

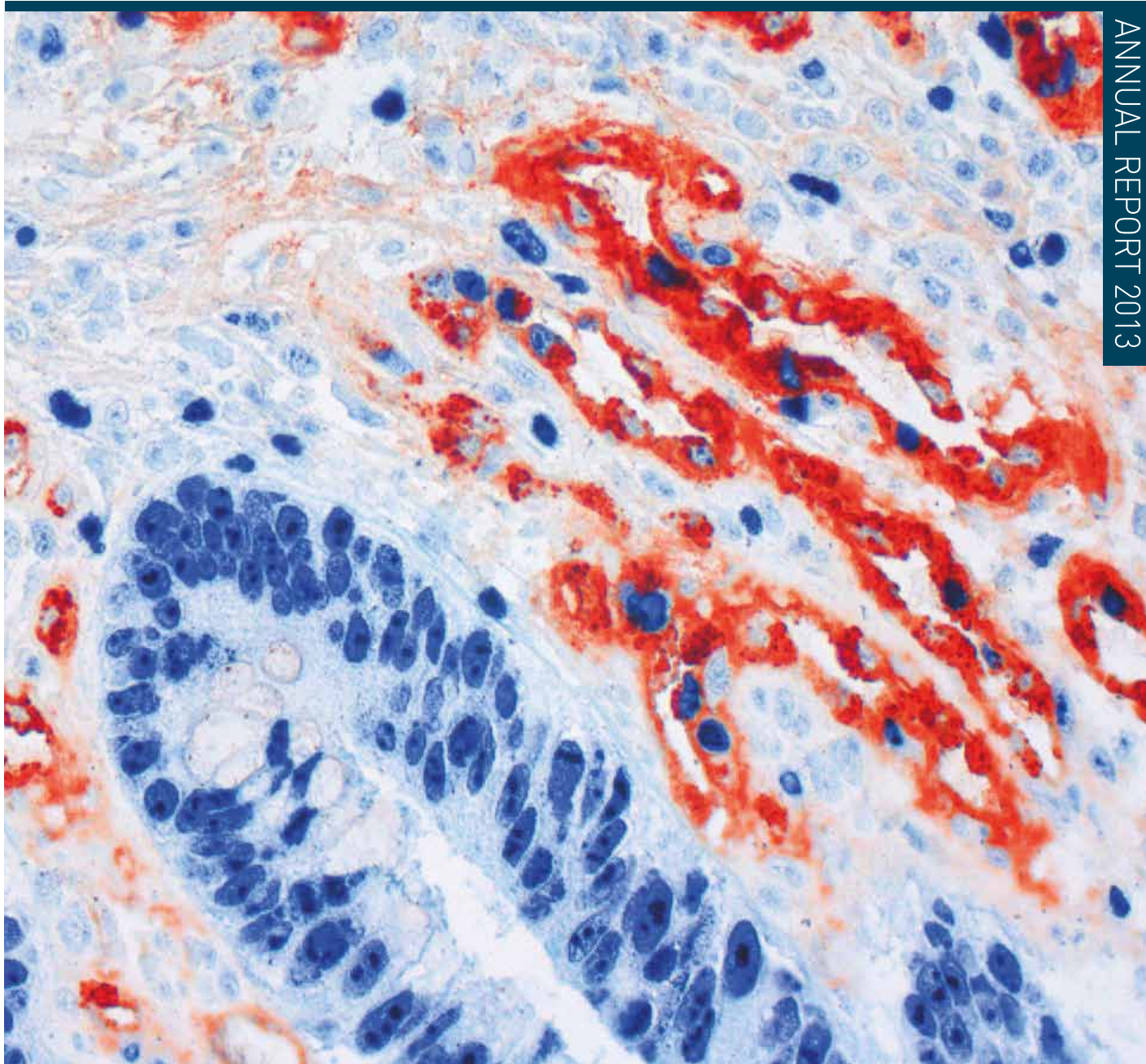


Centre for Cancer Biomarkers



ff Norwegian
Centre of
Excellence
The Research Council of Norway

ANNUAL REPORT 2013



08

Research Activities

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Research School

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Seminars and Symposium



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Director's Comments

We have had a busy start-up period at CCBIO, with important research data published in high-impact journals, and an international recruitment process. We have laid the fundament for our research school, and we've done multiple media appearances.

On November 12, 2012, the Research Council of Norway officially announced that the *Centre for Cancer Biomarkers CCBIO* was awarded a Norwegian Centre of Excellence. This completed 19 rewarding months of prequalification proposals and applications at different levels. Nine founding teams in the field of translational cancer research, working together with three associated groups in bioinformatics, economy and ethics, were excited to receive this stimulating challenge. The centre was opened by RCN Director Arvid Hallén on May 30, 2013, during the 1st CCBIO Symposium.

The centre has a bold aim: *to improve biological understanding, early diagnosis of and treatment of cancer, by using novel biomarkers*. This is a major challenge in today's personalized medicine. The complexity of cancers, in space and time, is an obstacle for effective therapy, combined with the many escape mechanisms of progressing tumors. For the task to be successful, we will focus on targeted projects across model studies (Program 1), biomarker discovery and validation (Program 2), and clinical studies (Program 3). We have established a Research School for Cancer Studies aimed for young recruits and future leaders, in addition to research seminars, annual symposia, and active international collaboration and networking. Taking advice from the CCBIO Council (local) and the CCBIO Scientific Advisory Board (Carl-Henrik Heldin, Uppsala; Ate van der Zee, Groningen; Bruce Zetter, Boston), we hope to fulfill our goals in the coming years and *make a difference* in the war against cancer.

Lars A. Akslen, Director of CCBIO





Vision and Research Programs

CCBIO aims to discover, validate and translate functional cancer biomarkers to improve biological understanding, early diagnosis of aggressive phenotypes and treatment of cancer.

CCBIO will focus on tumor-micro-environment interactions in primary and metastatic lesions that can define and predict cancer progression patterns and aggressive tumor features. The center will study how cross-talk between tumor cells and various cell types in the tumor microenvironment reflect cancer complexity and heterogeneity, and determine cancer prognosis, beyond what is given by the accumulation of genetic alterations in tumor cells.

By three overlapping research programs, CCBIO will re-focus its cancer research into the following fields, each with specific projects.

Mechanisms of Tumor Micro - environment Interactions

Exploration and Validation of Cancer Biomarkers

Clinical Applications and Trial Studies

Biomedical project areas have been supplemented with integrated ethics and economy projects, focused on how to prioritize and fund expensive cancer treatment in the era of expanding and costly personalized medicine. New collaboration partners, both national and international, have been included to support our efforts. • •

Organization of the Centre

CCBIO is organized as a matrix structure across six departments and four faculties. Its main activities are located at the Faculty of Medicine and Dentistry (FMD)'s departments, Department of Clinical Medicine (K1), Department of Clinical Science (K2) and Institute of Biomedicine (IBM).



The majority of the CCBIO staff also holds positions and funding at Helse Bergen. Day to day administration is taken care of by the departments, enabling researchers to interact with their familiar support staff. In the establishment phase, this structure and interaction has been highly successful with excellent cooperation. The model is robust and reduces vulnerability to a minimum. It gives CCBIO common interests with the departments, thus easing interaction.

The research projects have been organized in three integrated programs (preclinical models, biomarkers, clinical studies) chaired by program coordinators (see page 7). Lab space and core facilities are available for CCBIO, as is the Clinical Trials Unit at Haukeland University Hospital. The team of investigators (PIs) have formed the principal investigator group with monthly meetings to discuss administrative and scientific issues, and with updates on developments and progress. This is a platform for increased collaboration within CCBIO.

CCBIO is managed by the Director, Prof. Lars A. Akslen, and the Administrative Leader Geir Olav Løken, assisted by four finance officers (total of one position) at the departments of FMD. New offices for the

CCBIO Management Group have been made available in the main hospital building (Sentralblokken, second floor).

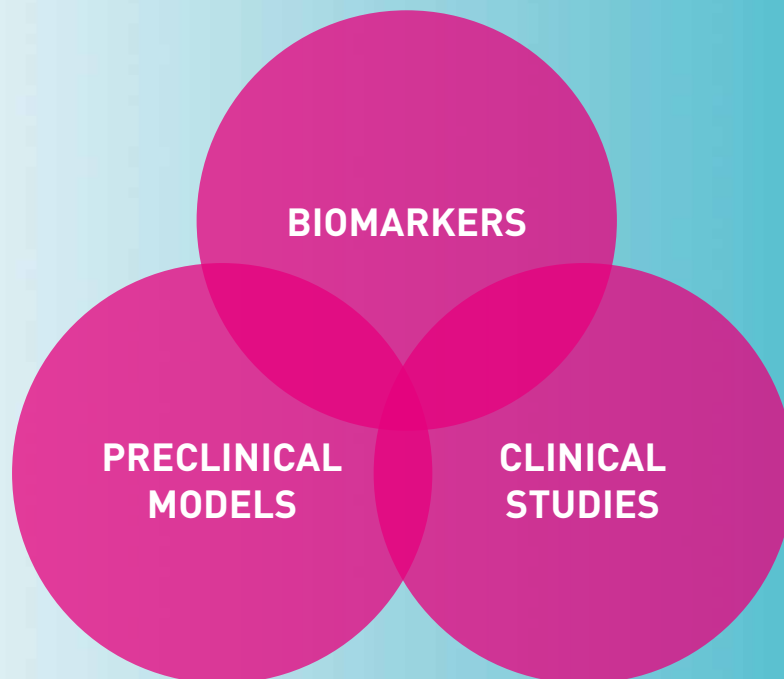
During 2013, core staff has been recruited, such as the Administrative Leader (Geir Olav Løken), three senior laboratory managers (PhDs), nine recruitment positions (PhD positions, postdocs), and one postdoc in ethics. One postdoc in bioinformatics will be advertised shortly. In addition, one adjunct professor (health economy) at 20% has been recruited (Prof. John Cairns, London School of Hygiene and Tropical Medicine), and more external 20% positions are in the recruitment process as part of international networking. The recruitment positions were advertised in *Nature* on April 25, 2013, in combination with comments on CCBIO in *Spotlight on Norway: Healthy outlook for Norwegian life science*. ••

Centre Director

Prof. Lars A. Akslen

Management Group

Scientific Advisory Board



ETHICS - ECONOMY

PRECLINICAL MODELS

animals and cell models
MIC - PROBE - FLOW
animal imaging

BIOMARKERS

biobanks - registries
immunohistochemistry
microarray - bioinformatics

CLINICAL STUDIES

multicenter studies
Clinical Trials Unit HUH
infrastructure and logistics

Research Activities and Highlights

Across the three different core programs, several areas of research and specific projects have been initiated at CCBIO, focusing on mechanisms of tumor-micro-environment interactions and tumor progress, discovery and validation of tumor biomarkers, and clinical studies.



