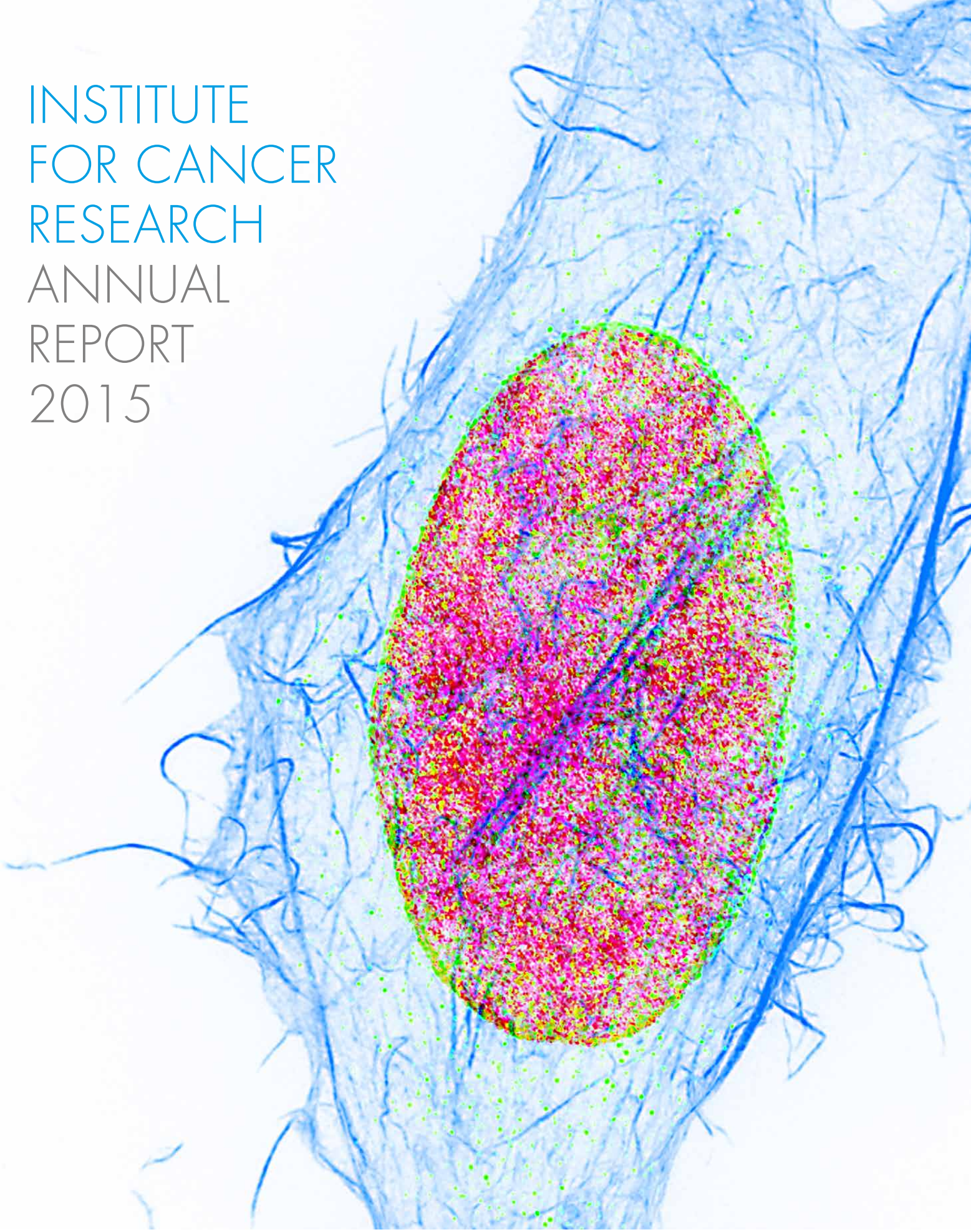
# INSTITUTE FOR CANCER RESEARCH ANNUAL REPORT 2015



Oslo University Hospital

HELSE SØR-ØST

UiO : University of Oslo

FRONT PAGE
Structured Illumination Microscopy image of a HeLa cell stained for filamentous actin (blue), DNA (red), and emerin (a nuclear envelope protein, yellow). Imaged on an OMX V4 super-resolution microscopy system. By Vigdis Sørensen, Advanced Light Microscopy Core Facility, Department of Core Facilities.

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# CONTENTS

# INTRODUCTION BY THE DIRECTOR

2015 has seen important developments in the Institute for Cancer Research (ICR). The revised ICR organisation was implemented in January 2015, reducing the number of research departments from 7 to 6 and the number of independent research groups from 28 to 24. The aim is to increase group strength, productivity, quality and collaboration. This report shows that the research output for 2015 shows significant improvement compared to all previous years, and although the reasons for this are many, it is likely that our strengthened focus and revised organisation have contributed. During the year individual researchers have received prestigious awards, including Anne-Lise Børresen-Dale: The Fritjof Nansen Award for Outstanding Research and The AACR Distinguished Lectureship in Breast Cancer Research; Sigrid Thoresen (Stenmark group): The King's Gold Medal for best PhD Thesis; Kaisa Haglund (Stenmark group): Anders Jahre's Prize for Young Medical Scientists; Harald Stenmark: The Research Council Møbius Prize; Guro E. Lind: Ragnar Mørk Legacy Prize and appointment as Leader of The Young Science Academy of Norway.

The Department of Core Facilities has been successfully established with an improved service capacity, uniform pricing policy and new cutting edge instruments (HiSeq 4000 Sequencer and CyTOF multichannel mass cytometer).

The ICR's international Scientific Advisory Board (SAB) conducted its first visit in September, and gave us both very positive feedback and valuable recommendations for further improvement. As regards cancer care and cancer research in OUH as a whole, a new Cancer Division has been established, with ICR as the core basic and translational research unit. Other institutional ongoing developments include the OECI Comprehensive Cancer Center (CCC) accreditation process, the formulation of an OUH Cancer Strategy, and the likely construction of a new clinical building at the Radium Hospital site. All these elements are key to the development of the CCC at OUH, and ICR is an essential contributor in all these processes.

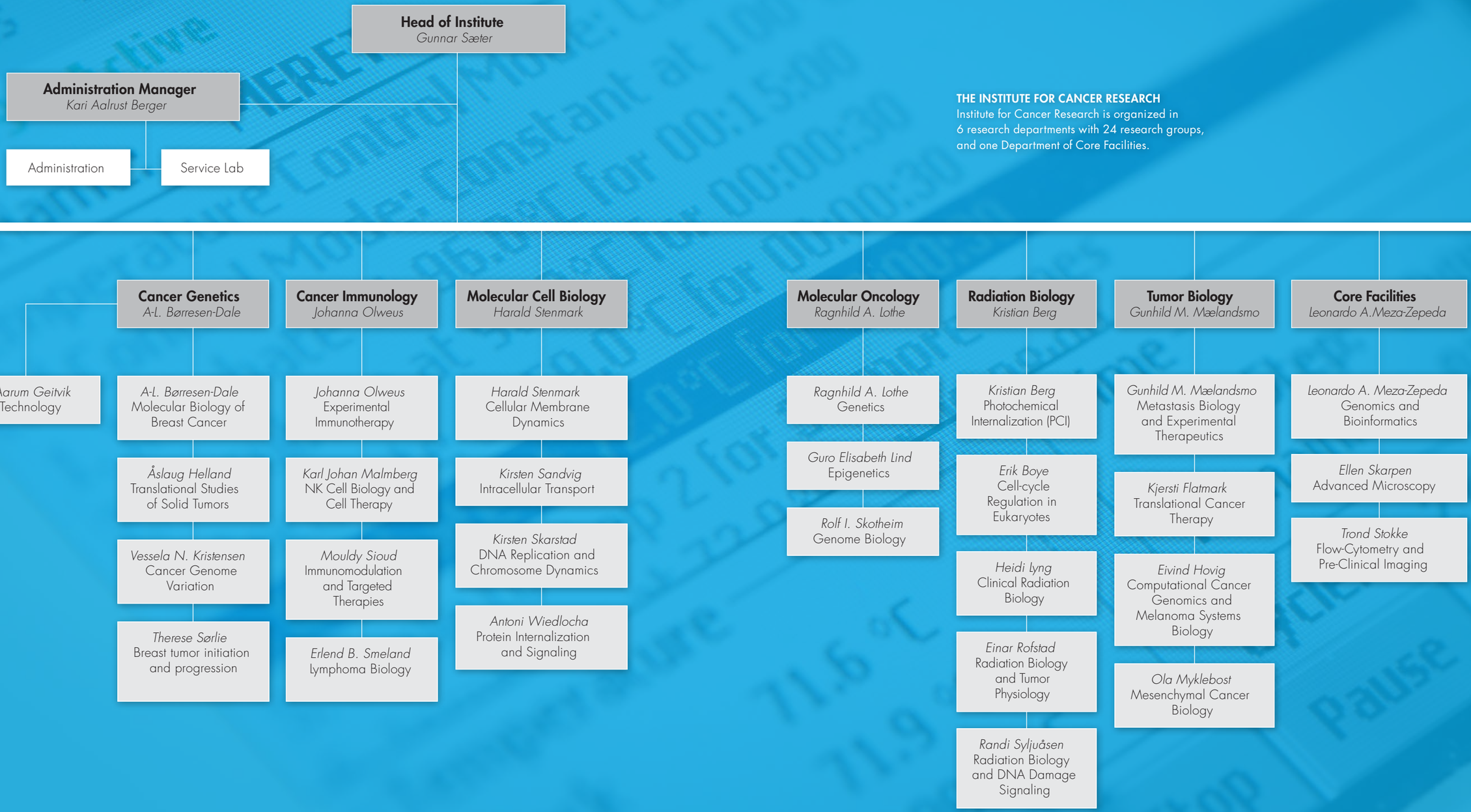
The new Oslo Cancer Cluster Innovation Park was opened next door in August, and in connection with this we hosted a successful international MD Anderson Global Academic Program (GAP) Young Investigator Workshop with focus on immunotherapy approaches in lung cancer, melanoma, lymphoma and glioblastoma. Apart from its novel Innovation Incubator, the OCCI structure houses the Norwegian Cancer Registry, and the OUH Department of Tumour Pathology, which includes the Section for Molecular Pathology co-localized with the ICR Core Facilities for Genomics and Bioinformatics, all in the spirit of knowledge transfer and collaboration.

2015 has been a very good year for ICR, and areas for further improvement include increases in collaboration with clinical researchers, partnerships and coordinator roles in more successful EU grants, and strengthened international visibility. To support this a specific ICR strategy for the coming years will be formulated in 2016, building on the OUH institutional cancer strategy.

**DIRECTOR**
**Gunnar Sæter**

*"Cancer Research of International Excellence"*

# ORGANISATION

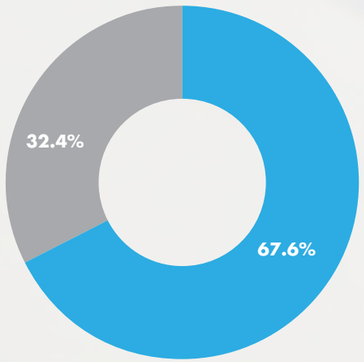



**THE INSTITUTE FOR CANCER RESEARCH**
Institute for Cancer Research is organized in 6 research departments with 24 research groups, and one Department of Core Facilities.

# KEY FIGURES 2015

## FUNDING

Percent



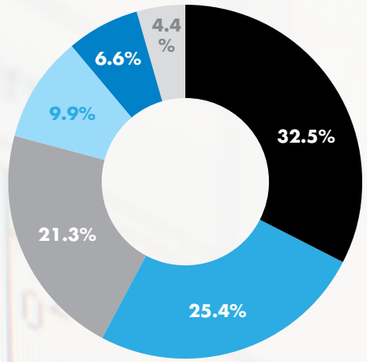

Actual Institute expenditure for 2015 by internal and external funding sources (total 293.2 MNOK = approx. 31.1 M€). The corresponding figures for budget allocation was 25% vs. 75%. This discrepancy is caused by external funds being transferable to the subsequent year, whereas internal funds are not.

*Source: Expenditure Accounts 2015.*

Internal funding
External funding

## EXTERNAL FUNDING BY SOURCE

Percent



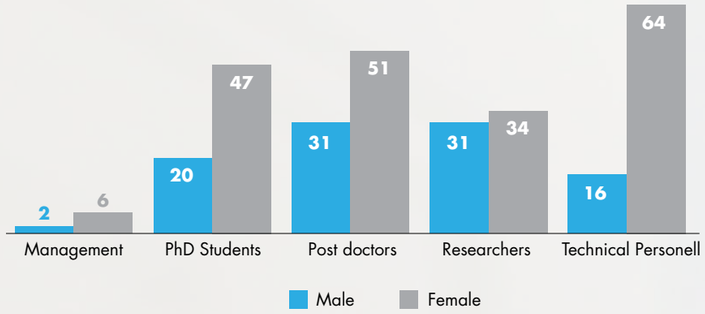

Sources of external competitive funding for 2015, based on actual expenditure (total 198.3 MNOK = approx. 21 M€)

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

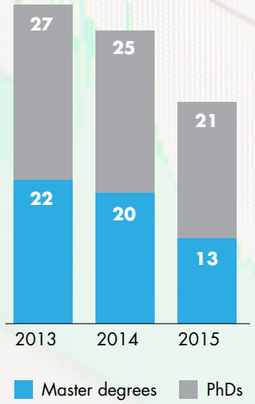
## EMPLOYEES

Compared to 2014 the number of full time positions has increased from 294 to 302. Most marked is the increase in post-docs (74 to 82), which is a deliberate development to increase the ratio of post-docs to Ph.D. students, as recommended by the SAB.

*302 Full Time Employees by type of position*




## COMPLETED PHDS AND MASTER DEGREES

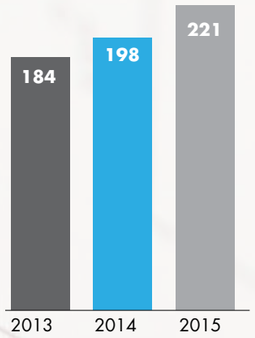



## ARTICLES PUBLISHED

The number of publications for 2014 and 2015 are based on actual lists of publications from the ICR research groups.

The publications for 2013 and Impact Factor (IF) data are based on the OUH Publika database.

