Centre for Cancer Biomarkers

Norwegian Centre of Excellence – University of Bergen

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CONTENTS

Cover picture: Malignant melanoma of the skin.

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Director´s Comments

Throughout 2014, CCBIO completed its first phase of recruitment, and many enthusiastic PhD students and postdoctoral fellows are in place and have initiated their work in different research groups. Basic studies are being performed, especially focusing on how tumor cells interact with the surrounding microenvironment, by epithelial-mesenchymal transition, plasticity programs, angiogenesis induction and matrix dynamics, leading to the initiation of metastatic spread. Different classes of biomarkers and their clinico-pathologic correlations are being explored, such as genetic markers, gene expression mining and profiling, and tissue based protein marker studies. As an example of implementation studies, the aim of the multicenter MoMaTEC projects on integrated biomarker profiling of endometrial cancer is to perform stratified surgery based on validated biomarkers and imaging data.

One of the goals for CCBIO is to push experimental therapy and diagnostics for our patients. We are facing significant and complex challenges in how to attack metastasizing tumors. Recent papers support the positive responses to immunological checkpoint blockers, and studies with multiple indications are in preparation. CCBIO is participating in this effort by planning substudies with novel technologies like single cell analysis of immunophenotype and intracellular signaling of patient immune cells. This is performed in collaboration with the Clinical Trials Unit at Haukeland University Hospital. During 2014, CCBIO investigators have headed directly into the immunotherapy domain by teaming up with Bergen Technology Transfer Office and angel investors. The first patients will be treated using dendritic cell based therapy after cryoablation of prostate cancer tissue in early 2015. In addition, the first AXL inhibitor, BGB324 from BerGenBio, entered a Phase I trial in Bergen, indicating a new era in biomedical research in our region, with CCBIO investigators participating. Through a five-year grant on liquid biopsies, various technologies for circulating cells and DNA will be explored in the setting of clinical trials.

During 2014, the CCBIO Research School for Cancer Studies was established, with several key courses, monthly research seminars, a junior scientist symposium (four times each year) and the CCBIO Annual Symposium as integrated parts. This program of educational and networking activities has been well received. Currently, CCBIO is now in the process of recruiting a team of international key collaborators in affiliated positions. This will be important to strengthen our research programs and excellence profile. Based on these efforts, 2015 will be an exciting year.

Lars A. Akslen, Director of CCBIO

Health Priorities Should Be Open, Just and Smart

ROGER STRAND // Medical innovations provide health benefits. They also tend to incur increased costs to the health care system, simply because a novel benefit can create a demand from which the supply side can profit. This is a basic fact of capitalist societies.

While Norwegian politicians, health personnel and citizens might disagree as to whether public health expenditures are too high or indeed too low, it remains a fact that they are increasing. In 2013, the amount of 288 billion NOK (37 billion euros) was spent on public health in Norway, representing an average expenditure of 56 700 NOK/ citizen. So far, Norway's wealthy oil economy has had little difficulty absorbing these costs. 2014, however, was the year when Norway experienced an awakening from its oil-lubricated financial slumber. The oil price dropped dramatically, with immediate consequences for employment. As a fortunate coincidence, the Norwegian governmental expert group on public health prioritization submitted its final report "Open and just - priorities in the Norwegian healthcare services". Its main conclusion is that health prioritization needs to be systematic, transparent, based on general criteria, effective and anchored in the goal of "as many good life-years for everybody, fairly distributed".

Exactly what this will imply for expensive cancer treatments remains to be seen. Recent cancer drug developments have created health benefits, hope, perhaps hype and definitely public controversy. Some of the ethics debates that emerged, appeared more as tragedies than dilemmas- sick individuals getting hopes from therapeutic options that simply cannot be afforded.

More scientific knowledge does not by itself alleviate the ethical tragedies. Indeed, research is in a sense their principal creator. When we call for smarter prioritization, the challenge is not mainly that public decision-makers should become better versed in science. Rather, from the CCBIO perspective, cancer research itself needs to become smarter, develop smarter knowledge that can resolve old problems and produce fewer new ones.

Research on cancer biomarkers bears this promise of smarter science. Part of the tragedy when the individual patient cannot receive a promising treatment because it is not cost-effective on a population level, is the lack of applicable knowledge on the sub-population level. Biomarkers that produce finer stratifications may reduce the tension between clinical wisdom and the need for general decision criteria. At least some biomarkers may have this effect.

This call for smarter science in the name of ethics may seem innocent. It is not. It marks what since the 1990s has been called "the new social contract of science" – a call for researchers to temper their passion for knowledge and not rush ahead, driven by their curiosity alone.

Rather, the researchers are asked to consider the social role and function of his knowledge before it is produced. It is a call for anticipatory ethics of science; a type of ethics that hardly exists and is profoundly inexact. Recently, European research policies have developed the concept of "Responsible Research and Innovation" (RRI; similar to what in the US is called anticipatory governance of science). In Horizon 2020, RRI was made a cross-cutting principle by the European Parliament. One can witness a new request from society onto science: the request not only to produce knowledge but smart knowledge that can promote socially robust decision-making. Some would say this is an impossible request; at CCBIO, claims of impossibility tend to whet our appetite.

Vision and Research Areas

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

CCBIO has a focus on tumor-microenvironment interactions in primary and metastatic lesions and how they can define aggressive tumor features and predict cancer progression patterns. The center is studying how cross-talk between tumor cells and components in the tumor microenvironment reflect cancer complexity and heterogeneity and determine cancer prognosis, beyond what is given by description of genetic alterations in tumor cells.

By three overlapping research areas, CCBIO will re-focus its cancer research into the following main programs:

1. **Mechanisms of Tumor-Microenvironment Interactions (Preclinical Studies)**
2. **Exploration and Validation of Cancer Biomarkers (Biomarker Validation)**
3. **Clinical Applications and Trial Studies (Clinical Studies)**

Biomedical project areas have been supplemented with integrated ethics and economics 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.

The Economics of Cancer Biomarkers

JOHN CAIRNS // There are several dimensions to the economics of biomarkers: including the analysis of the pharmaceutical market, the economic evaluation of biomarkers, and the study of how biomarkers influence behavior.

An example of the first dimension is an analysis of the economic incentives to invest in biomarker-based diagnostic tests. The development of a diagnostic test is valuable from a social point of view if the aggregate cost of testing (including the development cost) is lower than its corresponding social value. The latter has a number of elements, such as reduced costs in the group of patients who would not respond to treatment, and the health gain as a consequence of adverse treatment effects. One important question, for instance, is - how likely is it that the current market structure for biomarker-based diagnostic tests and their companion treatments will produce the optimal amount of R&D for biomarker-based diagnostic tests? And if the current situation is sub-optimal, what policies could be introduced to improve it?

There are several important questions that economic evaluation can address. Where there is a choice of diagnostic tests which is most cost-effective? Where in the clinical pathway is it best to test? A further example concerns whether it is more cost effective to test all patients with a particular condition and treat selectively, or to treat all patients.

One question of major interest is the effect of biomarkers on the cost-effectiveness of treatments. The use of a biomarker may improve the cost-effectiveness of a treatment, assessed by comparing the incremental costs to the incremental benefits (usually measured in terms of QALYs or quality-adjusted life-years). Although the mean cost per patient will generally increase because of additional testing costs and increased treatment costs (e.g. because of increased progression-free survival), the mean QALY per patient will increase if it becomes possible to target therapies on those who are likely to receive greater benefit. If the incremental QALYs increase proportionately more than incremental cost the cost-effectiveness of the treatment will improve (that is, the incremental cost per QALY will fall).

Addressing these questions will (almost) always involve evaluation of treatment and testing, and not just evaluation of the diagnostic test. Diagnostic tests are rarely of value in themselves and

their value lies in their implications for treatment. Thus the cost-effectiveness of biomarkers will also be influenced by how biomarkers influence behaviour of clinicians and patients, for example, the extent to which treatment decisions or adherence to treatment are influenced by additional diagnostic information.

In short, the development and use of cancer biomarkers raises a wide range of economic questions and provides exciting opportunities for economists to work collaboratively to improve understanding in this rapidly evolving sphere.

Organization of the Centre

CCBIO is organized across six departments and four faculties. Its main activities, nine PIs and most of the other staff, are located at the Faculty of Medicine and Dentistry´s departments (FMD), Department of Clinical Medicine (K1), Department of Clinical Science (K2), and Institute of Biomedicine (IBM). The majority of CCBIO´s PIs also hold positions and funding at Helse Bergen and Helse Vest. In addition, CCBIO has activities and employees at the Departments of Informatics and Economics and Centre for the Study of the Sciences and the Humanities at University of Bergen.

Research Management
In terms of science management, CCBIO´s research has been organized in three integrated areas and programs (preclinical studies, biomarkers, clinical studies) (see figure). Lab space and core facilities are available for CCBIO, as is the Clinical Trials Unit at Haukeland University Hospital. The team of nine principal investigators as well as three associate investigators have monthly meetings to discuss administrative and scientific issues and update each other on developments and progress. The group has also met twice a year for a two-day strategy seminar. This is a platform for increased collaboration within CCBIO.

Scientific Advisory Board
In March 2014, the CCBIO Scientific Advisory Board (SAB) met for the first time. The board members for 2014 are:

- **Carl-Henrik Heldin** (SAB chairman), Professor and Director, Ludwig Institute for Cancer Research, Uppsala university, and chairman of the Nobel Foundation
- **Bruce Zetter, Charles Nowiszewski** Professor of Cancer Biology, Harvard Medical School and Boston Children's Hospital, Boston, MA
- **Ate van der Zee**, Professor and board member, University Medical Center Groningen

The SAB provided an overall favorable review of CCBIO as well as advice on how to proceed with improving CCBIO´s research performance.

Integration with host institution and administrative support

In terms of administrative support, CCBIO aims to use its funds as efficiently as possible, ensuring excellent administrative services for its scientists and a good climate of collaboration with its partners. Consequently, CCBIO is organized to retain full control over resources while the day to day administration is delegated to involved departments. As a main principle, funds and positions are located at the department where the research takes place. The intention has been to enable researchers to interact with their familiar support staff, to minimize resources used on day-to-day administration and give CCBIO common interests with the departments. This organization has been successful as it has proved to be efficient and robust, and the model has ensured excellent collaboration with the involved departments.

Management group

CCBIO is currently managed by the Director, Prof. Lars A. Akslen and the Administrative Leader Geir Olav Løken, assisted by five finance officers and other administrative staff allocated CCBIO in parts of their positions. The co-located offices for the CCBIO Management Group are in the main building of Haukeland University Hospital (Sentralblokken, second floor).

During 2013 and early 2014, core staff has been recruited (administrative leader, three senior laboratory managers, 11 recruitment positions (PhDs, postdocs), including one postdoc in ethics and one postdoc in bioinformatics. One adjunct professor (health economics) at 20% was recruited in 2013 (Prof. John Cairns, London School of Hygiene and Tropical Medicine). During late 2014, recruitment of international positions (10-20%) was initiated.

