and ensures consistent results. The work has resulted in two patent applications. A US patent was granted for VIM in bladder cancer. Using methylome sequencing in combination with the standardized digital PCR technology, we have identified novel DNA methylation biomarkers for non-invasive monitoring of bladder cancer. In urine from bladder cancer patients and healthy controls* the biomarker panel has a sensitivity of 97% and specificity 100%. To evaluate the accuracy of the panel in detecting recurrence of bladder cancer, we are, in collaboration with the Wahlqvist team at Aker, following a group of post-surgery individuals for two years.

We have demonstrated prognostic value of the epigenetic phenotype CIMP, which can stratify the microsatellite stable/BRAF mutated poor prognostic group of colorectal cancer patients (Vedeld et al., Int J Ca 2017). An overview of epigenetic biomarkers in gastrointestinal cancer was presented in Semin Cancer Biol (Vedeld et al., 2017). Mariella Güere completed her MSc.

*Thanks to colleagues at the Institute who contributed to the control group

DEPARTMENT OF MOLECULAR ONCOLOGY

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. Mutation analyses in cancer clearly benefit from knowing which genes and variants that are actually expressed. In this line, the group has particularly specialized in RNA-level analyses, and the projects focus on prostate cancer, although we are also involved with projects on testicular and colorectal cancers. An interdisciplinary set of competences is required to perform meaningful genome-scale cancer research. As such, personnel in the group have their basic education across the disciplines of biology, informatics, and medicine. Through 2017, the group consisted of ten members, including three postdocs, two engineers, two PhD students, one MSc student, a study nurse and the group leader.

AIMS

The research aim is to identify and characterize genes that are critical for development of cancer. Such genes may serve as diagnostic or prognostic biomarkers and as targets for future molecularly tailored therapy.

PROJECTS

- Genome-based prostate cancer biomedicine
- Fusion transcripts and other qualitative RNA variation in cancer
- Modelling heterogeneous solid tumours from multi-omics data

RECENT ACHIEVEMENTS

During 2017, the group continued the development of a large prostate cancer research program, primarily utilising a biobank resource with multiple frozen tissue cores from multifocal primary prostate cancer. Large effort has been spent on processing of tissue samples, isolation of nucleic acids, generation of genomics and transcriptomics data. A postdoc in the group, Andreas M. Hoff, spent twelve months at the Broad Institute, a world-leading site for genomics technologies, where he for example worked on structural genome changes and mutation analysis from cell-free DNA derived from plasma samples. The group continued to develop bioinformatics pipelines for high-throughput sequencing of DNA and RNA and utilized these in analyses of data from several cancer cohorts. For example, the group identified a set of fusion transcripts which are overexpressed in prostate cancer (Zhao *et al.*, Oncotarget). Further, a novel software has been developed for visualizing fusion transcripts (Lågstad *et al.*, Bioinformatics). Altogether, seven papers were published during 2017, including the two abovementioned papers with first and/or last authors from the research group. In 2017, Kristina Totland Carm completed her MSc degree.

OUR GOAL IS TO DEVELOP NEW PREDICTIVE METHODS AND TREATMENT STRATEGIES FOR IMPROVED RADIATION THERAPY

DEPARTMENT OF

RADIATION BIOLOGY

HEADED BY: **KRISTIAN BERG**

The Department has more than 60 employees organized in 4 research groups and 6 project groups. The research at the department is focused on the biological responses to ionizing and non-ionizing radiation, including γ-radiation, radiation from radionuclides, ultraviolet radiation, visible light as well as proton therapy. Our department is actively engaged in revealing the mechanisms involved in DNA repair, cell-cycle regulation, genomic instability and immune responses after radiation, the impact of hypoxia on the radiation response and predictive markers for the outcome of radiotherapy of cancer patients. The department is also involved in delivering radionuclides to cancer tissue. Another research area is the use of visible light to activate photosensitive compounds that are used for cancer detection and therapy. In that respect a technology has been developed, photochemical internalization (PCI), which may be utilized for site-directed intracellular delivery and activation of therapeutics into cancer cells. This technology induces reactive oxygen species that has similarities to the biological response to ionizing radiation. Our vision is to develop a radiobiological understanding of response to ionizing and non-ionizing radiation on the molecular, cellular and physiological level, and to utilize this knowledge to design new strategies for the treatment of cancer. Our research strategy involves basic radiobiological research, translational and clinical studies.

OUR GOALS ARE

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

KEY ACHIEVEMENTS THE LAST 3-4 YEARS INCLUDE

- Novel patient-derived xenograft models of carcinoma of the uterine cervix showing functional intratumoral lymphatics have been established and characterized
- Increased knowledge about how Chk1 and Wee1 inhibitors work to kill cancer cells
- PCI has been found efficient as a methodology to enhance antigen presentation during anti-cancer vaccination. Several new recombinant targeted protein toxins have been developed and are under preclinical evaluation. A phase I clinical trial documenting the safety and efficacy of PCI has been published in Lancet Oncology
- A production unit for biomolecular therapeutics has been established
- A new method to image hypoxia in prostate cancer based on integration of images reflecting oxygen consumption and supply has been developed
- We gained important new knowledge about the regulation of translation in response to cellular stress as well as about the function of the stress-response kinase GCN2 in human cells

DEPARTMENT OF RADIATION BIOLOGY

PHOTOCHEMICAL INTERNALIZATION

GROUP LEADER:
KRISTIAN BERG

OUR GOAL IS TO DEVELOP AND OPTIMIZE THE PCI TECHNOLOGY FOR TREATMENT OF SOLID CANCERS

ABOUT

Group members: 17, including 5 researchers, 2 postdocs, 3 PhD students and 6 technical positions, including the project groups of Asta Juzeniene, Pål Kristian Selbo, Anette Weyergang and Theodossis Theodossiou.

Endocytic entrapment is a hurdle for therapeutic utilization of macromolecular therapeutics with intracellular targets. Photochemical internalisation (PCI) is a technology for release of endocytosed therapeutic macromolecules into the cells cytosol that has been development from experimental studies to clinical evaluation.

