Centre for Cancer Biomarkers

Norwegian Centre of Excellence – University of Bergen

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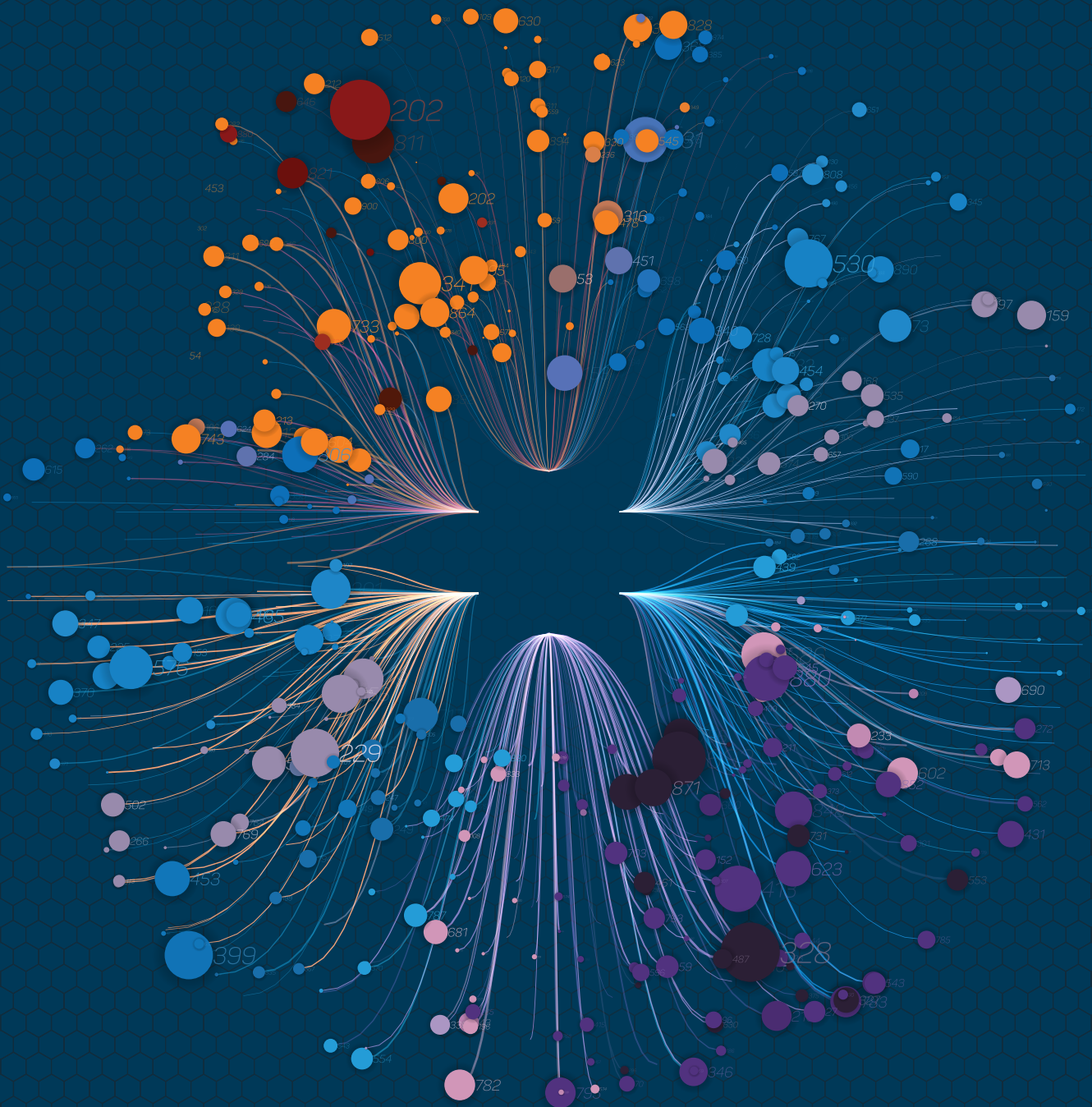

ANNUAL REPORT 2017

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THE 5TH ANNUAL SYMPOSIUM

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DIRECTOR'S COMMENTS

CCBIO2.0 has been approved, and we are proud to congratulate the entire CCBIO family with this achievement. It is most stimulating and motivating to move towards the second term and to fully promote our many ideas and different activities. This applies to a range of biomedical projects, from basic studies towards biomarker intense clinical trials as well as implementation and improved practice. On top of this, our activities in the field of ethics and economics, related to the principles and practices of priority setting, will be strengthened since this is a key component in contemporary precision medicine.

Studies of individual tissue biomarkers are still frequently performed, by us and others, and successful validation is more important than ever to increase the likelihood of clinical application. In breast cancer, the traditional TNM-classification of tumor stage has now been upgraded by including histological grade, expression of estrogen receptors and progesterone receptors as well as HER2 status into the novel concept of "prognostic stage groups" for clinical use. This represents a very exciting perspective for validated biomarkers.

A major challenge today is to account for tissue complexity and heterogeneity in malignant tumors, to study it without loosing the tissue coordinates, and to eventually report it with potential clinical consequences and perspectives. The prospects of high-dimensional tissue profiling, using multiplexing immuno-histochemical techniques or the powerful mass cytometry approach, combined with advanced bioinformatics and machine learning, are motivating. In the setting of biomarker programs in our clinical trials, such aspects are promising.

Many topics have received increased attention. The smartness of cancers is as fascinating as ever. During the past few years, aspects of tumor cell plasticity, including interactions with the immune and vascular systems, have started to emerge. This represents a huge potential for increased understanding of cancer strategies, but also challenges and possibilities of improved combination treatment.

During the last year, and according to a repurposing strategy, a panel of more than 600 commercially available FDA-approved drugs was screened to detect compounds with the novel features of inhibiting the Wnt-ß-catenin signaling pathway, and exciting results were presented. The identification of nitazoxanide (NTZ) as a blocking compound is a novel mechanism. A national patient trial combining anti-Axl treatment with immunotherapy is actively recruiting patients. The dendritic cell based cryoimmunotherapy trial on prostate cancer (CryoIT) is progressing well. An interim analysis of the patients included was conducted during late 2017 with encouraging results. In particular, ultradeep TCR-sequencing indicated several prevalent new T-cell clonotypes as a reflection of new immunity. In leukemia, single cell profiling can be used to monitor CML patients treated with the kinase inhibitor nilotinib. In AML, a wide phospho-protein screen was performed, and the data support the impact of intracellular phospho-signaling pathways in reflecting differentiation stage and recurrent mutations. The identified proteins represent a possibility for further development of protein based biomarkers in leukemia.