Compared to 2014 the number of publications in 2015 increased by 31% overall, from 40 to 60 in the IF 5-10 group (+50%), and from 25 to 30 in the IF >10 group (+20%).




| IMPACT FACTOR | 2013 | 2014 | 2015 |
|---|---|---|---|
| Mean | 5.5 | 6 | 5.7 |
| Median | 3.9 | 4.3 | 4.3 |

**Professor Carl-Henrik Heldin**, Ludwig Institute of Cancer Research, Uppsala (Chair)

**Professor Eric Solary,** Director of Research, Institut Gustave Roussy, Paris

**Professor Per Eystein Lønning**, Haukeland University Hospital, Bergen

**Professor Josep Tabernero,** Director, Vall d´Hebron Institute of Oncology, Barcelona

**Professor Mef Nilbert,** Head, Regional Cancer Centre South, Lund

**Professor Odd Stokke Gabrielsen,** University of Oslo



# ICR'S SCIENTIFIC ADVISORY BOARD

## VISIT FROM ICR'S SCIENTIFIC ADVISORY BOARD (SAB) SEPTEMBER 16-17, 2015.

*Short summary from the SAB Chair, Professor Carl-Henrik Heldin:*

The SAB was very impressed by the strong leadership and overall scientific accomplishments of the scientists at ICR. Several of the groups are international leaders in their fields and regularly report important scientific discoveries in high impact journals. The high quality of the research at ICR is illustrated by the fact that scientists at ICR have leading roles in no less than three K.G. Jebsen Centers, as well as in one Center of Excellence and in the Norwegian Cancer Genomics Consortium. The SAB feels that the recent reorganization of ICR was timely and appears to have been implemented successfully, and that it has enhanced the scientific competitiveness and productivity at ICR.

A particular strength of the research at ICR is that excellent basic research is combined with very successful translational research. For the moment, about one third of the groups perform mainly basic research and about two thirds perform mainly translational research. The SAB feels that this is a good balance. Even though the special mission of ICR is to promote translational research, close contacts with excellent basic researchers is a prerequisite for the development of a strong translational research program.

Recommendations for further improvements:

1. Formulate a strategy for ICR for the coming 5-10 years.
2. Enhance clinical partnership.
3. Aim at developing a Comprehensive Cancer Center at Oslo University Hospital.
4. Develop the well-functioning core facilities further aiming at a national coordination.
5. Advertise open positions internationally.
6. Enhance visibility of ICR.

## FOLLOW-UP OF THE SAB REPORT.

*Gunnar Saeter, ICR Director*

The ICR is very fortunate to have an international SAB with very high scientific expertise and strategic insight, and a thorough and very constructive review was performed during their visit. Oslo University Hospital (OUH) has during 2015 gone through a reorganization process resulting in the formation of a dedicated Cancer Division where ICR is an important unit, and an institutional Cancer Strategy is currently under development. Building on this ICR will during 2016 also develop its own complementary strategy for the coming years, and how to develop increased ICR-clinical partnerships will be a core element. A revised application for Comprehensive Cancer Center accreditation to the OECI will be submitted in June 2016. The Core Facilities (CFs) are under constant development; we are in 2016 completing the co-localization and integration of the CFs for genomics and bioinformatics with the OUH Department of Molecular Pathology, and new cutting edge instruments have been added to the CFs. Towards the end of 2015 a new ICR group lead position was announced internationally, 31 of 54 applicants were from outside Norway and the evaluation process is currently ongoing with an international search committee.

The next SAB visit is planned for 2017.

# DEPARTMENTS AND RESEARCH GROUPS





INSTITUTE FOR CANCER RESEARCH | ANNUAL REPORT 2015

DEPARTMENT OF

# CANCER GENETICS

Headed by
Anne-Lise Børresen-Dale,
Gry AA Geitvik is acting
from 1. november

Our vision is to perform integrated molecular and epidemiological studies to reduce risk, achieve early diagnosis, improve prognosis, and to tailor treatment for individual patient with breast, lung, pancreatic and ovarian cancer. We are an interdisciplinary team of 50 with MDs, molecular biologists, bioinformaticians and highly educated engineers organized in 4 research groups and one lab-technology unit. The engineers are connected to a specific research group but organized in a separate unit which enhances the skills of "state of the art" technology and improves exchange of knowledge across research groups and cancer types, leading to increased quality of the department's laboratory work and project management.

The research focus is molecular classification, data integration, translation, and pan-cancer analyses, with a common goal of achieving deeper molecular understanding of inter- and intra-tumor heterogeneity between tumor entities and tumor subgroups, and within a single tumor. We have established a pipeline for high-quality biobanking (>100 000 vials) and data handling of patient cohorts with long-term follow-up, and perform multilevel molecular characterization down to the single cell level. Our database consists of > 3000 patients with analyses at 2-6 molecular levels, and includes samples from the following clinical trials:

- **MetAction**, focusing on metastastatic disease with targeted sequencing for selection of therapy in an N-of 1 Precision Oncology study;
- **NeoAva Phase-II**, neoadjuvant chemotherapy (breast cancer) with/without bevacizumab, samples before/during and after treatment;
- **IBCT phase-II**, Improved Breast Cancer Therapy in the neoadjuvant and metastatic setting
- **EMIT,** Establishment of Molecular profiling for Individual Treatment decisions in Early BC
- **TREM**, EGFR-mutated patients (lung) with primary TKI-resistance
- **ThoRaT**, lung cancer patients receiving radiotherapy
- **NorPACT-1**, Neo-adjuvant chemotherapy for pancreatic cancers

Mouse modelling of human cancers to understand the cancer evolution, heterogeneity and therapy resistance is also part of the department's project portfolio.

We have extensive institutional, national and international collaborations and are partners inn several networks and consortia: The Regional Research Network on Extracellular Vesicles (RRNEV), Personalized Cancer Treatment and Metaflammation, ICGC (International Cancer Genome Consortium), EU funded projects (Eurocan, BASIS, EpiMark, Cancer-ID), BCAC (international breast cancer consortium). We host the K.G. Jebsen Center for Breast Cancer Research and The National Competence Center for Lung Cancer.

The total number of peer reviewed publications in 2015 was 54

*"Molecular classification to understand tumor progression, to improve prognosis and tailor treatment"*

# MOLECULAR BIOLOGY OF BREAST CANCER

Group leader Anne-Lise Børresen-Dale

*"Exploring inter- and intra-tumor heterogeneity at various molecular levels and perform integrated analyses to develop prognostic and predictive signatures for breast cancer"*

## ABOUT

The group counts 4 scientists, 4 postdocs, 3 phDs, one MD/PHD, 1 master student, and 6 research engineers. 1 part-time oncologist, 1 study-nurse and a professor in bioinformatics (UiO) are associated with the group. We seek to reach a more fundamental understanding of the biological dynamics of breast cancer through high-throughput molecular analyses of DNA, mRNA, miRNA and protein. 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, from consecutive patient series with up to 25 years follow-up (OsloVal, Oslo0, Oslo1 and Oslo2), and on samples from several clinic trials: The MetAction-, NeoAva- I-BCT and the EMIT-studies.

## AIMS

Our group aims at elucidating the impact of inter- and intra-tumor heterogeneity on response to therapy and patient outcome. We also focus on development of molecular diagnostic assays for an earlier and more detailed diagnosis to improve tailoring of treatment. To do this we have a strong effort on characterizing breast carcinomas at multiple molecular levels in a "systems biology framework", and our ultimate goal is to translate the biological findings into improved clinical management including development of new therapeutic approaches.

## PROJECTS

- Single level classification at DNA/RNA/protein/metabolic level of both primary tumors and metastases
- Somatic Genetics, single genes, genome-panels, WGS
- Genomic alterations to elucidate the genomic landscape
- Intra-tumor heterogeneity, implication for diagnosis/treatment
- Cell-free tumor DNA in blood
- HER2 positive cancer, treatment response
- Genomic and functional analysis of therapeutic targets
- The role of lncRNA and miRNA's
- Integrated classification

## RECENT ACHIEVEMENTS

- 22 original publications (plus 5 in press) and one invited book chapter
- Three PhDs dissertations
- The group leader received The Fritjof Nansen Medal and Award for Outstanding Research, The Oslo University Hospital's Excellent Researcher Award, and The AACR Distinguished Lectureship in Breast Cancer Research



# TRANSLATIONAL STUDIES IN SOLID TUMORS

Group leader Åslaug Helland

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

## ABOUT

Our group focuses on translational studies on solid tumors, with a special interest in pancreatic, lung, ovarian and colorectal cancers. With starting point in clinical studies and clinical questions, we do analyses on mRNA, miRNA, DNA, methylation, glycosylation, mutations and proteins. By elucidating underlying biology of tumor development, and identifying predictive and prognostic biomarkers, we aim to improve patient care. The group has three project groups, with a total of 16 members. Eight of these are MDs. India, Great Britain and Israel are represented. We are three researchers, two postdocs, eight PhD-students, one study nurse and two engineers.

## AIMS

The ultimate goal is to personalise cancer treatment and improve prognosis.
Initiate and perform clinical studies
Identification of circulating biomarkers
Identification of tumor biomarkers for prediction of therapy response and for prognosticaton

## PROJECTS

- Serum miRNA-signatures: Diagnostics of lung and pancreatic cancers
- Serum miRNA-signatures: Prediction of therapy response in ovarian cancers
  – Part of the ICON7-study with chemo + \ - bevacizumab
- Molecular characterisation of lung and pancreatic carcinomas
- Improving radiotherapy in lung cancer (ThoRaT-study)
  – Radiotherapy + \ - erlotinib
  – Cytokine-analyses in serum samples
  – PET-CT analyses before, during and after radiotehrapy
- Mechanisms behind TKI-resistance in EGFR-mutated tumors (TREM-study)
  – AZD9291 treatment. Molecular analyses of resistance mechanisms
- Genome-wide detection of diagnostic plasma miRNAs in pancreatic cancer patients
  – NorPACT-1 study (Neo-adjuvant chemotherapy)
- Exosome profiles of proteins and miRNAs in plasma of pancreatic cancer patients
- Serum N-glycans as prognostics markers in pancreatic and colorectal cancers

## RECENT ACHIEVEMENTS

- Involved in Eurocan-meeting "Circulating biomarkers in cancer", May 2015
- Involved in two SFF-applications
- Published 18 papers in peer-review journals, (1 published in "Nature")
- Presentations at national and international meetings
- The group has PIs on >20 translational and clinical studies
- One PhD-student had her dissertation
- Two PhD-students submitted her thesis in December 2015

# 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: 2 research engineers, 5 postdocs, (2 of the postdocs 50% in collaboration with other groups at the Department and Institute), 1 PhD student and 1 MSc student. Vessela Kristensen is a professor I at the Faculty of Medicine, UiO, and works towards a fruitful collaboration between KRF and University of Oslo, where she leads the group of Oncogenomics with a molecular branch consisting of 3 postdocs, 2 PhD students, 1 MSc student and 1 research engineer. Both groups work closely together with a total of 5 male and 11 female members, and includes members from France, India, Pakistan and Serbia. Kristensen is on the advisory committee of 3 graduate students at Princeton University.

## AIMS

The Cancer Genome Variation group works to understand how genetic variation affects occurrence of somatic alterations, gene expression patterns and genome wide copy number alterations. Understanding inherited genetic variability and how it affects biological pathways will lead to new prevention and treatment strategies. http://ous-research.no/kristensen/

## PROJECTS

- Genome variation; fine mapping characterization of susceptibility loci continues with in depth next generation re-sequencing analyses
- DNA methylation at specific CpGs affects the expression genome wide, pointing to signaling and effector pathways such as immune signaling
- Data integration towards identification of signaling pathways involved in response to treatment. Integrated analysis of high-resolution DNA methylation profiles, gene expression, germ-line genotypes and clinical end points in time-course studies of breast cancer patients under treatment
- Non-canonical transcriptomes. Long non-coding RNAs in normal versus primary breast tumor tissues; converse changes to cancer-related protein-coding genes
- Immune signaling. Interleukin signaling in focus since our 2012 discovery of massive cytokine signaling.
- Nano-dissection applied to identify multiple types of immune cells in silico

## RECENT ACHIEVEMENTS

Publication activity: 31 publications and 2 PhD dissertations, 1 MSc thesis in 2015.



# BREAST TUMOR INITIATION AND PROGRESSION

Group leaderTherese Sørlie

*"Understanding cell fate decisions in tumor progression"*

## ABOUT

The group counts 10 people including one senior scientist (TS), one scientist, three postdocs, three PhD students, one bioengineer and one MD-PhD student.

Our group is interested in breast tumor initiation and progression; from the cell of origin in which the first oncogenic events take place, the specific pathways and processes that are deregulated in the further progression of the tumors, to the specific events that are essential for the transition from in situ to invasive cancer. We use patient cohorts and animal models (transgenic and patient-derived xenograft - PDX) in our studies. We apply high-throughput genomic technologies, functional assays, lineage-tracing, in situ hybridization techniques and statistical and bioinformatics methods in our research.

## 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 tumors progress to more advances stages, improved strategies for early intervention and more precise treatment can be developed.

## PROJECTS

- Characterize the functional effect of breast cancer risk variants
- Characterize subtype-specific progression pathways of pre-invasive lesions in the breast
- Identify and test potential molecular progression markers in large patient cohorts, and model their interactions
- Characterize genetic, phenotypic and functional heterogeneity in PDX models of breast cancer and the effect of treatment
- Investigate the role of Hedgehog/GLI1 signaling in breast cancer progression
- Explore the tumorigenic potential of LGR5 expressing cells in the mammary gland
- Study tissue homeostasis upon anti-cancer treatment by in vivo lineage tracing
- Define genetic and epigenetic regulatory events in breast cancer progression, using transgenic animal models

## RECENT ACHIEVEMENTS

- 15 publications in 2015
- One PhD defense
- Secured funding for 2016-2019 through the Research Council's FRIMEDBIO program

DEPARTMENT OF

# CANCER IMMUNOLOGY

Headed by
Johanna
Olweus

## ABOUT

DCI has 4 research groups. Among the PIs, 3 are full professors at UiO (MD, PhD) and one is visiting professor (DEA pharm, PhD). One PI was recently recruited from Karolinska Institute in 2011. Groups in the DCI are partners of: Center of Excellence for Cancer Biomedicine (CCB), two K.G. Jebsen Centers (Cancer Immunotherapy and Inflammation Research, with leadership in the former) and OUH focus area for Cancer Immunotherapy. With emphasis on translation and extensive involvement in clinical trials, the DCI is the department with the highest number of MDs at the Institute. The DCI counts 39 members (62% women); 5 scientists, 11 postdocs, 8/1 PhD/Master students, and 10 technical staff. Norwegians/recruited from abroad: 64/36%.