Research Activities and Highlights

Across the three main research areas, several different projects are being conducted, including work on exploration and validation of various cancer biomarkers, clinical studies, and projects on mechanisms of tumor-microenvironment interactions.

Nine principal investigators and group leaders are instrumental for CCBIOs biomedical research: Lars A. Akslen, Bjørn T. Gjertsen, Donald Gullberg, Anne Chr. Johannessen, Karl H. Kalland, James B. Lorens, Rolf K. Reed, Helga B. Salvesen, and Oddbjørn Straume.

Three associate investigators have been a vital part of intersecting research areas in CCBIO: John Cairns (economics), Inge Jonassen (bioinformatics), Roger Strand (ethics).

PHOTO: Ingvild Festervoll Melien

Principal Investigators at CCBIO

During 2014, research efforts have been increasing in the core groups, as reflected in the list of publications. Several papers have been published in high-ranking journals during 2014, such as studies on genetic and protein biomarkers in gynecologic cancers, breast cancer, hematologic cancer, and melanoma. Also, a study on how prostate cancers can limit their own spread was published. These studies exemplify how local teams can collaborate successfully with international environments and networks.

CANCER BIOMARKERS
LARS A. AKSLEN GROUP

Professor Akslen is a specialist in surgical pathology and is directing the Tumor Biology Research Group at the Department of Clinical Medicine (University of Bergen). Since 2013, he is also the director of Centre for Cancer Biomarkers CCBIO. Akslen´s team, and now CCBIO, are engaged in translational cancer research. The group has a strong focus on molecular biomarkers for improved classification and grading of malignant tumors, as a better guide for targeted and precise treatment. The team is currently focusing on two main programs. Firstly, the studies of the tumor microenvironment, especially tumor-vascular interactions and angiogenesis markers. Secondly, genetic and molecular markers of aggressive tumors, with focus on tumor cell proliferation and cell cycle regulation.

The Akslen group has initiated projects on various cancers, such as breast cancer, malignant melanoma, and prostate cancer. Studies of human tumor samples (primary and metastatic lesions) are combined with experimental cell and animal models to improve translation. Biobanks with fresh and paraffin embedded tumor tissue with detailed clinical annotations are applied in these projects. The team has extensive national and international collaboration.

The team has reported several novel angiogenesis biomarkers which provide better grading of malignant tumors and might prove important for targeted treatment and response prediction. In breast cancer, 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 biomarkers in trials of metastatic melanoma, renal cancer, and breast cancer. Ongoing studies have shown that vascular invasion by tumor cells is a strong predictor of aggressive tumors. By gene expression analysis, signatures predicting vascular proliferation and vascular invasion have been identified and validated, also suggesting novel candidates for targeted therapy and prediction of treatment response.

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Senior Researchers:
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May Britt Kalvenes, PhD
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Hanne Puntervoll, PhD

CANCER CELLS AND REPROGRAMMING PLASTICITY

KARL-HENNING KALLAND GROUP

Professor Kalland is directing the Prostate Cancer Therapy Research Group at the Department of Clinical Science, and he is engaged in translational cancer research with a focus on molecular mechanisms and regulatory principles underlying reprogramming plasticity that may be exploited by aggressive cancer cells, such as epithelial to mesenchymal transition (EMT), stem cell and neuroendocrine differentiation of prostate cells and asymmetric cell division.

The idea is that research using appropriate experimental cell culture, animal models and relevant patient materials will provide insights that may guide innovative cancer therapy and identify important molecular targets.

Currently, the group is focused on prostate cancer. One approach is based on an experimental model of stepwise prostate carcinogenesis. This model has been developed by the group starting with a benign human prostate epithelial cell with basal cell features. Using only physiological selection, i.e. different growth conditions and selection over time, gene expression reprogramming gave rise to a series of progeny cells with an accumulating number of malignant features. The model encompasses cells that underwent EMT acquired ability to grow anchorage independently and eventually formed tumors in mice models. Human prostate tumor cells have been recovered from the animal tumors. All these cell types seem to be relatively stable and can be passaged indefinitely in subconfluent cultures. The passage history is carefully recorded. The experimental model has generated detailed molecular insight into reprogramming plasticity of prostate derived cells, including EMT, as presented in a series of publications. Currently, manuscripts and work are in progress regarding mechanisms of stem cell differentiation and asymmetric division. A drug discovery and developmental program is ongoing based upon the model, and this has identified novel small compounds and their molecular targets in cancer cells.

The studies on reprogramming plasticity have yielded increased insight into sources of cancer cell heterogeneity. This has resulted in a Phase I Clinical Trial of cryoimmunotherapy against metastatic prostate cancer, in order to exploit the tumor neo-antigenome and address subcellular heterogeneity. The cryoimmunotherapy module will be combined with specific molecular targeting of gene expression that is preferentially activated in tumor initiating cell subpopulations in ongoing innovative strategies against prostate cancer.

RESEARCH GROUP:

Senior Researchers:
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Research Program in Medicine:
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Technicians:
Hoang, Hua My, Research Technician
Johannessen, Beth, Engineer

MATRIX BIOLOGY
DONALD GULLBERG GROUP

Professor Donald Gullberg has his background in medical chemistry from Uppsala University, and has been working on collagen receptors and integrin biology. He was recruited to the University of Bergen in 2004 and is now directing the Matrix Biology Group at the Department of Biomedicine where he is collaborating closely with Marion Kusche-Gullberg (proteoglycan-related research), Rolf K. Reed (physiology) and Linda Stuhr (physiology).

Since the 1990s, projects have been focused on integrin α11, which was previously discovered in the Gullberg group. Integrin α11beta1 is a collagen receptor with a number of features which makes it a key molecule in tissue fibrosis and tumor-stroma interactions in different types of solid tumors. The group has generated new animal models (mouse and zebrafish) to study the role of integrin α11 during development, in fibrosis and in tumors, and reached a better understanding of the role of integrin α11 in cancer-associated fibroblasts (Marie Curie ITN funded project).

The CCBIO projects deals with the role of integrin α11 in tumor stroma using:

a) tumor-fibroblast heterospheroids as a 3D model system to understand bidirectional communication between tumor cells and fibroblasts; a long-term aim is to develop this system to a large scale in vitro assay to screen for compounds targeting integrins/integrin signalling and with the potential to inhibit tumor growth and spread:

b) new reagents/animal models to conditionally inactivate genes in an integrin α11 specific manner. The long-term aim is to develop new animal models to better analyze the role of cancer associated fibroblasts in tumor stroma interactions.

During 2014, a mouse strain enabling conditional inactivation of integrin α11 has been successfully generated, and a mouse strain for studies of the tumor stroma is currently being analyzed. Two major efforts to generate mouse monoclonal antibodies against α11 are ongoing, and the group will determine the role of integrin α11 during EMT using human lung cancer cells and mouse mammary gland epithelial cells.

RESEARCH GROUP:

Donald Gullberg, PhD, Prof.
Ning Lu, PhD, Senior Laboratory Engineer
Marion Kusche-Gullberg, PhD , Prof.
Kiran Kumar Katta, PhD., Post-doc
Cedric Zeltz, PhD., Researcher
Mona Grønning, Laboratory Engineer

MECHANISMS OF TUMOR CELL PLASTICITY

JAMES LORENS GROUP

Professor Lorens´ team is working on how epithelial cell plasticity between epithelial and mesenchymal phenotypic states provides a 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, the team is investigating the relationship between regulators of EMT in tumor cells in maintenance of normal stem and progenitor cells. Recent results highlight the Axl receptor tyrosine kinase as a key regulator of both normal adult epithelial stem- or progenitor cells and a determinant of carcinoma cell plasticity. These studies on Axl signaling have provided new insights into the regulation of tumor phenotypic heterogeneity and formed a basis for the recent clinical translation of novel Axl inhibitors. Further studies are ongoing on how distinct combinations of microenvironmental factors regulate phenotypic plasticity in normal and cancer cells using new a screening technology.

Using these mechanistic insights Lorens and his team are exploring how microenvironmental factors regulate tumor cell plasticity underlying contextual drug responses.

RESEARCH GROUP:

Bougnaud, Sebastien, Post-doc, PhD
Davidsen, Kjersti, PhD candidate, M.D.
Engelsen, Agnete, Post-doc, M.S., PhD
Ertsås, Henriette, PhD candidate, M.S.
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Lie, Maria, PhD candidate, M.S.
Pelissier, Fanny, PhD candidate, M.S.
Vik Berge, Sissel, Staff Engineer

TRANSCAPILLARY EXCHANGE

ROLF REED GROUP

The Rolf Reed Group is working on the role of the collagen matrix as a determinant for the biophysical properties of tumors. The ongoing studies on experimental cancers originate from a long-term collaboration with Professor Kristofer Rubin at Lund University, Sweden and more recently with Professor Donald Gullberg at UiB. The studies have demonstrated that the connective tissue in general, including experimental tumors, can modify the interstitial fluid pressure via an interaction between cellular tension in the fiber networks in the tissue and the cellular collagen binding integrin receptors. In tumors,"interstitial hypertension" is a functional barrier against the movement of substances across the tumor microcirculation.

The studies focus on the role of collagen binding integrin α11 and αVα3 since the latter is taking over for the former when this is lacking. It has been demonstrated that carcinomas from integrin α(3)-deficient mice have a denser collagen network compared to controls and with elevated interstitial pressure in experimental carcinomas. The studies are extended to more tumor types and also to study the effect on tumor stroma when the stromal cells are lacking integrin α11.

As an extension of the above studies, a collaboration also including Professors Gullberg and Akslen has been initiated to investigate integrin α11 in human cancers.

The CCBIO projects involve collaborations with professors Donald Gullberg and Marion Kusche Gullberg in the Matrix Biology group on the role of integrins α11 and αVα3 in the tumor stroma, using tumor-fibroblast heterospheroids as a 3D model system to understand communication between the tumor cells and fibroblasts. A long-term aim is to develop an vitro system to screen for compounds targeting integrins/integrin signaling and with the potential to inhibit tumor growth and metastsis.

A collaboration with Professor F.-R. Curry at University of California at Davis and Professor Torfinn Taxt at UiB on transcapillary exchange focus on development of methods for its measurement in genetically modified mice with subsequent use for studies in experimental tumor using dynamic contrast enhanced magnetic resonance (DCE-MRI) to study transcapillary exchange. 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.

RESEARCH GROUP:

Rolf K. Reed, M.D., PhD, Prof.
Ning Lu, PhD, Senior Laboratory Engineer
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Trude Skogstrand, PhD postdoctoral fellow
Caroline Schmid, PhD postdoctoral fellow
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Hilde Smeland, PhD student/engineer
Gerd Salvesen, Engineer
Maria Tveitarås, Engineer
Kristina Sortland, Engineer
Tonje Sønstevold, Engineer

GYNAECOLOGIC CANCER

HELGA SALVESEN GROUP

The Salvesen group 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, The 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 molecular alterations that are prevalent in aggressive gynaecological disease. 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).