The creation of a stimulating science culture is one of the most important goals of CCBIO. How can we apply the seed and soil principles in the scientific microenvironment? In an exchange between Francis Bacon and Roger Strand, the CCBIO Organon should be regarded as a colorful, energetic beehive. ••

Lars A. Akslen, Director of CCBIO

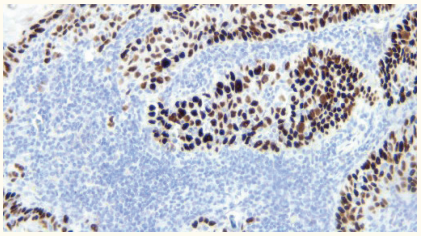
VISION AND RESEARCH AREAS

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

CCBIO is focusing on tumor-microenvironment interactions in primary and metastatic lesions, and how tissue context can educate and 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.

CCBIO concentrates on the following overlapping and fully integrated 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 are 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. ••

CCBIO Opinion

Text: Lars A. Akslen

Prospects of Next Generation Tissue Profiling

The gold standard for a diagnosis of cancer, following clinical and radiological suspicion, has for a long time been the microscopic analysis of simply stained tissue samples. In addition to studying the criteria of malignancy, more features will be reported, such as histologic grade and detailed stage information. Using breast cancer as an example, the last edition of the TNM classification system (AJCC, 8.ed, 2017) has now included histologic grade (G) and expression status of key biomarkers such as estrogen receptor (ER), progesterone receptor (PR), and HER2 on top of the basic TNM parameters, in a new prognostic stage group concept. This upgrade of the TNM classification is significant.

In recent times, translational efforts have made extensive use of tissue samples for large-scale research purposes including discovery and validation of omics profiles, and biobanks with clinical annotations (TCGA, METABRIC, Human Protein Atlas and many others) have become valuable tools for hypothesis-based studies and more extensive discovery-oriented mapping of different classes of biomarkers. However, some problems are evident. First, many biomarkers are mostly based on samples from primary tumors, whereas metastatic disease represents the real clinical problem. Second, even when considering the primary lesion alone, or the metastatic lesions, tissue heterogeneity as a reflection of biological diversity within a tumor mass adds a significant challenge.

A large majority of biomarker studies on intact tissue samples have focused on individual tumor cell features. There is a need for higher order studies of multiple characteristics, or profiles, or phenotypic patterns, such as those starting to emerge from multiplex immuno-histochemistry or immuno-fluorescence analyses. This will be necessary to build more precise tissue based models of co-expression patterns and functional biomarkers within different tissue compartments, with particular attention to the tumor microenvironment, and including the interacting immune and vascular systems. The use of mass cytometry might be necessary to increase the potential for even deeper learning of the tissue composition as well as proximity patterns and functional tissue domains. To support such ambitious plans, studies will have to be supported by intense bioinformatics and artificial intelligence resources to be successful. Modeling of the tumor-microenvironmental interactions based on studies of solid biopsies, is a challenge in this field. In translational studies, researcher networks will be needed to increase our insight of the complexity and heterogeneity of biological networks in cancer. A deep and integrated understanding of morphology and biology is necessary to obtain better models of how malignancy is driven in the context of tissue landscapes. ••

CCBIO Opinion

Text: John Cairns, Ole F. Norheim & Roger Strand

Precision Fairness?

The concept of precision medicine emerged on US health policy agendas in the early 2010s and has since gained increasing prominence on both sides of the Atlantic, in part replacing the similar concept of personalised medicine. In the more optimistic imaginations of precision cancer care, every patient will receive uniquely tailored treatment on the basis of perfectly sensitive and specific biomarkers, thereby maximising clinical benefit and minimising the risk of adverse effects. Sometimes, even the old imaginaries of "the cure for cancer" and "winning the war on cancer" are invoked.

The reality of cancer, however, is also a matter of the success of hygiene, welfare and modern medicine: As fewer (affluent) people die from infectious diseases or malnutrition, more of us reach old age and get the opportunity to develop cancer. While modern medicine may reach the stage of curing some cancers sometimes, we should expect to also uphold the rest of the Hippocratic maxim: Relieving often and comforting always.

Life is not fair. Life simply *is*. Fairness, on the other hand, is a property of human decisions, practices and institutions. The Scandinavian welfare state emphasizes the value of fairness and distributive justice and is, at least in theory, less prone to accept inequalities in health as a fact of life or a matter of bad luck. May biomarkers help to identify those patients we can help the most and who need it more?

On a general level and in a short-term perspective, they might not. Many biomarkers relate to the health problems of the rich and rely on technically sophisticated healthcare systems to be of clinical relevance. In the long run, however, there is room for optimistic imagination. While the introduction of new medical technologies in general tends to increase healthcare costs, biomarkers could become the exception if they lead to less ineffective treatment. More fundamentally, biomarkers challenge the business models of the pharmaceutical industry and the political economy of a sector characterized by high profit margins, especially if innovative use of biomarkers can revive the interest in older drugs that are off patent.
Still, biomarkers, as they are conceived so far, are limited to biological information. They indicate what will happen to the patient if she or he is given (or not given) a particular treatment. The fairness of the healthcare system is supposed to be ensured by general guidelines. In the many public controversies over expensive cancer drugs, however, other unique features of patients are emphasized than their conventional biomarker profile. Media and citizens suggest, for example, that it may be unfair to treat a 40-year single parent of small children in the same (restrictive) way as an elderly person without similar responsibilities. In the era of precision medicine, could we imagine a similar development towards precision fairness, in which many more specific features of also the *needs, e.g the severity of disease of a particular individual,* are taken into account? Would precision fairness secure the accountability, transparency and predictability of decisions, and would it indeed change our notion of what is fair? ••