## AIMS

Improve cancer diagnostics and therapy through cutting edge research on tumor immunology and lymphocyte biology.

## PROJECTS

- Lymphocyte biology, by deciphering
  - ontogeny 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 local immunotherapy in lymphoma (LYMVAC)

## RECENT ACHIEVEMENTS

In 2015, 21 original publications and 13 reviews were published of which 12 with IF>5 (mean IF 5.6), with 21 as first/last authors of which eight with IF>5. Two DOFIs/one patent application were filed. One article subject of commentary in Blood (IF=10). Edited special edition on Cancer Immunotherapy in Molecular Oncology, to which two groups contributed (IF 5.3).

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

# 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), 1 scientist, 3 postdocs, 5 PhD students and 2.5 engineers. Four members have MD background. Eight members are recruited from abroad (seven different countries) and five are Norwegians. The group is partner of two K.G. Jebsen Centers (2013-); "Cancer Immunotherapy" and "Inflammation Research", respectively, and Olweus is Director of the former.
The main focus is to develop new strategies for cancer immunotherapy and to couple clinical trials with penetrating mechanistic analyses.

## AIMS

To find new immunotherapeutic T-cell based strategies that overcome the major challenge of self-tolerance in cancer. Two principally distinct approaches are pursued in an interdisciplinary and translational program
Strategy 1: Use of T cell-based allo-reactivity 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, identify T cells reactive towards such epitopes, and identify their T-cell receptors for future genetic transfer in adoptive cellular therapy

**Strategy 2**

- Target neo-antigens neglected by the patient's own immune system
- Profile T-cell receptors as a tool to identify T-cell reactivities
- Identify neo-antigens and reactive T cells in biobanked material from patients responding to immunotherapy in LYMVAC trial
- Identify auto-antibody targets by protein arrays

## RECENT ACHIEVEMENTS

Eight articles accepted for publication (five original) with Olweus as senior author on all and group member as first author on six, of which six in journals with IF>5 and two with IF 10 or higher (Hepatology, Blood). Olweus was invited to be scientific editor for a special issue on cancer immunotherapy in the journal Molecular Oncology (IF 5,3), and the issue appeared in December 2015. One filed patent application.



# NATURAL KILLER CELL BIOLOGY AND CELL THERAPY

Group leader Karl-Johan Malmberg

*"Our focus is to develop the next generation natural killer (NK) cell therapy"*

## ABOUT

The group counts 19 members (F/M: 10/9); 1 full professor (KJM), 2 scientists, 4 postdocs, 5 PhD students, 2 engineers, 2 master students. Seven members have MD background. Malmberg is a visiting Professor at the Karolinska Institutet (KI) and the group is partner of the K.G. Jebsen Center for Cancer Immunotherapy (2013-) and of three focus area centers in Immunotherapy and Regenerative Medicine at both KI and OUH. The main focus is to develop new strategies for cell-based immunotherapy based on insights into the molecular regulation of natural killer (NK) cells.

## AIMS

The long-term goal of the laboratory is to advance our fundamental understanding of NK-cell development and function, and use this progress to design new immunotherapeutic approaches and clinical trials for patients with cancer. We focus on basic questions concerning 1) the formation of killer cell immunoglobulin-like receptor (KIR) repertoires and regulation of effector cell function, 2) translational questions of how NK cells may be function-enabled for anti-cancer activity and 3) clinical studies in the context of allogeneic stem cell transplantation (HSCT) and adoptive cell therapy.

## PROJECTS

- Functional plasticity and diversification of human NK-cell repertoires in health and disease
- Metabolic reprogramming and NK-cell homeostasis
- Clinical trial program; harnessing adaptive NK cells in cancer therapy

## RECENT ACHIEVEMENTS

Eight original articles and two reviews.

# IMMUNO-MODULATION AND TARGETED THERAPIES

Group leader Mouldy Sioud

*"Our goal is to enhance patient responses to immunotherapy and navigate therapeutic agents to cancer cells"*

## ABOUT

The group consists of five members (3 women); one senior scientist, two engineers, one PhD, one master student, and one 50% postdoc. Sioud is a visiting professor at University of Tunis since 1997. The group is a part of the OUH-focus area cancer immunotherapy and H2020 NANO-D-SIRE consortium. The thematic focus areas of the group are immunotherapy, RNAi, and phage display technology.

## AIMS

To direct innate immune cells towards cancer cells via new recombinant protein therapeutics and to develop siRNA therapeutics that block immune checkpoints.

Notably, our current research has led to the discovery of new cancer cell-binding peptides used worldwide (e.g., Wang XF et al. 2007 *Cancer Res,* Moreno M et al. 2014, *J Control Release*), peptide-Fc fusions able to activate innate cells against cancer cells, single chain Fv antibodies targeting various cancer types, and the first siRNA modulated-dendritic cell cancer vaccine. Moreover, some of our previous work has led to a deeper understanding of RNA sensing by the immune system and gene regulation by endogenous antisense transcripts [e.g., Røsok & Sioud 2004 *Nature Biotech.,* Sioud 2006 *Nature Biotech* (IF=39), Sioud, 2006 *Trends Mol Med* (IF=10.1)].



## PROJECTS

- Checkpoint blocking siRNAs in cancer immunotherapy
- Targeting antigens to dentritic cells
- Engineering peptide-Fc fusions and scFv antibody fragments for cancer therapy

## RECENT ACHIEVEMENTS

- New peptide-Fc fusion proteins for cancer therapy (Mol. Ther-M 2015)
- A peptide-Fc fusion protein with dual function (Oncotarget, in revision)
- Single chain Fv antibody-based tumour targeting (to be submitted)
- siRNA-modified DC vaccines tested in compassionate use

So far the group has published 180 PubMed-indexed papers, including 2 original papers and 9 methods/review papers in 2015. One filed patent regarding peptide-Fc fusions. Sioud participated as expert reviewer for EU (H2020-NMBP10 Formulation of biologicals).



# LYMPHOMA BIOLOGY

Group leader Erlend Bremertun Smeland/June Myklebust

*"We are working to identify better prognostic markers and to improve therapeutics for lymphoma by a translational research approach"*

## ABOUT

The group consists of 13 members with research background in medicine, biology, biochemistry and biotechnology, and includes 1 professor (EBS), 1 assistant professor (JHM), 1 senior scientist (50% position), 5 postdocs, 4 PhD students and 1 technician. Four of the members are recruited from abroad (USA, China, Switzerland, Sweden).

The group is part of the Centre for Cancer Biomedicine (Centre of Excellence). Our research is focused on B-cell lymphoma, a heterogeneous group of malignancies originating from B cells of the immune system. Although new therapeutic approaches have significantly improved overall survival, some types are still considered incurable. The lab has a strong translational focus, and we use exome sequencing, advanced flow cytometric analysis and cutting edge mass cytometry (CyTOF) to identify tumor cell heterogeneity, and to characterize tumor microenvironment composition. The molecular biology expertise has been strengthened with establishment of CRISPR/Cas9 genome editing to create gene knockout models. Lymphoma xenograft mouse models have been established for testing of new drugs in vivo.

## AIMS

To identify biomarkers and to develop novel therapeutic strategies in B-cell lymphoma.

## PROJECTS

- Proteomics characterization of tumor cells and tumor microenvironment in follicular lymphoma (FL), mantle cell lymphoma (MCL) and diffuse large B-cell lymphoma (DLBCL) by use of immunohistochemistry, flow cytometry and mass cytometry (CyTOF)
- Characterize how crucial mutations affect drug responsiveness in B-cell lymphoma (drug assay, phospho-specific flow cytometry, genetic manipulation)
- Identify abnormal cell signaling in lymphoma cells by phospho-specfic flow cytometry
- Exome and RNA sequencing projects in diffuse large B-cell lymphoma and follicular lymphoma to identify recurrent mutations associated with therapy relapse
- Exome and RNA sequencing to describe clonal evolution and disease progression in serial biopsies of FL

## RECENT ACHIEVEMENTS

Nine publications in 2015 with four as first author.
One PhD dissertation (Idun Fiskvik, June 2015), and one new DOFI.

DEPARTMENT OF

Headed by
Harald Stenmark

# MOLECULAR CELL BIOLOGY

The department has a staff of about 60 and hosts 4 research groups (Stenmark, Sandvig, Wiedlocha and Skarstad), 9 project groups, and a departmental service unit. It was previously known as Department of Biochemistry and acquired one group (Skarstad group) in 2015 from the previous Department of Cell Biology. Research in the department comprises various aspects of cancer relevant cell biology, including membrane traffic, receptor signaling, and cell division. Translational research on cancer cell-derived exosomes is a recent development in Sandvig´s group. 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 the identification of novel molecular mechanisms for control of DNA replication, cell division, growth factor signaling, cellular protrusion outgrowth, cell migration, and intracellular transport. In general, the department's groups have been successful in obtaining national and international external funding. The groups of Stenmark, Sandvig and Wiedlocha are associated with a Centre of Excellence, Centre for Cancer Biomedicine. 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.

*"Uncovering the cellular basis of cancer development"*

# CELLULAR MEMBRANE DYNAMICS

*"Diving into cellular membranes to find the keys of cancer"*

Group leader Harald Stenmark

## ABOUT

The group studies the dynamics of cellular membranes and tries to understand their relevance to cancer. Cellular processes studied by the group include endocytosis, autophagy, and cell division. Initially focusing on the membrane lipid phosphatidylinositol 3-phosphate (PtdIns3P) and its downstream effectors, the group has also contributed to our understanding of how the endosomal sorting complex required for transport (ESCRT) machinery controls processes as different as receptor downregulation and sealing of the nuclear envelope during mitotic exit. The group employs standard and advanced molecular biology methods in combination with biochemistry and imaging technologies such as standard transmission electron microscopy, immunoelectron microscopy, electron tomography, correlative light and electron microscopy, live-cell microscopy, confocal microscopy, light-sheet microscopy and super-resolution microscopy. 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). It contains 4 project groups, led by Andreas Brech, Kaisa Haglund, Camilla Raiborg and Tor Erik Rusten. The group consists of 11 men and 19 women, and 11 nationalities are represented. The staff consists of 1 group leader, 5 senior researchers, 4 researchers, 8 postdocs, 7 PhD students, 1 visiting MSc student, 3 technicians, and 1 laboratory assistant.

## 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
- Cell signalling and membrane dynamics in tumour-microenvironment interactions
- Control of cell polarity by membrane dynamics
- Centrosome dynamics in cancer
- Cytokinesis in development and carcinogenesis
- The Beta-catenin destruction complex in physiology and cancer
- Membrane dynamics in promotion of genome integrity

## RECENT ACHIEVEMENTS

- Discovery that the ESCRT machinery mediates sealing of the newly formed nuclear envelope during mitotic exit, and that this mechanism is essential for genome integrity (Vietri et al., Nature, 2015).
- Identification of a novel mechanism for controlling intracellular positioning of late endosomes via their contacts with the endoplasmic reticulum, and demonstration that this mechanism promotes outgrowth of cellular protrusions (Raiborg et al., Nature, 2015).
- Two PhD students were graduated in 2015, and 18 papers were published by group members.
- In 2015, Sigrid Bratile Thoresen received H.M. the King's Gold Medal for best PhD thesis, Kaisa Haglund received Anders Jahre's prize for younger medical scientists in the Nordic countries, and Harald Stenmark received the Research Council's "Møbius" prize for outstanding research.



# INTRACELLULAR TRANSPORT

*"All the way from basic research to translation"*

Group leader Kirsten Sandvig

## ABOUT

Sandvig's group, counting 17 members plus master students, 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 of our 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. We also characterize exosomes from prostate cancer cells and patients with the goal of detecting lipid 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 71 (more than 300 publications). The group has extensive national and international collaboration.

The group consists of 5 men and 12 women. 11 Norwegians, 6 with other nationalities. 7 nationalities represented in the group. 1 group leader, 4 project leaders (researchers), 8 postdocs, 2 PhD students, 2 technicians.

## AIMS

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

## PROJECTS:

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

## RECENT ACHIEVEMENTS

In 2015 the group published 13 articles and a book chapter, and one Ph.D. student finished his degree. The work on exosomes from prostate cancer patients resulted in 2015 in a DOFI as well as patent applications (for more details, see separate paragraph about innovations).

# DNA REPLICATION AND CHROMOSOME DYNAMICS

*"Studying DNA transactions to understand disease mechanisms"*

Group leader Kirsten Skarstad

## ABOUT

The group counted 6 members for most of 2015, and studies proteins and mechanisms which act on DNA. We wish to understand the mechanisms by which DNA is replicated, moved and repaired. Of special interest is replication fork collapse which contributes to genome instability. Stability of the genome is important to prevent development of cancer. We also study regulation of the cell cycle, and are interested in how initiation of replication and segregation are controlled and coordinated with cell growth and cell division. Most of our projects are basic science projects using the model organism *Escherichia coli.*

The group consists of 6 women. Two nationalities (Norwegian and Finnish) are represented. 1 group leader, 2 postdocs, 2 PhD students, 1 technician.

## AIMS

The principal aim is to increase the knowledge about DNA transactions and use this knowledge to combat disease.

## PROJECTS

- Mechanisms of replication fork collapse and repair
- The roles of the beta clamp and PCNA proteins in replication fork rescue
- The roles of SeqA, topoisomerases and Dam methylase in stabilization of the replication fork and daughter chromosome segregation
- The roles of the DnaA initiator protein and RNA polymerase transcriptional activity in control of replication frequency

## RECENT ACHIEVEMENTS

Two PhD students (Emily Helgesen and Ida Benedikte Pedersen) completed their degrees.

PhD student/postdoc Emily Helgesen and postdoc Kay Oliver Schink (from the Stenmark group) managed by super resolution microscopy to visualize details of the SeqA nucleoprotein structure and found that although the SeqA structures trail behind the replisome at a distance, the two sister SeqA structures were kept closer together than 30 nm. The result was commented on at international meetings and is reported in Helgesen et al, 2015, *Nucleic Acids Res* 43 (5), 2730-43.

We contributed to a better understanding of the bacterial cell cycle with Flåtten et al, 2015, *PLoS Genetics,* 11 (6), e1005276.

Postdoc Emily Helgesen's manuscript on the importance of the nucleoid associated protein, H-NS, received a spotlight comment in J. Bacteriology (Helgesen et al, 2016, Feb 8. JB.00919-15, Epub ahead of print).