As a partner in the CCBIO clinical node we are developing methods in close collaboration with the clinical staff to promote improved preclinical models (orthotopic mouse models, patient derived short term cell cultures) for drug testing in parallel with advanced imaging.

RESEARCH GROUP:

Clinical staff:
Bjørge, Line, Prof. II, M.D., PhD
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HELSE BERGEN

ORAL CANCER

ANNE CHRISTINE JOHANNESSEN GROUP

Research at Bergen Oral Cancer Research Group (BOCG) lead by professor Johannessen aims to identify the key molecules of importance for oral cancer development, in order to identify patients who risk 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 behavior of oral cancer. For that purpose, the team has established human tissue-based 3D cell culture models of normal mucosa and oral cancer tissue. These models have opened 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 the crucial role played by carcicoma-associated fibroblasts (CAFs) on oral carcinoma development and progression, 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 and developed a cancer index system of diagnostic and prognostic value based on this panel of molecular 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. The team is now working to expand this cancer index to include molecules from connective tissue and to validate it in the newly formed multi-center 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-center studies on biomarkers in oral cancer are important. The team is part of a collaborative network which includes universities and health institutions in Norway, UK, Romania, India, Nepal and Sudan.

RESEARCH GROUP:

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Martha Rolland Jacobsen, Student Researcher
Parajuli, Himalaya, DDS, PhD candidate
Salwa, Suleiman, DDS, PhD candidate
Sapkota, Dipak, Post-doc, DDS, PhD
Saroj Rajthala, PhD candidate, DDS
Victoria Konstantinova, MPhil candidate, DDS
Øijordsbakken, Gunnvor - Senior Engineer

ANTI-ANGIOGENIC TREATMENT

ODDBJØRN STRAUME GROUP

Dr. Straume has a background in medical oncology with special interest in cutaneous melanoma, renal cancer, and breast cancer. His CCBIO related research activity focuses on three main projects:

Predictive markers of anti-angiogenic treatment in malignant melanoma
Cutaneous melanoma is dependent on angiogenesis to progress and metastasize. Previous results of a clinical phase II study of the anti-VEGF antibody bevacizumab in patients with metastatic melanoma documented that ~30 % of the patients experienced clinical benefit of the treatment. The main objective of this project is to identify predictive markers of response to bevacizumab. During 2014, a series of candidate angiogenic biomarkers have been investigated, and the results will soon be submitted for publication.

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 45 cases with metastatic clear cell renal carcinoma, the team is now working on a set of candidate biomarkers for their predictive value. Blood and tissue samples are under investigation. During 2014, the clinical data, response data as well as quality of life data has been analyzed.

The 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". HSP27 is also a promising predictive marker for anti-angiogenic treatment. 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.

RESEARCH GROUP:

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Gry Haaland, PhD candidate, MD.
Kjersti Davidsen, PhD candidate, MD.
Hanna Dillekås, M.D. (Pre-PhD-project)
Monica Transeth, Stud med

SIGNALLING-TARGETED THERAPY

BJØRN TORE GJERTSEN GROUP

Professor Gjertsen's research interest has its background in the study of intracellular signal transduction by protein phosphorylation in regulation of cell death (apoptosis). Early works included the first proof-of-principle concept of apoptosis-resistance mechanism in myeloid leukemia through point mutation in protein kinase A. Following this observation, 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 tightly regulated through protein modifications, 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). The concept of phosphoprotein signaling response and phenotypic profiling for prognostic information in cancer and as biomarkers in clinical trials was later proposed. In collaboration with Emmet McCormack, state-of-the-art animal models and advanced molecular imaging of acute myelogen leukemia has been established for development of p53- and signaling-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 the last two decades and a two-year survival below 20% in patients above 65 years of age, several clinical trials for Norwegian patients have been established. The CCBIO Centre of Excellence forms an ideal platform for extensive biomarker and functional sensitivity testing for individualized signal transduction therapy. During treatment, the clonal repertoire of AML is usually highly remodeled, and the most dangerous clones may be hardly detectable at diagnosis but strongly amplified during the intensive chemotherapy.

In the ongoing phase I trial BGBC003 we are currently employing sensitivity screen, exome sequencing, functional signaling analyses and avatar creation of enrolled patients. Several of these techniques allow precise evaluation of clonal evolution during therapy. This early phase clinical trial of the orally available Axl kinase inhibitor BGB324 is the first trial of Axl inhibitor in cancer patients.
Through CCBIO and the Helse Bergen clinical trials units, the team will continue to develop new therapy options and novel diagnostics for cancer patients.

RESEARCH GROUP:

Researchers:
Hans Petter Brodal, MS
Vibeke Andresen, M.S., PhD
Haugse, Ragnhild, RPH

Postdoctoral fellows:
Jørn Skavland, M.S., PhD
Rakel Brendsdal Forthun, M.S., PhD
Sigrun Margrethe Hjelle, M.S., PhD

PhD Candidates:
Andre Sulen, M.S.
Calum Leitch, M.S.
Caroline Benedicte Engen, M.D.
Maria Omsland, M.S.
Stein Erik Gullaksen, M.S.
Elise Aasebø, M.S
Katharina Bishof, M.D.
Shaba Shafiee, MS.
Trung Quang Ha, M.D.
Pre-PhD Projects:
Benedicte Sjo Tislevoll
Carina Hinrichs
Ehsan Hajjar
Tara Dowling

Technicians:
Wenche Hauge Eilifsen
Marianne Enger
Siv Lise Bedringaas


SCANLAF

Associated Investigators

INTEGRATING ELSA INTO CCBIO

ROGER STRAND

In 2014, CCBIO's research group on ELSA – ethical, legal and social aspects – was fully manned as our new postdoctoral fellow Anne Blanchard joined the team consisting of professor Roger Strand and research assistant Ina Hannestad Nygaard.

Thematically, the ELSA team focus its efforts on three main lines of inquiry: (1) Issues of social justice and public legitimacy in priority decision-making in public health care, and how biomarkers and personalised cancer medicine affect these ethical issues by providing increased scientific knowledge - but also changed business models for the pharmaceutical industry; (2) The tension between the need for universal rules and values in public health decision-making and the ethical relevance of biological and clinical understanding of individual cancer patients (or small subgroups); and (3) The ethical aspects of the challenges of reproducibility and clinical (ir) relevance in biomarker research. In our vision, these three lines are interrelated and also closely related to the economic aspects studied by economist colleagues in CCBIO.

The ELSA model of CCBIO is that of "integrated ELSA", drawing upon the learning process that ELSA research went through in the 2000s. A separate team of social scientists and philosophers "dealing with the ethical issues" tends not to work well. Rather, the vision is to build ELSA awareness and capacity within the entire CCBIO, through frequent informal interaction as well as participation in the junior scientists symposia (Blanchard), selected CCBIO seminars and the P.I. meetings (Strand). The team aims at gradually integrating ELSA thinking into the research and governance practices of the entire centre.

A specific focus in 2014 was to create and prepare a designated ph.d. course, "CCBIO 903 Cancer Research: Ethical, economic and social aspects", that runs January-February 2015.

RESEARCH GROUP:

Roger Strand, Prof.
Anne Blanchard, Postdoc
Ina Hannestad Nygaard, Research assistant

BIOINFORMATICS
INGE JONASSEN

In the context of CCBIO, Professor Inge Jonassen and part of his team from the CBU (Computational Bioinformatics Unit) at the University of Bergen are working on development and application of bioinformatics methods for analysis of data resulting from high-throughput measurement technologies applied to cancer samples. A primary focus is on deconvolution of gene expression data sets, resulting from samples composed of a combination of tumor cells and the surrounding and supporting microenvironment. The research aims to decompose the signal into that originating from the tumor cells and those originating from other tissue and cell types in the sample. This will enable us to study interactions between tumor cells and the environment and to identify relations to choice of treatment, outcome, and prognosis.

In this first phase, we are analyzing public gene expression data sets with a variety of methods to find out if any of the tools can be adapted to suit our needs. Part of this work also involves analysis of earlier published tumor type specific expression signatures. In the longer perspective, we want to to perform network and module analysis, using the output from the deconvolution approach to improve our understanding of the networks involved in different tumor types and their microenvironments. We further intend to integrate other omics data on DNA methylation, copy number variation and protein expression to achieve a more holistic view of the underlying mechanisms.

RESEARCH GROUP:

Inge Jonassen, Professor
Konstantina Dimitrakopoulou, Postdoc
Kristian Brakstad Samdal, Master student

THE ECONOMICS OF CANCER BIOMARKERS

JOHN CAIRNS

Professor John Cairns from London School of Hygiene & Tropical Medicine is an international capacity within health economics and has unique competences in relation to economic evaluation of new types of clinical treatment. In the capacity as adjunct professor and Associate PI at CCBIO, Cairns, in collaboration with professors Oddvar Kaarboe and Jan Erik Askildsen from the UiB Department of Economics, works on two main CCBIO projects: 1. The industrial economics of biomarkers – how the interplay between the diagnostic market and the pharmaceutical market affects the incentives to invest in R&D for biomarker-based diagnostic tests; 2. How cancer biomarkers change the cost-effectiveness of different therapies and the opportunities for economic models to contribute to optimising the development of cancer biomarkers.

In 2014, the economics team has been working on an economic model for the relationship between developers of cancer biomarkers and drug manufacturers, the preparation of a seminar paper "Assessing the cost-effectiveness of bevacizumab in the treatment of metastatic melanoma", and the development of the nationally unique PhD course CCBIO 903 Cancer research: ethical, economic and social aspects.

In 2015, PhD candidates will be recruited for the two above projects. Also, a review of economic evaluations to identify how introduction of cancer biomarkers has changed the cost-effectiveness of treatment will be prepared. Further, an economic evaluation of bevacizumab in the treatment of metastatic melanoma will be issued. Presentations of models and results will be held during CCBIO seminars and the CCBIO annual symposium. The PhD-course on the ethical, economic and social aspects of cancer research will be held in January and February 2015.

INVOLVED RESEARCHERS IN 2014:

John Cairns, Professor
Oddvar Kaarbøe, Professor
Jan Erik Askildsen, Professor

CCBIO Research School for Cancer Studies

The CCBIO Research School for Cancer Studies (RSCS), which was officially opened in September 2014, focuses on translational cancer research and innovation, including international exchange and mobility as well as ethical-, legal- and societal aspects of cancer research and treatment. The research school courses are available for all interested students within the field of cancer research. The RSCS is directed by Professor and Vice-Rector Anne Christine Johannessen in collaboration with the director of CCBIO.