CCBIO Opinion

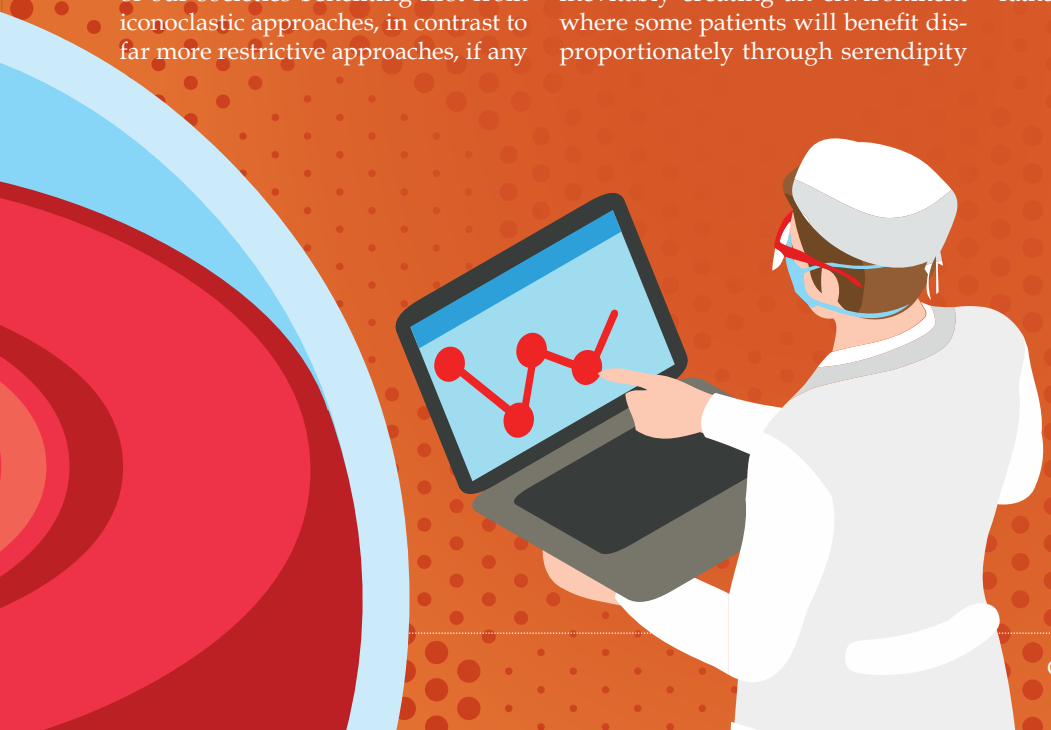
Text: Hani Gabra

Precision Medicine - Fairness and the Big Pharma Perspective

The days of the Blockbuster drug are over in oncology. The requirement to demonstrate convincing benefit for patients for a new cancer drug in order to license it is driving increasingly rigorous patient stratification as a means to unambiguously demonstrate precise patient cohorts in whom treatment is justified. Big pharma understand that these cohorts are increasingly precisely molecularly stratified, and in general there is an accompanying push to use new drugs earlier in the disease journey as this trends to an increase in seeing benefit. Thus, big science in big pharma, richer nations' health budgets and insurance systems that can cope with this complexity and therefore spiraling costs, together with the ability to present cogent cases for novel treatments in increasingly sophisticated ways result in the more affluent microcosmos of our societies benefiting first from iconoclastic approaches, in contrast to far more restrictive approaches, if any access at all, from poorer public health care systems earlier in the life cycle of new drugs. The recent examples of the eye-watering cost associated with FDA approval of CD19 targeted Chimaeric Antigen Receptor T Cell therapy for relapsed paediatric acute lymphoblastic leukemia is no doubt based on the hope of future quality of life and productivity for that child together with the relative rarity of the condition.

The typical patient utilised en-route to registration of new anti cancer drugs is not typical of the general population of cancer patients and clearly demographic and socioeconomic issues contribute to that difference (awareness through education, nutrition, earlier presentation etc). Nevertheless, big pharma has a responsibility to follow the science and turn that science into good medicine, inevitably creating an environment where some patients will benefit disproportionately through serendipity born out of personalisation in addition to better access through socioeconomics. The successes of precision medicine are creating a complex mosaic of trade-offs where fairness and equity of access to life lengthening or curative but expensive treatments have to be scrutinised. This of course has a "reverse translational" effect on the way drug development decisions are made in pharma, and the symbiosis of big pharma and society continuously evolves around these issues.

Despite these caveats I remain optimistic that good science will give us solutions to disease both preventative and curative, and that big pharma has an essential role in creating the landscape of clinically available options that can create the debate around fairness through an embarrassment of riches rather than desert of hopelessness. ••



Organization of the Center

CCBIO is organized across seven departments and four faculties at the University of Bergen (UIB). Its main activities, eight PIs and most of the other staff are located at the Faculty of Medicine´s departments (MF): Department of Clinical Medicine (K1), Department of Clinical Science (K2), and Department of Biomedicine (IBM).

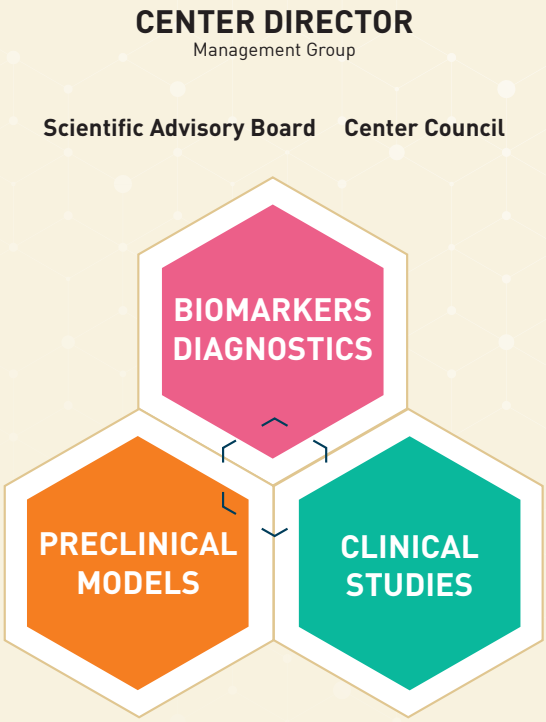
The majority of CCBIO´s PIs also hold positions and funding at the regional health authorities Helse Bergen and Helse Vest. CCBIO has activities and employees at additional departments and institutions. These are the Department of Informatics, Department of Economics, Department of Global Public Health and Primary Care, as well as the Center for the Study of the Sciences and the Humanities, all at the University of Bergen, and also at the London School of Hygiene and Tropical Medicine.