# PROTEIN INTERNALIZATION AND SIGNALLING

*"Searching for molecular targets in FGF-related malignancies"*

Group leader Antoni Wiedlocha

## ABOUT

The group is composed of 6 members from 3 nationalities. 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.
The group consists of 3 men and 3 women. 3 nationalities represented. 1 group leader, 1 researcher, 3 postdocs, 1 medical student.

## AIMS

The main goal of the research group is to elucidate differences in mechanisms of signaling induced by FGF/FGFR in normal and in tumour cells.

## PROJECTS

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

## RECENT ACHIEVEMENTS

We explored the role of HSP90 in stabilisation of oncoproteins and in protecting them against proteasomal degradation. We have shown that the novel HSP90 inhibitor NVP-AUY922 impairs stability of a permanently active fusion protein containing the FGFR1 tyrosine kinase domain. The small HSP90 molecule was able to inhibit proliferation of leukemic KG-1 cells and cause cell death in vitro, indicating a HSP90-dependent addiction of the fusion protein. Moreover, combined treatment of cytarabine and NVP-AUY922 showed synergistic anti-leukemic activity in vivo (Wendel T., et al., Exp. Cell Res. 2015).
We have elucidated the relationships between intrinsic stability of FGF proteins and their biological activities. We demonstrated that the biological activity of many FGFs is critically regulated by their half-life, reflecting both stability and degradation. This has several important implications for understanding of the FGF-signaling system in healthy and disease (Buchtowa M., et al., CMLS, 2015).

DEPARTMENT OF

# MOLECULAR ONCOLOGY

Headed by
Ragnhild A. Lothe

The department of Molecular Oncology (MO) has 3 research groups and counts 38 employees. The group leaders are all professors at the University of Oslo, affiliated with the Institute for Biosciences, the Institute for Clinical Medicine, and the Institute for Informatics. The PIs are partners in the Centre of Excellence for Cancer Biomedicine (2007-17), the K.G. Jebsen Colorectal Cancer Research Centre (2014-18), and the OUH priority area for Colorectal Cancer (2014-18). The PIs are also partners in the Norwegian Cancer Genomics Consortium, the Global Testicular Cancer Research Consortium, European Network for the Study of Cholangiocarcinoma and Cooperation Studies on Inherited Susceptibility to Colorectal Cancer (COST action).

The employees hold a trans-disciplinary competence and hands-on experience in a broad range of technologies, including multilevel genomics, epigenetics and cell biology. The MO research activity comprises the molecular biology of solid tumors and transfer of such knowledge into clinical use. Our main goal is to contribute to solve clinical challenges for colorectal cancer and prostate cancer. The strategy for the next three years is to explore spatio-temporal tumor heterogeneity in CRC and prostate cancer, and combine the results with drug sensitivity and resistance patterns found by high throughput screening of cell cultures. This will be followed by implementation of selected findings in clinical trials.

During the last 3 years, we have published 76 papers, with 1st and/or last authorships on two-thirds. The mean IF = 7.9 in the 3 ye period, including 7 papers with IF> 10. The MO total innovation activity (since 2007) include 13 patent applications, several innovation grants, two signed license agreements with a British biotech company.

In the period 2013-15, 11 PhDs and 7 MSc have received their academic degrees with supervisors from MO.

As part of the research quality, we emphasize work satisfaction and the deparment has had the highest possible score in the employee surveys the last three years from South-East Health Regional authorities.

*"Biological discoveries for precision cancer medicine"*

# GENETICS

Group leader Ragnhild A. Lothe

*"Genomics – irreversible mistakes in cancer and a source for clinical biomarkers"*

## ABOUT

Our group studies the underlying genetics of solid tumors, with particular focus on colorectal cancer (CRC). We combine multilevel genomics, genetics, immunohistochemistry and cell biology to i) identify and develop clinically useful cancer biomarkers and ii) better understand the molecular heterogeneity and mechanisms that promote cancer development and metastasis. The group has 23 members, including 7 post docs/scientists, 7 PhD students and 7 research assistants/engineers.

## AIMS

Our overarching goal is to transfer novel biomedical knowledge into improved cancer patient stratification and treatment.

## PROJECTS

- Prognostic and predictive biomarkers for CRC and malignant peripheral nerve sheet tumors (MPNST)
- Genomic tumor heterogeneity and clonal evolution in primary CRCs and their liver metastases
- miRNA expression, function and biomarker potential in CRC
- Ubiquitin system in intercellular communication and CRC pathogenesis
- Identification of drug targets by multilevel genomics combined with drug sensitivity screens of CRC and MPNST cell lines

## RECENT ACHIEVEMENTS

Our group identified novel prognostic biomarkers for CRC and MPNST in 2015. In CRC, we showed that loss of expression of the cell cycle protein regulator of chromosome condensation 2 (RCC2), identifies patients with a high-risk of relapse after surgery. (Bruun J et al., Clin Cancer Res). In MPNST, we published novel biomarkers that identify patients with a high risk of relapse after assumed complete resection. (Danielsen SA et al., Neuro Oncology; Kolberg et al., Molecular Oncology). Last year, we published three comprehensive review papers about non-coding RNA in CRC (Cekaite et al., Oncotarget), splicing mechanisms and aberrant RNA expression in cancer (Sveen et al., Oncogene) and PIK/AKT signaling in CRC (Danielsen et al., BBA-reviews on cancer). Altogether, we published 12 papers, with 1st and/or last authorship on 7.

## CLINICAL TRANSLATION

In 2015 we suggested an immunotherapy clinical trial for MPNST patients. The protocol was recently approved with patient recruitment starting in April. PI: Tormod Guren; Ragnhild A Lothe and Matthias Kolberg are co-investigators.





# 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 carefully selected methylome approaches with detailed candidate gene characterization. The research is performed across cancer types, with a main focus on colorectal cancer. In 2015 the group counted eight members, including three postdocs, two PhD students, one engineer, one MSc student 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
- Epigenetic drivers of tumor development

## RECENT ACHIEVEMENTS

During 2015 the group has focused on innovation and explored alternative ways forward for developing a DNA methylation based urine test for bladder cancer detection and monitoring, including collaboration with a Norwegian start-up company. In collaboration with Inven2, the project received Kreft-Biotek funding from the Research Council of Norway and the Norwegian Cancer Society at the end of the year. The group has published high-performing DNA methylation biomarkers for minimally invasive detection of the rare cancer type cholangiocarcinoma, by use of biliary brushes (Andresen et al., Hepatology), and is currently exploring the use of bile as a source for biomarker testing. Autumn 2015 The Young Academy of Norway was established. Lind was selected to lead the Academy, consisting of 20 young researchers from various disciplines. Lind was also awarded the Ragnar Mørks legacy award in November.

# 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, 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. We are a group of nine members, including three postdocs, two engineers, three MSc students 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

We have developed bioinformatics pipelines for high-throughput sequencing of DNA and RNA, and during the past year, we have published on both exome-sequencing and RNA sequencing. Our exome-sequencing study was the first such publication on testicular germ cell tumours. This revealed a low mutation frequency, resembling that of childhood cancers, and that bilateral testis cancers have independent developmental lineages (Brabrand, Johannessen et al., Neoplasia). We developed a new methodology for RNA-sequencing which we have named RACE-seq, where we sequence pools of multiplexed RACE (rapid amplification of cDNA ends) products. This led to discovery of several novel fusion transcripts in colorectal cancers (Hoff, Johannessen *et al.*, Oncotarget). Altogether, we have published 10 papers during 2015, including three with first and/or last author from the research group. In 2015, Andreas Midbøe Hoff and Sigbjørn Brabrand defended their PhD theses.

DEPARTMENT OF

# RADIATION BIOLOGY

Headed by
Kristian Berg

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

The Department has more than 60 employees organized in 5 research groups. The research at the department is focused on the biological responses to electromagnetic radiation, including γ-radiation, ultraviolet radiation and visible light. Our department is actively engaged in revealing the mechanisms involved in DNA repair, cell-cycle regulation and genomic instability after radiation, the impact of hypoxia on radioresponse and predictive markers for the radiosensitivity of neoplastic 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. The department is also involved in revealing the impact of solar radiation on cancer development and protection by UV-induced vitamin D formation. 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.

Professor Erik Boye retired at the end of 2015. His former group is continued in 2016 as a project group led by Dr. Beata Grallert, as part of the group Radiation Biology and DNA damage signalling group, headed by Dr. Randi Syljuåsen. Following the retirement of Professor Johan Moan in 2014, his group´s research on photobiophysics, led by Dy. Asta Juzeniene, has been continued as a project group in Kristian Berg´s research group.

## 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 malignancies
- 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

## RECENT ACHIEVEMENTS

- Novel theory has been established explaining apparently conflicting clinical observations on associations between lymph node metastasis and tumor interstitial fluid pressure, hypoxia, and microvascular density
- Increased knowledge about how Chk1 and Wee1 inhibitors work to kill cancer cells
- PCI: 1) enhanced antigen presentation during anti-cancer vaccination; 2) Several new recombinant targeted protein toxins have been developed
- A prognostic hypoxia biomarker has been found for patients with cervical cancer
- A G1-S checkpoint has been identified in fission yeast which is not only dependent on the DNA repair capacity of repair deficient cells, but also the nature of the repair deficiency

# 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 4 researchers, 2 postdocs and 4 PhD students

Photochemical internalisation (PCI) is a technology for release of endocytosed macromolecules into the cytosol. The technology is based on the use of photosensitizers located in endocytic vesicles that upon activation by light cause formation of reactive oxygen species inducing rupture of the endocytic vesicles and hence allowing release of the macromolecules such as type I ribosome inactivating proteins (RIPs), gene-encoding plasmids, adenovirus, oligonucleotides, vaccine antigens and some chemotherapeutics into the cytosol. Endocytic escape is a hurdle for therapeutic utilization of macromolecular therapeutics with intracellular targets. The PCI technology is under development to overcome this hurdle. For clinical utilization a novel photosensitizer has been developed and evaluated for PCI of bleomycin. PCI is currently evaluated in a phase II clinical trials.

Solar ultraviolet (UV) radiation is the main source of vitamin D production and also the most important risk factor for skin cancer development. Vitamin D deficiency is a causal risk factor for several types of cancer. We need to understand what a balanced level of sun exposure is to maintain an adequate level of vitamin D with a minimal risk for skin cancer.

## AIMS

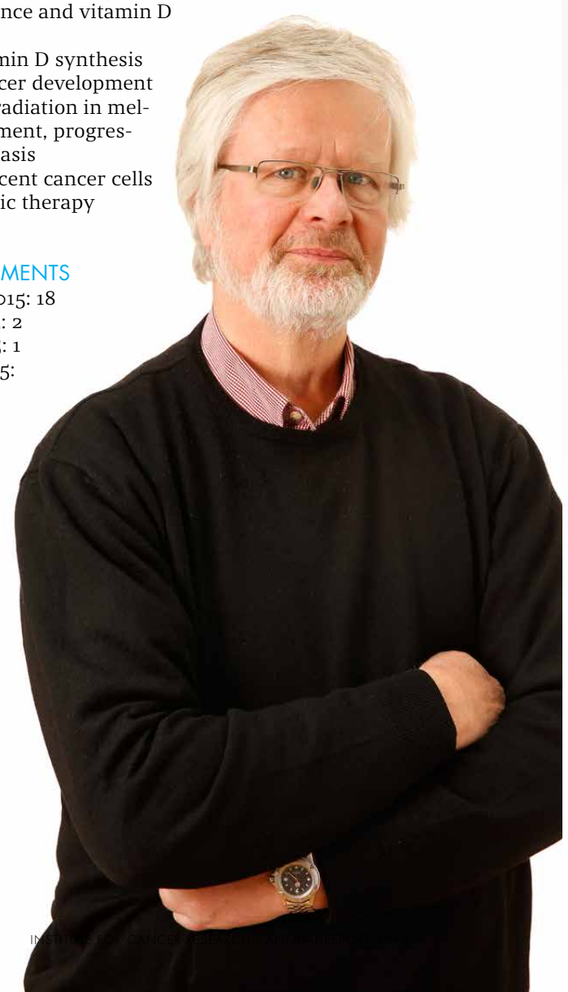
The main aim of our group is to develop and optimize the PCI technology for treatment of solid cancers with a curative endpoint.

## PROJECTS

- Design and develop recombinant immunotoxins based on type I ribosome-inactivation
- protein toxins to achieve high treatment efficacy and specificity
- Reveal the potential of the PCI technology as a treatment option for therapy resistant cancers, including cancer stem cells
- 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 treatment and seek treatment options to further utilize these effects to reach a curative endpoint
- Document and utilize the anti-tumor immunity potential of the PCI technology
- Develop PCI as a strategy for improving anti-cancer vaccines
- The role of UVB and/or UVA in skin cancer development, induction of premature cellular senescence and vitamin D synthesis
- Cutaneous vitamin D synthesis versus skin cancer development
- The role of UV radiation in melanoma development, progression and metastasis
- Targeting senescent cancer cells by photodynamic therapy

## RECENT ACHIEVEMENTS

No. of papers in 2015: 18
PhD thesis in 2015: 2
MSc thesis in 2015: 1
New grants in 2015:
EuroNanoMed II: PCINano with the PCI-group as PI; grants from the Norwegian Cancer Society, including a career stipend, from South-Eastern Health Authorities and from Simon Fougner Hartmanns Familiefond.





# CELL-CYCLE REGULATION IN EUKARYOTES

Group leader Erik Boye

*"Our goal is to understand the basic aspects of cell-cycle regulation to develop new treatment strategies"*

## ABOUT

The group was fully active in 2015, but following Professor Erik Boye's retirement towards the end of the year the research will be continued as a project group led by Dr. Beata Grallert, as part of the group Radiation Biology and DNA damage signalling group, headed by Dr. Randi Syljuåsen

Group members: 1 group leader, 1 project leader, 3 postdocs, 1 Ph D student, 1 research assistant, 1,5 technicians, 1 MSc student, 2 visiting international students

The group works to characterize the molecular mechanisms regulating cell-cycle progression in the model organisms yeast and mammalian cells in culture. The methods used are whichever are necessary to solve our biological problem: molecular genetics, cell synchronization, flow cytometry and different in vitro analyses.

## AIMS

We study two aspects of the cellular response to stress: Checkpoint regulation of the cell cycle, which is central in cancer development, and inhibition of translation, which is related to cell survival after stress. We are characterizing a G1-S checkpoint that we discovered some years ago (Genes Dev 2007, PNAS 2012) and which involves the kinase Gcn2 and also affects protein translation. Our aims are to fully understand the molecular interactions involved, including the activation mechanism of Gcn2 and its role in cancer. We have discovered a novel mechanism that inhibits protein synthesis after different forms of stress.