Project *Radionuclide therapy (project leader Juzeniene)*: Targeted radionuclide therapy, based on systemic, regional or local application of radiopharmaceuticals alone or in combination with a cell-targeting molecule, are developed to improve patient's quality of life, prolong survival and may even lead to cure.

AIMS

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

Project *Radionuclide therapy*:

The main goal is to optimize alpha radionuclide delivery and to study its efficacy for treatment of bone, lung and peritoneal micrometastases.

PROJECTS

- Design and development of recombinant immunotoxins for activation by PCI
- Light-controlled delivery of cancer immunotherapeutics including PCI of 1) immunotoxins targeting cancer stem cells (CSCs) and 2) CSC-derived vaccines.
- Utilize new vehicles for targeted delivery of small molecular drugs to endocytic vesicles for activation by PCI
- Evaluation of the vasculature as a target for PCI and further utilize these effects to reach a curative endpoint
- A novel therapy for osteosarcoma by dual targeted alpha particle radiation
- Targeted alpha radionuclide therapy for bone metastasis of prostate and breast cancer
- Alpha-emitting ^{224}Ra-labeled microparticles for the treatment of intraperitoneal ovarian cancer

RECENT ACHIEVEMENTS

- Documented the anti-tumor immunity potential of PCI of bleomycin.
- Established a biomolecule production unit based on recombinant technology.
- New grants in 2017: Protonics (Open project support, Theododdiou);
- Researcher stipend (Selbo), 1 PhD (HSØ)
- Three project groups were established in 2017
- No. of papers in 2017: 10
- PhD thesis: 1
- MSc thesis in 2016: 1

CLINICAL RADIATION BIOLOGY

GROUP LEADER:
HEIDI LYNG

OUR GOAL IS TO DISCOVER BIOMARKERS AND MOLECULAR TARGETS FOR COMBINATION THERAPIES WITH RADIATION

ABOUT

Group members: 11, including one researcher, five postdocs, two PhD students, one master student and two technicians.

The focus is to develop molecular biomarkers that can identify patients at risk of radiotherapy failure and to find targets for therapeutic intervention in a combined radiotherapy regimen. The research projects are run in close collaboration with medical doctors and physicists. 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. In collaboration with Department of Medical Physics, 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 radiotherapyof 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 2017, the group has published 4 articles.
One PhD student (Jonsson) achieved her degree with the thesis: Hypoxia-induced aggressiveness in cervical and prostate cancer with special emphasis on gene regulation, metabolism and biomarkers.

One master student (Gjølberg) graduated with the thesis: Phenotypic changes following upregulation of miR-105-5p, miR-767-5p and miR-6499-5p in SW756 cervical cancer cell lines.

We received HSØ grant to establish regional research network in precision radiotherapy, a collaborative effort between researchers (radiobiologists, medical physicists and medical doctors) at Sørlandet Hospital, Innlandet Hospital and OUH.

DEPARTMENT OF RADIATION BIOLOGY

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: 10, including 2 researchers, 4 postdocs, 2 PhD students, and 2 technicians.

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 physiological 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 physiological 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 physiological microenvironment, metastatic propensity, and radiocurability of tumors
- To develop treatment strategies for normalizing the physiological microenvironment, decreasing the metastatic propensity, and enhancing the radiocurability of tumors

PROJECTS

- Clinical MRI of locally-advanced cervical carcinoma
- Preclinical MRI of cervical carcinoma, pancreatic carcinoma, and malignant melanoma
- Antiangiogenic and antifibrotic treatment of tumors
- Mechanisms governing the physiological microenvironment of tumors

RECENT ACHIEVEMENTS

The group published 10 papers in 2017. In these papers, we report novel relationships between

(a) parametric images obtained by dynamic contrast-enhanced MRI and the outcome of cervical cancer patients treated with chemoradiotherapy,
(b) parametric images obtained by dynamic contrast-enhanced and diffusion-weighted MRI, tumor hypoxia, and tumor extracellular matrix,
(c) lymph node metastasis, pulmonary metastasis, and the physiological tumor microenvironment,
(d) tumor angiogenic signature and effect of antiangiogenic treatment, and
(e) tumor hypoxia and microvessel architecture.

RADIATION BIOLOGY AND DNA DAMAGE SIGNALING

GROUP LEADER:
RANDI G. SYLJUÅSEN

OUR GOAL IS TO OBTAIN NEW KNOWLEDGE ABOUT CELLULAR RESPONSES TO RADIATION AND UTILIZE IT TO IMPROVE CANCER THERAPY

ABOUT:

Group members: 12 including 3.9 researchers, 3 postdocs, 2.8 PhD students and 2.3 technicians.

Theme: In radiotherapy ionizing radiation is used to cause DNA damage in cancer cells. The DNA damage is rapidly sensed and a network of intracellular DNA damage signaling cascades is activated. These signaling cascades influence whether the cells die or survive, through regulation of DNA repair, cell cycle checkpoint and cell death pathways.

Our group works on the border between basic and translational radiation research. We conduct basic projects to identify novel mechanisms of DNA damage checkpoint signaling, in addition to more applied projects to understand how inhibitors of checkpoint signaling can be used in an optimized manner for cancer treatment. Two project groups, headed by Beata Grallert and Trond Stokke, are members of our group.

AIMS

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

PROJECTS

- Pre-clinical exploration of the effects of checkpoint kinase (CHK1, WEE1, ATR) and PARP inhibitors
- The functional role of Protein phosphatase 1 (PP1) targeting subunits in DNA damage checkpoint signaling
- Identification of promising DNA damage combination treatments through flow cytometry-based large-scale compound screens
- Centrosomal and ciliary proteins in cell cycle regulation and genome integrity – roles and targets in cancer etiology, diagnostics and treatment
- The role of GCN2 and translational regulation in the cell cycle and cellular stress

RECENT ACHIEVEMENTS

In 2017 the group published 6 articles. Members of the group were senior author on 3 of these (published in Oncotarget, Journal of Cell Science, Plos One). One PhD student graduated in 2017 (C. Rothe: "Regulation of Cdk activity in the cell cycle"). In December 2017 the group obtained grants from the Norwegian Research Council (FRIPRO) and the South-Eastern Norway Regional Health Authority.