Main goals and 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 paraclinical and clinical research environments with a common focus on translational studies of cancer biomarkers. PhD candidates and postdoctors get the opportunity to meet renowned international researchers, and the candidates meet each other and deliberate

upon their research projects across the established research groups.

In order to attain this goal, CCBIO has allocated basic funding to the RSCS. In addition, RSCS has been integrated into CCBIO's strategic activities like CCBIO Annual Symposium and the CCBIO Monthly Seminars where world leading scientists and opinion leaders give keynote lecturers and interact with students and PIs. Other established RSCS key activities are the CCBIO Junior Scientist Symposium where junior scientists from CCBIO and beyond meet four times each year to present and discuss their research. A series of specially designed courses have been planned and will be launched in early 2015. Apart from the main focus on relevant biomarker studies, PhD candidates are to be trained in inter-disciplinary collaboration, and ethical, economic and societal aspects pertaining to CCBIOs research.

CCBIO also aims to actively use its international networks to provide the ground for exchange of PhD candidates and post doctors both to and from CCBIO. The RSCS will collaborate with local and national research schools.

Courses currently running or established

All courses are open according to available capacity, albeit giving CCBIO´s PhD candidates first right of entry in case of capacity problems. The below list

denotes CCBIO's courses approved by the UiB. The courses, apart from CCBIO901 and CCBIO902 which run continiously.

which runs continuously, will run once a year or every second year.

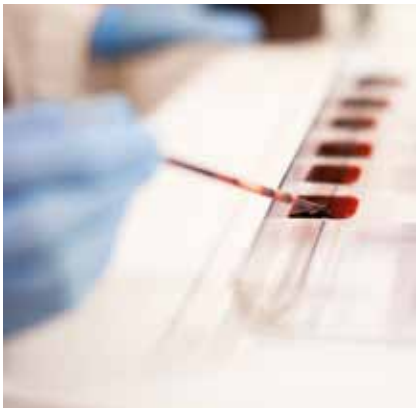
- **CCBIO 901: CCBIO Junior Scientist Symposium. PhDs and PDs present their results four times a year. Postdocs are chairing the meeting and discussions after each presentation.**

- **CCBIO 902: CCBIO Seminar and Symposium Series. This course combines 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.**

• **CCBIO 903: Cancer Research: Ethical, economical and societal aspects. The course focuses 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.**

• **CCBIO 905: 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.**



• **CCBIO 904: Tumour Biology in the Clinic. The course leaders have experience from equivalent courses arranged by the Norwegian M.D.s association. CCBIO aims to extend the existing course with a focus also on bio-banking in practice.**

CCBIO RESEARCH SCHOOL FOR CANCER STUDIES

Opening of CCBIO Research School for Cancer Studies

Faculty of Medicine and Dentistry – University of Bergen

September 11th 2014 - Auditorium II – BB Building

13.00-13.10	Welcome and opening remarks Lars A. Akslen (Director of CCBIO)
13.10-13.30	Presentation of CCBIO Research School for Cancer Studies. Anne Christine Johannessen (Head of the Research School)
13.30-13.40	Anne Lise Fimreite (Prorector, UiB)
13.40-13.50	Robert Bjerknes (Vice Dean, Research, Faculty of Medicine and Dentistry)
13.50-14.00	Nils Erik Gilhus (Head, Department of Clinical Medicine, UiB)
14.00-15.00	Keynote Lecture: Professor Anne-Lise Børresen-Dale (Institute for Cancer Research, UiO, Oslo) Challenges in Translational Cancer Research
15.00-16.00	Reception

CCBIO
Junior Scientist Symposium 2014

The CCBIO Junior Scientist Symposium represents an integrated part of the CCBIO Research School for Cancer Studies. This is a seminar series that aims to improve scientific interaction and networking among junior researchers. The symposia are held four times annually, and the first seminar took place on June 11th 2014. The symposia have been well visited, with 40-60 registered attendants at the meetings.

This symposium is an arena where PhD candidates and postdocs gain experience with oral presentations and academic discussions. The meetings have proved to be an excellent place for young researchers to get input for potential collaborations in ongoing and future projects. The program has covered a broad range of topics, from basic studies to clinical research. Further, trial lectures have been presented, and invited speakers from research groups outside of CCBIO have also presented their projects.

Each symposium has a format where 3-5 PhD candidates and postdocs present their research, followed by short discussions. The participants have been well satisfied with these seminars. They have commented on the high level of the research and presentations, as well as the positive side of getting to know colleagues in other CCBIO research groups. The small-talk goes lively in the breaks, suggesting that new and fruitful research collaborations might get started here.

Senior researcher Camilla Krakstad and postdoc Elisabeth Wik, coordinators of the junior seminars, have been planning and chairing these meetings. They report that there is great interest in the symposia, and the participants have been active and enthusiastic during the sessions. They also tell that being in charge of such seminars is a highly relevant experience.

Centre for Cancer Biomarkers

PROGRAM - CCBIO Junior Scientist Symposium

June 11th 2014 - Auditorium 4, BBB

Symposium Chairs: Camilla Krakstad & Elisabeth Wik

10.00-10.10 **Lars A. Akslen.** Welcome and introduction

10.10-10.30 **Tarig Al-Hadi Osman**
Multiple immunostaining identifies separate cancer stem cellsubpopulations in oral squamous cell carcinoma

10.30-10-50 **Mari Halle**
Molecular profiling in fresh tissue with high tumour cell content promotes enrichment for aggressive uterine adeno carcinomas

10.50-11.00 **Break**

11.00-11.20 **Ingrid Moen**
Anti-metastatic action of inhibiting FAK and VEGFR-2 together in pancreatic neuroendocrine tumors

11.20-11.40 **Agnete Engelsen**
Axl regulates stemness in adult lung alveolar epithelial homeo stasis and NSCLC drug resistance

11.40-12.30 **Lunch**

12.30-12.50 **Anne Blanchard**
The ELSA team of CCBIO: some ethical questions around cancer biomarkers

12.50-13.10 **Emilia Hugdahl**
BRAF-V600E expression in primary nodular melanoma: significance for survival and association with pathological features

13.10-13.20 **Break**

13.20-13.40 **Ning Lu**
Integrin α11β1 integrin regulates tensional homeostasis in fibroblast/A549 carcinoma heterospheroids

13.40-14.00 **Rakel Brendsdal Forthun**
Phosphoprotein expression in AML patients reflects patient stratification

Centre for Cancer Biomarkers

PROGRAM - CCBIO Junior Scientist Symposium

August 28th 2014 - Auditorium 4, BBB

Symposium Chairs: Camilla Krakstad & Elisabeth Wik

10.00-10.45 Gro Vatne Røsland
Trial lecture: Role of quiescent tumour cells in therapy resistance

10.45-11.00 Break

11.00-11.20 Erling Høivik
Exome sequencing of matched primary and metastatic tissues in endometrial cancer

11.20-11.30 Info CCBIO-901

11.30-12.30 Lunch

12.30-12.50 Cornelia Schuster
Predictive markers for treatment with bevacizumab monotherapy in metastatic melanoma

12.50-13.10 Maria Omsland
Cell-to-Cell Communication in Acute Myeloid Leukemia by Tunneling Nanotubes

13.10-13.20 Break

13.20-13.40 Jan Roger Olsen
Signal transduction and transcription factor activation in prostate cancer

13.40-14.00 Even Birkeland
The rationale behind a proteomics approach to discover breast cancer biomarkers

Centre for Cancer Biomarkers

PROGRAM – 3rd CCBIO Junior Scientist Symposium

October 30th 2014 - Auditorium 4, BBB

Symposium Chairs: Camilla Krakstad & Elisabeth Wik

10.00-10.45 Lars Herfindal
Therapeutic nanocarriers for improved cancer chemotherapy

10.45-11.00 Break

11.00-11.20 Elisabet Ognedal Berge
WBC BRCA1 methylation predicts risk of OC

11.20-11.40 Rakel Brendsdal Forthun
Phosphoprotein expression in AML patients reflects patient stratification

11.40-12.30 Lunch

12.30-13.00 Anne Blanchard
"Why your new cancer biomarker may never work": Cancer research between hope and despair

13.00-13.20 Himalaya Parajuli
Expression of integrin Ð-11 by carcinoma associated fibroblasts modulates oral squamous cell carcinoma behavior

13.20-13.40 Break

13.40-14.00 Sebastien Bougnaud
Tumor/stroma dynamics during tumor development and treatment

CCBIO Seminars

CCBIO has a monthly research seminar where invited guests and international speakers or the principal and associate investigators focus on current research topics and updates. The CCBIO seminar has been well visited and received.

The CCBIO Seminar series fulfills several aims. Firstly, it conveys relevant biomarker research to the local scientific community and students and younger researchers in particular, providing the ground for future recruitment. Secondly, 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. Last, but not least the CCBIO Seminars, 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.

Whereas the CCBIO seminars in the fall of 2013 mainly served the purpose of introducing CCBIO and its PIs research focus to the local research environment, more international guests have been invited in 2014. All CCBIO seminars so far have had very high attendance with the allocated auditorium mostly being overfilled.

CCBIO Seminars in 2014

30.01.2014

Karl-Henning Kalland, CCBIO
Heterogeneity and reprogramming plasticity of cancer cells – therapeutic possibilities.

20.02.2014

Roger Strand, CCBIO
Crossing the Styx.

20.03.2014

Cédric Gaggioli, Institute for Research on Cancer and Aging (IRCAN), Nice, France: Production of LIF cytokine by cancer cells and fibroblasts contributes to the establishment of a pro-invasive tumor microenvironment.

24.04.2014

Angela Nieto, Instituto de Neurociencias Consejo Superior de Investigaciones Científicas (CSIC)–Universidad Miguel Hernández (UMH), San Juan de Alicante, Spain: Epithelial plasticity in development and disease.

22.05.2014

Emmet McCormack, Department of Clinical Science, UiB. Pharmacological inhibition of the SIRT1 deacetylase with the small molecule inhibitor Tenovin-6 enhances ablation of FLT3-ITD+ LSC in combination with TKI treatment.

28.08.2014

Inge Jonassen, CCBIO
Towards characterizing tumour microenvironments – experimental and computational approaches.

02.10.2014

Zena Werb, Department of Anatomy, and Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, CA, USA: New insights into mechanisms underlying breast cancer metastasis.

30.10.2014

Boris Hinz, Laboratory of Tissue Repair and Regeneration, University of Toronto, Canada. Myofibroblasts can have it all: matrix mechanics, integrins, and pro-fibrotic growth factor activation.

27.11.2014

Bjørn Tore Gjertsen, CCBIO
Oncogene-addicted cancer: chronic myelogen leukemia as a model of a tyrosine kinase driven malignancy.