## PROJECTS

- Regulation of the G1-S transition in fission yeast
- Regulation of the G2-M transition in fission yeast
- Regulation of the G1-S transition in mammalian cells
- Regulation of translation after stress
- The function of Gcn2 in cancer

## RECENT ACHIEVEMENTS

Publications printed in 2015:
T.W. Håland, E. Boye, T. Stokke, B. Grallert and R.G. Syljuåsen. Simultaneous measurement of passage through the restriction point and MCM loading in single cells.
Nucl Acids Res 43(22):e150. doi: 10.1093/nar/gkv744. Epub 2015 Aug 6. PMID: 26250117

J.H.J. Knutsen, G.E. Rødland, C.A. Bøe, T.W. Håland, P. Sunnerhagen, B. Grallert, and E. Boye. Inhibition of translation independently of eIF2α phosphorylation.
J. Cell Sci 128(23):4420-7.
doi: 10.1242/jcs.176545.

One Ph.D. thesis defended (Haaland: Mechanisms regulating the G1-S transition in mammalian cells.)

One M.Sc. thesis (Noorland: Exploring the kinase GCN2 and what activates it)

Three popular science articles in newspapers

# CLINICAL RADIATION BIOLOGY

Group leader Heidi Lyng

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

## ABOUT

Group members: 10, including one researcher,five postdocs, one PhD student and two master students.

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 clinicians. 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 cancers
- Develop biomarkers and find drug targets for personalized radiotherapy of patients with these diseases

## PROJECTS

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

## RECENT ACHIEVEMENTS

Publications in 2015: 3

Selected paper: Lando M, Fjeldbo CS, Wilting SM, Snoek BC, Forsberg MF, Kristensen GB, Steenbergen RD, Lyng H. Interplay between promoter methylation and chromosomal loss in gene silencing at 3p11-p14 in cervical cancer. Epigenetics, 10(10):970-80, 2015.





# RADIATION BIOLOGY AND TUMOR PHYSIOLOGY

Group leader: Einar K. Rofstad

*"Our goal is to develop strategies for enhancing the radiocurability of tumors"*

## ABOUT

Group members: 9, including 2 researchers, 3 postdocs, 2 PhD students, and 2 technicians.

The focus of the group is to reveal mechanisms causing tumor resistance to radiation therapy. The research is based on the hypothesis that radiation resistance is primarily a consequence of microenvironmental abnormalities in the tumor tissue. 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

The main aim is to develop strategies for personalized radiation therapy of cancer to improve the outcome for patients with treatment-resistant tumors. The research is divided into two arms with the following aims:

- To develop MRI-based methods that can provide information on the physiological microenvironment and radiocurability of tumors
- To develop antiangiogenesis-based treatment strategies for normalizing the physiological microenvironment and enhancing the radiocurability of tumors

## PROJECTS

- Mechanisms Governing the Microenvironment and Radiocurability of Tumors
- Interstitial Fluid Pressure and Hypoxia in Tumors: Causes and Consequences
- Preclinical and Clinical MRI
- Antiangiogenic Tumor Treatment

## RECENT ACHIEVEMENTS

No. of papers in 2015: 6

Together with a group at the University of Science and Technology in Trondheim, we published a paper in Neoplasia showing that 1H-HR-MAS-MRS may be a valuable tool for evaluating the role of hypoxia and lactate in tumor metastasis and radiocurability. Moreover, together with Department of Gynecological Cancer at Oslo University Hospital, we published a paper in Radiotherapy and Oncology presenting a novel method for analyzing DCE-MRI data. By using this method, we showed that MR images acquired within 1 min after contrast administration have significant prognostic effect in patients with locally advanced cervix cancer.

# RADIATION BIOLOGY AND DNA DAMAGE SIGNALING

Group leader Randi G. Syljuåsen

*"Our goal is to obtain new knowledge about DNA damage signaling and utilize it to improve cancer therapy"*

## ABOUT

Group members: 11.5, including 3.5 researchers, 3 postdocs and 2 PhD students.

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. In the beginning of 2015 the Molecular Radiation Biology group was merged into this group.

## AIM

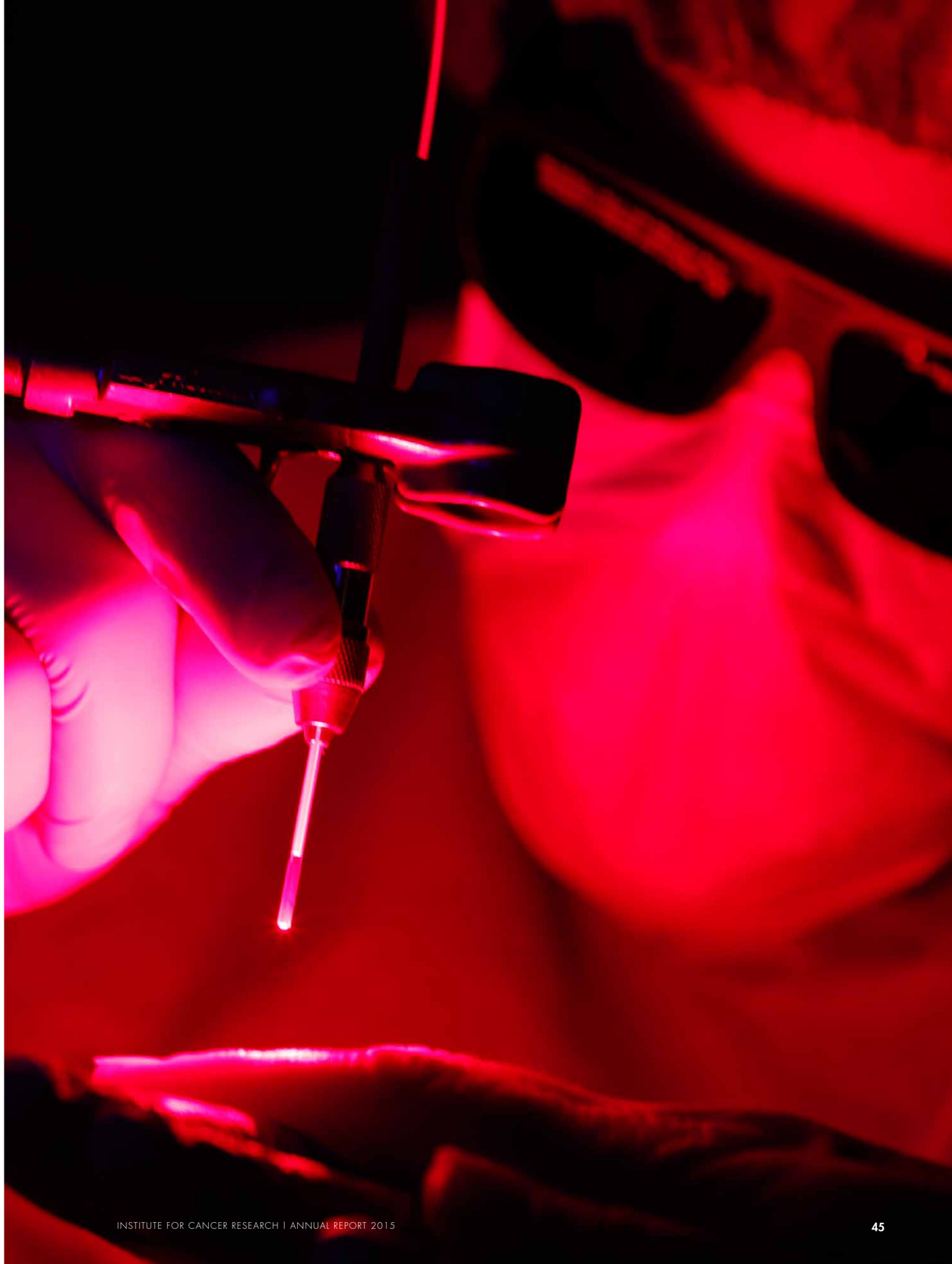
- Obtain new knowledge about DNA damage signaling, with focus on the S and G2 checkpoints, and explore how such knowledge can be used to improve cancer therapy.

## PROJECTS

- Pre-clinical exploration of checkpoint kinase inhibitors (Chk1, Wee1, Atr) as a strategy for cancer treatment in normoxic and hypoxic cancer cells in the absence and presence of ionizing radiation
- The functional role of Protein phosphatase 1 (PP1) targeting subunits in regulation of checkpoint signaling after radiation
- Identification of novel regulators of DNA damage signaling through flow cytometry-based large-scale compound screens
- Effects of Parp inhibitors
- The function of the centrosome and selected centrosomal proteins in cell cycle regulation and genome integrity

## RECENT ACHIEVEMENTS

In 2015 the group published 8 articles. Members of the group were senior or first author on 5 of these (published in Nucleic Acids Research, Cell Cycle x 2, Frontier Genetics and Plos One). During 2015 one PhD student (Johan A.W. Sternemalm: "Functional characterization of CSPP1 proteins and their evaluation as biomarkers in breast cancer"), one associated Ph.D student and three master students graduated from our group.



DEPARTMENT OF

# TUMOR BIOLOGY

Headed by
Gunhild M.
Mælandsmo

The department has 4 research groups and 62 employees, with a common vision to better understand the biological mechanisms involved in cancer development, progression and metastasis, and to utilize this knowledge to improve cancer treatment. We are mainly performing translational research, and the main pillars in our research program are cancer genomics, computational science and investigations on biological mechanisms underlying metastatic progression. Our ambition is to identify candidate biomarkers and therapeutic targets, followed by validation in preclinical models and clinical trials. To foster high quality translational research we emphasize a close collaboration with clinical scientists, and have several researchers holding part-time clinical positions. Another prerequisite for the ongoing research is a large collection of patient-derived tumor models established 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. We expect such patient-derived xenografts (PDX) to be crucial for clinical translation of precision medicine and the department aims to actively participate in this effort. In that regard it will be of high priority to maintain the national and international networks and collaborations as mentioned below.

Key achievements over the last 3-4 years include external funding of several large collaborative projects in the area of precision oncology:

- NCGC - The Norwegian Cancer Genomics Consortium, funded by The Research Council of Norway, (RCN), a national project aiming to sequence tumors across nine tumor types
- NoSarC - Norwegian Sarcoma Consortium, funded by The Norwegian Cancer Society (NCS), a national project studying disease development and treatment of sarcoma
- MetAction - Actionable targets in cancer metastasis (RCN), the first clinical trial in Norway offering targeted treatment based on biomarker detection in metastatic lesions
- MOVEMBER - Identifying biomarkers distinguishing indolent and aggressive prostate cancer (NCS)

Other clinical intervention studies with substantial collateral research;

- NeoAva: Bevacizumab in combination with neoadjuvant chemotherapy in breast cancer (in collaboration with Dept. of Cancer Genetics - patient inclusion complete)
- I-BCT: DNA targeted chemotherapy to breast cancer patients with an aggressive phenotype
- ImmunoPeCa: Immunotoxin in Peritoneal Carcinomatosis

*"Preclinical and clinical efforts towards precision oncology"*

# METASTASIS BIOLOGY AND EXPERIMENTAL-THERAPEUTICS

*"Context-induced cellular plasticity in metastasis and resistance"*

Group leader Gunhild M. Mælandsmo

## ABOUT

- Employees: The group has 18 members with multidisciplinary background and experience (cell- and molecular biologists, medical doctors, physicists and animal technicians), and includes two MDs in shared clinical positions
- Research focus: Metastasis biology and therapeutic targets/experimental drugs.
- Methodology: Molecular and functional analyses utilizing clinical samples, human cell cultures and in vivo models.

## AIMS

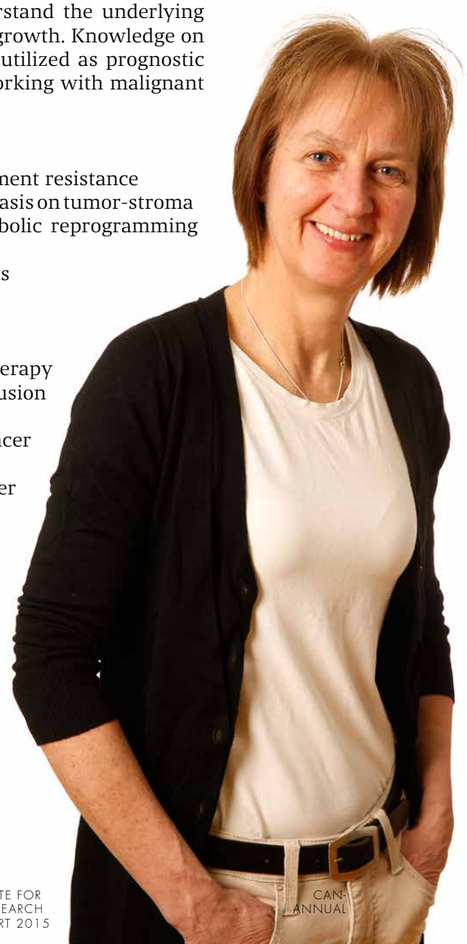
Metastatic progression is the major clinical challenge and the principal cause of death in cancer patients. To combat metastatic cancer our goal is to understand the underlying biological mechanisms causing therapy resistance, invasion and re-growth. Knowledge on these processes is vital for identification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

## PROJECTS

1. Basic research revealing mechanisms causing metastasis or treatment resistance
   - Metastasis associated proteins and regulators, with special emphasis on tumor-stroma interactions and effects on cellular plasticity (invasion, metabolic reprogramming and immune responses)
2. Preclinical research evaluating novel drugs and drug combinations
   - Efficacy and mechanistic studies in vitro and in vivo
   - Biomarker detection by molecular and functional techniques
3. Clinical trials for precision medicine
   - NeoAva: bevacizumab in combination with neoadjuvant chemotherapy for patients with locally advanced breast cancer (patient inclusion closed, data processing ongoing)
   - 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

## RECENT ACHIEVEMENTS

- Metrics: Group members were credited with 14 publications in 2015, six with group members as first and/or last author; 1 PhD degree completed
- Two clinical intervention trials open for inclusion (MetAction and I-BCT)
- Marie Sklodowska-Curie mobility grant and partnership in the EU-grant "Imaging the Force of Cancer"
- Several collaborative projects with industry partners (eg: funding from BIA and BioTek2021)





# TRANSLATIONAL CANCER THERAPY

*"New treatment for peritoneal metastases"*

Group leader Kjersti Flatmark

## ABOUT

The Translational Cancer Therapy group comprises 16 members; it was relatively recently established, and several projects are in an early phase. Our strength is a broad variety of expertise spanning from basic biologists through translational scientists to clinicians; this year, 5 group members were MDs. The 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 prognostic and predictive biomarkers and implement improved cancer therapy using a collaborative, transdisciplinary, and translational approach.