PRECLINICAL AND CLINICAL EFFORTS TOWARDS PRECISION ONCOLOGY

DEPARTMENT OF TUMOR BIOLOGY

HEADED BY: **GUNHILD M. MÆLANDSMO**

The department has four research groups and 56 employees with a common vision to better understand the biological mechanisms involved in cancer progression and metastasis. Our strategy is, through basic and translational research in the areas of cancer biology and computational science, to enhance systems understanding and thereby 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 xenograft models from different types of human cancer. The models are utilized for biological studies of disease progression, and for preclinical evaluation of novel drugs and drug combinations.

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 large collaborative projects in the area of precision cancer medicine:

NCGC - The Norwegian Cancer Genomics Consortium, a national project aiming to sequence tumors across nine tumor types. Currently most of the exomes have been sequenced and are being analyzed. Several papers are now under publication.
NoSarC - Norwegian Sarcoma Consortium, a national project aiming to collect a prospective biobank and study disease development and treatment of sarcoma. Exome sequencing is ongoing and preclinical models are generated for studies of candidate drugs.
MetAction - Actionable targets in cancer metastasis. An efficient diagnostic pipeline has been established in this first clinical trial in Norway offering treatment based on targeted NGS data. 50 patients were enrolled and in 11 cases treatment was commenced.
MOVEMBER - Identifying biomarkers distinguishing indolent and aggressive prostate cancer. Candidate biomarkers have been identified using Norwegian cohorts of serum, urine and tissue, and are currently undergoing validation in independent national and international cohorts.

Other clinical studies with substantial collateral research;
NeoAva: Bevacizumab in combination with neoadjuvant chemotherapy in breast cancer (patient inclusion ended)
I-BCT: DNA targeted chemotherapy to breast cancer patients with an aggressive phenotype
ImmunoPeCa: Immunotoxin in Peritoneal Carcinomatosis
Biobank Norway - a national initiative to coordinate biobank activities for research purposes

DEPARTMENT OF TUMOR BIOLOGY

METASTASIS BIOLOGY AND EXPERIMENTAL THERAPEUTICS

GROUP LEADER:
GUNHILD M. MÆLANDSMO

CONTEXT-INDUCED CELLULAR PLASTICITY - THE ROUTE TO RESISTANCE AND METASTASIS

ABOUT

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

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

Project groups:
Kristin Austlid Tasken – Urological Molecular Biology
Lina Prasmickaite – Tumor stroma interactions in metastasis and resistance

AIMS

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

PROJECTS

1. Basic research revealing mechanisms causing treatment resistance and metastasis
   - Metastasis associated proteins and regulators, with special emphasis on tumor-stroma interactions and effects on cellular plasticity (cancer cell invasion, metabolic reprogramming and immune responses)
2. Preclinical research investigating novel drugs and drug combinations
   - Mechanistic studies and assessment of treatment efficacy in patient-derived xenografts
   - Biomarker detection by molecular and functional techniques
   - Response evaluation of experimental drugs (often in collaboration with commercial partners, *eg.*: Lytix Biopharma, Arctic Pharma/Biomolex, Oncoinvent)
3. Clinical trials in precision medicine
   - NeoAva: bevacizumab in combination with neoadjuvant chemotherapy for patients with locally advanced breast cancer (patient inclusion closed)
   - I-BCT: extended DNA-targeted chemotherapy to breast cancer patients with an aggressive phenotype
   - MetAction: Actionable target identification in metastatic cancer for palliative targeted treatment (patient inclusion closed)

RECENT ACHIEVEMENTS

- Metrics: Group members were credited with 14 publications in 2017, of which five with group members as first and/or last author; two PhD degrees and two Master degrees completed
- Successful establishment of the MetAction diagnostic pipeline allowing treatment decisions based on targeted NGS-data (50 enrolled patients)
- One clinical intervention trial open for inclusion (I-BCT)

TRANSLATIONAL CANCER THERAPY

GROUP LEADER:
KJERSTI FLATMARK

NEW TREATMENT FOR METASTATIC COLORECTAL CANCER

ABOUT

The Translational Cancer Therapy group comprises 16 members with a broad variety of expertise, including students, 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 develop new, efficacious treatment(s) for colorectal cancer (CRC). This will be accomplished by bringing the clinic and lab together in translational research projects utilizing 1) preclinical models for efficacy and mechanistic studies 2) clinical cohort studies to understand CRC biology and identify biomarkers and therapeutic targets 3) clinical intervention trials to test new drugs and therapeutic concepts in patients

PROJECTS

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

RECENT ACHIEVEMENTS

- Group members were credited with 24 publications in 2017; 1 masters degree was completed
- Successful completion of the MetAction study, including establishment of the diagnostic pipeline enabling treatment decisions based on targeted NGS-data for 50 enrolled patients
- Successful completion of the ImmunoPeCa trial investigating intraperitoneal administration of MOC31PE immunotoxin in patients with resectable peritoneal metastases from CRC
- Successful completion of the first of its kind Laparoscopic Versus Open Resection for Colorectal Liver Metastases: The OSLO-COMET Randomized Controlled Trial.
- Preparations for the multicenter METIMMOX trial have been completed and the trial will start accrual in March 2018
- Preparation of a COST action proposal for the Cure4PMP European Research Network

DEPARTMENT OF TUMOR BIOLOGY

COMPUTATIONAL CANCER GENOMICS

GROUP LEADER:
EIVIND HOVIG

ENABLING THE TRANSITION TO CLINICAL UTILITY

ABOUT

The 10-member group has strong interest in the development of computational approaches in cancer genomics in general, and in melanoma systems biology, with an emphasis on the MITF master switch of melanocytes. Currently, activity is centred on computational aspects of deep sequencing for cancer, with downstream analysis. The group facilitates precision cancer medicine towards the clinic, leveraging the participation in the BIGMED RCN-financed ICT lighthouse project.