Research Management

In terms of science management, CCBIO is organized in three integrated research areas and programs (preclinical studies, biomarker studies and clinical studies) and four associate programs (ethics, economics, prioritization and bioinformatics) that support the three main research areas (see organizational chart). Lab space and core facilities are available for CCBIO, as is the Clinical Trials Unit at Haukeland University Hospital. The eight principal investigators meet monthly to discuss administrative and scientific issues and update each other on development and progress. In addition to taking part in some of the monthly meetings, CCBIO's associate investigators together with the principal investigators take part in a full day strategy seminar bi-annually. The monthly meetings and the bi-annual strategy seminars are important platforms for increased collaboration within CCBIO.

Management group

In 2017, CCBIO was managed by the director, Professor Lars A. Akslen, the



co-director, Professor Bjørn Tore Gjertsen and the administrative leader, Geir Olav Løken. From August 2017, Ragna Breines filled the position as administrative leader while Geir Olav Løken was on leave until August 2018. The management group is assisted by four finance officers, a web and newsletter editor, the faculty communications officers and a wide range of other administrative staff allocated to CCBIO in parts of their positions. The co-located offices for the management group are in the main building of Haukeland University Hospital (Sentralblokken, second floor).

Integration with the 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 for collaboration with its departmental and institutional partners. Consequently, CCBIO is organized to retain full control over resources while the day-to-day administration is delegated to the involved departments. As a main principle, funds and positions are located at the respective department where the research takes place. This enables researchers to interact with their familiar support staff, thereby minimizing resources used on day-to-day administration. In addition, it creates common interests between CCBIO and the departments. This model has proven successful due to its efficiency and robustness, and it has ensured excellent collaboration with the involved departments. ••

Scientific Advisory Board

The CCBIO Scientific Advisory Board (SAB) consists of Professors Carl-Henrik Heldin, Bruce Zetter and Ate van der Zee, all three being internationally leading researchers in CCBIO-relevant fields. The SAB's mandate is to give the center director and center staff advice on science and scientifically relevant matters. The SAB has convened once a year for a full day meeting with the CCBIO PIs and associate PIs, following the CCBIO Annual Symposium.

From the left: Bruce Zetter, Carl-Henrik Heldin, and Ate van der Zee.

In its 2017 report, the SAB stated that it was impressed with the interactions between the center and the Board and that CCBIO has gone to great lengths to revise the direction in accordance with the SAB's advice. This especially applies to CCBIO's efforts on improving the bioinformatics infrastructure, initiation of clinical trials, integration of imaging modalities into the work of the center, increased emphasis on liquid biopsy in cancer management, and acquisition of supplemental funding.

In the SAB's opinion, CCBIO displays excellence and scientific rigor in its commitment to translate discoveries to a clinical setting and is rapidly becoming one of the world leaders in the study, discovery, application and translation of cancer biomarkers. It sees CCBIO's basic biomarker research as a core strength and finds it encouraging that the new clinical trials are now in the process of accruing patients. The SAB found it especially promising that two of the trials are in collaboration with industry partners and that CCBIO is closely integrated with the Clinical Trials Unit at Haukeland University Hospital. The SAB encouraged the continued exploration of biomarkers associated with immunotherapy efficacy as well as research on biomarkers associated with drug sensitivity and with the acquisition of chemo resistance in solid and liquid tumors. CCBIO's effort within economics and Ethical Legal and Societal Aspects (ELSA) was characterized as unique, fundamental and important, and the SAB recommended a continued expansion of these programs and further integration into CCBIO's medical research effort.

The 2017 SAB report mainly focuses on research activities and ongoing clinical trials at CCBIO. In general, the SAB finds that the three integrated programs complement each other nicely and provide an exemplary translational research effort. They also applauded the degree of fruitful interactions and collaborations between the PIs of CCBIO. Further, the high quality of clinical studies performed in the context of CCBIO was a pleasant surprise to the SAB since several studies now are moved from preparation phase to including patients. Including biomarkers in tissue or liquid form significantly strengthens the clinical trials protocols. A strong asset for the CCBIO program is the presence of basic, translational and clinical researchers in combination with an ambitious local oncology pharmaceutical company (BerGenBio).

Further, CCBIO's efforts in recruiting international collaborators were characterized as excellent, especially CCBIO's program of 10% adjunct positions as it has given very good collaborative ties both in terms of scientific quality and range. The SAB was pleased that CCBIO now has a total of 13 international, highly qualified adjunct professors who collaborate with CCBIO PIs. The SAB was also pleased with CCBIO's efforts to improve the gender balance in its PI group by recruiting female junior- and associate investigators. The SAB concludes that during its 4-5 years of running, CCBIO has developed into a well-functioning Centre of Excellence and that among its many strengths, the high quality research programs on biomarkers that span from basic science, to translational research and clinical trials are specially mentioned. ••

Carl-Henrik Heldin is the chairman of CCBIO's SAB and is professor and director at the Ludwig Institute for Cancer Research, Uppsala University, Sweden, and chairman of the Nobel Foundation.

Ate van der Zee is professor of gynecological oncology and member of the Board of Directors at the University Medical Center Groningen, the Netherlands.

Bruce Zetter is the Charles Nowiszewski Professor of Cancer Biology at Harvard Medical School and Boston Children's Hospital, Boston, MA, USA.

Center Council

The Center Council's mandate is to provide advice to the CCBIO management team, mostly on administrative and some strategic issues, and to contribute towards ensuring that the activity is in accordance with the contract with the Research Council of Norway (RCN). The Center Council has its focus mainly on potential local synergies, whereas the CCBIO Scientific Advisory Board addresses the scientific and international perspective. The Council is composed of the Faculty of Medicine (MF) dean (chair) and vice-dean for research, the heads of department from the Department of Clinical Medicine (K1), the Department of Clinical Science (K2) and the Department of Biomedicine (IBM), the director of research from Haukeland University Hospital (Helse Bergen) and the CCBIO and MF directors as observers. The CCBIO administrative leader is the council secretary. During the establishing phase in 2013 and 2014, the Center Council met twice a year and has thereafter, by its own choosing, met annually. ••

Scientific Activities and Progress

CCBIO has a focus on tumor-microenvironment interactions and plasticity programs in primary and metastatic lesions and how these can define aggressive tumor phenotypes and predict cancer progression and treatment response.