## PROJECTS

1. Colorectal cancer (CRC) – a majority of the projects in the group focus on locally advanced and metastatic CRC, involving basic, preclinical, translational and interventional clinical trials
2. Cancer metastasis projects – employ basic, translational and clinical methodology to identify and characterize factors of importance in the metastatic process
   - Exosomes in cancer metastasis
   - Experimental models and therapy in ovarian carcinoma
   - miRNA in cancer metastasis
   - B7H3 protein in metastasis and therapy resistance
   - MetAction clinical trial – actionable targets in cancer metastasis
   - Brain metastasis project
3. Sarcoma
   - Gastrointestinal stromal tumors – therapy resistance and circulating DNA
   - NoSarC; DNA sequencing of annual cohorts of sarcoma patients in Norway

## RECENT ACHIEVEMENTS

- Group members were credited with 15 publications in 2015; 1 PhD completed, 1 Master degree completed.
- Two clinical intervention trials are ongoing (ImmunoPeCa and MetAction)
- A public, revised database of all human miRNAs (MirGeneDB.org; http://MirGeneDB.org)
- Establishment of the Cure4PMP European Research Network
- Commercialization MOC31PE immunotoxin

# COMPUTATIONAL CANCER GENOMICS AND MELANOMA SYSTEMS BIOLOGY

*"Systems solutions for precision medicine"*

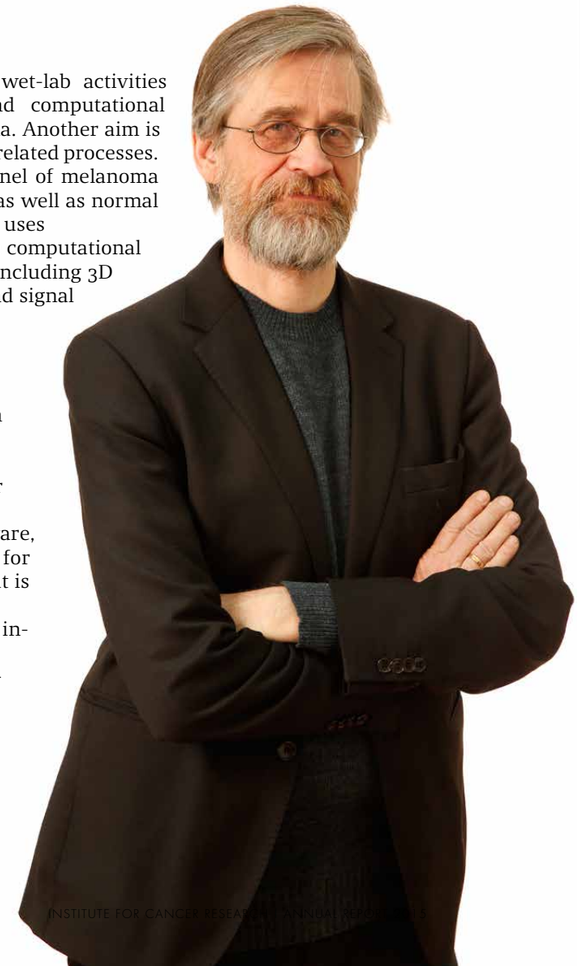
Group leader Eivind Hovig

## ABOUT

The 12-member group has strong interest in the development of computational approaches in cancer genomics in general, and in melanoma systems biology more specifically. Currently, activity is centred on computational aspects of deep sequencing pipelines for cancer, and downstream analysis. The lab biology focus is on understanding various aspects of melanoma biology, with an emphasis on the MITF master switch of melanocytes, and studies on key signaling systems in melanoma.

## AIMS

The overarching approach is to feed the computational and wet-lab activities reciprocally, using high-throughput genomic technologies and computational modeling, to understand important signaling systems in melanoma. Another aim is to develop novel methodology for computational studies of cancer-related processes. The main wet-lab approach is the use of a well-characterized panel of melanoma cell lines representing different stages of melanoma progression, as well as normal melanocytes to chart causative molecular features. The group also uses lentiviral constructs to build lab models of melanoma. Among the computational aspects addressed are immune aspects of melanoma, chromatin, including 3D models of nuclear DNA, understanding of mutational processes and signal modeling.



## PROJECTS

- The MITF transcriptional master switch of melanocytes
- Use of lentiviral systems with bi-cistronic MITF constructs with ChIP-seq mapping of active signal pathways
- Development of solutions for integrative cancer sequencing towards diagnostics, and participation in international efforts for development of best practice methods
- Further development of statistical genomics based on our software, theGenomic HyperBrowser. This is an internationally used tool for multipurpose integrated statistical analysis of genomic data that is being further developed
- Melanoma signalling perturbations for systems understanding, including MITF, BRAF and CDKN2A aberrations
- Understanding the consequences for modulation of immune responses in melanoma

## RECENT ACHIEVEMENTS

Publications: 13
PhDs completed: 2



# MESENCHYMAL CANCER BIOLOGY

*"Drug repurposed for orphan cancer"*

Group leader Ola Myklebost

## ABOUT

The 14-member group has a long standing interest in the biology of mesenchymal tumors (sarcomas). The current focus is on precision medicine for these tumors, and Ola Myklebost is head of the Norwegian Cancer Genomics Consortium (NCGC, www.kreftgenomikk.no) and Norwegian Sarcoma Consortium (NoSarC, www.nosarc.no).

## 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 biology – Gaining further understanding of the development and progression of osteo- and liposarcomas, and potentially identify biomarkers and novel drug targets
- Studies of metabolic reprogramming in sarcomas and during mesenchymal transformation of breast cancer
- 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

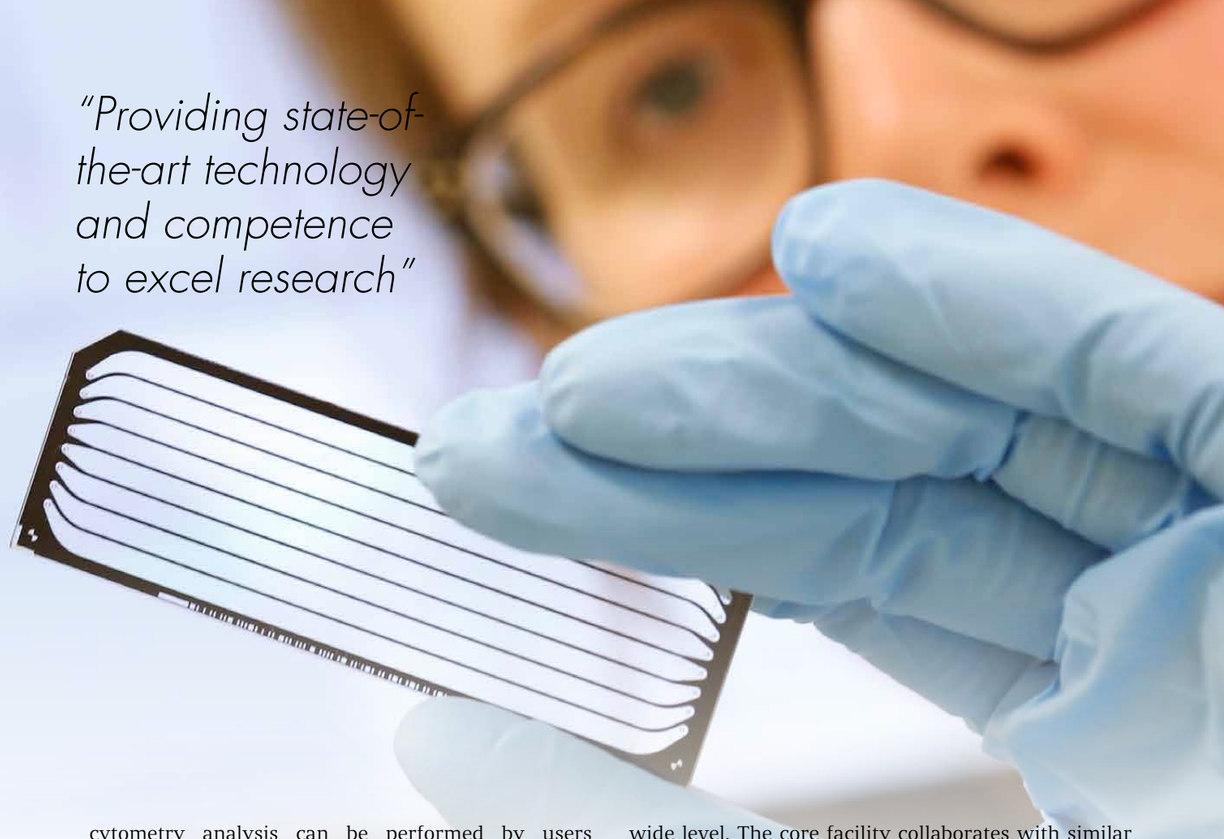
Publications: 12
PhDs completed: 1

DEPARTMENT OF

# CORE FACILITIES

Headed by
Leonardo A.
Meza-Zepeda

*"Providing state-of-the-art technology and competence to excel research"*



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 facilities is organised in three units; Flow Cytometry and Pre-Clinical Imaging, Advanced Microscopy, and Genomics and Bioinformatics, with a total of 22 employees. 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 super-resolution microscopy. Current instruments include a Zeiss LSM710 confocal microscope, a DeltaVision live-cell microscope and an OMX Blaze structured illumination (and STORM) super-resolution microscope. The core facility cooperates with nodes at the Rikshospitalet and Ullevål campuses of Oslo University Hospital, as well as the light microscopy core facility at the Institute for Biosciences, University of Oslo. Recently, the core facility for ALM was accepted as 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. Our current instrumentation includes 3 transmission electron microscopes and sample preparation tools such as microtomes (cryo), high-pressure freezers and freeze substitution units. We actively cooperate with the imaging platform at the Institute for Biosciences, University of Oslo. In 2015 the core facility received funding for new large research infrastructure from the Research Council of Norway.

## BIOINFORMATICS

**Leonardo A. Meza-Zepeda**

*Facility staff: 5*

The Bioinformatics Core Facility provides service, support and advice on most aspects of bioinformatics, including a wide array of topics ranging from simple identifier mapping tasks to mathematical modelling of biological processes, sequence and sequencing data analysis, analysis protein structure, DNA variation, genetic linkage, microarrays, association studies, statistical genomics, database access, web services and network analysis. The complementary competence of the core facility personnel is backed by strong links to leading bioinformatics and biostatistics research groups in the region. The operation of the Bioinformatics Core Facility is aligned with the national and local Elixir bioinformatics infrastructure project, and also interacts with USIT, University of Oslo, for facilitating use of high-performance computing resources.

## FLOW CYTOMETRY

**Trond Stokke**

*Facility staff: 4*

The Flow Cytometry Core Facility (FCCF) provides analysis and sorting services for users within the South-Eastern Health Region of Norway. Flow cytometry analysis can be performed by users themselves, but sorting experiments are done by core facility employees. The facility also offers high-throughput screening, processing and staining of cells in 96- or 384-well plates, followed by automated flow cytometry and/or microscopy analysis. We have installed a new mass-spec "flow cytometer", the CyTOF. In this instrument a number of parameters may be measured, up to 50-60, i.e. several times what is achievable by regular flow cytometry. The FCCF collaborates with facility nodes at the Rikshospitalet and Ullevål campuses of OUH.

## GENOMICS

### HIGH-THROUGHPUT SEQUENCING AND MICROARRAYS

**Leonardo A. Meza-Zepeda**

*Facility staff: 8*

The Genomics Core Facility (GCF) provides state-of-the-art laboratory technology and high-throughput genomic services to the Norwegian scientific community. Today, GCF is an Illumina CSPro certified service provider, and offers an extensive set of complex technologies to study genome structure, dynamics and function using high-throughput sequencing with the complete range of Illumina sequencers 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 a founder member of the newly established National Consortium for Sequencing and Personalised Medicine (NCS-PM). The GCF provides the sequencing infrastructure and competence for the National Personalised Medicine initiative, and received in 2015 large research infrastructure funding from the Research Council of Norway as part of NCS-PM.

## PRECLINICAL MAGNETIC RESONANCE IMAGING (MRI)

**Trond Stokke**

*Facility staff: 2*

The Preclinical MRI Core Facility provides access to a state-of-the-art 7T Bruker MRI system and 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 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 MRI 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. In 2015 an IVIS pre-clinical in vivo imaging service was established, suitable for whole body 2D imaging using fluorescence and luminescence.

# RESEARCH CENTRES OF ICR



## 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.

## 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. The selected Centres receive 16 million NOK in basic funding from the Foundation.

## 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.


# CENTRE FOR CANCER BIOMEDICINE (CCB)

HEADED BY
HARALD STENMARK AND
RAGNHILD A. LOTHE

*"Uniting basic and translational cancer research for the benefit of the patient"*



## ABOUT

CCB was inaugurated in September 2007 with the vision of joining cell biological research aimed at discovering new mechanisms in tumour development with translational cancer research aimed at discovering novel molecular and phenotypic hallmarks that can be exploited in cancer diagnostics and therapeutics. Aided by 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 colorectal cancer, lymphomas, prostate cancer or malignant peripheral nerve sheath tumors (MPNST). CCB's interdisciplinary strategy has turned out to be a very fruitful one, and there has been a steep increase in publications that involve several of the PI and associated groups of the centre. Most of the publications have CCB scientists as leading authors, and several CCB publications can be classified as real breakthroughs. Moreover, a large number of innovation paths have surfaced from CCB scientists.

## 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 internalization and signalling
- Cellular membrane dynamics
- Intracellular transport
- Cancer genetics
- Cancer epigenetics
- Cancer cytogenetics
- Cancer genome biology
- Large-scale genomic instability
- Statistical analyses in cancer
- Biomedicine of:
  - Colorectal cancer
  - Lymphomas
  - Prostate cancer
  - Malignant peripheral nerve sheath tumours

## RECENT ACHIEVEMENTS

CCB graduated 7 PhD degrees in 2015 and published 70 articles, many of these in leading international journals. Papers with CCB scientists as corresponding authors were published in leading journals such as *Nature* (two papers), *Clinical Cancer Research*, *Hepatology* and *Nature Reviews in Clinical Oncology*. CCB scientists have also been active in popularizing the centre´s research in the form of newspaper chronicles, blog posts and interviews in the mass media.