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

AIMS

We aim to

- apply and develop novel methodology for computational studies of cancer-related processes, including statistical genomics, 3-dimensional DNA conformation, drug prediction algorithms and mutational processes
- contribute insight on heritable cancer-predisposing DNA-variation in the Norwegian population
- characterize the geographical stratification aspects of the Norwegian population
- develop solutions for precision cancer medicine towards the clinic
- understand signaling processes in melanoma

PROJECTS

- Development of solutions for integrative cancer sequencing towards diagnostics, and participation in international efforts for development of best practice methods, including being computational leaders of the Norwegian Cancer Genomics Consortium, partner of the BIGMED ICT lighthouse and of Elixir Norway, and participates in the Center of Innovation Excellence Big Insight for the knowledge economy.
- Further development of statistical genomics based on our software, the Genomic HyperBrowser. This is an internationally used tool for multipurpose integrated statistical analysis of genomic data.
- Melanoma signaling perturbations for systems understanding, including MITF, BRAF and CDKN2A aberrations
- Understanding the consequences for modulation of immune responses in melanoma
- Familial cancer project, including a close collaboration with deCODE, Iceland

RECENT ACHIEVEMENTS

- Group members were credited with 18 publications in 2017, of which 7 with group members as first and/or last author.
- 2 Master degrees were completed
- Pink ribbon funding was obtained

MOLECULAR BIOLOGY OF SARCOMA

GROUP LEADER:
JØRGEN WESCHE

USING PRECISION MEDICINE TO IMPROVE TREATMENT OF SARCOMAS

ABOUT

The 15-member group has a long standing interest in the biology of mesenchymal tumors (sarcomas). Jørgen Wesche started as a new group leader 1st of April 2017. The group was previous led by Heidi Maria Namløs and Ola Myklebost. The current focus is on precision medicine for sarcomas. To achieve this, the group has broad expertise in basic cell biology and translational research and, in addition, one MD in a shared clinical position.

AIMS

As an overall approach, the group is combing genetic characterization by deep genomic analysis of patient material with preclinical investigation in cell cultures and human tumor models in mice. The generation and characterization of in vitro and in vivo sarcoma models make the framework for the pre-clinical analyses. Sarcomas are rare cancers, with poor treatment options, and can gain much from personalized cancer treatment. The choice of treatment would be based on the tumor's mutations, opening for the opportunity to use treatments currently approved for other cancers with similar mutations. The ultimate aim is to work towards future precision medicine for sarcomas.

PROJECTS

- Norwegian Sarcoma Consortium (NoSarC) – Biobanking and genomic characterization of patient material of 2-3 national cohorts of sarcomas, estimated to at least 500 samples. The project will provide unique, population based datasets including the many rare subtypes of sarcomas.
- Preclinical investigation – Using in vitro and in vivo models to evaluate the therapeutic potential of drugs that target mutations identified in patient tumors.
- Sarcoma cell biology – Gaining further understanding of development and progression of rhabdomyosarcoma, liposarcoma and osteosarcoma, and potentially identify biomarkers and novel drug targets.
- Establishment of ex-vivo drug sensitivity/resistance screen for sarcoma primary tumors, and search for novel anti-sarcoma drugs using drug screens on panels of liposarcoma and osteosarcoma cell lines.
- Implementation of sequencing in diagnostics.
- Exploration of "liquid biopsies", the detection of tumor-derived DNA in blood, to monitor disease progression and therapeutic markers.

RECENT ACHIEVEMENTS

Publications: 13
2 master degrees and 1 PhD completed.

PROVIDING STATE-OF-THE-ART TECHNOLOGY AND COMPETENCE TO EXCEL RESEARCH

DEPARTMENT OF

CORE FACILITIES

ACTING HEAD: **TROND STOKKE**

The Department of Core Facilities runs seven regional and national technology platforms financed by the South-Eastern Regional Health Authorities and the Research Council of Norway, providing advanced services to regional, national and international users. The Department aims to deliver easy access to state-of-the-art advanced technologies, to improve research quality through assistance by experienced personnel and optimal choice of technology, and ultimately increase the scientific competitiveness of our users. The Department of Core Facilites is organized in six units; Flow Cytometry, Pre Clinical Imaging, Advanced Light and Electron Microscopy, Genomics, and Bioinformatics, with a total of 19 employees. In 2016, the Genomics and Bioinformatics units relocated to the new Oslo Cancer Cluster Innovation Park, colocalising their activities with the Section for Molecular Diagnostics at Oslo University Hospital. This strategic move aims to facilitate the implementation of sequencing-based molecular cancer diagnostics. More information at: www.ous-research.no/corefacilities.

ADVANCED LIGHT MICROSCOPY

Ellen Skarpen
Facility staff: 2

The Core Facility for Advanced Light Microscopy (ALM) offers services in various types of ALM, including confocal microscopy, live-cell microscopy and superresolution microscopy. Current instruments include a Zeiss LSM710 confocal microscope and an OMX Blaze microscope for structured illumination and STORM super-resolution imaging, as well as live-cell microscopy. The core facility cooperates with nodes at the Rikshospitalet and Ullevål campuses of OUH, as well as the light microscopy core facility at the Institute for Biosciences, University of Oslo. The core facility for ALM is a Eurobioimaging node, providing state-of-the-art technologies in the fields of biological and medical imaging. Services include training, courses, access to microscopes and microscopy performed by core facility personnel.

ADVANCED ELECTRON MICROSCOPY

Ellen Skarpen
Facility staff: 1

The Core Facility for Advanced Electron Microscopy includes nodes at the Radium Hospital and Rikshospitalet, and provides service, training and access to microscopes for ultrastructural studies. The core facility offers a wide range of techniques including conventional plastic embedding, immune EM, correlative light/electron microscopy (CLEM), high pressure freezing and electron tomography. Current instrumentation includes 3 transmission electron microscopes and sample preparation tools such as microtomes (cryo), high-pressure freezers and freeze substitution units. The core facility actively cooperates with the imaging platform at the Institute for Biosciences, University of Oslo.