Nine principal investigators and group leaders are instrumental for CCBIO's biomedical research:

Lars A. Akslen, Bjørn T. Gjertsen, Donald Gullberg, Karl H. Kalland, James B. Lorens, Rolf K. Reed, Anne Chr. Johannessen, Helga B. Salvesen, and Oddbjørn Straume.

In addition, three associated investigators represent a vital part of intersecting research areas in CCBIO:

Inge Jonassen (bioinformatics), Oddvar Kaarbøe (economy), Roger Strand (ethics).

CCBIO is funded by the Research Council of Norway and the University of Bergen, with additional funding from the Norwegian Cancer Society, Helse Vest RHF and Helse Bergen HF.

Principal Investigators



CANCER BIOMARKERS

LARS A. AKSLEN GROUP

The team is currently focusing its efforts in two areas: Firstly, studies of the tumor microenvironment, especially tumor-vascular interactions and angiogenesis markers. Secondly, the genetic and molecular markers of aggressive tumor behaviour, particularly related to cell cycle regulation and tumor cell proliferation.

Akslen is a certified specialist in surgical pathology and is directing the *Tumor Biology Research Group* (since the establishment in 1995) at Department of Clinical Medicine (University of Bergen). Since 2013, Akslen is the director of Centre for Cancer Biomarkers CCBIO. Akslen's team, and now CCBIO, are engaged in translational cancer research with a strong focus on exploration and validation of novel biomarkers for more biologically based classification and grading of malignant tumors, as a better guide for targeted treatment. The group has included projects on various cancers, such as breast cancer, malignant melanoma, prostate cancer, and gynecologic cancers. Studies of human tumor samples are combined with experimental cell and animal models to improve translation. The overall aim is to provide novel biomarkers which can assist in prediction of aggressive tumor behavior and be helpful in tailored treatment.

As examples, the team reported that HSP27 represent a critical regulator and biomarker of tumor dormancy and angiogenesis as shown in studies of breast cancer models with clinical validation (Straume et al., PNAS 2012). In collaboration with researchers at Harvard Medical School and Cornell University, the team recently reported a novel mechanism related to tumor spread and showed how a protein (prosaposin) secreted by tumor cells might induce a metastasis-resistant microenvironment (niche) and inhibit metastatic spread (Catena et al., Cancer Disc 2013). The findings were clinically validated. Akslen and

his co-workers have reported several novel angiogenesis biomarkers which provide better grading of malignant tumors and might prove important for targeted treatment. In breast cancers, angiogenesis is particularly increased in the aggressive basal-like subtype, and the mechanism behind this finding is being studied. Also, the group is currently exploring predictive markers in trials of metastatic melanoma and renal cancer.

In ongoing and future projects, the team will continue to combine studies of tumor tissue from patients (primary and metastatic lesions), through the use of biobanks and registry data, with experimental cell and animal models. This approach will make it possible to explore novel mechanisms and validate potential targets and biomarkers in the human setting. The current goal is to extend studies of prognostic and predictive biomarkers towards an integrated role in clinical trials and personalized patient management. The team has extensive national and international collaboration. ••

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SIGNALLING-TARGETED THERAPY

BJØRN TORE GJERTSEN GROUP

Professor Bjørn Tore Gjertsen's research interest has its background in the study of intracellular signal transduction by protein phosphorylation in regulation of cell death (apoptosis). As a medical student these early works includes the first proof-of-principle concept of apoptosis-resistance mechanism in myeloid leukemia through point mutation in protein kinase A (J Biol Chem 1993). With this background, studies of protein phosphorylation in chemotherapy induced apoptosis in vitro and in patients have elucidated novel mechanisms of cell death regulation. The tumor suppressor protein p53 is heavily modified and tightly regulated, and the impact of this key protein was described by analysis of p53 protein isoforms modulation and p53 directed gene expression in patients during high dose chemotherapy of acute myeloid leukemia (AML) (Oncogene 2012). Development of single cell phosphoprotein analysis in patient AML cells for phenotype analysis of mutations in signalling pathways, and proposed the concept of phosphoprotein signalling response for prognostic information in cancer and as biomarkers in clinical trials (Cell 2004, Blood 2007). In collaboration with Professor Emmet McCormack, state-of-the-art animal models and advanced molecular imaging of acute myelogenous leukemia has been established for development of p53- and signalling-targeted therapy (2012, Cancer Res 2013, Blood 2013). Together this has formed a therapy and biomarker program focusing on development of signalling and p53 targeted therapy.

The research has focused on the aggressive blood cancer acute myeloid leukemia (AML), affecting approximately 150 new cases in Norway per year. Because of limited therapeutic advances last decades and currently three year survival below 20% in patients above 65 years of age, Gjertsen has established several clinical trials for Norwegian patients. Gjertsen has been national coordinator several academic HOVON/SAKK clinical trials in AML. Clinical trials in collaboration with Novartis and Boehringer-Ingelheim is currently exploring single cell signalling analysis in trials with novel signal transduction inhibitors.

CCBIO Centre of Excellence form an ideal platform for the upcoming 2014-15 early phase clinical trial of the Axl kinase inhibitor BGB324 in AML. BGB324 is a per oral medicine that will be tested for clinical benefit in acute leukemia. The use of single cell signalling biomarkers in response prediction will be examined. Single cell signalling analysis of selected solid tumors, as well as in normal blood cells, will be examined for disease stratification and therapy response prediction. ••

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INTEGRINS

DONALD GULLBERG GROUP

Ever since his graduate studies Dr. Gullberg has worked on integrins. For almost two decades this work has focused on work related to integrin alpha11, which was discovered in the Gullberg group. Integrin alpha11beta1 is a collagen receptor with a number of features which makes it an interesting molecule in tissue fibrosis and tumor-stroma interactions in different types of solid tumors.

The research group has accumulated a number of reagents to perform detailed molecular studies of cell-collagen interactions. A recent review article summarizes some of the current research challenges in this field (Zeltz et al., 2013).

Current projects aim to generate new animal models (mouse and zebrafish) to study the role of integrin alpha11 during development, in fibrosis and in tumors. Also, the Gullberg Group wants to generate new function blocking reagents to integrin alpha11. The scientists want to reach a better understanding of the role of integrin alpha11 in cancer-associated fibroblasts (Marie Curie ITN funded project).

Last, but not least, the Gullberg Group aim to characterize the role of integrin alpha11 in scleroderma/fibrosis (EEA-funded bilateral Norway-Poland project).

The CCBIO projects deals with the role of integrin alpha11 in the tumor stroma using two main techniques. The first is the use of tumor-fibroblast heterospheroids as a 3D model system to understand bidirectional communication between the tumor cells and fibroblasts. A long-term goal is to develop this system to a large scale in vitro system. This way one could screen for compounds targeting integrins/integrin signaling, with the potential to inhibit tumor growth and spreading.

The second way of working is to use new reagents to conditionally inactivate genes in an integrin alpha11 specific manner. The long-term aim here is to develop new animal models to more stringently be able to analyze role of cancer associated fibroblasts in tumor stroma interactions.

Integrins play a key role in many severe diseases, and the goal of the Donald Gullberg Group is that the research will result in better and more effective treatments. ••

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ORAL CANCER

ANNE CHRISTINE JOHANNESSEN GROUP

Research at Bergen Oral Cancer Research Group (BOCG) lead by professor Johannessen aims at identifying the key molecules of importance for oral cancer development, in order to identify patients at risk for developing oral cancer from premalignant lesions, and to reveal potential targets for more efficient, individualized therapy of oral cancer.

The focus is on understanding the cancer-host interactions, particularly the interaction between the surface epithelium and the underlying connective tissue, and their role in the aggressive behaviour of oral cancer. For that purpose we have established human tissue-based 3D cell culture models of normal mucosa and oral cancer tissue (Costea et al J Amer Pathol 2006). These models open up for further testing of the role of potential biomarkers that have been identified on patient biopsy material.

Using patient material, the 3D models and animal models, the group has shown a crucial role for carcinoma-associated fibroblasts (CAFs) on oral carcinoma development and progression (Costea et al, Cancer Research, 2013), and characterised at the molecular level how CAFs are actively involved in carcinoma development and invasion. The group has also identified 16 diagnostic biomarkers implicated in the regulation of cell cycle, genomic stability, chromatin maintenance, and stem cell regulation (Teh et al., Int J of Cancer, 2013) and developed a cancer index system of diagnostic and prognostic value based on this panel of molecular epithelial biomarkers. This study validated the use of a molecular-based analysis on two geographically distinct patient cohorts consisting of oral tissue biopsies donated by patients from the United Kingdom and Norway. We plan now to expand this cancer index to include molecules from connective tissue and to validate it in the newly formed multi-centre platform for biomarker testing in oral cancer.

Oral cancer is a burden of disease especially in the Sub-Saharan and Indian Subcontinent. For that reason, international, multi-centre studies on biomarkers in oral cancer are important. Our research group is part of a collaborative network which includes universities and health institutions in Norway (Bergen, Tromsø, and Ålesund, UK (Queen Mary University of London and Bradford Institute for Cancer Therapy), Romania (University of Bucharest), India (Advanced Centre for Treatment Research & Education in Cancer, Tata Memorial Centre, Mumbai, and D.A Pandu Memorial R.V Dental College, Bangalore), Nepal (BP Koirala Memorial Cancer Hospital, Bharatpur) and Sudan (University of Science and technology, Umdurman, and University of Khartoum, Khartoum). ••

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PROSTATE CANCER

KARL-HENNING KALLAND GROUP

Kalland and his team have been focusing of regulatory molecular mechanisms of gene expression in normal cells, virus infected cells and cancer cells; Biochemistry, molecular biology, immunology, morphology and genome-wide methods and bioinformatics have been applied in experimental cell culture systems and in patient samples; Major previous achievements are the discovery that the HIV-1 Rev protein is a nucleocytoplasmic shuttle protein (1994) and the discovery of the now prototypic nuclear export signal first described in Rev (1994/1995); Recently, an experimental model of stepwise malignant transformation of human prostate cells were established in the group and studied using genome-wide analyses of gene and microRNA expression and epigenetic changes, using microarray and next generation sequencing technology and phenotypic assays. The model is exploited in a drug discovery program.