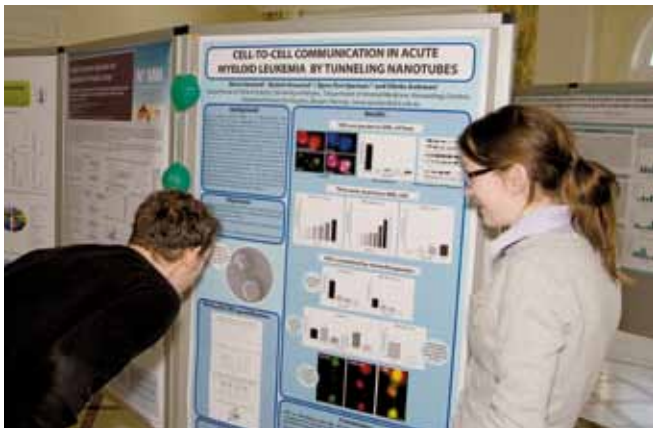
18.12.2014

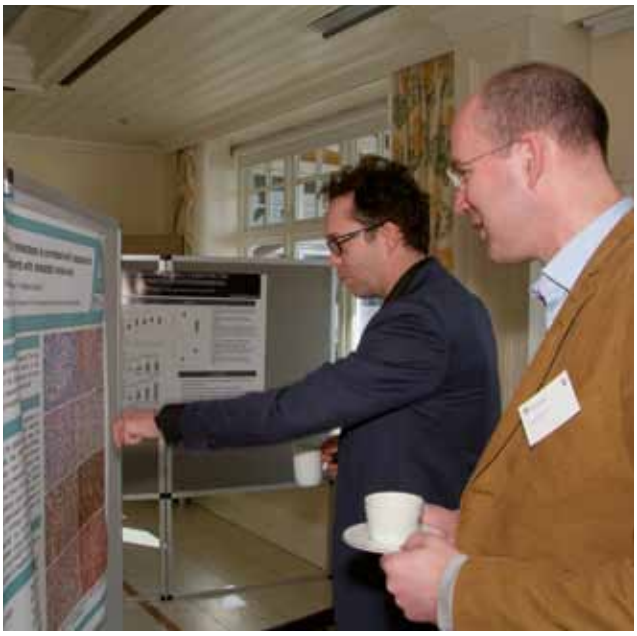
Arne Östman, Dept. of Oncology-Pathology, KI, Stockholm, Sweden. Impact of PDGFR-regulated fibroblasts and pericytes on tumor progression, prognosis and drug response.

The 2nd Annual Symposium

25th-26th March
at Solstrand Hotel & Bad.

160 participants





The 2nd CCBIO Annual Symposium was held 25th-26th March at Solstrand Hotel & Bad. More than 160 participants took part. The symposium was a veritable success both scientifically and socially and even the notoriously unstable weather in the Bergen region collaborated to provide CCBIO with a perfect frame for its annual gathering.

The lectures held by invited international and national speakers, the former in majority, were very well received by the audience and focus was kept on biomarkers and the tumor's microenvironment. 46 younger researchers took the opportunity to present their research with posters during two long combined lunch- and poster sessions of two hours each. The poster sessions proved a successful catalyst for interaction between younger and more senior researchers from Norway and abroad. Most participants also took the opportunity to have a late dinner together and stay at the hotel overnight for the second day of lectures.

Centre for Cancer Biomarkers

Norwegian Centre of Excellence
The Research Council of Norway

2nd CCBIO Symposium 2014

Solstrand, March 25-26, 2014 - Bergen - Norway

SCIENTIFIC PROGRAM

Day 1: Tuesday March 25, 2014

09:00-10:00 Registration and coffee

10:00-10:15 **Lars A. Akslen (Director of CCBIO)**
Introduction to CCBIO Symposium 2014.

Chair: Professor James Lorens

10:15-11:00 **Rameen Beroukhim (Boston)**
Interpreting cancer copy-number alterations.

11:00-11:30 **Helga Salvesen (Bergen)**
Molecular profiling of primary compared to metastatic lesions in gynecologic cancers.

11:30-12:00 **Therese Sørlie (Oslo)**
Gene expression patterns and biomarkers in subtypes of breast cancer.

12:00-14:00 LUNCH AND POSTER SESSION

Chair: Professor Donald Gullberg

14:00-14.45 **Mark LaBarge (San Francisco)**
Insights into aging and cancer through de construction and recapitulation of human mammary microenvironments in culture.

14:45-15:15 **James Lorens (Bergen)**
The role of the Axl receptor tyrosine kinase in drug resistance and metastasis.

15:15-15:45 COFFEE

15:45-16:15 **Ian Mills (Oslo)**
An Interplay Between Transcription and Metabolic Reprogramming in Prostate Cancer.

16:15-16:45 **Karl-Henning Kalland (Bergen)**
Cancer cell heterogeneity and reprogram-ming plasticity - therapeutic possibilities

19:00 DINNER

Day 2: Wednesday March 26, 2014

Symposium Chair: Helga B. Salvesen

09:00-09:45 **Valerie Weaver (San Francisco)**
Tissue tension reprograms the tissue to metastasis.

09:45-10:15 **Donald Gullberg (Bergen)**
Fibroblast integrins in wounds, scars and tumors - emerging molecular themes.

10:15-10:45 **Randolph Watnick (Boston)**
Development of a novel multimodal therapeutic agent targeting the tumor microenvironment.

10:45-11:15 COFFEE

11:15-12:00 **Johanna Ivaska (Turku)**
Cell-matrix interactions in cancer

12:00-12:45 **Taina Pihlajaniemi (Oulu**
Multiplexin Collagens in Development and maintenance of tissue homeostasis and in malignant growth.

12:45-14:15 LUNCH AND POSTER SESSION II

Chair: Karl-Henning Kalland

14:15-14.45 **Bruce Zetter (Boston)**
New approaches to metastatic cancer.

14:45-15:15 **Kjetil Taskén (Oslo)**
Regulation of anti-tumor immune responses in colorectal cancer.

15:15-15:45 **Bjørn Tore Gjertsen (Bergen)**
Personalized medicine and clonal evolution in acute leukemia?

15:45-16:00 **Lars A. Akslen (Bergen)**
Closing remarks.

CCBIO in the 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 during 2014.

02.01.14

BT - Hun så sin far dø. Selv kan hun bli reddet av medisinske framskritt – Bjørn Tore Gjertsen

OPTIMIST: – Jeg kom utrolig raskt til behandling og får tett oppfølging, sier Gunn Hatland Engebretsen, som for bare noen uker siden fikk diagnosen kronisk leukemi. Målet er at hun skal bli helt frisk av den kroniske sykdommen.

Hun så sin far dø. Selv kan hun bli reddet av medisinske fremskritt.

KARI PEDERSEN
kari.pedersen@bt.no
foto MARITA AAREKOL

Diagnosen kom kastende på henne for bare noen uker siden. Gunn Hatland Engebretsen (64) var til legen på halvårlig kontroll siste fredag i november. Mandag satt hun hos frisøren da telefonen ringte. Det var hematologisk avdeling på Haukeland universitetssykehus, som ba henne komme dagen derpå for å ta flere blodprøver.

– Hva er det dere frykter? spurte Engebretsen og tenkte på sin far, som døde av kronisk myelogen leukemi i 1975, 64 år gammel.

Dagen etterpå fikk hun samme diagnose. Men hun trenger ikke frykte farens skjebne.

– Veldig optimistisk

– Jeg er veldig optimistisk på hennes vegne, sier professor Bjørn Tore Gjertsen.

Han leder en forskningsgruppe ved Senter for kreftmarkører ved Universitetet i Bergen (Centre for Cancer Biomarkers). Forskerne her jobber med å finne bedre og mer skreddersydd kreftbehandling. Nøkkelen til det er jakten på biomarkører, som avslører nøyaktig hvilken form for kreft pasienten har.

I Engebretsens tilfelle har det vært en lang vei fra biomarkør til tablettene hun nå tar to ganger om dagen. Allerede på 1960-tallet identifiserte forskerne det såkalte Philadelphia-kromosomet, en genforandring som finns hos 98 prosent av pasienter med kronisk myelogen leukemi. Først 40 år seinere kom kuren.

Den er svært virkningsfull, for-teller Gjertsen.

– Så seint som på 1990-tallet var halvparten av disse pasientene døde innen fem år, med mindre de ble beinmargtransplantert. Det er en risikabel behandling med høy dødelighet. Nå regner vi med at 98 prosent av pasientene vil kunne kontrollere sykdommen med tabletter, sier Gjertsen.

Tar to år å bli frisk

For Engebretsen er ambisjonene høyere enn som så. Hun deltar i et forsøk ledet av Gjertsens gruppe, der målet er å helbrede den kroniske sykdommen. Etter to år med tablettkur og sprøyter med et immunstimulerende stoff, er planen å avslutte behandlingen. Da skal hun være frisk.

– Det tok 40 år fra forskerne fant biomarkøren til den ble omsatt til virksom medisin. Vil andre kreftkurer ta like lang tid å utvikle?

– Ja, det tok mange år for kronisk myelogen leukemi, og det finns eksempler på andre gener som forskerne vet gir kreft, men som det fortsatt ikke finns effektiv behandling mot. Målet for en satsing som Senter for kreftmarkører er å forsere den utviklingen, sier Gjertsen.

Gjertsens forskergruppe vil undersøke om Engebretsen har arvelig kreft. En bror er død av lungekreft, og hun og faren fikk begge kronisk myelogen leukemi.

– Dersom hun og faren har den samme sykdommen og vi kan forklare det i studier av gener, kan det bli en liten verdenssensasjon, påpeker Gjertsen.

Sikker på at det går bra

Gunn Hatland Engebretsen er glad tilfeldighetene avdekket den snikende sykdommen.

– Er det skremmende å vite at du har samme sykdommen som tok livet av din far?

– Jeg har egentlig ikke hatt tid til å reagere. Det gikk bare noen dager før diagnosen var bekreftet, og noen dager deretter var jeg i gang med behandling. De er blitt så flinke med denne sykdommen, at jeg er sikker på at dette skal gå bra.

FAKTA

Biomarkører

- BT presenterte nyttårsaften Senter for kreftmarkører (Centre for Cancer Biomarkers) som er tilknyttet Universitetet i Bergen og Haukeland universitetssykehus.
- Senteret jobber med å finne biomarkører, som kan gi mer målrettet kreftbehandling. Biomarkører kan være gener, et protein eller egenskaper i vevet rundt kreftsvulsten.
- Den effektive kuren for kronisk leukemi er et godt eksempel på at biomarkører kan gi nye medisiner.
- Engebretsen deltar i et forsøk der hun over to år får dasatinib-tabletter i kombinasjon med interferon.