DEPARTMENT OF CORE FACILITIES

BIOINFORMATICS

Susanne Lorenz

Facility staff: 5

The Bioinformatics Core Facility (BCF) provides service, support and advice in the field of bioinformatics. By combining biology with computer science, statistics and mathematical modelling we offer support for analysis and interpretation of biological data including genomics, transcriptomics and proteomics for basic and translational research. The BCF has a specific focus on developing and providing solutions for precision medicine and cancer-related projects. 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, to facilitate the use of high performance computing resources.

FLOW CYTOMETRY

Trond Stokke

Facility staff: 3

The Flow Cytometry Core Facility (FCCF) provides analysis and sorting services for users within the South-Eastern Health Region of Norway. Flow cytometry analysis can be performed by users themselves, as well as assisted by core facility personnel. We have 3 analyzers and two sorters with up to 6 lasers each that may measure up to 21 fluorescence parameters simultaneously. Sorting experiments are either performed by core facility staff, or by the users in the Sony SH100 sorter. The FCCF has possibilities for high-throughput screening, processing and staining of cells in 96- or 384-well plates, followed by automated analysis. We have installed a new "mass-spec flow cytometer", the CyTOF. This instrument can measure up to 50-60 parameters simultaneously at single cell resolution. The FCCF collaborates with facility nodes at the Rikshospitalet and Ullevål campuses of OUH.

GENOMICS HIGH-THROUGHPUT SEQUENCING AND MICROARRAYS

Susanne Lorenz

Facility staff: 6

The Genomics Core Facility (GCF) provides state-of-the art high-throughput genomic services to the Norwegian scientific community. The GCF offers an extensive portfolio of complex technologies to study genome structure, dynamics and function using high-throughput sequencing and different commercial microarray platforms. Our highly competent and experienced service personnel provide advanced support to clinical, translational and basic researchers. Our services include standard and custom solutions to study the transcriptome, genome and epigenome from multi-genes to genome wide level. The core facility collaborates with similar nodes at the Ullevål campus for sequencing and microarray services. The GCF is a member of the Norwegian Genomics Consortium, and the Norwegian Consortium for Sequencing and Personalised Medicine (NorSeq). The GCF provides the sequencing infrastructure and competence for the National Personalised Medicine initiative, and in 2016 has renewed its sequencing instrumentation by a large infrastructure grant financed by Research Council of Norway.

PRECLINICAL IMAGING FACILITY

Trond Stokke

Facility staff: 2

The Preclinical Imaging Facility provides access to a state-of-the-art non-invasive imaging equipment for mice and rats. The equipment is situated within the animal facility and consist 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. 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

60

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 is funded for 5 + 5 years (if recommended following a mid-term evaluation). The total basic funding is ~100 million NOK.

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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 million NOK in basic funding from the Foundation and support from the host institutions, the University of Oslo (Centre for Cancer Immunotherapy) or Oslo University Hospital (Colorectal Cancer Research Centre).

66

NORWEGIAN CANCER GENOMICS CONSORTIUM

The establishment of Norwegian Cancer Genomics Consortium was recommended by the Regional Health Authorities and the Universities. The consortium includes research groups and clinicians from the Norwegian University Hospitals, and its total basic funding is 75 million NOK received from the Norwegian Research Council.

> UNITING BASIC AND TRANSLATIONAL CANCER RESEARCH FOR THE BENEFIT OF THE PATIENT

CENTRE FOR CANCER BIOMEDICINE (CCB)

HEADED BY **HARALD STENMARK AND RAGNHILD A. LOTHE**

Centre for Cancer Biomedicine

ABOUT

CCB was a Norwegian Centre of Excellence that was funded by the Research Council of Norway from 01.09.2007 to 31.08.2017. The centre's vision was to join cell biological research aimed at discovering new mechanisms in carcinogenesis and tumour suppression with translational cancer research focusing on discovery of novel molecular and phenotypic hallmarks of cancers that can be exploited in diagnostics, prognostics and therapy. Through collaboration with CCB's experts in biostatistics, this has indeed proven to be a fruitful strategy, and CCB scientists have made several discoveries and innovations that promise to be useful for future patients with lymphoma, colorectal cancer or prostate cancer.

AIMS

- Discovery of novel mechanisms in tumour suppression and cancer development
- Discovery of novel molecular and phenotypic hallmarks of cancers that can be exploited in cancer diagnostics, prognostics and therapy

PROJECTS

- Protein internalisation and signalling
- Cellular membrane dynamics
- Intracellular transport
- Cancer genetics
- Cancer epigenetics
- Cancer genomics
- Tumour heterogeneity and clonal expansion
- Cancer Biostatistics
- Advanced image analyses

RECENT ACHIEVEMENTS

CCB's interdisciplinary research strategy has continued to yield discoveries that will benefit the future cancer patient. A paper that received considerable attention came from PhD student Nadja Katheder in Tor Erik Rusten's CCB project group. Katheder, Rusten and their co-workers published in *Nature* that tumours instruct cells in their microenvironment to turn on autophagy, a cellular process that entails degradation of some of the cell's own proteins into amino acids. These amino acids are then transported back to the tumour as constituents of new cancer cell proteins. If this mechanism is inhibited, the tumour shrinks, which provides us with a new target for future cancer therapy. These findings were dedicated commentary articles in *Cell Metabolism, Developmental Cell* and *Scientific Reports* and were covered by the news on national TV. Another project leader in CCB, June Myklebust, has, in collaboration with colleagues at Stanford revealed individual differences in B-cell receptor signalling in patients with non-Hodgkin's lymphomas that correlate with differences in therapy responses (published in *Blood*). Postdoc Hege Marie Vedeld and her co-workers in Guro E. Lind's CCB group have identified a specific DNA methylation phenotype that identifies high- risk patients among microsatellite stable BRAF mutated colorectal cancers (published in *International Journal of Cancer*). Researcher Anita Sveen and colleagues in Ragnhild A. Lothe's CCB group have analysed a large number of microsatellite-instable colorectal cancers and revealed molecular hetereogeneity with clinical relevance, including mutations that predict favourable prognosis (published in *Genome Medicine*).

CCB graduated 6 PhD candidates in the period of 01.01-31.08.2017 and published 51 articles, several of these in leading journals. During the whole 10-year centre period, CCB has graduated 61 PhD candidates and published 655 papers.