The current main interests are cancer associated transcriptional reprogramming potential, such as the EMT (epithelial to mesenchymal transition) and specific gene expression activation of cancer initiating cell subpopulations. These studies have led to an increased insight into sources of cancer cell heterogeneity and have motivated the implementation of a cryoimmunotherapy strategy in order to exploit the tumor neoantigenome and address subcellular heterogeneity. The cryoimmunotherapy module will be combined with specific molecular targeting of gene expression that is preferentially activated in cancer initiating cell subpopulations. ••

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TUMOR CELL PLASTICITY

JAMES LORENS GROUP

Epithelial cell plasticity between epithelial and mesenchymal phenotypic states provides the repertoire of cellular functions required during embryonic development, organogenesis and adult tissue repair and homeostasis. This phenotypic plasticity also allows adaptation of tumor cells to microenvironmental challenges such as hypoxia, inflammation and drug treatment that facilitate malignant progression, metastasis and drug resistance. Gene expression programs related to the epithelial-to-mesenchymal transition (EMT) are utilized both by normal and neoplastic epithelial cells to access stem cell-related functions.

Using comparative functional approaches, we are investigating the relationship between regulators EMT in tumor cells in maintenance of normal stem and progenitor cells. Our recent results highlight the Axl receptor tyrosine kinase as a key regulator of adult epithelial and carcinoma cell plasticity. Mechanistic studies on Axl signaling have provided new insights into tumor EMT regulation and formed the basis for the recent clinical translation of novel Axl inhibitors. We are further investigating how distinct combinations of microenvironmental factors regulate phenotypic plasticity in normal and cancer cells using new a screening technology (MEArrays). Using these mechanistic insights we are exploring how microenvironmental factors regulate tumor cell plasticity underlying contextual drug responses. ••

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TRANSCAPILLARY EXCHANGE

ROLF REED GROUP

The studies on the interstitial matrix and the long-term collaboration with Professor Kristofer Rubin at Uppsala University, Sweden has since the early 1990s been on acute inflammation and subsequently on experimental cancers, and in particular on the role of the hydrostatic pressure (Pif) and how a lowering of Pif will explain the initial and rapid edema formation in acute inflammation. In a series of collaborative studies it has been demonstrated that fiber networks in the loose connective tissues are compressed by cellular tension mediated from the cells to the fibre networks via the beta1-integrin receptors. When this tension is released, the tissue expands due its content of glycosaminoglycans, in particular hyaluronan, and the Pif is lowered in turn pulling in water from the circulation to create a local edema. The tissue can be compacted again, with reversal of Pif, via the action of several chemokines and also prostaglandins, but now uses the alfaVbeta3-integrin to mediate cellular tension on to the fibre networks. The enhanced transcapillary fluid flux in the tumors during the lowering of Pif will raise the transport of cytostatic agents into the tumor, in turn slowing tumor growth compared to control.

A recent collaboration with Professor F.-R. Curry at University of California at Davis has focused on transcapillary exchange and development of methods for its measurement in genetically modified mice.

The CCBIO projects in which Rolf Reed participates builds strongly on the above collaborations and also with collaborations with Professors Linda Stuhr, Donald Gullberg and Marion Kusche Gullberg in the Matrix Biology group. The current focus has a particular focus on the role of integrins alpha11 and alfaVbeta3 in the tumor stroma using:

- a) tumor-fibroblast heterospheroids as a 3D model system to understand bidirectional communication between the tumor cells and fibroblasts. A long-term aim is to develop this system to a large scale in vitro system to screen for compounds targeting integrins/integrin signaling and with the potential to inhibit tumor growth and spreading.
- b) transvascular exchange in acute inflammation and experimental cancers.
- c) integrins alpha11 and alfaVbeta3 in the tumor stroma and how they modify tumor growth and preproperties.
- d) the use of dynamic contrast enhanced magnetic resonance (DCE-MRI) to study transcapillary exchange in genetically modified mice.

The long term goal of the research is to understand the tumor-stroma and its dynamic properties, and how this insight can be used to alter therapeutic principles of solid tumors. ••

KEY PUBLICATIONS

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C. Österholm-Corbascio, N. Lu, Å. Lidén, T. V. Karlén, D. Gullberg, R.K. Reed and M. Kusche-Gullberg. Fibroblast EXT1-levels influence tumor cell proliferation and migration in composite spheroids. *PLoS One*. 7:e41334, 2012.

T. Friman, R. Gustafsson, L. B. Stuhr, J. Chidiac, N. E. Heldin, R. K. Reed, Å. Oldberg and K. Rubin. Increased fibrosis and interstitial fluid pressure in two different syngeneic murine carcinomas grown in integrin $\alpha 3$ -subunit deficient mice. *PLoS One* 7:e34082, 2012.

Å. Lidén, A. Berg, T. Nedrebø, R. O. Hynes, R. K. Reed and K. Rubin. PDGF BB-mediated normalization of dermal interstitial fluid pressure after mast cell degranulation depends on $\alpha 3$, but not $\alpha 1$ -integrins. *Circulation Research* 98: 635-641, 2006.

Å. Oldberg, S. Kalamajskij, A. Salnikov, L. Stuhr, M. Mörgelin, R. K. Reed, N.-E. Heldin and K. Rubin. The small leucine-rich repeat proteoglycan fibromodulin determines stroma structure and physiology in experimental carcinoma. *Proceedings National Academy of Sciences* 104: 13966-13971, 2007

C. B. Rygh, G. Løkka, T. Taxt, R. Heljasvaara, T. Pihlajaneimi, F.-E. Curry, O. Tenstad and R. K. Reed. Non-invasive MRI reveals vascular leakage in mice deficient of basement membrane collagens XV and XVIII. *Journal of Physiology* 592:325.36, 2014.

STAFF

Moen, Ingrid – postdoctoral fellow
 Lu, Ning – senior engineer
 Reigstad, Inga – PhD student
 Salvesen, Gerd – engineer
 Skogstrand, Trude – postdoctoral fellow
 Smeland, Hilde – PhD student/engineer
 Stuhr, Linda – professor
 Tveitarås, Maria – engineer



GYNAECOLOGIC CANCER

HELGA SALVESEN GROUP

Professor Salvesen's research is focused on molecular alterations in gynaecologic cancer, to define potential targets for new therapies and develop reliable biomarkers for individualised therapy. The goal is to perform a comprehensive molecular profiling of primary- and metastatic lesions from cervical, endometrial- and ovarian carcinomas in order to improve trials with molecularly targeted therapy. This project represents clinical research with a strong focus on translational aspects. The study is part of a collaborative platform with Harvard, Dana Farber Cancer Institute, and MIT working towards the global characterisation of molecular alterations in metastatic gynaecologic cancer.

Through this work we have identified potentially targetable genetic alterations that are prevalent in aggressive gynaecologic disease (PNAS 2008 and 2009, Nature 2013). Based on this background, we have launched a prospective multicentre study to reduce morbidity, promote individualised treatment and facilitate the implementation of molecularly based targeted therapy for women with gynaecologic cancer. Tissue from primary tumours is collected nationally from several hospitals in the region and internationally through members of the Nordic Society for Gynaecologic Oncology and from European Cancer centres (MoMaTEC1).

During this project we plan to take our previous studies of global molecular classification of primary tumours to a new level, with global characterisation of genetic alterations in fresh tissues from corresponding metastatic lesions and characterisation with advanced imaging techniques (fMRI, PET-CT). The project will focus on molecular alterations in primary tumours and metastatic lesions from the same patient with the goal of identifying targetable and measurable molecular alterations in malignant lesions. A unique sample collection with freshly frozen primary-metastatic sample pairs will be used as an investigation set, and larger series with paired primary-metastatic formalin fixed paraffin embedded lesions will be used for clinical validation.

The ultimate goal is to apply the new knowledge regarding distribution of genetic alterations in malignant lesions to improve the ability to detect these by advanced imaging methods and ultimately develop of trials with molecularly targeted therapy. ••

KEY PUBLICATIONS

Ojesina AI, Salvesen HB*, Meyerson M*. Landscape of genomic alterations in cervical carcinomas. *Nature* 2014; 506(7488):371-5.

*Joint senior authors.

Salvesen HB, et al. Integrated genomic profiling of endometrial carcinoma associates aggressive tumors with indicators of PI3 kinase activation. *PNAS* 2009; 106(12):4834-4839.

Trovik J, Wik E....., Amant F, Akslen LA, Salvesen H. Stathmin overexpression identifies high risk patients and lymph node metastasis in endometrial cancer. *Clin.Cancer Res.* 2011.

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STAFF

Clinical staff:

Bjørge, Line - Prof. II
Valen, Ellen - study nurse

Postdoctoral fellows/scientists:

Bredholt, Therese
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Husby, Jenny (imaging)
Karlsson, Thomas
Thorbjørnsen, Ingild
Werner, Henrica

Medical students:

Engerud, Hilde
Mauland, Karen
Mjøs, Siv



ANTI-ANGIOGENIC TREATMENT

ODDBJØRN STRAUME GROUP

The research activity focuses on three main project:

-Predictive markers of anti-angiogenic treatment in malignant melanoma

Malignant melanoma is dependent on angiogenesis to progress and metastasize(1). We have previously published the results of a clinical phase II study of the anti-VEGF antibody bevacizumab in patients with metastatic melanoma(2) and found that ~30 % of the patients experienced clinical benefit of the treatment. The main objective of the project is to identify predictive markers of response to bevacizumab. We are currently launching a larger national randomized clinical phase II trial to validate the findings in the first trial. PhD project.

- Predictive markers of anti-angiogenic treatment in renal cell carcinoma

The VEGF receptor inhibitor Sunitinib is first line treatment in metastatic or non-resectable clear cell carcinoma of the kidney. About 50 % of the patients are expected to respond. In a patient series of 50 patients with metastatic clear cell renal carcinoma we will identify, evaluate and validate a set of candidate biomarkers for their predictive value. Blood samples, tissue samples and clinical data are under investigation. PhD project.