CCBIO in the media

09.01.14
Dagens Medisin – Fond for uavhengige kliniske studier – Oddbjørn Straume

09.01.14
Dagens Medisin - Forventer bråk rundt forskningsplan - Rolf Reed
http://www.dagensmedisin.no/nyheter/venter-brak-rundt-forskningsplan/

14.05.14
NRK Hordaland P1 – Føflekk-dagen – Oddbjørn Straume

05.06.14
Forskning.no – Søren Falchs juniopris 2014 til kreftforsker – Camilla Krakstad
http://www.forskning.no/begivenheter/393425

12.06.14
UiB.no – Great interest in the CCBIO Junior Scientist Symposia – Camilla Krakstad, Elisabeth Wik, Lars Akslen
http://www.UiB.no/en/ccbio/78959/great-interest-ccbio-junior-scientist-symposia

14.06.14
NRK Her og Nå – Dagens gjest – Camilla Krakstad -
http://radio.nrk.no/serie/her-og-naa-hovedsending/DMNH01013914/14-07-2014#t=58m29s

22.06.14
BT – Nå skal kreften fryses bort - Karl-Henning Kalland, Bjørn Tore Gjertsen -
http://www.bt.no/nyheter/lokalt/Na-skal-kreften-fryses- bort-3143505.html

OPTIMIST: - Vi skal være forsiktige med å love for mye, men hvis det virker slik vi har sett i andre mindre forsøk, kan vi få kreften til å gå tilbake, bedre pasientens allmenntilstand og redusere smerter, sier professor Karl-Henning Kalland. Han skal prøve ut en helt ny behandlingsmetode for prostatakreft. FOTO: TOR HØVIK

Nå skal kreften fryses bort

07.08.14
UiB.no – On a quest to cure cancer – Agnete Engelsen - http://www.UiB.no/en/news/79919/quest-cure-cancer

19.09.14
Vest24 – Cellekaos på Festplassen – Jessica Furriol, Henriette Christie Ertsås - http://tjinfo.UiB.no/Vedlegg?id=9ff8c38883371ba948474c58dc86a6a7

Molekylærbiolog Henriette Christie Ertås fra Kreftforeningen spiller skuespill med engasjerte elever. Hun prøver å få dem til å forstå hvor slitsomt og kaotisk det er å være cellearbeider når personen man er «inni» har falt ned fra et tre og slått foten. Foto: VIDAR LANGELAND

Cellekaos på Festplassen

CCBIO in the media

20.09.14
Onkonytt – CCBIO satser på biomarkører – Lars Akslen

30.10.14
BT – Ble overrasket med 33 millioner – Lars Akslen, Bjørn Tore Gjertsen, Karl-Henning Kalland, James Lorens, Helga Salvesen - http://www.bt.no/nyheter/lokalt/Ble-overrasket-med-33-millioner-3231019.html

31.10.14
På Høyden – Pengedryss til kreftforskinga – Lars Akslen, Bjørn Tore Gjertsen, Karl-Henning Kalland, James Lorens, Helga Salvesen - http://pahoyden.no/2014/10/pengedryss-til-kreftforskinga

CCBIO satser på biomarkører

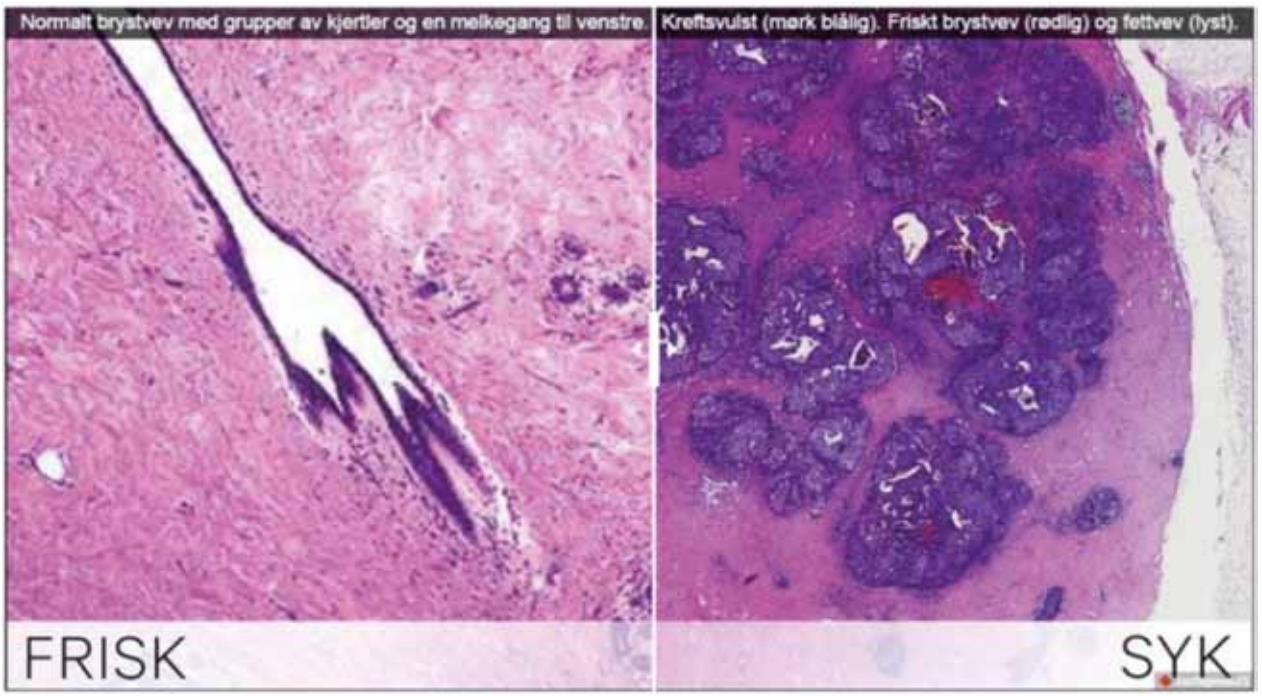
Pengedryss til kreftforskinga

Publisert: 31. oktober 2014 **Oppdatert:** 31. oktober 2014, 09.27

Det var stor glede på UiB då Kreftforeningen kom til byen med historisk pengedryss til kreftforsking. Foto: Karl Kristian Langeland

12.11.2014
Youtube.com - CCBIO - an introduction. - Lars A. Akslen et al
https://www.youtube.com/watch?v=uofcuV-JAyA&feature=youtu.be

16.11.14
BT – Derfor går kreftcellene berserk – Lars Akslen - http://www.bt.no/nyheter/innsikt/Derfor-gar-kreftcellene-berserk-3240101.html



Derfor går kreftcellene berserk

Innsikt: Når blodkarene rundt svulsten bestemmer seg for å invadere, da går kreftcellene berserk.

Lars A. Akslen UiB og Haukeland universitetssykehus

Publisert: 16.nov. 2014 08:00 Oppdatert: 16.nov. 2014 08:00

Lagre i leselisten

Kreft er som en krig. Mange kreftsvulster må gi tapt etter god medisinsk behandling. En del av kroppen, immunsystemet, overvåker situasjonen og kan eliminere uønskede celleopprør, som tidlige kreftsvulster. Men noen blir aggressive og angriper kroppen. De oppfører seg som en terrorgruppe som

ARTIKKELFORFATTEREN

Lars A. Akslen har skrevet denne artikkelen. Han er professor ved Klinisk institutt I ved UiB og overlege ved Avdeling for patologi ved Haukeland universitetssykehus. Akslen leder også Centre for Cancer Biomarkers (CCBIO), et Senter for fremragende forskning (SFF) ved UiB.

CCBIO in the media

20.11.14
Dagens Medisin – Gensignatur er «motorvei» for spredning – Lars Akslen, Monica Mannelqvist, Elisabeth Wik

Gensignatur er «motorvei» for spredning

Bergensforskere har funnet en gensignatur som kan identifisere de mest aggressive brystkreftsvulstene. Målet er mer målrettet behandling

Center for Cancer Biomarkers

08.12.14
soundcloud.com – Podkast Kreft – Lars A. Akslen & Marion Solheim
https://soundcloud.com/mof-UiB/podcast-kreft

20.12.14
BT – Synet som vil forfølge dem resten av livet –
Anne Christine Johannesen
– http://www.bt.no/nyheter/utenriks/article3265562.ece

CCBIO and social media

#ccbio




Social media has grown to be the inbound marketing tool and connector for organizations, businesses and individual users alike. It is a global tool to stay in touch, meet, greet, communicate, network and market. CCBIO promotes our researchers, scientific findings, happenings, media appearances and behind-the-scenes glimpses via the faculty Facebook, Twitter and Instagram accounts. The hashtag is of course **#CCBIO**, and we will continue to work further with social media.









Presentation of PhD candidates and Postdocs

AASEBØ, ELISE: Born 1986, holds a M.S. in Medical Cell Biology from UiB. She is currently a PhD candidate in the acute myeloid leukemia (AML) group at PROBE and connected to the Gjertsen group. She applies quantitative mass spectrometry-based proteomics on AML cells, and the aim is to identify biomarkers which can improve prognostication of AML patients.

AHMED, LAVINA: Born 1983, holds an M.S. in Molecular Medicine from the University of Sussex and in 2011 started as a PhD in the Akslen group. This is a combined academic-industrial PhD project, in collaboration with BerGenBio AS, focused on the validation of Axl antibodies and studies of Axl expression in breast cancer and other tumors.

AZEEM, WAQAS: Born 1985 in Pakistan, has both a veterinary degree from Pakistan and an M.S. in molecular biology from Sweden. He is now a PhD candidate in the Kalland group. His research project is on the identification of molecular therapeutic targets in prostate cancer cell sub-populations.

Presentation of PhD candidates and Postdocs

AZIZ, SURA: Born 1978 in Iraq, is a M.D. from Al Nahrain University of medicine in Iraq. She is now a PhD candidate in the Akslen group. Her research project aims to identify new biomarkers in aggressive breast cancer with special focus on proliferation in metastases and the influence of the tumor microenvironment on the metastatic site.

BERG, ANNA: Born 1984, is a M.D. from UiB. In 2012 she started as a PhD candidate in the Salvesen group. In her PhD-project she has a focus on premalignant lesions in endometrial tissue, aiming to find biomarkers to improve diagnostics and to guide treatment strategies.

BIRKELAND, EVEN: Born 1982, holds a M.S. in medical cell biology and finished in 2013 a PhD on genetic alterations in endometrial cancer, both at the UiB. He is now a post-doc in the Akslen group. His research interests are in the field of cancer proteomics, especially related to breast cancer subtypes and the tumor microenvironment.

BISCHOF, KATHARINA: Born 1981 in Austria, M.D. and now a PhD candidate in the Gjertsen group. Her research focus is on identifying biomarkers in ovarian cancer, which can predict response to standard chemotherapy regimens.

BLANCHARD, ANNE: Born 1985 in France, has a background in earth sciences and ecological economics. She did her PhD on inter-disciplinarity related to climate change, and her interests since then have been the complex science-policy interface and the role of science in society. She is a post-doc based at the Centre for the Study of the Sciences and the Humanities (SVT), in the group of Roger Strand. Her project focuses on ethical, legal and societal aspects of cancer biomarkers.