Even though CCB will not continue as a centre, key elements of CCB's research will be sustained in the form of other centres and projects. These include a new Centre of Excellence, Centre for Cancer Cell Reprogramming, KG Jebsen Colorectal Cancer Research Centre, KG Jebsen Centre for B-Cell Malignancies, Lighthouse project "DoMore", Toppforsk project "Modeling tumor htereogeneity in colorectal cancer", Toppforsk project "Deciphering tumor-host biology", and NANO2021 project ""Biodegradable nanoparticles in cancer diagnosis and therapy".

EXECUTIVE GROUP (IN 2017):

Harald Stenmark, director
Ragnhild A. Lothe, co-director
Håvard E. Danielsen
Knut Liestøl
Kirsten Sandvig
Guro E. Lind
Erlend B. Smeland

ASSOCIATE PIS:

Sverre Heim
Rolf I. Skotheim
Antoni Wiedlocha

ASSOCIATE CLINICAL RESEARCHERS:

Arild Nesbakken
Harald Holte
Karol Axcrona

OUR GOAL IS TO DEVELOP NEW THERAPEUTIC STRATEGIES THAT OVERCOME IMMUNE TOLERANCE TO TARGET CANCER

K.G. JEBSEN CENTER FOR CANCER IMMUNOTHERAPY

HEADED BY **JOHANNA OLWEUS**

STIFTELSEN KGJ Kristian Gerhard Jebsen Foundation

ABOUT

In the K.G. Jebsen Center for Cancer Immunotherapy (JCIT) hosted by the University of Oslo, five Norwegian and one Dutch research group have come together to find new immunotherapeutic strategies that overcome the major challenge of self-tolerance in cancer. JCIT was granted prolongation following the first 4-year period, throughout 2020. The partnering groups of JCIT span complementary competencies ranging from basic proteomics, cell signaling and T-cell receptor engineering to expertise in experimental clinical immunotherapy trials. This places the center in a unique position to pursue novel therapeutic opportunities, and the strong focus on translating therapeutic opportunities is a fundamental characteristic of JCIT. Results from basic research are pursued through the necessary translational steps to testing in patients, and in-depth mechanistic studies of patient material obtained in experimental clinical trials are performed with the aim of improved designs of immunotherapeutic strategies.

AIMS

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

PROJECTS

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

RECENT ACHIEVEMENTS

- Reported the first Phase I/II clinical trial based on transfer of allogeneic NK cells to patients with high-risk AML and MDS. *Clinical Cancer Research.*
- Partner Kjetil Taskén received King Olav Vs Prize for Cancer Research.
- Launched an intervention trial based on PGE_2 inhibition in metastatic colorectal cancer (2 x 400 pts)
- Launched Lymvac-2, combining intratumoral immunotherapy with anti-PD1 for treatment of patients with follicular lymphoma, in collaboration with Merck.
- Entered into partnership with Fate Therapeutics Inc. to develop off-the-shelf NK cell therapy.
- Joined forces with Kite Pharma to use her TCR technology for identification of therapeutic TCRs to defined targets.

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

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

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

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

Kjetil Taskén (MD, PhD), Institute for Cancer Research, Dept of Cancer Immunology, Centre for Molecular Medicine Norway, Nordic EMBL Partnership and Dept of Infectious Diseases, OUH

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

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

HIGH QUALITY TRANSLATIONAL RESEARCH FOR THE BENEFIT OF COLORECTAL CANCER PATIENTS

K.G. JEBSEN COLORECTAL CANCER RESEARCH CENTRE

HEADED BY **RAGNHILD A. LOTHE**

STIFTELSEN KGJ Kristian Gerhard Jebsen Foundation

ABOUT

Colorectal cancer (CRC) is a major health burden, and the focus of our Centre is translational and clinical research to meet challenges in the management of the disease, including early detection and improved patient prognostication and treatment. The Centre is hosted by the Clinic for Cancer Medicine, Oslo University Hospital (OUH). The Centre PIs are also partners in the OUH SMART-Colorectal cancer priority area.

Home page: www.colorectalcancer.no

GROUP LEADERS/STEERING COMMITTEE

- **Professor Ragnhild A. Lothe** (MSc, PhD, leader), Dept. Molecular Oncology, Institute for Cancer Research, OUH and University of Oslo (UiO)
- **Professor Arild Nesbakken** (MD,PhD, deputy leader), Department of Gastrointestinal Surgery, OUH and Institute for Clinical Medicine, UiO
- **Associate Professor Mette Kalager** (MD, PhD), Institute of Health and Society, UiO, and Dept. Epidemiology, Harvard T.H.Chan School of Public Health, USA
- **Professor Rolf I. Skotheim** (MSc, PhD), Department of Molecular Oncology, Institute for Cancer Research, OUH
- **Senior Consultant Marianne Guren** (MD, PhD), Department of Oncology, OUH and Institute for Clinical Medicine, UiO

AIMS

Translate biomedical knowledge to improve the prevention and treatment of CRC by uniting a translational multidisciplinary research environment and following the patient through the course of the disease.

PROJECTS

- Effectiveness of screening and colonoscopy procedures
- Clinical and molecular biomarkers for improved risk stratification of patients
- Improved treatment efficacy from chemotherapy and/or targeted drugs by biologically guided treatment
- Model tumor heterogeneity and clonal evolution to monitor early relapse and treatment failure
- Pharmacogenomics of the patients' own tumor cells for therapy guidance and prediction of response

KEY ACHIEVEMENTS

In 2017, 34 peer reviewed papers related to CRC were published from the PI groups, and three PhDs were defended.

New insights into the effectiveness of CRC screening from long-term trials were published, including a low benefit from sigmoidoscopy for women older than 60 years (Holme et al., Brit Med J 2017), and reduced benefit and increased risk of adverse events from screening colonoscopy in elderly beneficiaries (Garcia-Albeniz et al., Ann Intern Med 2017).