CCBIO has three overlapping and well integrated research areas: basic studies of cancer mechanisms, discovery and validation of cancer biomarkers, and clinical studies. An ambition is to obtain rapid transfer of knowledge to practical medicine. In addition, several integrated studies on economics and priority setting are up and running. An increasing range of activities have been established at the CCBIO Research School for Cancer Studies, including programs made possible through the INTPART Program and funding from The Olav Thon Foundation. Increased internal and external collaboration and networking is taking place.

An ambition is to obtain rapid transfer of knowledge to practical medicine.

In the area for basic studies, projects are focusing on how tumor cells interact with the surrounding microenvironment, by epithelial-mesenchymal transition, plasticity and transdifferentiation, angiogenesis induction, fibroblast activation and matrix dynamics, leading to growth and metastatic spread.

During the last year, and according to a repurposing strategy, a panel of more than 600 commercially available FDA-approved drugs was screened to detect compounds with the novel features of inhibiting the Wnt-ß-catenin signaling pathway, and exciting results were reported. The identification of nitazoxanide (NTZ) as a blocking compound that binds to the enzyme PAD2 followed by citrullination and degradation of ß-catenin is a promising novel mechanism (Qu et al., 2017).

The dendritic cell based cryoimmunotherapy trial on prostate cancer (CryoIT Phase I) is progressing well. An interim analysis of included patients was conducted with encouraging results. In particular, ultradeep TCR-sequencing indicated that CryoIT was followed by several prevalent new T-cell clonotypes as a reflection of new immunity (work in progress).

In leukemia, single cell profiling can be used to monitor CML patients treated with the kinase inhibitor nilotinib (Gullaksen et al., 2017). In AML, a wide phosphoprotein screen was performed using phospho-protein-enriching columns and differential gel electrophoresis (Forthun et al., 2017). The data supports the impact of intracellular phospho-signaling pathways in reflecting differentiation stage and recurrent mutations. The identified proteins represent a possibility for further development of protein based biomarkers in AML.

The SonoCURE team have demonstrated the preclinical development and par-

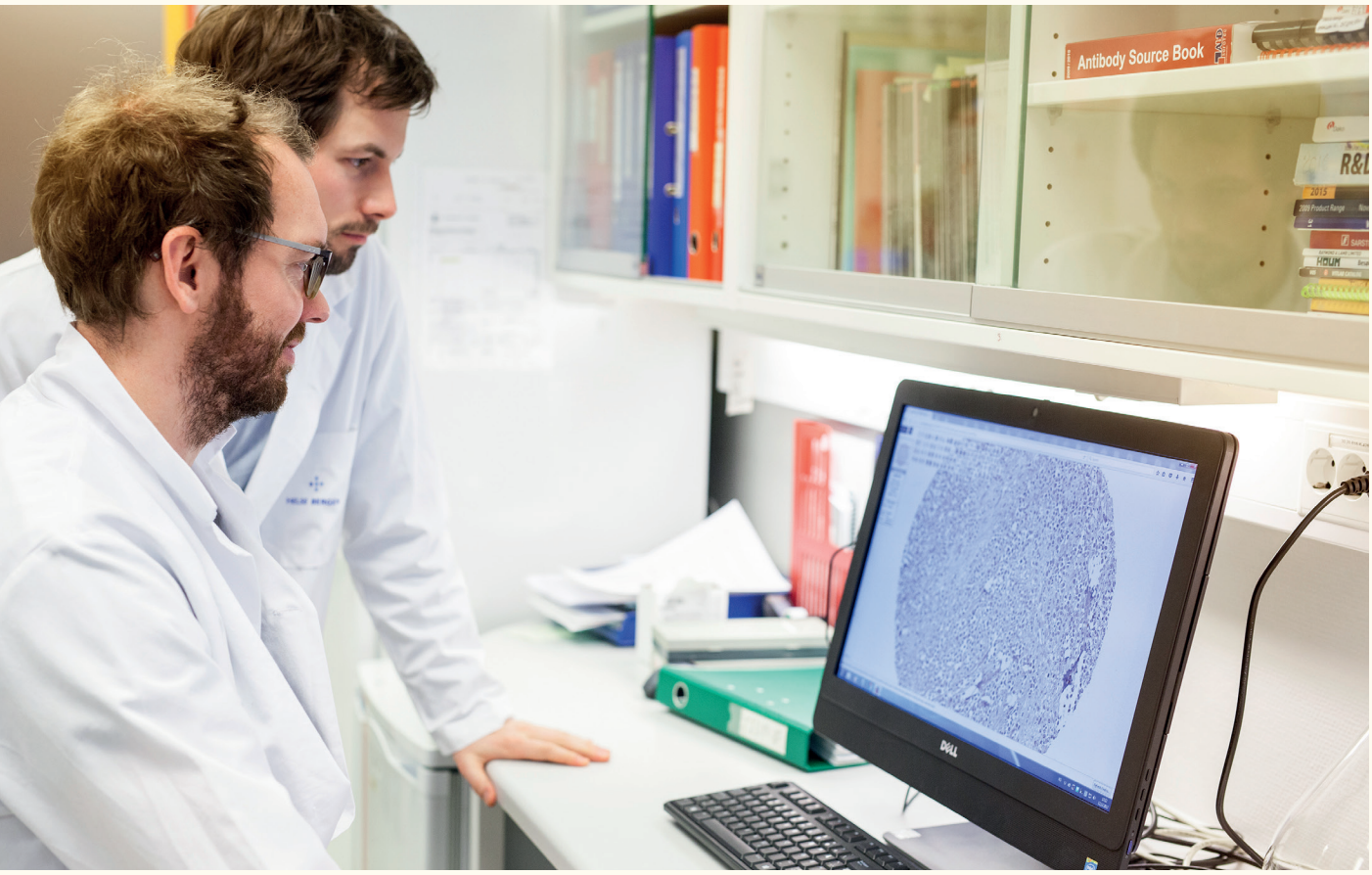
ticipated in the clinical application of sonoporation in the first clinical trial in pancreatic ductal adenocarcinoma. In this study, patients survived on average 17.6 months, compared with 8.9 months through the simple addition of sonoporation to a standard of care treatment protocol (Kotopoulis et al., 2017).