- Role of HSP27 in cellular stress, wound healing and tissue trauma

The small heat shock protein (HSP27) is involved in human tumor dormancy and the "angiogenic switch"(3). HSP27 is also a promising predictive marker for anti-angiogenic treatment (Schuster et al, in prep). The research group will investigate how tissue trauma and wound healing can initiate tumor growth and synchronize growth of occult micrometastases. The role of cellular stress response mechanisms following tissue trauma with focus on HSP27, will be evaluated. ••

KEY PUBLICATIONS

Straume O & Akslen LA (2001) Expression of vascular endothelial growth factor, its receptors (flt-1, kdr) and tsp-1 related to microvessel density and patient outcome in vertical growth phase melanomas. *Am J Pathol* 159(1):223-235.

Schuster C, Eikesdal HP, Puntervoll H, Geisler J, Geisler S, Heinrich D, Molven A, Lonning PE, Akslen LA, & Straume O (2012) Clinical efficacy and safety of bevacizumab monotherapy in patients with metastatic melanoma: predictive importance of induced early hypertension. *PLoS One* 7(6):e38364.

Straume O, Shimamura T, Lampa MJ, Carretero J, Oyan AM, Jia D, Borgman CL, Soucheray M, Downing SR, Short SM, Kang SY, Wang S, Chen L, Collett K, Bachmann I, Wong KK, Shapiro GI, Kalland KH, Folkman J, Watnick RS, Akslen LA, & Naumov GN (2012) Suppression of heat shock protein 27 induces long-term dormancy in human breast cancer. *Proceedings of the National Academy of Sciences of the United States of America* 109(22):8699-8704.

STAFF

Martin Pilskog, MD, PhD student
Cornelia Schuster, MD, PhD student

Associated Investigators



Roger Strand



Inge Jonassen



Oddvar Kaarbøe

SCIENCE IN SOCIETY

ROGER STRAND

Roger Strand is a Professor at the Centre for the Study of the Sciences and the Humanities (SVT), University of Bergen, and affiliated with CCBIO with 25% of his position.

Strand is a trained natural scientist (cand. scient. (biochemistry, 1992) and dr. scient., (biochemistry, 1998), both degrees from the University of Bergen, Norway). Ever since his dissertational work, which combined biochemistry with philosophy of biochemistry, he has worked on issues of methodological underdetermination in science, scientific uncertainty and complexity. This has gradually led his research into broader strands of philosophy, ethics and social research and broader issues of policy, decision-making and governance at the science-society interface.

In 2005, Strand was appointed Professor and Director of SVT. During his directorship, SVT grew in size and produc-

tion, mainly because of externally funded ELSA research projects on nanotechnology, biotechnology and emerging S&T coordinated by Strand. ELSA being “ethical, legal and social/societal aspects”, a central interest in these projects has been the attempt to create broad approaches to ethical and societal aspects of S&T that include the political dimension of the governance of science and technology and not only focus on ethical dilemmas or other more technical issues. This research interest was also pursued together with Kjetil Rommetveit and others in the two FP7 research projects TECHNOLIFE and EPINET, both coordinated by SVT. This has been combined with more practical work on ethics through appointments to regional, national and European ethics committees. In 2014, Strand was appointed by the European Commission as Chair of their Expert Group on Indicators for Responsible Research and Innovation.

At the same time, and related to the interest in clarifying the political dimension of the governance of science and technology, a part of Strand’s research has been devoted to the understanding of the internal foundational problems of life science – and their relationships to their social, political and cultural context. In particular, together with Dominique Chu he has sought to understand biological and social complexity and how it is and is not adequately dealt with by various scientific approaches. Both these strands of research – a broad-scoped approach to ELSA as well as the interest in biological complexity – are key to Strand’s engagement with the CCBIO and its ethical and societal aspects. ••

KEY PUBLICATIONS

K. Rommetveit, R. Strand, R. Fjelland & S. Funtowicz (2013): What can history teach us about the prospects of a European Research Area? JRC Scientific and Policy Reports, Report EUR 26120, Luxembourg: Publication Office of the European Union.
R. Strand (2011): “Health Ideologies, Objectivism and the Common

Good: On the Rights of Dissidents”, Cambridge Quarterly of Healthcare Ethics, 20(4): 605-611.

J. R. Karlsen, & R. Strand (2009): “Annexation of Life: The Biopolitics of Industrial Biology”, in: J. H. Solbakk, S. Holm, and B. Hoffman (eds): The Ethics of Research Biobanking. Dordrecht:

Springer Verlag, pp. 315-329.

D. Chu, R. Strand & R. Fjelland (2003): “Theories of Complexity,” Complexity, 8:19-30.

BIOINFORMATICS DATA MINING

INGE JONASSEN

Jonassen's research has largely been focused on development of bioinformatics methods for the analysis of molecular biology data. He developed methods for the automatic discovery of sequence motifs and contributed to early methods for the automatic discovery of regulatory signals in the Yeast genome. The group contributed methods for the analysis and prediction of protein structure. The Jonassen group has also developed methods for analysis of microarray gene expression data including methods for identification of genes, and pairs of genes, useful for classification of expression profiles obtained from biological samples, e.g., tumour samples. Later, the

group has also developed methods for analysis of high-throughput sequencing data. The group has produced a number of software packages made available to the user community.

The Jonassen group has been involved in a number of collaborations with experimental groups within a wide range of areas including basic biology, cancer studies, genetics, and fish and fish parasite genomics. For example, the group has contributed to the analysis of a number of different microarray gene expression studies of panels of cancer cases identifying marker genes associated with different outcomes, response

to treatment etc. The group has contributed to several genome sequencing projects including those for the bacteria *Methylococcus capsulatus* and *Francisella noatuensis*, the cod and salmon fishes, and the copepod salmon louse.

Jonassen has since 2003 led Norwegian infrastructure projects for bioinformatics, first through the FUGE Bioinformatics platform, and since 2012 through the Elixir.no project. The latter is linked with the European research infrastructure ELIXIR for bioinformatics where Jonassen is leading the initiative to establish a Norwegian Node. ••

KEY PUBLICATIONS

Jonassen I, Collins JF, Higgins DG. 1995. Finding flexible patterns in unaligned protein sequences. *Protein Science* 4, 1587-1595.

Brazma A, Jonassen I, Vilo J, Ukkonen, E. 1998. Predicting Gene Regulatory Elements in Silico on a Genomic Scale. *Genome Research* 8, 1202-1215.

Bø TH, Jonassen I. 2002. New feature subset selection procedures for classification of expression profiles. *Genome Biol* 2002; 3 (4) Research 0017.

Taylor WR, Bartlett GJ, Chelliah V, Klose D, Lin K, Sheldon T, Jonassen I. 2008.

Prediction of protein structure from ideal forms. *Proteins: Struct, Funct, and Bioinfo.* 70, 1610-1619.

PATIENTS AND ECONOMY

ODDVAR KAARBØE

Oddvar Kaarbøe is currently professor of economics at the University of Bergen, and research director of Health Economics Bergen (HEM). After finishing his PhD in 2000 (game theory, UiB) he joined HEB. His theoretical research

is within contract theory with a specific focus on financing and organizing of health care organizations. His empirical work is centered around prioritization of patients in specialized care and on evaluations of reforms in the health care

sector. Kaarboe has also worked with health authorities in Norway to develop reimbursement models for hospitals in Norway. ••

KEY PUBLICATIONS

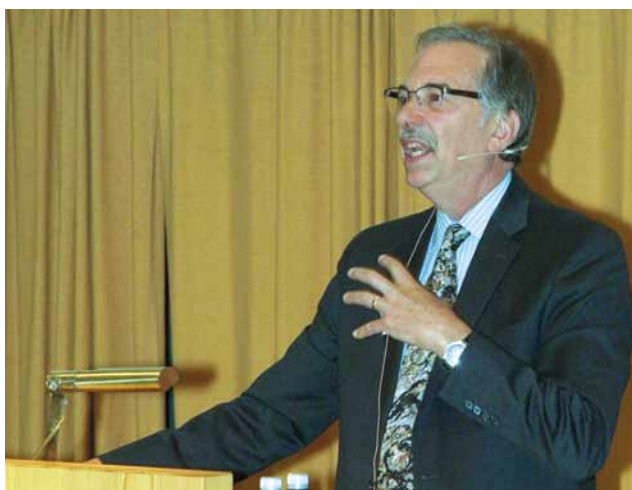
Paying for Performance in Hospitals. *Economic Analysis and Policy*, 41(1):49-70, 2011. With Burkhard Hehenkamp. Monitoring Prioritization in a Public Health Care Sector. The Case of Norway. *Health Economics*. 20(8), 958-970, 2011.

With Jan Erik Askildsen, Tor Helge Holmås. The Impact of Different Prioritisation Policies on Waiting Times. A Comparative Analysis of Norway and Scotland. *Social Science & Medicine*, 97, 1-6, 2013. With Jurgita Januleviciute, Jan Erik Askildsen, Tor Helge Holmås, Matt Sutton.

Waiting times and socioeconomic status. Evidence from Norway, *Health Economics*, 23(1), 93-107, 2014. With Fredrik Carlsen.

Highlights





During 2013, research efforts have been increasing in the CCBIO groups as reflected in the list of publications. Technically, the budgetary start was July 1, 2013, and the recruitment process was active and ongoing until the end of the year. Thus, the results as shown in Appendix 1 reflects the ongoing activity in the CCBIO research teams as detailed in the application.

Several papers have been published in high-ranking journals during 2013, such as studies on genetic and protein biomarkers in gynecologic cancers, breast cancer, melanoma and hematologic cancer. Also, a study on how prostate cancers can limit their own spread was published. These studies indicate how local teams can collaborate successfully with international environments and networks.

Research School for Cancer Studies (RSCS)

The CCBIO Cancer Research School is directed by Professor and Vice-Rector Anne Christine Johannessen. RSCS will be officially opened in the fall of 2014. The research school will be available for all interested students in the field of cancer research (not exclusive for CCBIO candidates).

Background.

The Research School for Cancer Studies (RSCS), under CCBIO's aegis, has been approved by the UiB. It will focus on translational cancer research and innovation including international exchange and mobility.

RSCS goals and main activities.

The main goal of the RSCS is to be a scientifically stimulating and inclusive meeting place for junior researchers within various areas of cancer research, ranging from basic medical to preclinical and clinical research environments with a common focus on translational studies of cancer biomarkers. PhD candidates and postdoctors will get the opportunity to meet renowned international researchers, and the candidates can meet each other and deliberate upon their research projects across the established research groups.