Benefiting from the national public health system and our collaboration with the Cancer Registry of Norway, the effect of preoperative chemoradiotherapy on reducing local recurrence rate, and trend towards increases survival, was demonstrated in a large population-based study (Åsli et al; Radiotherapy & Oncology 2017). We are currently assembling a national population-representative patient series withdrawn from diagnostic tumor material of 5,000 patients from all health regions. Tissue microarrays (TMA) will be used for multiplex biomarker studies.

Due to a recent FDA-approval, microsatellite instability (MSI) status currently receives much attention as a marker for response to immunotherapy in advanced cancers (May 2017). We discovered tumor heterogeneity with clinical relevance in MSI+ CRC, including molecular associations of resistance to anti-PD1 treatment conferred by *JAK1* mutations (Sveen *et al.*, Genome Med, 2017). Additional studies related to the clinical implications of tumor heterogeneity are ongoing in the Centre.

In our high throughput drug screening project more than 100 preclinical models have been included. In a pharmacogenomic study we combined gene expression subtyping and drug screening data from cell lines, and HSP90 inhibitors were identified as potent drugs in an aggressive subtype of CRC. A "xenotrial" of patient-derived xenografts confirmed a potential to overcome chemoresistance in this subtype *in vivo*, encouraging clinical testing of HSP90 inhibitor combination therapy in CRC (Sveen*, Bruun* et al. Clin Cancer Res 2017). Ex vivo drug screening combined with genomics of multiple samples from resected CRC liver metastases is ongoing.

PATIENT ADVISORY BOARD

Our Centre has an active patient advisory board with the following members: Marianne Guriby, teacher, Lars Reed, engineer, Thorvald Stoltenberg, retired politician, and Jack Waitz, athlete coach.

CLINICAL TRANSLATION

Members of our Centre have participated in the European Society for Gastrointestinal Endoscopy (ESGE) guideline panels for quality improvements of endoscopy in clinical use (Kaminsky M, et al. Endoscopy 2017).

The international clinical study KEYNOTE-177 evaluates immunotherapy (pembrolizumab) vs. chemotherapy for MSI metastatic CRC. We have participated in this study and patient inclusion is completed.

The international phase III study ARRAY-818-302 evaluates targeted combination therapies for BRAF-mutated metastatic CRC. Together with Prof. Tabernero at VHIO, Barcelona, we have applied to conduct a bilateral translational substudy for treatment response prediction.

THE USE OF TUMOR GENOME ANALYSIS TO BETTER TAILOR CANCER TREATMENT

NORWEGIAN CANCER GENOMICS CONSORTIUM

HEADED BY **OLA MYKLEBOST**

CancerGenomics.No

ABOUT

The Norwegian Cancer Genomics Consortium (NCGC) is a group of oncologists and researchers from all health regions of Norway, who are collaborating to determine the potential of cancer genome analysis for prediction of therapeutic outcomes or selection of novel targeted therapies.

AIMS

Precision oncology, or personalized cancer medicine, is expected to provide huge benefits to the patients by better adapting the treatment, especially by targeted drugs, to the specific properties of the disease of the individual. The hope is that this will at least give prolonged survival and better quality of life, and at the same time reduce the morbidity, expense and wasted resources on unsuccessful treatments. A main obstacle is the difficulty to prove the efficacy in ever smaller patient groups, and thus the reluctance of the public health services to introduce the new treatments.

PROJECTS

- Exome sequencing and mutation profiling of nine selected cancer types
- Establishment and characterisation of relevant preclinical models
- Validation of novel targets in preclinical models
- Investigation of predisposing gene variants
- Establishing of national infrastructure for the storage and analysis of large-scale sensitive patient data
- Design of small-scale trials to identify potential of candidate drugs
- Develop decision support tools for pathologists and oncologists to better interpret genome diagnostic data for therapeutic interventions

The projects include the determination of the DNA sequence, the detailed structure, of all genes in the patient and the tumour, identification of mutations that reveal mechanistic insights or can suggest specific treatments. Trial-derived biobanks from melanomas, leukemias, sarcomas, and breast cancers are being investigated for predictive biomarkers, as are biobanks containing sarcomas, colon, prostate, myeloma, and lymphoma samples from standard-of-care treated patients. The leukemia trial investigated is from the first-in-man trial of an Axl inhibitor from BerGenBio. A prospective, population-based cohort of all Norwegian sarcoma patients for 3 years is being accrued (see NoSarC.no), and in addition to the 200 sample pairs exome sequenced by NCGC, about 150 additional pairs are being sequenced with additional funding from the Radium Hospital Legacy. Up to now approximately 1800 samples from 630 patients have been sequenced. Promising targets for which drugs are available, but without documentation of clinical effect in the cancers investigated, are tested pre-clinically in relevant cell culture and xenograft models. The intention is to propose small, exploratory clinical trials to indicate activity in selected patients, and that promising results could lead to extension to phase II studies. Several trials are in progress by the partners.

The main hub of NCGC is at the ICR and its core facility for genomics, and five of the co-principal investigators are from the ICR. The other main nodes are at the University of Oslo, Haukeland University Hospital (Bergen), St Olav University Hospital (Trondheim), University Hospital of Northern Norway (Tromsø), and the University of Tromsø. The NCGC also has an ELSA work package, which addresses important societal issues including innovation, health economy, law and ethics, as well as professional and societal dialogue.

RECENT ACHIEVEMENTS

The data from the sequenced samples are currently being deeply investigated, and a number of preclinical studies in cell lines are under way. A database has been generated at 1000genomes.no with all the genetic variants (SNPs) detected in the germ lines (blood samples), and the frequencies in the cohort. Other environments are preparing to add Norwegian SNP data, which will be a valuable resource for many types of genetic research and diagnosis.

CLINICAL TRANSLATION

The project is investigating patient samples either prospectively collected, or being part of clinical trials, with the aim to gain biologically based clinical insight. Oncologists are strong partners. The detection of novel therapeutic targets and their evaluation in pre-clinical studies may have immediate clinical value. The team maintains a systematic professional outreach and dialogue, with continuous discussions on the strategies and how they may be implemented in the clinics at institutional meetings, external conferences and public meetings.