Recent results highlight the Axl receptor tyrosine kinase as a key regulator of both normal adult epithelial progenitor cells and a determinant of carcinoma cell plasticity. A multicenter trial combining anti-Axl treatment with immunotherapy is actively recruiting patients. Further, Axl kinase inhibition blocked the aggressive traits of pancreatic cancer cells and enhanced the efficacy of gemcitabine in patient-derived xenografts and late-stage murine models by targeting the tumor-immune interface. Axl inhibition drove tumor cell differentiation and reversed gemcitabine resistance mechanisms, and potentiated an immune stimulatory microenvironment by targeting immune suppressive myeloid cell types (Ludvig et al., 2017).

Studies are being performed on biomarker discovery and validation in breast and gynecologic cancers, using protein levels, as well as omics data on mRNA and DNA alterations. Efforts are made to map tumor diversity and associations with clinico-pathologic phenotype. In breast cancer, expression of the stem cell marker Nestin was found to correlate strongly with basal-like and BRCA1-related tumors, and associated with EMT and angiogenic profiles (Krüger et al., 2017). Markers for tumor vascular content have been reported to correlate with prognosis (Ramnefjell et al., 2017), and pattern of vascular invasion by tumor cells, either blood or lymphatic vessels, correlate with tumor aggressiveness (Klingen et al., 2017). In a study of perinodal invasion of lymph node metastases in breast cancer, results were obtained that have been included in national guidelines from the Norwegian Breast Cancer Group (Aziz et al., 2017). Novel data on the relationship between genetic alterations and protein expression in cutaneous melanoma has been reported (Hugdahl et al., 2017a,b).

Studies on extracellular matrix biology are progressing.

In studies of gynecologic cancers, protein expression differences between primary tumors and their metastases, as well as the prognostic value, have been published (Tangen et al., 2017; Fonnes et al., 2017; Halle et al., 2017). Proteomic profiling of tumor tissue showed differences between obese and non-obese patients (Mauland et al., 2017). Also, biomarkers for low-grade endometrial neoplasia have been reported (Berg et al., 2017). The use of estrogen and progesterone receptor status for endometrial



cancer to stratify for lymphadenectomy is continued in a Phase 4 implementation trial (MoMaTEC2).

Studies on extracellular matrix biology, in particular integrin profiling, are progressing. Development of novel antibodies and mouse models are being performed. In one study, increased expression of integrin alpha11 was found in head and neck carcinomas (Parajuli et al., 2017). In a study of human breast cancer xenografts, tumor growth and metastases were dependent on the oxygen levels (Yttersian Sletta et al., 2017). It was further shown that imatinib increases oxygen delivery in extracellular matrix-rich but not in matrix-poor experimental carcinoma (Burmakin et al., 2017).

Several efforts and initiatives within CCBIO, with increased internal and external collaboration, are now up and running. The projects are spanning from tumor plasticity programs and microenvironment biology, through discovery and validation of biomarkers and signatures, to clinical trials with targeted biomarker panels using liquid biopsies and single cell analysis.

The programs on ethics and economics of biomarker based therapy are also expanding and are being integrated in the recently established clinical trials. The activities of the CCBIO Research School for Cancer Studies are increasing. CCBIO performs research on cancer biomarkers along the entire chain from studies of biological mechanism to clinical trials. Our main societal impact resides in this sense in medical innovation and the improvement of cancer diagnostics and therapies. The main measure of this impact is ultimately its effect on the quality and cost-effectiveness of cancer treatment; it cannot be precisely measured on the short-term. Better knowledge of cancer biomarkers is likely to affect the prioritization dilemmas; however, the nature of that effect depends on the nature of the knowledge to be discovered.

CCBIO aims to further strengthen the work on societal perspectives by developing one interdisciplinary humanities and social science team to study the opportunities and challenges of precision cancer medicine. This team will deepen the collaboration with CCBIO cancer researchers to promote the integration of ELSA perspectives and RRI into practice. Furthermore, the group will continue their European and US collaborations on the more conceptual research into RRI and the coproduction of science, technology and society. Finally, as the research progresses, the team plans to take a more active and visible stand vis-à-vis the Norwegian society and public sphere.

Through 2017, several papers have been published, and CCBIO has presented two books. We have conducted a range of educational activities within the research school, and communications and media appearances have reflected many of our scientific findings. ••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SOCIETAL IMPACT, INNOVATION AND INDUSTRIAL IMPACT

CCBIO performs research on cancer biomarkers along the entire chain from studies of biological mechanisms to clinical trials. Our main societal impact resides in this sense in medical innovation and the improvement of cancer diagnostics and therapies. The main measure of this impact is ultimately its effect on the quality and cost-effectiveness of cancer treatment; it cannot be accurately measured on the short-term. By cost-effectiveness we refer to the challenges of the increased cost of medical services and notably of cancer treatment, which also raise difficult ethical issues of which conditions and patients to prioritize in the public health services. Better knowledge of cancer biomarkers is likely to affect the prioritization dilemmas; however, the nature of that effect depends on the nature of the knowledge to be discovered.