Several CCB scientists received prestigious prizes in 2015. These include Sigrid B. Thoresen, who received H.M. the Kings´s Gold Medal for best PhD thesis, Kaisa Haglund, who received Anders Jahre´s prize for younger medical scientists in the Nordic countries, Guro E. Lind, who received Dr. Ragnar Mørk´s prize for excellent cancer research, and Harald Stenmark, who received the Research Council´s "Møbius" prize for outstanding research. Guro E. Lind was elected as the first chair of the newly started Academy of Young Scientists, an initiative from the Norwegian Academy of Science and Letters.

## CLINICAL TRANSLATION

The research groups of Erlend B. Smeland, Ragnhild A. Lothe and Rolf I Skotheim are in collaboration with associate clinicians Harald Holte, Arild Nesbakken and Karol Axcrona running major tumour heterogeneity studies for the three main cancer types of CCB (lymphoma, colorectal, and prostate cancer). Some of the obtained next-generation sequencing results are likely to identify prognostic or predictive biomarkers.

In 2015 Harald Holte co-authored a paper in *Blood* from Oslo University Hospital about immunotherapy of advanced follicular lymphoma (FL) using 3 treatment modalities resulting in regression of disseminated FL. In another study (national cross-sectional study) co-authored by Holte in *Journal of Clinical Oncology*, side effects in lymphoma survivors after autologous transplantation were studied, and the results may aid in establishing new surveillance strategies.

A clinical phase II trial on the MPNST type of sarcoma was recently approved. The Lothe group published two papers in 2015 that identified high-risk biomarkers for MPNST patients with and without the hereditary disease of von Recklinghausen (Danielsen et al., *Neuro Oncol;* Kolberg et al ., *Mol Oncol.*). So far, no treatment beyond surgery is proven to have effect in these patients. Based on the similarities with melanoma, Lothe suggested an immunotherapy-based clinical trial for these patients. The study was approved late 2015 with collaborating oncologist Guren as PI. A preclinical study of high- throughput drug sensitivity and resistance therapy was perfomed by Matthias Kolberg and Jarle Bruun, and novel findings will be implemented in another protocol. All biomarker studies will be performed in the Lothe lab at CCB.

## EXECUTIVE GROUP (PI's) IN 2015

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

## ASSOCIATE PI's

Sverre Heim
Guro E. Lind
Antoni Wiedlocha

Centre for Cancer Biomedicine

# K.G. JEBSEN CENTER FOR BREAST CANCER RESEARCH

HEADED BY
ANNE-LISE
BØRRESEN-DALE

*"From bed to bench to byte to bedside"*

## ABOUT

The vision of the Center was to move towards personalized therapy for breast cancer, using integrated molecular analyses to reduce risk, improve prognosis, and tailor treatment. The Center was built on the Oslo Breast Cancer Research Consortium (OSBREAC), and after its funding period expired at the end of 2015 this consortium will continue to move the field forward, also through a Regional Research Network grant from The South Eastern Regional Health Board to the OSBREAC consortium.

## AIMS

The overall aim has been to open up for stronger collaboration between clinical and basic scientists, and to motivate exchange of ideas on how to best utilize the huge collection of patient materials and data generated. By such synergism we have been able to explore genes/pathways/networks involved in basic processes like cell cycle regulation, DNA repair, apoptosis, and immune response and their impact on breast cancer development, progression and response to therapy.

## PROJECTS

- High throughput molecular characterization of primary tumors
- Detection and characterization of occult tumor cells in bone marrow, blood and sentinel lymph nodes as well as detection of cell free tumor DNA in blood
- Functional studies in experimental model systems
- Metabolic and physiological characterization
- Data integration

## RECENT ACHIEVEMENTS

- Combined analyses of molecular data (copy number, mRNA, miRNA, methylation, protein expression, metabolic profiles) from 450 cases from Oslo2 have identified novel biological functions and molecular pathways being deregulated. These results have paved the grounds for initiating clinical trials to identify novel patient subgroups for tailored therapy and monitoring
- The NeoAva study demonstrated that patients with a significantly higher expression of genes enriched for immune-related pathways responded to the antiangiogenic treatment. Analysis of CNA demonstrated significant differences in genomic instability and differences in specific loci between good and poor responders. Specific treatment-induced changes were also seen in protein expression (RPPA) and the metabolome (HR-MAS)
- Deep sequencing of selected samples has identified new genes involved, and novel mutational processes that evolve across the lifespan of a tumor, with patient-specific signatures of point mutations and chromosomal instability
- Advanced in-situ techniques, iFISH, and novel software demonstrated that HER2+ tumors display several types of intratumor heterogeneity important for predicting response and cell-type dynamics during neoadjuvant treatment
- Comparing DNA alterations of several single DTCs per patient to each other, to the corresponding primary tumor and lymph node, suggests a continuous dissemination of single tumor cells throughout the tumor evolution. By demonstrating subclonality in the lymph node metastasis, and their copy number profiles resemblance to primary tumor, we provide novel insight into the metastatic process

## CLINICAL TRANSLATION

The research project utilizes a number of previously and newly collected clinical cohorts. We have performed "state of the art" analyses of patient material, both on bulk tumors, single cells and liquid biopsies, at various stages of the disease, from consecutive series with up to 25 years of follow-up (OsloVal, Oslo0, Oslo1, Oslo2). Several clinical trials have been initiated: NeoAva (neoadjuvant treatment with/without bevacizumab), analyses of 3 different time-points completed, EMIT (Establishment of Molecular profiling for Individual Treatment decisions in Early Breast Cancer - analyses ongoing), and I-BCT (a phase2 clinical trial studying biological rationale for the optimal selection of treatment regimens - under collection ).

## GROUP LEADERS/STEERING COMMITTEE

The Center has consisted of 6 research groups,

- Clinical group: Dr.Med Ellen Schlichting and Prof. Em Rolf Kåresen (surgery), Prof. Torill Sauer, Dr.Med Elin Borgen, and Dr.Med Hege G. Russnes (pathology), Prof. Erik Wist, Dr.Med Olav Engebråten and Prof. Bjørn Naume (oncology)
- Molecular group : Prof. Anne-Lise Børresen-Dale (Director), Prof. Vessela N. Kristensen (deputy Director)
- Micro-metastases group: Prof. Bjørn Naume
- Model-systems and functional group: Prof. Gunhild M. Mælandsmo and Prof. Em. Øystein Fodstad
- Metabolic profiling and imaging group: Prof. Tone F. Bathen NTNU Trondheim
- Bioinformatics/biostatistics group: Prof. Ole Christian Lingjærde, UiO

In the period 2011-2015 there have been 23 PhD students who have defended or delivered their thesis. More than 250 scientific publications have been published or are in press from the Center.

STIFTELSEN KGJ Kristian Gerhard Jebsen Foundation

# K.G. JEBSEN CENTER FOR CANCER IMMUNOTHERAPY

HEADED BY JOHANNA OLWEUS




## 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. This consortium of PIs is assembled based on highly complementary expertise in proteomics, cell signaling, T-cell receptor (TCR) and HLA-engineering and animal models, translational research and expertise as PI for clinical trials in immunotherapy. Of the 53 center employees 55% are recruited from abroad (60/40 women/men). The center is part of Oslo University Hospital Focus Area for Cancer Immunotherapy, lead by partner AK.

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

## 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 (WP 1)
- Identify T cells that recognize and kill cells that express the identified targets (WP 2)
- Molecular cloning, genetic transfer and profiling of immune receptors (WP 3)
- Enhance effector T-cell function by overcoming inhibitory mechanisms (WP 4)
- In vivo evaluation of immune modulating therapies (WP 5)

## RECENT ACHIEVEMENTS

- Clinical responses are strongly correlated to anti-tumor T-cell reactivity in patients with follicular lymphoma treated with novel immunotherapy *(Blood 2015, commentary same issue, OncoImmunology 2015)*
- TCRs isolated from cell-type specific T cells can be used to engineer T cells to kill patient-derived lymphoma/leukemia cells *(OncoImmunology, accepted 2015)*
- High-throughput discovery of antigen-specific CD4+T cells and T-cell receptors *Nature Medicine 2015)*
- Developed novel technology in which 8000 different proteins are coupled to separate beads for multiplexed proteomics to determine serum-antibody specificities for target identification
- Obtained new insights into the functional plasticity of human NK cells *(J. Immunol 2015, Immunity 2015)*, paving the way for development of the next generation of NK-cell therapy
- Characterized a new potential mechanism of regulation of Treg-mediated immunosuppression *(patent application, Invent2 Idea Prize 2015)* and performed a chemical biology screen that has delivered a set of candidate compounds to perturb this mechanism to be tested (on-going).

## CLINICAL TRANSLATION

A key strength of the center is the ability to couple clinical trials with penetrating mechanistic analyses, facilitating the continuous refinement of experimental immunomodulatory therapeutic trials.

- Results from **LYMVAC cancer vaccine trial**, in which a novel local immunotherapeutic strategy resulted in 36% clinical responses in patients with follicular lymphoma, were published in ***Blood 2015*** *(see achievements)*. Based on this successful study two follow-up studies were designed to i) identify T-cell targets (on-going) (supported by Roche), and ii) improve the local immunotherapy regime with addition of systemic anti-PD-1 in patients, supported by *Merck*. Enrollment of patients has started.
- **Adoptive NK-cell trial:** A first phase I/II clinical trial based on adoptive transfer of haploidentical NK cells to patients with high-risk hematological malignancies (MDS and AML) who have no other treatment options was completed with promising results. The results pave the way for a Nordic trial with a JCIT partner as PI.

## GROUP LEADERS/ STEERING COMMITTEE

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

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

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

**Professor Kjetil Tasken (MD, PhD**), Centre for Molecular Medicine Norway, Nordic EMBL Partnership and Biotechnology Centre, UiO and Dept of Infectious Diseases, OUH

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

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

STIFTELSEN KGJ Kristian Gerhard Jebsen Foundation

# K.G. JEBSEN COLORECTAL CANCER RESEARCH CENTRE

HEADED BY
RAGNHILD A. LOTHE

*"High quality translational research for the benefit of the colorectal cancer patient"*



## ABOUT

Colorectal cancer (CRC) is a major health burden, and the focus of our Centre is translational and clinical research on several of the remaining challenges in the management of the disease, including early detection and improved patient prognostication and treatment. The Centre was opened in August 2014, and is hosted by the Clinic for Cancer, Surgery and Transplantation, Oslo University Hospital (OUH). The Centre PIs are also partners in the OUH SMART-Colorectal cancer priority area, which is granted for the period 2014-18 and lead by Ragnhild A. Lothe and Arild Nesbakken. The Centre projects involve translational and clinical co-investigators from all the four main sites at OUH, and from the Institute of Clinical Medicine, University of Oslo. The research leaders have competence /experience in biomarker research and development, as well as in running various clinical trials. Ongoing international collaborations include researchers at Harvard, MD Anderson, Oxford University and Vall d'Hebron Research Institute.
Home page: www.colorectalcancer.no

## AIMS

The research groups unite a translational multidisciplinary research environment with focus on high quality in all steps of the research process, following the patient through the course of the disease and aiming to transfer biomedical research into improvements in prevention and treatment of CRC.

## PROJECTS

- Clinical and molecular biomarkers for improved risk stratification of patients
- Personalised drug treatment of patients by biologically justified use of chemotherapy and/or targeted drugs
- Biomarkers for monitoring early relapse of CRC by exploring the clonal evolution resulting in molecular intra and inter-tumour heterogeneity of primary and metastatic lesions
- Identification of high risk precursor lesions and novel biomarkers in population-based screening studies

## RECENT ACHIEVEMENTS

During 2015, 23 relevant peer reviewed papers were published from the PIs, including in relevant journals as GUT, Oncogene and Clinical Cancer Res.

Bioinformatic pipelines are implemented for analyses of multilevel genomic data, including high resolution DNA copy number variation, exome sequencing (Bruun et al., CCR 2015; Brabrand et al., Neoplasia 2015) and RNA sequencing (Hoff et al., Oncotarget 2015), as well as for data integration to analyse tumor clonality and immunogenicity, the latter by predicting neoantigen presentation by patient-specific HLA molecules (Sveen et al., submitted).

Prognostic value is demonstrated for the cell cycle protein Regulator of chromosome condensation 2 in CRC (n>900) (Bruun et al., CCR 2015). Validation studies in independent patient series are currently being analysed in international collaboration. Prognostic value of intra-patient, inter-metastatic genetic heterogeneity is recently identified (Sveen et al., submitted).

Associate investigator Guro E. Lind appointed as the first leader of the Young Academy of Norway, and receiver of Ragnar Mørk legacy prize 2015. Michael Bretthauer and Ragnhild A. Lothe both received major grants through "TOPPFORSK" – Norwegian Research Council and the University of Oslo.

KGJ Colorectal Cancer Research Centre has arranged two whole day seminars in 2015; Institute for Cancer Research, 10th of February 2015, 55 participants. Grand Hotel, Oslo, 12th of November 2015, 60 participants. PIs have contributed to dissemination of supercomputing and personalized medicine to the general public by articles in Apollon, META, Vi Menn, Aftenposten.

## CLINICAL TRANSLATION

The **EPoS trial** was opened May 2015 –PI Michael Bretthauer. The European Polyp Surveillance Trial (EPoS) has started patient recruitment and will include 30,000 patients over the next three years. The EPoS-project is addressing one of the most important challenges in the prevention of colorectal cancer; the surveillance of patients that have had colorectal polyps removed (polypectomy).
A **phase II clinical trial** initiated in the KGJ Centre was approved late 2015 by the Regional Ethics Committee and by The Norwegian Medicines Agency and patient inclusion will start spring 2016. "Adjuvant chemotherapy in elderly with colon cancer stage III – geriatric assessment and prognostic gene signatures". PI Marianne Guren, co-investigators: Ragnhild A. Lothe, Arild Nesbakken, Anita Sveen, Jørgen Smedby (PhD student).