In order to attain this goal, CCBIO will integrate the RSCS into CCBIO's strategic activities like the annual CCBIO Symposium as well as the monthly CCBIO Seminars where world leading scientists and opinion leaders will give key-note lectures and interact with students and PIs. Other RSCS key activities will be a journal club and an array of specially designed courses. Apart from the main focus on translationally relevant biomarker studies, PhD candidates will be trained in

inter-disciplinary collaboration, project management, communication skills and ethical, economic and societal aspects pertaining to CCBIO's research. CCBIO aims to actively use its international networks to provide the ground for exchange of PhD candidates and postdoctors both to and from CCBIO. The RSCS will collaborate with local and national research schools.

Organization. The RSCS is directed by Professor Johannessen, and all PIs in CCBIO will contribute towards the activities.

Administrative support for coordination is provided by the Department of Clinical Medicine (DCM), whereas local administrative support for each course is provided by the relevant departments. Apart from its allocated own annual budget of 150 000 NOK, the RSCS will be able to draw upon the resources allocated to other parts of CCBIO, boosting its total resources.

Courses currently being established.

According to CCBIO's scientific and organizational philosophy, courses will be controlled and flagged by CCBIO, but also be formally located at and credited to the relevant department. All courses will be open according to available capacity after CCBIO's PhD candidates have enrolled. The below list illustrates CCBIO's current ambition for courses to be established





during the next year. Courses with a given registration number are already approved by CCBIO. For the remainder, course descriptions are currently being elaborated.

- **CCBIO 901 Junior Scientist Mini Symposium Series.** PhDs and PDs will present their results four times a year. If the PhD-candidates have the need to meet more often, one will consider organizing a retreat or other meeting points.

- **CCBIO 902 CCBIO Seminar and Symposium Series.** This course combines the CCBIO part of the BMED 380 (the monthly CCBIO Seminar series) with the CCBIO Annual Symposium to make a 3 point 900-level course.

- **BMED 904 Biomedical Research Course: Matrix Biology.** This is an established course where CCBIO members will now have first right of entry.

- **Methods in Biomarker Research.** This course will focus on the full panel of advanced and standard methods with relevance for cancer biomarkers. The intention is a methodological course that also includes components of ethics and economy. This is a strongly needed course with potential national interest.

- **Tumour Biology in the Clinic.** The course leaders have experience from equivalent courses arranged by the Norwegian MDs association. CCBIO aims to extend the existing course with a focus also on bio-banking in practice.

- **Cancer Research: Ethical, economical and societal aspects.** The course will focus on ethical, economical and societal aspects of cancer and cancer research and aims to equip PhD candidates with tools for systematic reflection on their own and related research as well as methods for assessing the cost benefit of health measures and methods of treatment. • •

Research Seminars

CCBIO has a monthly seminar, where principal investigators or invited guests focus on current research. During the start-up phase, CCBIO's PIs have presented ongoing research within their groups. The CCBIO seminar has been well visited and received.

Background.

The CCBIO Seminar series fulfils several aims. First, it conveys relevant biomarker research to the local scientific community and students and younger researchers in particular, providing the ground for future recruitment. Second, it is part of two formal courses, BMED 380 on the master level, and together with the CCBIO Annual Symposium, forms

CCBIO 902, a PhD level course. Third, the CCBIO seminars with their subsequent open pizza get together are an important arena for informal interaction between international researchers, CCBIO PIs and other CCBIO staff as well as interested researchers and students in general.

The CCBIO-seminars in the fall of 2013 mainly served the purpose of intro-

ducing CCBIO and its PIs research focus to the local research environment. The CCBIO seminars in 2014, mainly consists of international researchers with a focus relevant for CCBIO. All CCBIO seminars so far have had very high attendance with the allocated auditorium being over-filled every time. • •



CCBIO seminars in 2013

29.8.2013: Lars A. Akslen, Director of CCBIO

CCBIO: Current concepts and challenges in cancer research.

26.9.2013: Helga B. Salvesen, Co-Director of CCBIO

Individualized therapy based on molecular alterations in gynecologic cancer.

31.10.2013: Oddbjørn Straume, CCBIO

Angiogenic biomarkers in malignant melanoma.

25.11.2013: CCBIO Special Lecture:

Sonja Loges, University Hospital Hamburg-Eppendorf, University Comprehensive Cancer Center II, Medical Clinic & Institute of Tumor Biology
Role of Gas6 - Axl axis in malignant interaction with the host.

28.11.2013: Bjørn Tore Gjertsen, CCBIO

Phosphoprotein signaling in acute myeloid leukemia.

Annual Symposium

The Opening Symposium on May 30-31, 2013 (1st CCBIO Symposium) was a success with more than 250 participants.



The Centre for Cancer Biomarkers CCBIO was officially opened by Arvid Hallén, Director of the Research Council of Norway, who handed over the SFF plaque to Prof. Lars A. Akslen, Director of CCBIO. Talks were held by representatives from

the University of Bergen, Haukeland University Hospital, the Norwegian Cancer Society, and others. The scientific program was well received, with keynote lectures by Bruce Zetter (Harvard Medical School), Mina Bissell (Lawrence Berkeley

National Laboratory), and John Cairns (London School of Hygiene & Tropical Medicine). Several other presentations on biomedical research as well as health ethics and economy attracted many positive comments. The poster session was a success. ••



CCBIO



**Norwegian
Centre of
Excellence**
The Research Council of Norway

Opening Symposium - May 30-31, 2013 Bergen - Norway

Official Opening and Scientific Program

Day 1: Thursday May 30, 2013

Store auditorium, 3rd floor, Haukeland University Hospital, Jonas Lies Vei 65

12.30-13.00 Registration, coffee and light food

Session 1 **Welcome and Official Opening** **Chair: Dean Nina Langeland**

13.00-13.30 Welcoming announcement and short presentation of Centre for Cancer Biomarkers by CCBIOs Director, Professor **Lars A. Akslen** (University of Bergen).

13.30-14.30 Official opening and short speeches and congratulatory statements
Arvid Hallén, Director, Research Council of Norway
Berit Rokne, Deputy Rector, University of Bergen
Eivind Hansen, Deputy Director, Haukeland University Hospital
Nils Erik Gilhus, Head, Department of Clinical Medicine, UIB
Jannikke Ludt, Head, Research Department, Norwegian Cancer Society
Nina Langeland, Dean, Faculty of Medicine and Dentistry, UIB

14.30-15.00 Coffee and light food

Session 2 **Biomarkers: Tradition and Future** **Chair: Professor Rolf Reed**

15.00-15.45 Keynote lecture I: Professor **Bruce Zetter** (Harvard Medical School)
New Mechanisms and Biomarkers of Chemoresistance.

15.45-16.30 Keynote lecture II: Professor **Mina Bissell** (Lawrence Berkeley National Laboratory).
Engineered models of dormancy and metastasis: the importance of the extracellular matrix

Day 2: Friday May 31, 2013

Store auditorium, 3rd floor, Haukeland University Hospital, Jonas Lies Vei 65

Session 3 **Biomarkers: Ethical and Economic Aspects** **Chair: Professor Oddvar Kaarbøe**

- 10.00-10.30 Keynote lecture III: Professor **John Cairns** (London School of Hygiene & Tropical Medicine)
The economic evaluation of cancer biomarkers.
- 10.30-11.30 Ethical, Legal and Economic aspects of CCBOs research,
Roger Strand (University of Bergen):
From Ethics to ELSA of Research on Cancer Biomarkers.
Oddvar Martin Kaarbøe (University of Bergen): Biomarkers, economic aspects.
Comments by **Ole Frithjof Nordheim** (University of Bergen).
- 11.30-13.00 Lunch & Poster Session, Assembly Hall, BBB, right across the pedestrian bridge
from Haukeland University Hospital.

Session 4 **Biomarkers: From Basic to Clinical Studies** **Chair: Professor Bjørn Tore Gjertsen**

- 13.00-15.00 **Arne Östman** (Karolinska Institute): PDGF-dependent CAFs and pericytes; impact
on metastasis and prognosis.
Christopher Hughes (University of California Irvine): Angiogenesis and the tumor
microenvironment.
Randolph Watnick (Harvard Medical School): Development of a novel therapeutic
peptide for the treatment of advanced cancer.
Rolf Brekken (University of Texas): Macrophages and metastasis: targeting
prometastatic macrophages and the products they make.
Ate van der Zee (University of Groningen): Examples of biomarker research in
gynaecologic oncology.
- 15.00-15.30 Coffee
- 15.30-17.30 **George N. Naumov** (Merck Research Laboratories Boston): Development and bio-
marker strategy of novel combination therapies using two investigational oncology
agents.
Oddbjørn Straume (University of Bergen): Angiogenesis as a treatment target in
metastatic melanoma.
Biaoyang Lin (University of Washington): Recurrent Targeted Genes of Hepatitis B
Virus in the Liver Cancer Genomes Identified by a Next-Generation Sequencing-
Based Approach.
James Lorens (University of Bergen): Stem cells, EMT and cancer: The role of Axl.
- 17.30-17.35 Summing up and closing (**Lars A. Akslen**)

Outreach and Media

CCBIO aims to communicate novel findings to the public in a timely and informative way, and has gotten quite a bit of media coverage since the start. Here are some of the many stories the CCBIO scientists have participated in:



NRK Dagsrevyen, 12.11.12: (the day the SFF's were announced by the Research Council of Norway) – “new malignant melanoma medicine”



I ferd med å knekke kreft-gåte

Kreftforskere i Bergen har gjort et stort internasjonalt gjennombrudd. Ny behandling kan stoppe kreftsvulsten og få den til å krympe, uten cellegift.

– Jeg føler nå at jeg er på vei tilbake til det livet jeg hadde, og kan fortsette å leve med barna og omgivelsene mine, forteller Trond Helge Karlsson.

Livet hans ble satt på vent da han oppdaget en fælles med ondartede kreftceller. Men ny medisin har gitt 34-åringen på Askøy i Bergen tilbake framtiden han fryktet å ikke bli en del av.

– Jeg hadde en svulst som vokste og vokste. Men bare noen uker etter at behandlingen begynte, merket jeg at jeg ble bedre. Så følte jeg at trykket begynte å vike seg i det området der svulsten var. Snartene forsvant, og så trakk svulsten seg tilbake, forteller han.