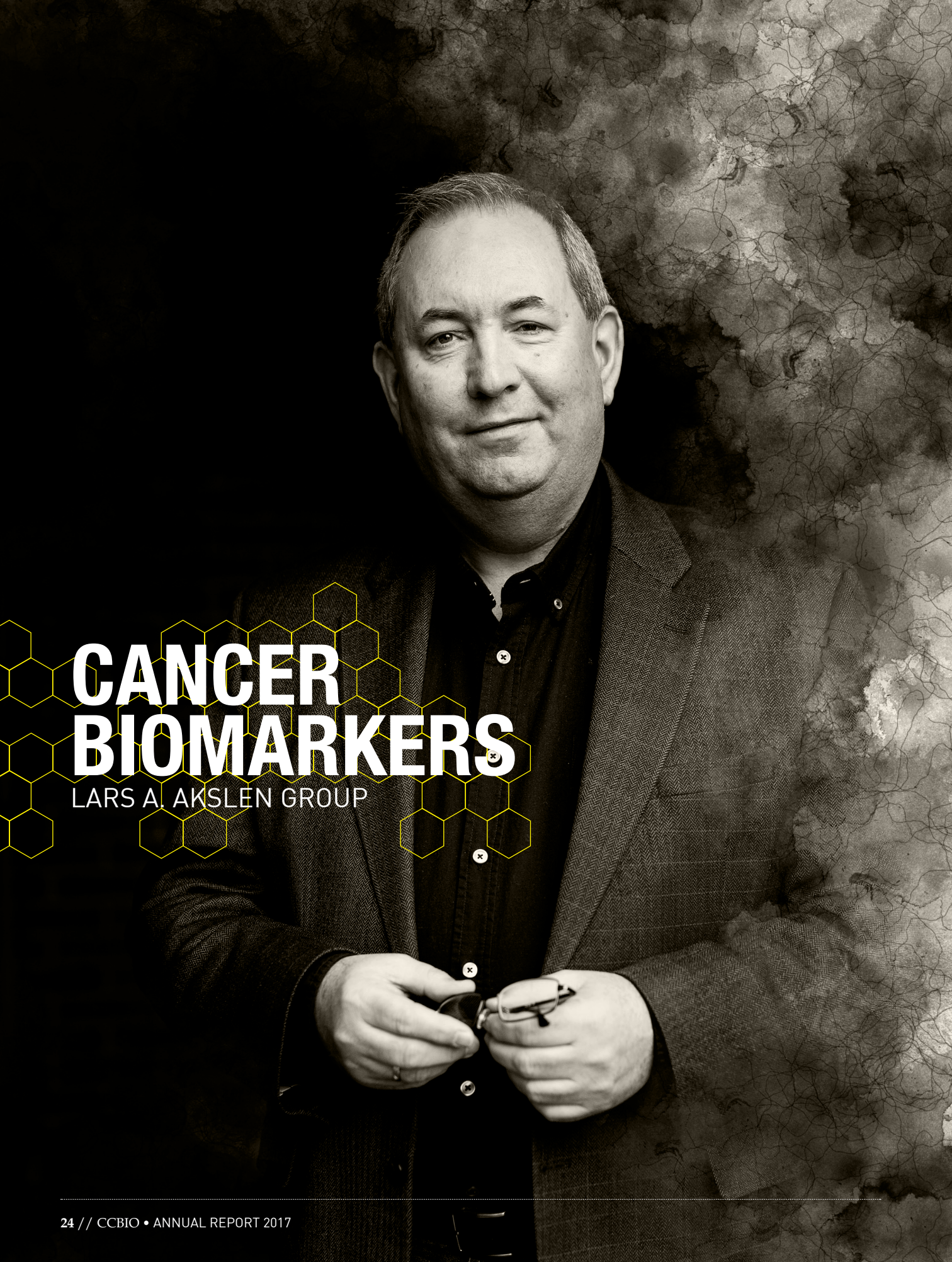
The question of the societal impact of CCBIO is accordingly also a question about the process of caring for and reflecting upon the societal impact. A specific feature of CCBIO is that it integrates research on its ethical, societal and economic aspects into the cancer research proper. A substantial part of the research budget is devoted to economists, ethicists and social scientists who continuously interact with cancer researchers at all levels in the consortium through workshops, informal meetings, PhD courses, conferences and co-authored papers, including the recently published anthology of the ethical, economic and societal aspects of cancer biomarkers.

Another feature integral to CCBIO's strategy of anticipation and reflection upon its societal impact is its continuous and extensive dissemination towards and interaction with civil society. As documented by our annual reports, we have invested a major effort into communicating prospects and challenges of cancer biomarkers in a number of media channels (including national and regional TV and newspapers), and we participate in public dialogue events, interacting with citizens, experts, authorities and non-governmental organisations such as the Norwegian Cancer Society. In this way, CCBIO adheres to and implements the European (and Norwegian) principle of Responsible Research and Innovation (RRI).

The research environment at CCBIO comprises a high degree of innovation. The European Commission defines innovation as "change that speeds up and improves the way we conceive, develop, produce and access new products, industrial processes and services. Changes that create more jobs improve people's lives and build greener and better societies." Since its inception, CCBIO has endeavoured to translate discoveries and facilitate the industrial and job-creating impact of research discoveries. An embodiment of this principle is the biotechnology company BerGenBio AS (www.bergenbio.com). Based on research from the Lorens group on the Axl receptor, supported by other CCBIO researchers and developed via support of Bergen life science innovation support mechanisms and venture capital, BerGenBio has grown into a top-tier biotechnology company developing first-in-class cancer treatments in world-wide clinical trials. Currently employing close to 40 people, with offices in Bergen and Oxford, and with many recruited from the University of Bergen/Haukeland University Hospital biomedical research community, BerGenBio demonstrates the ability of the Bergen research environs to drive innovation. Several CCBIO principal investigators (Lorens, Gjertsen, Straume, Akslen) have contributed to the successful clinical translation of the BGB324 Axl inhibitor, providing new basic research insights, novel clinical trial design and development of new biomarker strategies for patient stratification through specific R&D collaborations and mentoring of shared industrial PhD candidates. These efforts have gained national and international recognition as BerGenBio expands its clinical trial portfolio. CCBIO continues to benefit from this strategic alliance that attests a high level of biomedical innovation. A CCBIO investigator-initiated clinical trial (Straume) with the Axl kinase inhibitor BGB324 in combination with targeted immunotherapeutics for melanoma has attracted collaborators from renowned US biomedical research centers (Harvard Medical School, MIT, Vanderbilt) to conduct in-depth biomarker studies. CCBIO supports national innovation initiatives through board memberships and active participation in dialogue with policy and funding institutions. ••

Research Groups with Principal Investigators (PIs)

During 2017, research efforts have been increasing in the core groups, as reflected in the list of publications. Many of the studies demonstrate an increased collaboration within CCBIO, but also exemplify how local teams can collaborate successfully with international environments and networks.



CANCER BIOMARKERS

LARS A. AKSLEN GROUP

Research focus
The aim has been to discover and validate novel tissue-based cancer biomarkers, for better biological understanding and improved prediction of aggressive tumor behaviour. Hopefully, such markers can assist in molecular classification and grading of malignant tumors, as a better guide for precise treatment of the patients. The group has concentrated on the tumor microenvironment.

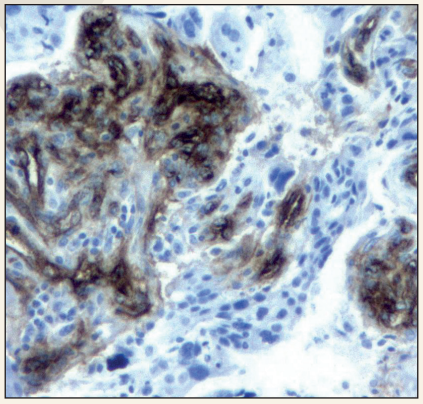
Projects
The team is currently targeting the following projects:
• Proteomic tissue profiling of luminal (receptor positive) and non-luminal (receptor negative) breast cancer.
• Role of Nestin as a marker of BRCA1-related, basal-like and aggressive breast cancer.
• Markers of tumor-vascular and angio-immunogenic interactions in breast cancer.
• Precision markers of tumor proliferation and invasive properties in relation to clinical applications in breast cancer.
• Role of stromal integrin alpha11 expression in breast cancer.