## PI's/STEERING COMMITTEE OF THE CENTRE

- **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
- **Professor Michael Bretthauer** (MD, PhD), Institute of Health and Society, UiO, and Department of Transplantation medicine, Section of Gastroenterology, OUH
- **Professor Rolf I. Skotheim** (MSc, PhD), Department of Molecular Oncology, Institute for Cancer Research, OUH and Institute for Informatics, UiO
- **Professor Kjell M. Tveit** (MD, PhD)/ **Senior Consultant Marianne Guren** (MD, PhD), Department of Oncology, OUH and Institute for Clinical Medicine, UiO

Administrative coordinator (20% position):
**Anette Sørensen**

STIFTELSEN KGJ Kristian Gerhard Jebsen Foundation

# NORWEGIAN CANCER GENOMICS CONSORTIUM

HEADED BY
OLA
MYKLEBOST

*"The use of tumor genome analysis to better tailor cancer treatment"*



## 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, promises huge benefits to the patients by better adapting the treatment, especially by targeted drugs, to the disease of the individual. The hope is that this will at least give prolonged survival and better quality of life to the patients, 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 sequence 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 and breast cancers are being investigated for predictive biomarkers, as are biobanks containing colon, prostate, myeloma, lymphoma and leukemia samples from standard-of-care treated patients. A trial biobank from leukemia patients participating in the first Axl inhibitor study from BerGenBio is planned. A prospective, population-based cohort of all Norwegian sarcoma patients for 2-3 years is now being accrued (see NoSarC.org). Up to now approximately 1300 samples from 530 patients have been sequenced.

Promising targets for which drugs are available, but without documentation of effect in the cancers investigated, are tested pre-clinically in relevant cell and xenograft models. The intention is then to propose small, exploratory clinical trials to indicate activity in selected patients, and that promising results could lead to proper phase II studies. Several trials are in progress by the partners.

The NCGC has received two major grants from the Research Council, and has embarked on projects to sequence tumour material from the selected biobanks. 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 SNPs detected in the germ lines, and the frequencies in the population. Other environments are preparing to add Norwegian SNP data, which will be a valuable resource for many types of genetic research and diagnosis. The NCGC was highlighted by a review article in Drug Discovery Today, in a special issue together with a number of other large cancer genomics and personalized treatment studies.

## CLINICAL TRANSLATION

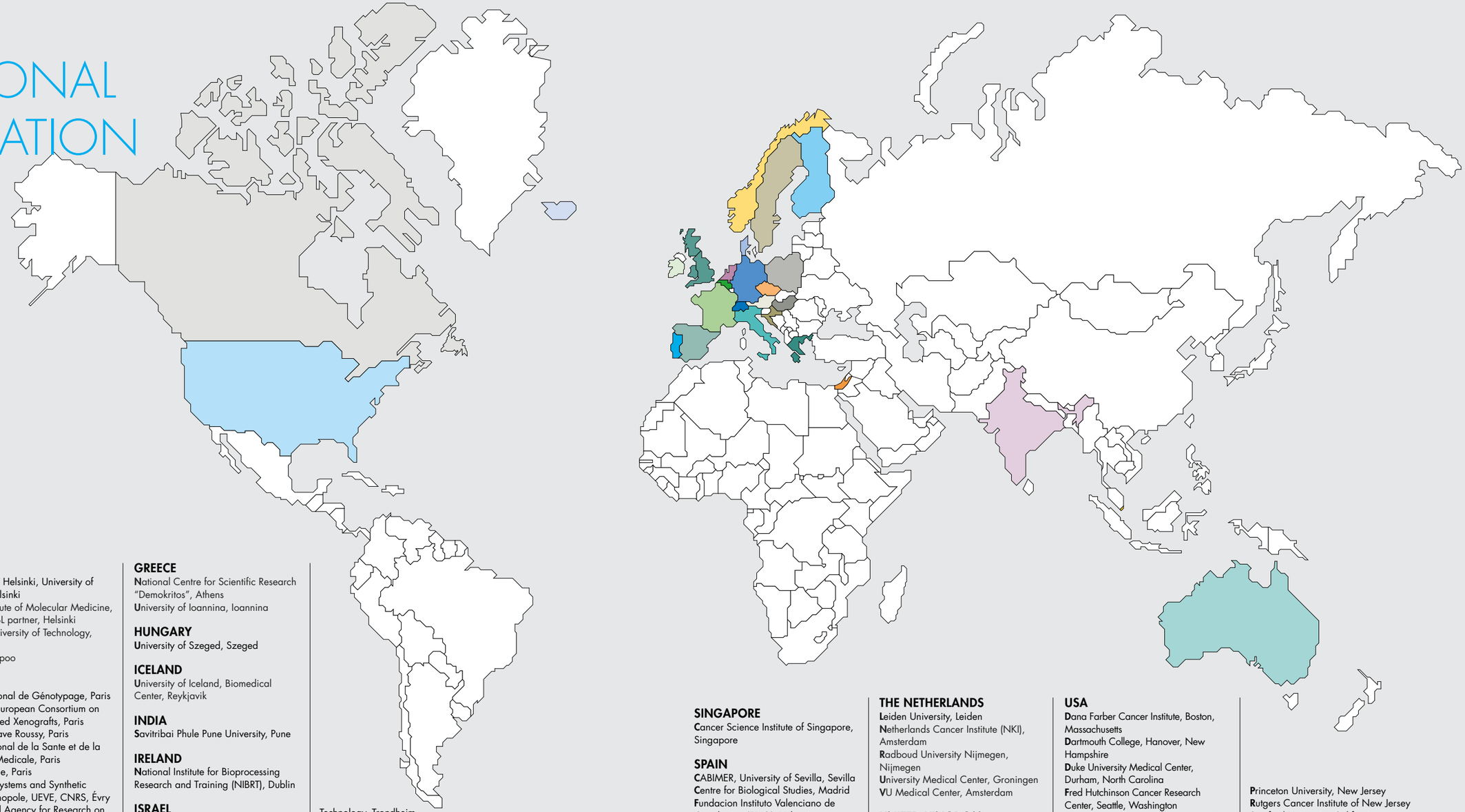
The project is investigating patient samples either prosepctively collected, or being part of clinical trials, with the aim to gain biologically based clinical insight. Oncologists are strong partners. The detection of novel therapeutic targets and their evaluation in pre-clinical studies may have immediate clinical value. The team maintains a systematic professional dialogue, with repeated discussions on the strategies and how they may be implemented in the clinic 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), Edvin Johannessen (UiO), Knut Martin Torgersen (Pfizer), Bjørn Gustafsson (NTNU), Tove Flem Jakobsen (Inven2), Olav Mella (UiB), Anne Sameline Grinsgaard (UNN).

CancerGenomics.No

# INTERNATIONAL COLLABORATION




**AUSTRALIA**
**G**arvan Institute, Sydney
**K**inghorn Cancer Centre, Sydney
**M**onash University, Melbourne

**AUSTRIA**
**M**edical University of Vienna, Vienna

**BELGIUM**
**G**hent University, Ghent
**K**atholieke University Leuven, Leuven
**U**niversiteit Hasselt, Genk

**CANADA**
**M**cGill University, Montreal
**P**rincess Margaret Hospital, Toronto
**U**niversity of Ottawa, Ottawa

**CROATIA**
**U**niversity of Zagreb, Zagreb

**CZECH REPUBLIC**
**C**harles University, Prague
**I**nstitute of Experimental Biology, Masaryk University, Brno
**I**nstitute of Molecular Genetics, Academy of Sciences of the Czech Republic, Prague
**N**ational Institute of Public Health, Prague

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**A**alborg University Hospital, Aalborg
**A**arhus University Hospital, Aarhus
**U**niversity of Copenhagen, Copenhagen
**U**niversity of Southern Denmark, Odense

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**F**innish Institute of Molecular Medicine, Nordic EMBL partner, Helsinki
**T**ampere University of Technology, Tampere
**Z**ora Oy, Espoo

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**E**urOPDX - European Consortium on Patient-derived Xenografts, Paris
**I**nstitut Gustave Roussy, Paris
**I**nstitut National de la Sante et de la Recherche Medicale, Paris
**I**nstitute Cürie, Paris
**I**nstitute of Systems and Synthetic Biology Genopole, UEVE, CNRS, Évry
**I**nternational Agency for Research on Cancer (IARC), Lyon
**U**niversité Lyon, Villeurbanne
**U**niversité Paris-Sud, Orsay

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**I**nstitut für Biochemie, University of Stuttgart, Stuttgart
**I**nstitute of Physiology and Pathophysiology, University of Mainz, Mainz
**J**acobs University, Bremen
**U**niversity of Bayreuth, Bayreuth
**U**niversity of Bochum, Bochum
**U**niversity of Cologne, Cologne
**U**niversity of Marburg, Marburg

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**U**niversity of Ioannina, Ioannina

**HUNGARY**
**U**niversity of Szeged, Szeged

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**IRELAND**
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**W**eizmann Institute, Rehovot

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**I**nternational School for Advanced Studies, Trieste
**I**stituto Nationale di Tumori, Milano
**T**he Rizzoli Institute, Bologna
**U**niversity of Bologna, Bologna
**U**niversity of Padova, Padova
**U**niversity of Salento, Lecce

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**H**aukeland University Hospital, Bergen
**N**orwegian University of Science and Technology, Trondheim
**S**tavanger University Hospital, Stavanger
**T**rondheim University Hospital- St. Olavs Hospital, Trondheim
**U**niversity hospital of North Norway, Tromsø
**U**niversity of Bergen, Bergen

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**J**agiellonian University, Kraków
**U**niversity of Gdansk, Gdansk

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**P**ortuguese Oncology Institute, Porto

**SINGAPORE**
**C**ancer Science Institute of Singapore, Singapore

**SPAIN**
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**C**entre for Biological Studies, Madrid
**F**undacion Instituto Valenciano de Oncologica (FIVO), Valencia
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**V**all d'Hebron Institute of Oncology, Barcelona

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**L**und University, Lund
**T**he Sahlgrenska Academy at the University of Gothenburg, Gothenburg
**U**ppsala University Hospital, Uppsala

**SWITZERLAND**
**U**niversity Hospital Zurich, Zurich

**THE NETHERLANDS**
**L**eiden University, Leiden
**N**etherlands Cancer Institute (NKI), Amsterdam
**R**adboud University Nijmegen, Nijmegen
**U**niversity Medical Center, Groningen
**V**U Medical Center, Amsterdam

**UNITED KINGDOM**
**C**ambridge Cancer Institute, Cambridge
**H**ampshire Hospitals/Southampton University, Southampton
**L**ondon Research Institute,The Francis Crick Institute, London
**R**oyal National Orthopaedic Hospital, Stanmore, Middlesex
**T**he Beatson Institute for Cancer Research, Glasgow
**T**he European Bioinformatics Institute (EMBL-EBI), Hinxton
**U**niversity College London Medical School, UCL, London
**U**niversity of Cambridge, Cambridge
**U**niversity of Liverpool, Liverpool
**U**niversity of Oxford, Oxford
**W**ellcome Sanger Institute, Hinxton

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**D**ana Farber Cancer Institute, Boston, Massachusetts
**D**artmouth College, Hanover, New Hampshire
**D**uke University Medical Center, Durham, North Carolina
**F**red Hutchinson Cancer Research Center, Seattle, Washington
**G**eorgetown University, Washington DC
**H**arvard University, Boston, Massachusetts
**J**ohns Hopkins Medicine, Baltimore, Maryland
**L**awrence Berkeley National Laboratory, Berkeley, California
**L**ineberger Comprehensive Cancer Center, Chapel Hill, North Carolina
**M**asonic Cancer Center and University of Minnesota, Minneapolis
**M**assachusetts General Hospital, Boston, Massachusetts
**M**D Anderson Comprehensive Cancer Center, Houston, Texas
**N**ational Institutes of Health (NIH), Bethesda, Maryland
**O**regon State University, Corvallis, Oregon
**P**rinceton University, New Jersey
**R**utgers Cancer Institute of New Jersey
**S**tanford University, California
**T**he Mount Sinai Hospital, New York
**T**he University of Kansas Hospital, Kansas
**T**isch Cancer Institute, New York
**U**CSF, Helen Diller Family Cancer Centre, San Francisco, California
**U**niversity of Albany, New York
**U**niversity of California, Berkeley
**U**niversity of Chicago, Illinois
**U**niversity of Colorado, Denver, Colorado
**U**niversity of Illinois, Champaign, Illinois
**W**ashington University, St Louis, Missouri
**W**eill Medical College of Cornell University, New York

# RECENT INNOVATIONS

Registered Declarations of Invention (DOFIs)
and Patent Applications

## 2013

Methods and biomarkers for detection of haematological cancers. (Lind, Lothe and Smeland groups)

Conjugate of a Photosensitiser and Chitosan and Uses Thereof. (Berg group)

Methods and biomarkers for detection and prognosis of cervical cancer - hypoxia gene expression signature. (Lyng group)

Treatment with MOC31PE immunotoxin in peritoneal carcinomatosis. (Flatmark group)

Identification of disease-driving antigens. (Olweus group)

CTL peptide epitopes and antigen-specific T cells, methods for their discovery, and uses thereof. (Olweus group)

An epigenetic prognostic signature in colorectal cancer. (Flatmark and Kristensen groups)

## 2014

Methods and biomarkers for analyses of colorectal cancer. (Lothe, Skotheim and Lind groups).

Biomarkers for cervical cancer - 3p gene expression signature. (Lyng group)

A serum microRNA signature predicts tumor relapse and survival in triple-negative breast cancer patients. (Børresen-Dale group)

Compositions and methods for targeting antigen presenting cell. (Sioud group)

Immortalized human bone marrow-derived mesenchymal stroma cells. (Myklebost group)

## 2015

Proteins in urinary exosomes as biomarkers for prostate cancer. (Sandvig group).

Prostate cancer markers and uses thereof. (Sandvig group).

Lipid species in urinary exosomes as biomarkers for prostate cancer. (Sandvig group).

Methods and biomarkers for detection and prognosis of cervical cancer - gene methylation signature for the identification of chemo-radioresistant disease. (Lyng group)

Peptide-Fc fusions for Cancer Therapy. (Sioud group)

Targeting cancer specific amino acid sequences with donor-derived T-cell receptor repertoires. (Olweus group)

Anti-CD37 chimeric antigen receptors and immune cells expressing them. (Smeland group)

A safe validation of therapeutic T cells. (Smeland group)

Selective Expansion of Educated NK Cells. (Malmberg group)

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## PUBLICATIONS 2015


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**Heterogeneous DNA Methylation Patterns in the GSTP1 Promoter Lead to Discordant Results between Assay Technologies and Impede Its Implementation as Epigenetic Biomarkers in Breast Cancer**
Genes (Basel), 6 (3), 878-900

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**Phase I trial of EpCAM-targeting immunotoxin MOC31PE, alone and in combination with cyclosporin**
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**Content of endothelial progenitor cells in autologous stem cell grafts predict survival after transplantation for multiple myeloma**
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**Photosensitizer and Light Pave the Way for Cytosolic Targeting and Generation of Cytosolic CD8 T Cells Using PLGA Vaccine Particles**
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