Centre for Cancer Biomarkers

- Sies karslagte melanomene som styrer samspillet mellom vevsnettet og andre molekylære identifikere diagnostiske kjennetegn for dette samspillet, og derved kreftens utvikling i kreftbehandlingen. Forskning gir små forbedringer hele tiden.
- Lars A. Akselsen utvalgte til utvalgte av samlet samlet

Nrk.no, 12.11.12: “Going for a cure”

Lindring og livsforlengelse

Steinar Aasmund
Professor, Avdeling for Kreftebehandling, OUS

Lars Andreas Akselsen
Professor, Centre for Cancer Biomarkers, ULS, Leder, Norsk Melanomgruppe

Andreas Stensvold
Overlege, Avdeling for Kreftebehandling, OUS, Leder Norsk Onkologisk Forening

LEGEMIDLER: Berge Solberg, professor i medisin og etikk og Stein Kaasa, professor i palliativ medisin og prosjektleder i Helsedirektoratet har i kronikk 29. november tatt til orde for at lindrende behandling bør prioriteres i livets sluttfase i stedet for behandling som ifølge dem gir minimal livsforlengelse. De setter kreftebehandling i et etisk dilemma. Spørsmålet er ikke enten-eller. Det er ikke uenigheter om at helsetilstanden aldri vil kunne oppfylle alle behandlingsønsker. Men rettsforholdene rundt skal ikke være bestemmende for behandling.

Kreft er ingen enkel gite som løses en gang for alle. Mens én av to overlevde kreftsykdom for 20 år siden, er det nå to av tre som gjør det. Det er forskning og utvikling av nye behandlinger, kombinert med tidligere og bedre diagnostikk, som har ført til denne positive utviklingen i kreftbehandlingen. Forskning gir små forbedringer hele tiden.

MÅ VELGE? «Pasientene skal ikke måtte velge mellom livsforlengende og lindrende behandling. De skal selvfølgelig få begge delene, skriver artikkelforfatterne.

Miljøet er utvikle bedre medikamenter for både å forlenge livet og lindrer plagene.

Mange pasienter med uheldig kreftsykdom har imidlertid lite eller ingen symptomer, og noen er i full jobb. De er på ingen måte i livets sluttfase. Solberg og Kaasa mener at pasienter med uheldig sykdom skal makte være omsorgsfull, lindrende behandling. Og ikke forlenge av levetid i uker og måneder.

Solberg og Kaasa bruker det nye medikamentet ipilimumab til pasienter med fellekreft som først gang hadde et medikament som virkelig virket. Medikamentet er godkjent i EU, alle andre land i Norden og de fleste land i Europa, (nå også Spania og England) bruker ipilimumab. I Norge kan behandlingen bare kjøpes privat. Lommeboka bestemmer hvilke pasienter som kan få ipilimumab. Det er ikke rettferdig for pasienter med uheldig kreft. Pasientene skal ikke måtte velge mellom livsforlengende og lindrende behandling. De skal selvfølgelig få begge deler.

Lommeboka bestemmer hvilke pasienter som kan få ipilimumab.

14.12.12: Dagbladet – “Solace and a longer life”

Opnar nytt kreftsenter

Med status som senter for framifrå forskning håper Centre for Cancer Biomarkers (CCB) å løpse kreftgåta.

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I november blei det klart at CCB ved Universitetet i Bergen (UiB), som einaste kreftforsknings-senteret denne runden, fekk status som senter for framifrå forskning (SFF). Løyvinga er på heile 17 millionar kroner årleg over ein femårsperiode, med moglegheit for utviding for fem nye år. I morgon er det tid for opning av det nye senteret.

Kan utvide

Midlane fører til at senteret kan intensivere forskinga dei har jobba med tidlegare, ved å betre forståinga, diagnostikken og behandlinga av kreft.

– Dette betyr at vi kan utvide repertoaret av analysemetodar og utvide pasientgruppa vi forskar på. Meir pengar gjev oss moglegheita til å utforske noko svært nytt og spanande, seier leiar Lars A. Akslen ved senteret.

– Kva betyr det for senteret at de har fått status som senter for framifrå forskning?

– Det er ei stor ære og ein fan-

fakta kreft

■ Samlenemning på rundt 200 ulike svulstformer. Ved kreft har det oppstått mutasjonar i arvestoffet til cellene, slik at cellene deler seg ukontrollert.

■ Kreft er den vanlegaste dødsårsaka i Noreg etter hjerte- og karsjukdommar. I 2010 blei 28.271 nordmenn diagnostisert med kreft. Av desse var 53 prosent menn og 47 prosent kvinner.

■ Dei vanlegaste kreftformene for menn er prostatakreft, lungekreft, og tjukk- og endetarmskreft. For kvinner er brystkreft mest utbreidd, følgd av tjukk- og endetarmskreft og lungekreft.

KJELDE: KREFTFORENINGA



TIL KRIG MOT KREFT: Centre for Cancer Biomarkers (CCB) forskar på utvikling av skreddersydd kreftbehandling. – Kunnskap om biomarkørar kan føre til ein revolusjon innan kreftbehandlinga, seier senterleiar Lars Akslen.

tastisk anerkjenning. Ein må også vere litt lokalpatriot og seie at det er bra at vi har dette i Bergen, og at ikkje alt kjem til hovudstaden, seier Akslen muntert.

– Ein revolusjon

Spesielt med CCB er at dei forskar på såkalla biomarkørar knytta til mikromiljøet, som er

viktige eigenskapar ved kreftsvulstane. Dette er eit lite undersøkt felt innan kreftforskinga, hevdar Akslen.

– Biomarkørane er fyrtårn som viser korleis ein skal behandle svulsten, og meir kunnskap om desse er noko av det som kan føre til ein revolusjon innan kreftbehandlinga, seier han.

Ved å lære meir om biomarkørane, kan ein drive betre og skreddersydd kreftforsking, og dermed tilpasse ei spesifikk behandling til kvar enkelt pasient.

– For å behandle ein kreftsvulst effektivt, må ein truleg ha behandling som både angrip kreftcellene og forsyningslinjene i mikromiljøet. Om ein gjer dette samtidig, reduserer ein faren for å at kreften sprer seg betydeleg, seier han.

– Knivskarp konkurranse

Det ligg stor nasjonal og internasjonal prestisje å få SFF-status.

– Det er en knivskarp konkurranse, og berre dei aller beste får midlar. Grunnen til at CCB vann er kvaliteten i forskningsplanane, seier divisjonsdirektør Anders Hanneborg i vitskapsdivisjonen hos Forskingsrådet.

– Dette er kanskje eit av dei mest spanande forskingsområdene i medisin i dag.

Av 149 søkarar, var det berre 13 som fekk midlar.

– Dei fleste SFF-senter utvidar ganske raskt, og aktiviteten er ofte tre-firedobla i løpet av nokre få år.

Internasjonalt samarbeid

Tre institutt ved Medisinsk Odontologisk Fakultetet ved UiB er involvert i senteret. Dekan Nina Langeland ved fakultetet er svært nøgd med opninga.

– Det gjer noko med dei andre fagmiljø at nokon får denne anerkjenninga. Eg trur det er viktig inspirasjon for andre miljø, og at fleire tør å søke på dei mest konkurranseutsette forskingsmidlane, seier Langeland.

Fleire grupper ved fakultetet har søkt tidlegare, utan gjennomslag.

– At kreftforskningsmiljøet i Bergen blir vurdert som betre enn mange andre plassar, er veldig bra.

I morgon har senteret opningsseremoni med store internasjonale kreftforskarar frå amerikanske prestisjeuniversitet til stades.

– Dette er viktige samarbeidspartnarar, og det er svært gunstig for oss at dei støttar senteret. Det betyr mykje for å styrke forskinga, og i tillegg bidrar dei med kunnskap og opplæring til dei nye forskingskandidatane, seier Akslen.



FORSKERGRUPPE: Professor James Lorens sammen med fire av hans PhD-stipendiater. Fra venstre Katarzyna Wnuk-Lipinska, Henriette Ertås, Fanny Pellissier og Crina Tiron. FOTO: SISSEL DYRSTAD, UIB

Bergensforskere fant ny kreftmedisin

Forskere fra Bergen har utviklet ny medisin som kan hemme spredning av brystkreft.

Kari Pedersen

Publisert: 02. okt. 2013 21:17 Oppdatert: 03. okt. 2013 06:21

Seiskapet BerGenBio AS er klar for å teste kreftmedisinen på pasienter over jul.

– Hvis dette virker slik vi håper, kan vi hjelpe mange pasienter. Tilsvarende medisiner redder mange liv, og er også

En mykstart på sommeren

Myk sko i nubuck med lett og dempende såle.

Herre

999,-

2.10.13: New drug from the Lorens team and BerGenBio.

30.05.13: Bergens Tidende – “new cancer research center”



PROSJEKTLEDERNE: Senteret har ni prosjekter, med hver sin prosjektleder. Fra venstre: Bjørn Tore Gjertsen, Karl Henning Kalland, Anne Christine Johannessen, Lars A. Akslen, Helga B. Salvesen, Oddbjørn Straume, Donald Gullberg. James Lorens og Rolf Reed var ikke til stede da bildet ble tatt. FOTO: JAN M. LILLEBØ

Skarpskytterne

■ 365 gode nyheter

En av årets beste helsenyheter i Bergen er etableringen av det nye Senter for kreftmarkører.

Kari Pedersen

Publisert: 31.des. 2013 07:47 Oppdatert: 31.des. 2013 08:22

Disse syv kreftforskerne jobber for å treffe bedre. Men nei, de tar ikke jegerprøven. Forskerne ved Senter for kreftmarkører jakter på nøkkelen til bedre og mer målrettet behandling av kreft.

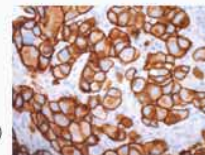
- Mye av dagens kreftbehandling er som å skyte med hagle. Vi ønsker å finne biomarkørene og medisinene som gjør det mulig å skyte skarpt, sier professor og senterleder Lars Andreas Akslen.

- Perspektivet vårt handler om å skape nye, smarte medisiner som vi kun



SENTER FOR KREFTMARKØRER

Forskningscenter tilknyttet Universitetet i Bergen og Haukeland universitetssykehus.



TALL: Senter for kreftmarkører (Centre for Cancer Biomarkers) er utpekt som Senter for fremragende forskning.

Senteret jobber med å finne biomarkører, som kan gi mer målrettet kreftbehandling. Biomarkører kan være gener, et protein eller egenskaper i vevet rundt kreftsvulsten.