GROUP LEADERS/STEERING COMMITTEE

The project has a leader group consisting of Ola Myklebost (ICR, head), Ragnhild A Lothe (ICR), Harald Holte (KRE), Leonardo A Meza-Zepeda (ICR), Eivind Hovig (ICR), Per Eystein Lønning (HUS), Bjørn Tore Gjertsen (HUS), Anders Waage (St Olav US), Ole Morten Seternes (UiT), Tom Dønnem (UNN). Our Board consists of Erlend Smeland (OUH, Head), Jónas Einarsson (RF/OCC), Hilde I. Nebb (UiO), Knut Martin Torgersen (Pfizer), Bjørn Gustafsson (StOlav/NTNU), Tove Flem Jacobsen (Link Medical), Olav Mella (HUS/UiB), Anne Sameline Grimsgaard (UNN/UiT).

see http://CancerGenomics.No

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Kinghorn Cancer Centre, Sydney
Monash University, Melbourne

AUSTRIA
Medical University of Vienna, Vienna

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

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

CROATIA
University of Zagreb, Zagreb

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

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Aarhus University Hospital, Aarhus
University of Copenhagen, Copenhagen
University of Southern Denmark, Odense

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Zora Oy, Espoo

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

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Institute of Physiology and Pathophysiology, University of Mainz, Mainz
Jacobs University, Bremen
University of Bayreuth, Bayreuth
University of Bochum, Bochum
University of Cologne, Cologne
University of Heidelberg, Heidelberg
University of Marburg, Marburg

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University of Ioannina, Ioannina

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IFOM, Milan
International School for Advanced Studies, Trieste
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University of Padova, Padova
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Portuguese Oncology Institute, Porto

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Institute of Cytology and Genetics, Novosibirsk

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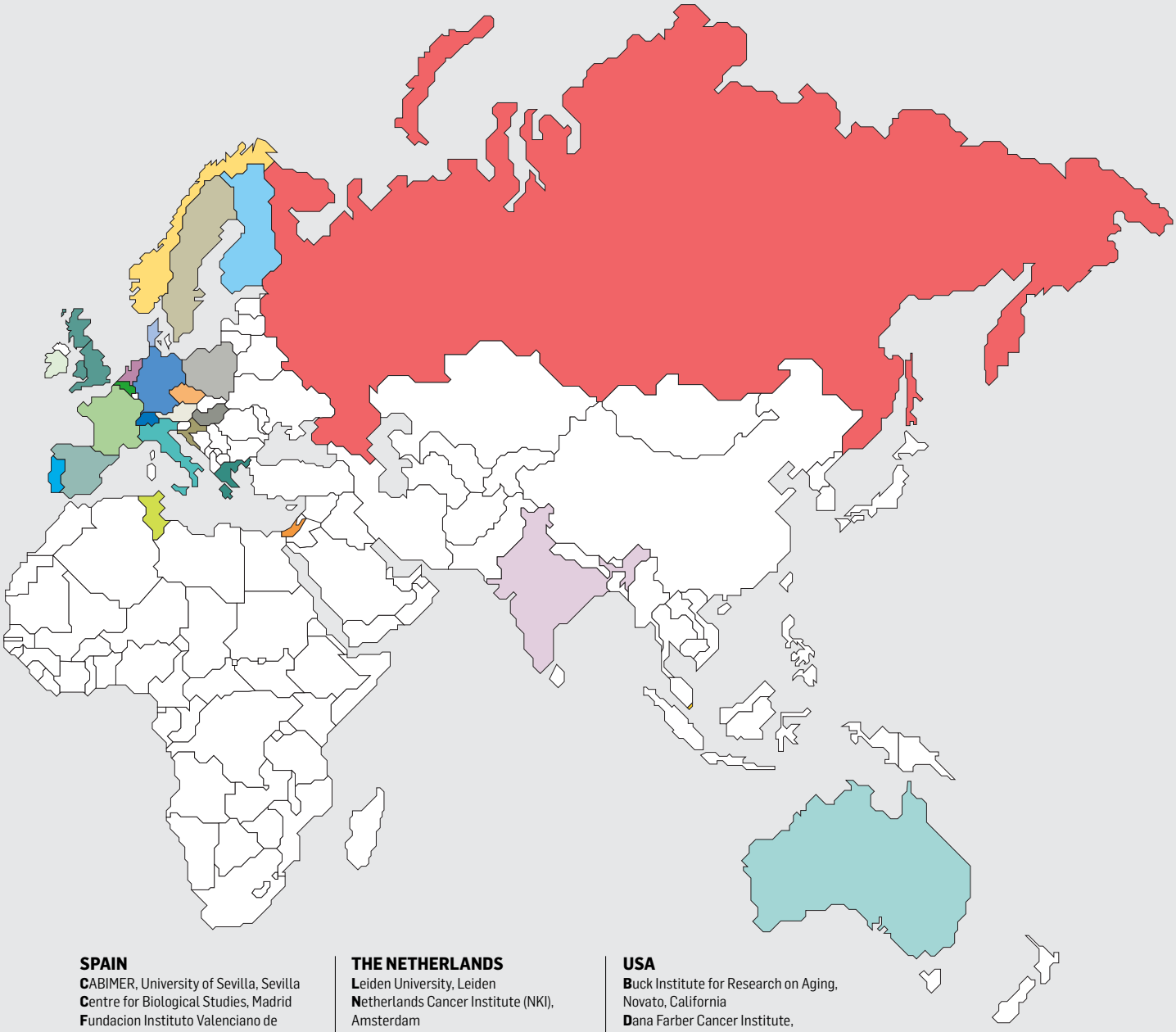
Cancer Science Institute of Singapore, Singapore



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University of Valencia, Valencia
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Lund University, Lund
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VU Medical Center, Amsterdam

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The University of Kansas Hospital, Kansas
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University of Chicago, Illinois
University of Colorado, Denver, Colorado
University of Illinois, Champaign, Illinois
Washington University, St Louis, Missouri
Weill Medical College of Cornell University, New York

RECENT INNOVATIONS

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2015

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2016

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2017

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The ICR will only achieve its goals if everybody on board joins forces

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