BLOIS, ANNA:Born 1977 in Italy, holds a M.S. in Animal Physiology and a PhD in Cell Biology, both from the University of Calabria, Italy. She is currently a post-doc in the Akslen group. Her research is focused on breast cancer, aiming to explore the angiogenic profile of different breast cancer subtypes, and to provide novel angiogenesis markers and potential treatment targets.

BOUGNAUD, SÉBASTIEN: Born 1983 in France, holds a M.S. in neuroscience from the University of Strasbourg and a PhD on brain tumor biology from Luxembourg. He is now a post-doc in the Lorens group and works on the development and characterization of animal models of tumor-stroma interactions in breast and lung cancer.

DAVIDSEN, KJERSTI TEFRE: Born 1980, holds an M.D. from the UiB and is currently doing her PhD project in the Lorens and Straume groups. She studies the Axl receptor and its involvement in therapy resistance in melanoma, aiming to inhibit Axl-dependent functions required for therapy resistance in Axl-expressing melanomas.

DIMITRAKOPOULOU, KONSTANTINA: Born 1983 in Greece, holds an M.S. in biomedical engineering (2007) and a PhD (2014), both from the University of Patras, Greece. Her doctoral thesis focused on complex disease analysis through systems biology approaches. She is now a post-doc in the Jonassen group with a focus on systems biology studies of the breast cancer microenvironment.

Presentation of PhD candidates and Postdocs

ENGELSEN, AGNETE: Born 1978, holds a M.S. in cell and developmental biology from UiB. In 2013 she received her PhD at UiB on studies of brain tumor biology. Since 2013 she is a post-doc in the Lorens group, working on Axl and tumor-stroma interactions, focusing on breast and lung cancer models.

ENGEN, CAROLINE: Born 1987, M.D. from UiB. She is currently a PhD candidate in the Gjertsen group. In her project she aims to elucidate aspects of clonal heterogeneity and clonal evolution in acute myeloid leukemia, with specific focus on possible therapeutic implications.

ERTSÅS, HENRIETTE: Born 1974, holds a M.S. in Virology from UiB and is currently a PhD candidate in the Lorens group. Her research goal is to understand how the microenvironment determines cell fate and tumor progression.

FONNES, TINA: Born 1988, has a veterinary degree from NMBU. She is now a PhD candidate in the Salvesen group and explores cell lines, clinical samples, and mouse models of endometrial cancer with a focus on imaging protocols and therapeutic studies.

FORTHUN, RAKEL: Born 1983, holds an M.S. in medical cell biology from UiB and in 2012 received her PhD from UiB, focused on acute myelogen leukemia (AML). She is now a post-doc in the Gjertsen group working on predictive biomarkers for AML treatment, especially related to the drug valproat.

FURRIOL, JESSICA: Born 1981 in Spain holds a M.S. in physiology from the University of Valencia and a PhD in 2013 on NF-KB in breast cancer. She is now a post-doc in the Aksl´s group. She currently works on genetic variants related to tumor-stroma interactions and protein expression patterns in breast cancer.

GULLAKSEN, STEIN ERIK: Born 1986, holds a M.S. in Nanotechnology from UiB and is currently a PhD candidate in the Gjertsen group. He is exploring several different types of cellular stress, when applied to leukemic cells.

HA, QUANG TRUNG: Born 1982, M.D. from Vietnam, holds a M.S. in Medical Biology from UiB and is currently a PhD candidate in the Gjertsen group. His research focus is on developing p53-independent and p53-dependent novel therapies for the treatment of acute myeloid leukemia.

HAALAND, GRY SANDVIK: Born 1982, M.D. from UiB, is currently doing her PhD in the Lorens group. Her research is focused on characterizing the receptor tyrosine kinase Axl, and its role in metastatic development, aiming to increase the knowledge about the receptor, its downstream effects on tumor cells, and to use this information in cancer treatment.

HALLE, MARI KYLLESØ: Born 1982, holds an M.S. in Molecular Biology from NMBU. She is now a PhD candidate in the Salvesen group, working on molecular changes occurring from primary endometrial cancer to metastatic disease.

HJELLE, SIGRUN MARGRETHE: Born 1983, holds a M.S. in Medical Cell Biology from UiB and completed in 2013 a PhD at UiB, focused on the expression and function of p53 full-length, p53b and p53g protein isoforms in leukemia. She is now a post-doc in the Gjertsen group continuing her focus on p53 in acute myelogen leukemia and breast cancer using proteomics analysis and functional studies of p53 isoforms.

HOLST, FREDERIK: Born 1971, received his M.S. in molecular biology and his PhD at the University of Hamburg in Germany. Currently he is a post-doc in the Salvesen group. He studies the somatic genetics of gynecological and other cancers with a special focus on cancer biomarkers.

HUA, YAPING: Born 1986, holds a M.S. in Pharmaceutical Chemistry and is a PhD candidate in the Kalland group. Her project is focused on discovery of leading compounds and their molecular targets in prostate tumor initiating cells.

HUGDAHL, EMILIA: Born 1980, M.D. from UiB. She is a PhD candidate in the Akslen group. Her project is focused on biomarkers for aggressive cutaneous melanoma, especially related to proliferation, BRAF mutations, and metastatic spread.

HUSBY, JENNY: Born 1973, M.D. from UiB. After completing her degree, she focused on radiology and nuclear medicine. Currently she is a PhD candidate in the Salvesen group. Her research focuses on functional imaging to promote individualized and targeted therapy in endometrial cancer.

JOKELA, TIINA: Born 1981 in Finland, holds a M.S. degree in biochemistry and a PhD from the University of Eastern Finland (2011), focusing on regulation of hyaluronan synthesis by UDP-sugars. As a postdoc, she is now conducting studies on Micro-Environmental Arrays (MEArrays) and breast cancer in the Lorens group. Her research focus is on how the microenvironment regulates mammary stem cell fate by using the Axl-receptor tyrosine kinase as a marker of a plastic cell phenotype.

KATTA, KIRANKUMAR: Born 1984 in India, holds a M.S. degree in Molecular Biology from the University of Skövde, and a PhD dealing with proteoglycans and their role in renal chronic transplant dysfunction (University Medical Center Groningen). Presently, he is a post-doc in the Gullberg group, focusing on the role of proteoglycans in tumor-stroma interactions using genetic tools and in vitro generated mini tumors.

KLINGEN, TOR-AUDUN: Born 1960, holds a M.D from the Aarhus University and is currently a PhD candidate in the Akslen group. He is working on tissue based biomarkers in breast cancer subtypes, with special focus on vascular invasion patterns and interactions with the tumor microenvironment.

KNUTSVIK, GØRIL: Born 1971, holds a M.D. from UiB, and is currently a PhD candidate in the Akslen group. She is working on proliferation biomarkers in breast cancer subtypes and how these can be used in molecular grading based on different tissue categories.

KRÜGER, KRISTI: Born 1987, M.D. from UiB and since 2014 a PhD candidate in the Akslen group. Her PhD project is focused on biomarkers in different breast cancer subtypes with emphasis on angiogenesis and tumor-vascular interactions.

LEITCH, CALUM: Born 1989 in Scotland, holds a M.S. in Molecular and Cellular Biology from the University of Glasgow. Since 2012 he has been a PhD candidate in the Gjertsen group. The primary aim is to identify novel pharmaceutical alternatives for the treatment of Acute Myeloid Leukaemia (AML) with a special focus on identification of novel drug combinations and biomarkers for drug sensitivity.

Presentation of PhD candidates and Postdocs

LIE, MARIA KOLNES: Born 1989, holds a M.S. in Nanoscience from UiB and is now a PhD candidate in the Lorens and Akslen groups. Her research is focused on how the tumor microenvironment regulates epithelial-mesenchymal transition (EMT) by focusing on the Axl tyrosine kinase receptor, and how this relates to cancer therapy responses.

LIU, HENGSHUO: Born 1984 in China, holds a M.S. in Biology from Uppsala University and is currently a PhD candidate in the Gullberg group. He is focusing on three projects: 1. the study of integrin a11 promoter in mechanically strained matrices; 2. to use 3D tumor spheroids to study integrin a11 function; and 3. to evaluate the role of integrin a11 on cancer associated fibroblasts.

MAULAND, KAREN KLEPSLAND: Born 1988, gained her M.D. at UiB in 2014 and then started as a PhD candidate in the Salvesen group. The main focus of her PhD project is on context dependent determinants of treatment targets and outcome in obese compared to non-obese endometrial cancer patients.

MOEN, INGRID: Born 1982, holds a M.S. in experimental- and human physiology from UiB and finished her PhD at UiB in 2011 on the influence of oxygen in breast cancer development, using hyperbaric oxygen treatment. She is now a post-doc in the Reed group and is investigating the effect of a novel focal adhesion kinase inhibitor on metastasis.

NALWOGA, HAWA: Born in 1966 in Uganda, holds both a M.D. and a Master of Medicine, the latter within Pathology and both from Makerere University College of Health Sciences. Her PhD from UiB was on biomarkers in breast cancer. She is now a post-doc in the Akslen group. Her current research is focused on breast cancer subtypes and biomarker comparisons between African and Caucasian populations, related to angiogenesis and tumor-microenvironment interactions.

NEGAHDAR, MARIA: Born 1973 in Iran, holds an M.S. in medical biochemistry and in 2012 received her PhD at the UiB with a focus on targets for diabetes treatment. She is now a post-doc in the Akslen group. Her research is focused on cell line studies of angiogenesis in breast cancer subtypes.

OLSEN, JAN ROGER: Born 1987, M.D. from UiB, currently a PhD candidate in the Kalland group. He works on prostate cancer models with a focus on cellular plasticity, differentiation and reprogramming.

OMSLAND, MARIA: Born 1988, has a M.S. in Medical Cell Biology and is currently a PhD candidate in the Gjertsen group. The aim of her project is to map the potential role of a newly discovered cell-to-cell communicator called tunneling nanotube (TNT) in leukemia, particularly in acute myeloid leukemia.

ONYANGO, THERESE BREDHOLT: Born 1975, has a M.S.in Molecular Biology and a PhD from UiB, the latter with a focus on mechanisms of importance for development and progression of uterine cancer. She is now a post-doc in the Salvesen group working on cell line studies of endometrial cancer to prove mechanisms and correlations that can be of importance for tumor development and progression.

OSMAN, TARIG: Born 1979 in Sudan, has a background as a dental surgeon from the University of Khartoum and in 2014 completed his PhD focusing on cancer stem cell related markers in normal and neoplastic oral mucosa at UiB. He is now a post-doc in the Akslen group working on experimental studies of angiogenesis, tumor microenvironment, and metastatic spread in breast cancer subtypes.

PARAJULI, HIMALAYA: Born 1977, holds a Bachelor in Dental Surgery from the Tribhuvan University Kathmandu and a M.S. in international Health from UiB. He is currently a PhD candidate in the Johannessen group. His research project is focused on the expression of integrin Ð11 in oral cancer.