List of Publications - CCBIO 2013

Appendix 1: List of Publications - CCBIO 2013

1. **Andresen, Vibeke; Wang, Xiang; Ghimire, Sakhila; Omsland, Maria; Gjertsen, Bjørn Tore; Gerdes, Hans-Hermann.**
Tunneling nanotube (TNT) formation is independent of p53 expression. *Cell Death and Differentiation* 2013;20:1124-1124
2. **Arnesen, Thomas; Glomnes, Nina; Strømsøy, Siri S.; Knappskog, Stian; Heie, Anette; Akslen, Lars A.; Grytaas, Marianne Aardal; Varhaug, Jan Erik; Gimm, Oliver; Brauckhoff, Michael.**
Outcome after surgery for primary hyperaldosteronism may depend on KCNJ5 tumor mutation status: a population-based study from Western Norway. *Langenbeck's archives of surgery (Print)* 2013 ; 398.(6):869-874
3. **Barczyk, Malgorzata; Bolstad, Anne Isine; Gullberg, Donald.**
Role of integrins in the periodontal ligament: organizers and facilitators. *Periodontology 2000* 2013 ;Volum 63. s. 29-47
4. **Barczyk, Malgorzata; Lu, Ning; Popova, Svetlana; Bolstad, Anne Isine; Gullberg, Donald.**
alpha 11 beta 1 integrin-mediated MMP-13-dependent collagen lattice contraction by fibroblasts: Evidence for integrin-coordinated collagen proteolysis. *Journal of Cellular Physiology* 2013 ;Volum 228.(5) s. 1108-1119
5. **Bayer, Monika Lucia; Schjerling, Peter; Heinemeier, Katja Maria; Gullberg, Donald; Herchenhan, Andreas; Krogsgaard, Michael; Kjær, Michael.**
CelluCCCLar changes in human tendon cells as a result to release of mechanical tension. *The FASEB Journal* 2013 ;Volum 27. (Meeting Abstract Supplement) 1217.23
6. **Bojesen, Stig E.; ... Dunning, Alison M.**
Multiple independent variants at the TERT locus are associated with telomere length and risks of breast and ovarian cancer. *Nature Genetics* 2013 ;Volum 45.(4) s. 371-384 (Salvesen group).
7. **Bredholt, Therese; Ersvær, Elisabeth; Erikstein, Bjarte Skoe; Sulen, Andre; Reikvam, Håkon; Aarstad, Hans Jørgen; Johannessen, Anne Chr.; Vintermyr, Olav Karsten; Bruserud, Øystein; Gjertsen, Bjørn Tore.**
Distinct single cell signal transduction signatures in leukocyte subsets stimulated with khat extract, amphetamine-like cathinone, cathine or norephedrine. *BMC Pharmacology & Toxicology* 2013 ;Volum 14. s. 35-41
8. **Busse-Wicher, Marta; Wicher, Krzysztof B.; Kusche-Gullberg, Marion.**
The exostosin family: Proteins with many functions. *Matrix Biology* 2013 Oct 12. [Epub ahead of print]
9. **Catena, Raúl; Bhattacharya, Nandita; El Rayes, Tina; Wang, Suming; Choi, Hyejin; Gao, Dingcheng; Ryu, Seongho; Joshi, Natasha; Bielenberg, Diane; Lee, Sharrell B.; Haukaas, Svein Andreas; Gravdal, Karsten; Halvorsen, Ole Johan; Akslen, Lars A.; Watnick, Randolph S.; Mittal, Vivek.**
Bone marrow-derived Gr1(+) cells can generate a metastasis-resistant microenvironment via induced secretion of thrombospondin-1. *Cancer Discovery* 2013 ;Volum 3.(5) s. 578-589
10. **Costea, Daniela Elena; Hills, Allison; Osman, Amani Hamza Ali; Thurlow, Johanna; Kalna, Gabriela; Huang, Xiaohong; Murillo, Claudia Pena; Parajuli, Himalaya; Suliman, Salwa Mustafa Nourelhuda; Keerthi, Kulasekara K; Johannessen, Anne Chr.; Partridge, Max.**
Identification of two distinct carcinoma-associated fibroblast subtypes with differential tumor-promoting abilities in oral squamous cell carcinoma. *Cancer Research* 2013 ;Volum 73.(13) s. 3888-3901
11. **Dabija-Wolter, Gabriela; Bakken, Vidar; Cimpan, Mihaela Roxana; Johannessen, Anne Chr.; Costea, Daniela Elena.**
In vitro reconstruction of human junctional and sulcular epithelium. *Journal of Oral Pathology & Medicine* 2013 ;Volum 42.(5) s. 396-404
12. **Delahanty, Ryan J.; Xiang, Yong-Bing; Spurdle, Amanda; Beeghly-Fadiel, Alicia; Long, Jirong; Thompson, Deborah; Tomlinson, Ian; Yu, Herbert; Lambrechts, Diether; Dörk, Thilo; Goodman, Marc T.; Zheng, Ying;**

Salvesen, Helga Birgitte; Bao, Ping-Ping; Amant, Frédéric; Beckmann, Matthias W; Coenegrachts, Lieve; Coosemans, An; Dubrowinskaja, Natalia; Dunning, Alison; Runnebaum, Ingo B.; Easton, Douglas; Ekici, Arif B.; Fasching, Peter A.; Halle, Mari Kylesø; Hein, Alexander; Howarth, Kimberly; Gorman, Maggie; Kaydarova, Dilyara; Krakstad, Camilla; Lose, Felicity; Lu, Lingeng; Lurie, Galina; O'Mara, Tracy; Matsuno, Rayna K.; Pharoah, Paul; Risch, Harvey; Corssen, Madeleine; Trovik, Jone; Turmanov, Nurzhan; Wen, Wanqing; Lu, Wei; Cai, Quiying; Zheng, Wei; Shu, Xiao-Ou.

Polymorphisms in inflammation pathway genes and endometrial cancer risk. *Cancer Epidemiology, Biomarkers and Prevention* 2013 ;Volum 22.(2) s. 216-223

13. **Dimcevski, Georg Gjorgji; Kotopoulos, Spiros; Hoem, Dag; Postema, Michiel; Gjertsen, Bjørn Tore; Bjånes, Tormod Karlsen; Biermann, Martin; McCormack, Emmet Martin; Sorbye, Halfdan; Molven, Anders; Gilja, Odd Helge.**
 Ultrasound-assisted treatment of an inoperable pancreatic cancer. I: *MedViz Conference 2013*. Bergen: MedViz, Haukeland University Hospital, University of Bergen, Christian Michelsen Research 2013 ISBN 978-82-998920-1-8. s. 49-52
14. **Engstrøm, Monica J; Opdahl, Signe; Hagen, Anne Irene; Romundstad, Pål Richard; Akslen, Lars A.; Haugen, Olav A.; Vatten, Lars Johan; Bofin, Anna M.**
 Molecular subtypes, histopathological grade and survival in a historic cohort of breast cancer patients. *Breast Cancer Research and Treatment* 2013 ;Volum 140.(3) s. 463-473
15. **Engstrøm, Monica J; Opdahl, Signe; Hagen, Anne Irene; Romundstad, Pål Richard; Akslen, Lars A.; Haugen, Olav A.; Vatten, Lars Johan; Bofin, Anna M.**
 Molekylære subtyper og overlevelse ved brystkreft. Kirurgisk høstmøte 2013; 2013-10-23 - 2013-10-25
16. **Engstrøm, Monica J; Opdahl, Signe; Hansen, Åse Kristin Skain; Romundstad, Pål Richard; Vatten, Lars Johan; Akslen, Lars A.; Hagen, Anne Irene; Haugen, Olav Anton; Bofin, Anna M.**
 Molekylære subtyper og overlevelse ved brystkreft. Årsmøte for Norsk Forening for Patologi; 2013-03-15 - 2013-03-16
17. **Fredly, Hanne Kristin; Ersvær, Elisabeth; Kittang, Astrid Marta Olsnes; Tsykunova, Galina; Gjertsen, Bjørn Tore; Bruserud, Øystein.**
 The combination of valproic acid, all-trans retinoic acid and low-dose cytarabine as disease-stabilizing treatment in acute myeloid leukemia. *Clinical Epigenetics* 2013 ; Aug 1;5(1):13.
18. **Fredly, Hanne Kristin; Gjertsen, Bjørn Tore; Bruserud, Øystein.**
 Histone deacetylase inhibition in the treatment of acute myeloid leukemia: the effects of valproic acid on leukemic cells, and the clinical and experimental evidence for combining valproic acid with other antileukemic agents. *Clinical Epigenetics* 2013 ; Jul 30;5(1):12.
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 High-throughput interrogation of PIK3CA, PTEN, KRAS, FBXW7 and TP53 mutations in primary endometrial carcinoma. *Gynecologic Oncology* 2013 ;Volum 128.(2) s. 327-334

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Cyclic AMP can promote APL progression and protect myeloid leukemia cells against anthracycline-induced apoptosis. *Cell Death and Disease* 2013; Volum 4. e516
22. **Geisler, Jürgen; Bachmann, Ingeborg M.; Nyakas, Marta Sølvi; Helsing, Per; Fjøsne, Hans E.; Mæhle, Lovise Olaug; Aamdal, Steinar; Eide, Nils; Svendsen, Henrik Løvendahl; Straume, Oddbjørn; Robsahm, Trude Eid; Dolven-Jacobsen, Kari; Akslen, Lars A.**
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23. **Getz, Gad; ... Shen, R.**
Integrated genomic characterization of endometrial carcinoma. *Nature* 2013;Volum 497.(7447) s. 67-73 (Salvesen group)
24. **Haldorsen, Ingrid S.; Grüner, Renate; Husby, Jenny Hild Aase; Magnussen, Inger Johanne; Werner, Henrica Maria Johanna; Salvesen, Øyvind; Bjørge, Line; Stefansson, Ingunn Marie; Akslen, Lars A.; Trovik, Jone; Taxt, Torfinn; Salvesen, Helga Birgitte.**
Dynamic contrast-enhanced MRI in endometrial carcinoma identifies patients at increased risk of recurrence. *European Radiology* 2013 ;Volum 23.(10) s. 2916-2925
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Increased microvascular proliferation is negatively correlated to tumour blood flow and is associated with unfavourable outcome in endometrial carcinomas. *British Journal of Cancer* 2014; Volum 110. s. 107-114 (Epub ahead of print Oct 31)
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27. **Helland, Øystein; Bishof, Katharina; Popa, Mihaela Lucia; Bishof, Katharina; Gjertsen, Bjørn Tore; McCormack, Emmet; Bjørge, Line.**
Histone deacetylase inhibisjon i kombinasjon med platinum i en klinisk relevant ortotopisk musemodel for ovarialcancer. Årsmøte i Norsk Gynekologisk Forening (NGF); 2013-10-24 - 2013-10-26
28. **Helland, Øystein; Popa, Mihaela Lucia; Gjertsen, Bjørn Tore; McCormack, Emmet; Bjørge, Line.**
Panobinostat / carboplatin delay postsurgical relapse of ovarian carcinomas in an orthotopic mouse model. The 18th International Meeting of the European Society of Gynaecological Oncology (ESGO); 2013-10-19 - 2013-10-22
29. **Herfindal, Lars; Myhren, Lene Elisabeth; Gjertsen, Bjørn Tore; Doskeland, Stein Ove; Gausdal, Gro.**
Functional p53 is required for rapid restoration of daunorubicin-induced lesions of the spleen. *BMC Cancer* 2013 ;Volum 13. s. 341
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31. **Iles, Mark M.; ... Barrett, Jennifer H..**
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32. **Jacobsen, Hege; Sleire, Linda; Wang, Jian; Netland, Inger Anne; Mutlu, Ercan; Førde, Hilde Elise Sundøy; Pedersen, Paal-Henning; Gullberg, Donald; Enger, Per Øyvind.**
Establishment of a novel dsRed NOD/Scid mouse strain to investigate the host and tumor cell compartments. *Cancer Investigation* 2013 ;Volum 31.(4) s. 221-230

33. **Johannessen, Tor-Christian Aase; Wagner, Marek; Straume, Oddbjørn; Bjerkvig, Rolf; Eikesdal, Hans Petter.**
Tumor vasculature: the Achilles' heel of cancer? *Expert opinion on therapeutic targets* 2013 ;Volum 17.(1) s. 7-20
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36. **Kloster, Martine Müller; Naderi, Elin Hallan; Haaland, Ingvild; Gjertsen, Bjørn Tore; Blomhoff, Heidi Kiil; Naderi, Soheil.**
cAMP signalling inhibits p53 acetylation and apoptosis via HDAC and SIRT deacetylases. *International Journal of Oncology* 2013 ;Volum 42.(5) s. 1815-1821
37. **Knutsvik, Gøril; Stefansson, Ingunn Marie; Collett, Karin; Akslen, Lars A.**
Proliferation markers PHH3, Ki67 and Mitotic count all show significant associations with features of aggressive breast carcinomas and reduced survival. *Laboratory Investigation* 2013 ;Volum 93. s. 50A-50A
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Proliferation markers PHH3, Ki67 and mitotic count all show significant associations with features of aggressive breast carcinomas and reduced survival. *Modern Pathology* 2013; Volum 26. s. 50A-50A
39. **Kotopoulos, Spiros; Delalande, Anthony; Popa, Mihaela; Dimcevski, Georg Gjorgji; Gilja, Odd Helge; Postema, Michiel; Gjertsen, Bjørn Tore; McCormack, Emmet Martin.**
Ultrasound and microbubble enhanced therapy of orthotopic human pancreatic cancer in mice. I: *MedViz Conference 2013*. Bergen: MedViz, Haukeland University Hospital, University of Bergen, Christian Michelsen Research 2013 ISBN 978-82-998920-1-8. s. 45-47
40. **Ladstein, Rita Grude; Bachmann, Ingeborg M.; Straume, Oddbjørn; Akslen, Lars A.**
Nestin expression is associated with aggressive cutaneous melanoma of the nodular type. *Modern Pathology* 2013 ; Volum 27. s. 396-401
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Molecular Determinants of Outcome With Mammalian Target of Rapamycin Inhibition in Endometrial Cancer. *Cancer* 2014 Feb 15;120(4):603-10. Epub 2013 Oct 25.
42. **McCormack, Emmet; Adams, Katherine J.; Hassan, Namir J.; Kotian, Akhil; Lissin, Nikolai M.; Sami, Malkit; Mujic, Maja; Osdal, Tereza; Gjertsen, Bjørn Tore; Baker, Deborah; Powlesland, Alex S.; Aleksic, Milos; Vuidepot, Annelise; Morteau, Oliver; Sutton, Deborah H.; June, Carl H.; Kalos, Michael; Ashfield, Rebecca; Jakobsen, Bent K.**
Bi-specific TCR-anti CD3 redirected T-cell targeting of NY-ESO-1-and LAGE-1-positive tumors. *Cancer Immunology and Immunotherapy* 2013 ;Volum 62.(4) s. 773-785
43. **McCormack, Emmet; Mujic, Maja; Osdal, Tereza; Bruserud, Øystein; Gjertsen, Bjørn Tore.**
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Nitroreductase, a near-infrared reporter platform for in vivo time-domain optical imaging of metastatic cancer. *Cancer Research* 2013 ;Volum 74.(4) s. 1276-1286

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Media Appearances - CCBIO 2013

Appendix 2: Media Appearances - CCBIO 2013

31.12.13	BT, «Finsikter seg inn på den beste medisinen mot kreft», «Skarpskytterne»
30.12.13	UiB Aktuelt, «Stort gjennombrudd i jakten på livmorhalskreft»
28.12.13	Aftenposten VITEN, «Måltrettet kreftbehandling til flere»
27.12.13	Helse Bergen web, «Første deltaljkart av arvestoffet ved livmorhalskreft»
25.12.13	Dagbladet/DN.no/Sunnmørsposten/Fædrelandsvennen/Altaposten/Framtid i Nord/ Harstad Tidende/Klassekampen/Adresseavisen/Folkebladet/NRK Hordaland nyheter, «Norske forskere med på gjennombrudd i kartleggingen av livmorhalskreft»
25.12.13	BT, «Bergens-forskere med på kreft-gjennombrudd»
25.12.13	Aftenposten, BT, «Har gjort viktige funn for bedre behandling av livmorhalskreft»
12.12.13	BT, «Skreddersyr medisiner mot kreft»
07.11.13	UiB Aktuelt, «Millioner til kreftforskning»,
05.11.13	Forskningsrådet, «Nytt SFF: Skreddersøm i sikte»
02.10.13	Kreftforeningen, «Ny medisin kan motvirke spredning av brystkreft»
02.10.13	BT, «Bergensforskere fant ny kreftmedisin»
02.10.13	UiB Aktuelt, Forskning.no, «Ny medisin kan motvirke spredning av brystkreft»
19.09.13	UiB News, HUBRO International, «Hunting psychopath cells»
Høst 2013	Annonsebilag for Oslo Cancer Cluster, «Utprøvende kreftbehandling gjennom kliniske studier», Bjørn Tore Gjertsen http://issuu.com/issuurim/docs/kampen-mot-kreft-2013_f333a5459d5b37?e=4296636/5327783#search
10.09.13	Nature Biotechnology, «First Axl inhibitor enters clinical trials»
Sept 2013	Bladet Forskning, «Skreddersøm i sikte»
Sept 2013	Forskningsdagene, «Jakten på kreften»

Sept 2013	Hubro 2-2013, « Blokkerer blodkar »
12.07.13	Kreftforeningen, « Paradigmeskifte i kreftbehandling? »
07.06.13	Oslo Cancer Cluster, Norwegian Cancer Biomarkers « Centre of Excellence »
06.06.13	BTO (Bergen Teknologioverføring), « Nytt håp i kreftkampen »
06.06.13	WN.com (WorldNews), « Nytt senter gir krefthåp i Bergen »
06.06.13	Aftonbladet, Sverige, « Cancer kan vara botemedelet – mot cancer »
04.06.13	VG, « Egne kreftceller knekker kreften – norsk gjennombrudd »
04.06.13	P5, « Norsk kreft-gjennombrudd »
01.06.13	TV2 Nyhetskanalen, Nytt kreftforskningssenter ved Universitetet i Bergen. Lars Akslen gjest i studio.
31.05.13	Kystradioen, Lars Akslen gjest i studio
31.05.13	På Høyden, « Åpnet krig mot kreft », From the opening
31.05.13	BA, « Gir nytt krefthåp »
31.05.13	UiB Aktuelt, « Startskotet avfyrt for kreftsenter », From the opening
30.05.13	Forskningsrådet, « Tre nye sentre for fremragende forskning er åpnet », From the opening
30.05.13	BA, « Nytt senter gir krefthåp i Bergen »
30.05.13	BT, « Opnar nytt kreftsenter », From the opening
30.05.13	NRK Hordaland (radio), Lars Akslen gjest i studio i morgonsendinga (radiosendinga med høgast lyttartal i Hordaland)
25.04.13	Nature, « Spotlight on Norway »

23.04.13	YouTube, video, «CCBIO – an introduction», On CCBIO
21.11.12	Kreftforeningens blogg, «Kreftforskere i elitedivisjonen», On CCBIO
13.11.12	Dagens Medisin, «Fem fremragende sentre innen medisin», On CCBIO
13.11.12	Hegnar Online, «Får 170 mill. til å forske på mulig kreftgjennombrudd», On CCBIO
13.11.12	NRK Hordaland, «I ferd med å knekke kreft-gåte»
12.11.12	NRK Dagsrevyen: Nytt senter for kreftforskning. http://tv.nrk.no/serie/dagsrevyen/nnfa19111212/12-11-2012#t=23m2s
12.11.12	BT, «Stor anerkjennelse til UiB»
12.11.12	Den norske patologforening (nettside), «Lars Akslen i spissen for Fremragende forskning», On CCBIO
12.11.12	UiB, fakultetets webside, «To nye sentre for fremragende forskning til fakultetet», On CCBIO
12.11.12	Forskningsrådet, «Tretten nye sentre for fremragende forskning», On CCBIO
12.11.12	På Høyden, «Vil sysselsette over 100 kreftforskere», On CCBIO
12.11.12	På Høyden, «Tre nye SSF-er til UiB», On CCBIO
12.11.12	UiB Aktuelt, «Tre nye sentre for fremragende forskning», On CCBIO
Høst 2012	HUBRO 2-2012, «Jakter på psykopatceller»
26.09.12	UiB Aktuelt, «Mikrososiologi mot kreft»



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Principal Investigators

From the left: Bjørn T. Gjertsen, James B. Lorens, Karl H. Kalland, Anne Chr. Johannessen, Lars A. Akslen, Rolf K. Reed, Helga B. Salvesen, Oddbjørn Straume, Donald Gullberg.

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Photo: Tove Lise Mossestad



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