PELISSIER, FANNY: Born 1988 in France, has a M.S in biotechnology from EPFL, Lausanne. She is currently a PhD candidate in the Lorens group. Her research is focused on the regulation of HMEC progenitors by the microenvironment and its alteration by age, the main research question being why women get more breast cancer with age.

PILSKOG, MARTIN: Born 1982, M.D. from UiB, is now a PhD candidate in the Straume group. His research project is about biomarkers and mechanisms of angiogenesis in relation to anti-angiogenesis treatment of metastatic renal cell carcinoma.

QU, YI: Born 1981 in China, has a M.S. in medicine from Peking Union Medical College. In 2013 she gained a PhD from UiB, focused on the generation of a stepwise prostate carcinogenesis model, a study of epithelial-to-mesenchymal transition and malignant transformation of prostate primary epithelial cells. Currently she is a post-doc in the Kalland group. Her research focus is on Wnt-related cancer drug screening and development.

RAMNEFJELL, MARIA: Born 1975, M.D. from UiB, is now a PhD candidate in the Akslen group. Her project is focused on molecular and clinico-pathologic characteristics of non-small cell lung cancer, aiming to explore novel biomarkers and potential treatment targets, with focus on the tumor microenvironment including activated angiogenesis and epithelial-mesenchymal transition.

REIGSTAD, INGA: Born 1984, M.D. from UiB and is currently a PhD candidate in the Reed group. Her PhD project is on the extracellular matrix (ECM) in experimental tumors where she is investigating the effects of $\alpha_v\beta3$ and $\alpha11\beta1$ integrins on the development of ECM.

SAPKOTA, DIPAK: Born in 1979, has a background within dental surgery and a PhD from the UiB. He is currently a post-doc in the Johannessen group. His research project is related to the expression profile and functional roles of the S100 protein members, in particular S100A16 as well as miRNA in oral cancer, and the prognostic role of S100A16.

SCHUSTER, CORNELIA: Born 1979 in Germany, holds an M.D. and a German Medical Doctor degree, both from Friedrich-Alexander University of Erlangen-Nuremberg in Germany. Since 2011, she has been a PhD candidate in the Straume and Akslen groups. Her research is focused on finding predictive biomarkers for treatment of metastatic melanoma.

Presentation of PhD candidates and Postdocs

SHAFIEE, SAHB: Born 1988 in Iran, holds a M.S. in Biomedical Cell Biology from UiB, currently a PhD student in Gjertsen´s group, in collaboration with prof. Emmet McCormack. She is working on translational development of preclinical models and therapies in Myelodysplastic Syndromes (MDS).

SKAVLAND, JØRN: Born 1972, holds a technical education in electronics and automation, a M.S. in Immunology and in 2013 gained a PhD at UiB. In his post-doc project in the Gjertsen group, he is aiming to monitor and evaluate signaling related patterns in leukemia.

SKOGSTRAND, TRUDE: Born 1977, holds a M.S. in Environmental Physiology and in 2013 gained a PhD in physiology with a focus on renal hypertensive fibrosis in rats. As a post-doc in the Reed group, she is now focusing on the properties of extracellular matrix in experimental tumors where she is investigating the effect of αVβ3-integrin.

SULEN, ANDRE: Born 1982, M.S. in biology from UiB with a focus on virus-host interactions using flow cytometric and proteomic techniques. He is currently a PhD candidate in the Gjertsen group, aiming to evaluate signaling related patterns in leukocytes as biomarkers for environmental stress exerted on the healthy population.

TANGEN, INGVILD LØBERG: Born 1980, has a M.S. in Pharmacology from the University of Oslo. She is now a PhD candidate in the Salvesen group. Her research focus is the investigation of expression levels of hormone receptors and hormone related co-factors in primary and metastatic endometrial carcinoma, and to investigate transcriptional alterations related to expression status.

TROVIK, JONE: Born 1961, is a M.D. and a PhD in 2012 from UiB on biomarkers in endometrial cancer. She is now a post-doc in the Salvesen group studying individualized therapy based on molecular alterations by incorporating preoperative biomarkers to tailor the treatment of endometrial cancer.

WERNER, HENRICA: Born 1976 in the Netherlands, is a M.D. and earned her PhD in 2014 at UiB with a focus on clinical and molecular features that can function as prognostic and predictive biomarkers to improve therapeutic decisions in connection with endometrial cancer. She is currently a post-doc in the Salvesen group. Her main focus is on the analysis of reverse phase protein array data of endometrial cancer samples including primary tumors and metastases.

WIK, ELISABETH: Born 1971, M.D. from UiB, earned her PhD (2013) with focus on biomarkers in endometrial cancer with emphasis on gene expression microarray analyses. She is now a post-doc in the Akslen group. Her present research focus is on biomarkers in breast cancer subtypes, gene expression analyses, and exploring transcriptional alterations related to the tumor microenvironment.

List of Publications - CCBIO 2014

List of Publications - CCBIO 2014

Publications are listed in the order they appear in PubMed with the most recent publications first.

Bruserud Ø, Reikvam H, Fredly H, Skavland J, Hagen KM, van Hoang TT, Brenner AK, Kadi A, Astori A, Gjertsen BT, Pendino F. Expression of the potential therapeutic target CXXC5 in primary acute myeloid leukemia cells - high expression is associated with adverse prognosis as well as altered intracellular signaling and transcriptional regulation. *Oncotarget*. 2014 Dec 26. [Epub ahead of print].

Hampson P, Wang K, Ersvær E, McCormack E, Schüler J, Fiebig HH, Gjertsen BT, Bruserud Ø, Lord JM. Up-regulation of anti-apoptotic genes confers resistance to the novel anti-leukaemic compound PEP005 in primary AML cells. *Oncoscience*. 2014 Aug 6;1(8):529-39.

Lee AW, Tyrer JP, Doherty JA, Stram DA, Kupryjanczyk J, Dansonka-Mieszkowska A, Plisiecka-Halasa J, Spiewankiewicz B, Myers EJ; Australian Cancer Study (Ovarian Cancer); Australian Ovarian Cancer Study Group, Chenevix-Trench G, Fasching PA, Beckmann MW, Ekici AB, Hein A, Vergote I, Van Nieuwenhuysen E, Lambrechts D, Wicklund KG, Eilber U, Wang-Gohrke S, Chang-Claude J, Rudolph A, Sucheston L, Odunsi K, Moysich KB, Shvetsov YB, Thompson PJ, Goodman MT, Wilkens LR, Dörk T, Hillemanns P, Dürst M, Runnebaum IB, Bogdanova N, Pelttari LM, Nevanlinna H, Leminen A, Edwards RP, Kelley JL, Harter P, Schwaab I, Heitz F, du Bois A, Orsulic S, Lester J, Walsh C, Karlan BY, Hogdall E, Kjaer SK, Jensen A, Vierkant RA, Cunningham JM, Goode EL, Fridley BL, Southey MC, Giles GG, Bruinsma F, Wu X, Hildebrandt MA, Lu K, Liang D, Bisogna M, Levine DA, Weber RP, Schildkraut JM, Iversen ES, Berchuck A, Terry KL, Cramer DW, Tworoger SS, Poole EM, Olson SH, Orlow I, Bandera EV, Bjorge L, Tangen IL, Salvesen HB, Krakstad C, Massuger LF, Kiemeney LA, Aben KK, van Altena AM, Bean Y, Pejovic T, Kellar M, Le ND, Cook LS, Kelemen LE, Brooks-Wilson A, Lubinski J, Gronwald J, Cybulski C, Jakubowska A, Wentzensen N, Brinton LA, Lissowska J, Yang H, Nedergaard L, Lundvall L, Hogdall C, Song H, Campbell IG, Eccles D, Glasspool R, Siddiqui N, Carty K, Paul J, McNeish I, Sieh W, McGuire V, Rothstein JH, Whittemore AS, McLaughlin JR, Risch HA, Phelan CM, Anton-Culver H, Ziogas A, Menon U, Ramus SJ, Gentry-Maharaj A, Harrington P, Pike MC, Modugno F, Rossing MA, Ness RB, Pharoah PD, Stram DO, Wu AH, Pearce CL. Evaluating the ovarian cancer gonadotropin hypothesis: A candidate gene study. *Gynecol Oncol*. 2014 Dec 17. [Epub ahead of print]

Chen Y, Klingen TA, Wik E, Aas H, Vigeland E, Liestøl K, Garred Ø, Mæhlen J, Akslen LA, Lømo J. Breast cancer stromal elastosis is associated with mammography screening detection, low Ki67 expression and favourable prognosis in a population-based study. *Diagn Pathol*. 2014 Dec 19;9(1):230.

Solheim O, Tropé CG, Rokkones E, Kærn J, Paulsen T, Salvesen HB, Hagen B, Vereide AB, Fosså SD. Fertility and gonadal function after adjuvant therapy in women diagnosed with a malignant ovarian germ cell tumor (MOGCT) during the "cisplatin era". *Gynecol Oncol*. 2014 Dec 12. [Epub ahead of print]

Carvajal-Carmona LG, O'Mara TA, Painter JN, Lose FA, Dennis J, Michailidou K, Tyrer JP, Ahmed S, Ferguson K, Healey CS, Pooley K, Beesley J, Cheng T, Jones A, Howarth K, Martin L, Gorman M, Hodgson S; National Study of Endometrial Cancer Genetics Group (NSECG); Australian National Endometrial Cancer Study Group (ANECS), Wentzensen N, Fasching PA, Hein A, Beckmann MW, Renner SP, Dörk T, Hillemanns P, Dürst M, Runnebaum I, Lambrechts D, Coenegrachts L, Schrauwen S, Amant F, Winterhoff B, Dowdy SC, Goode EL, Teoman A, Salvesen HB, Trovik J, Njolstad TS, Werner HM, Scott RJ, Ashton K, Proietto T, Otton G, Wersäll O, Mints M, Tham E; RENDOCAS, Hall P, Czene K, Liu J, Li J, Hopper JL, Southey MC; Australian Ovarian Cancer Study (AOCS), Ekici AB, Ruebner M, Johnson N, Peto J, Burwinkel B, Marme F, Brenner H, Dieffenbach AK, Meindl A, Brauch H; GENICA Network, Lindblom A, Depreeuw J, Moisse M, Chang-Claude J, Rudolph A, Couch FJ, Olson JE, Giles GG, Bruinsma F, Cunningham JM, Fridley BL, Børresen-Dale AL, Kristensen VN, Cox A, Swerdlow AJ, Orr N, Bolla MK, Wang Q, Weber RP, Chen Z, Shah M, Pharoah PD, Dunning AM, Tomlinson I, Easton DF, Spurdle AB, Thompson DJ. Candidate locus analysis of the TERT-CLPTM1L cancer risk region on chromosome 5p15 identifies multiple independent variants associated with endometrial cancer risk. *Hum Genet*. 2015 Feb;134(2):231-45.

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