Important results
• Studies have used proteomic profiling of whole tumor tissues, laser capture microdissected tissues (epithelial component, tumor stroma), whole cell lysates and secretome profiling (6 basal-like and 6 luminal-like cell lines). Data indicate significant differences of the stromal proteome across breast cancer subtypes. Disease progression might be modeled based on stromal protein profiles. Follow-up studies are ongoing.
• Expression of Nestin was found to correlate strongly with basal-like and BRCA1-associated breast cancer, and associated with stemness and angiogenic profiles. Cell studies using knock-in and knock-out strategies are ongoing.
•Data indicate that there is a difference between blood vessel and lymphatic involvement by tumor cells in high-grade breast cancer, and tumor associated macrophages (TAM) seem to be involved in this process. As a novel observation, increased microvascular proliferation was related to certain gene expression patterns and 6p21 amplification. Microvessel density predicted the response to bevacizumab in large and locally advanced breast cancers, and HSP27 associated with response to bevacizumab in metastatic melanoma.
• The team reported on tumor proliferation markers in breast cancers and how they change from primary tumors to metastases. The group found that 15% of breast cancers changed from low proliferation (primary tumors) to high in metastases. Data on extra-nodal spread of lymph node metastases and prognostic impact has been published and included as novel measures in national breast cancer guidelines by NBCG (HDir).
• Studies on the expression of alpha11 integrin in human breast cancers are ongoing in collaboration with Drs. Reed and Gullberg.
• In other projects, BRAF-V600E protein expression represented a novel progression marker in cutaneous melanoma. In a collaborative study with Dr. Watnick (Boston), the importance of prosaposin (PSAP) and thrombospondin-1 (TSP-1) for cancer progression was found.

Future plans
Ongoing projects will further explore the phenotypic diversity in breast cancer, with special focus on tumor-microenvironment-based classification (vascular response, immune response, neural response) and concentrate on tissue-based proteomics profiling. Studies aim to be extended by mass cytometry (CyTOF).

Current challenges in the field
A major challenge in the field of tissue profiling is to fully account for the complexity and heterogeneity within malignant tumors. Thus, a key development will have to account for how these features shall be represented and reported, when using multiple simultaneous biomarkers (multiplex studies, mass cytometry). Ultimately, complex biomarker profiles should translate into improved biological understanding and precise diagnostics and treatment.

What has it meant for your group to be part of CCBIO so far?
"To be an active member of the CCBIO family, and to direct this scientific enterprise, has been most stimulating and motivating. There is no better way to perform science than to combine project work with networking and mutual learning. Our colleagues on the international faculty play important instruments in the CCBIO orchestra." ••



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SIGNALING-TARGETED THERAPY

BJØRN TORE GJERTSEN | GROUP

Research focus
The Signaling-Targeted Therapy Group focuses on signaling-targeted therapy in chronic myeloid leukemia (CML) and acute myeloid leukemia (AML), two blood cancers derived from the myeloid cell lineage of the bone marrow. The goal has been to employ single cell analysis to risk stratify patients, and to measure effect of target inhibitors of signaling. An underlying hypothesis is that tumor suppressors, with particular focus on p53, is tightly regulating intracellular signaling.

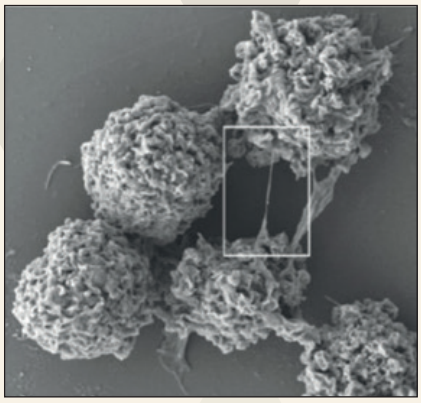
Projects
• Single cell signaling profiling is hypothesized to predict optimal disease control after serial testing of peripheral blood cells before and within one week of first dosing with kinase inhibitor monotherapy. CML is used as a model disease, where signal transduction inhibitors of the Abl kinase provide superior disease control and a long time overall survival that equal healthy comparators.
• Phase Ib/II trial in AML with Axl inhibitor BGB324. This inhibitor does not target a particular driver mutation, but may represent intrinsic resistance against such targeted therapy. Additionally, BGB324 seems to address the tumor-host interaction, and it will be particularly important to determine to which degree this occurs in AML.
• The tumor suppressor p53 is tightly regulated through cell signaling, and additional complexity is added through its multiple expressed isoforms. The group has previously observed that p53 isoform profiles reflect recurrent mutations in genes encoding for signaling molecules. They are currently addressing this relation of intracellular signaling to p53 regulation in cancer.

Important results
• A wide phosphoprotein screen in AML patient cells was performed using phosphoprotein-enriching columns and differential gel electrophoresis (Forthun et al. 2017). The data supports the impact of intracellular phospho-signaling pathways in reflecting differentiation stage and recurrent mutations. The identified proteins represent a possibility for further development of protein based biomarkers in AML.
• The group's key publication from 2017 indicated how single cell profiling can be used in CML treated with the kinase inhibitor nilotinib (Gullaksen et al. 2017).

Future plans
The most important work of 2018 will be to examine single cell analysis of BGB324 treated AML. Two grants were secured in 2017 for startup in 2018. In collaboration with the biotech company BCI Pharma, the group has piloted preclinical development of new kinase inhibitors for the FLT3 kinase. This project is now supported by the Norwegian Cancer Society for four years, where BCI Pharma has the ambition to initiate a phase I early trial in 2019. FLT3-ITD mutations are found in approximately 25% of AML patients, and are strong negative prognostic markers for these patients.

Current challenges in the field
Clonal evolution during cancer therapy is likely the most important challenge in low intensity therapy of acute myeloid leukemia. If single cell immune and signaling profiling could be used to monitor clonal evolution, future therapy could be guided to efficiently keep the disease in check.

What has it meant for your group to be part of CCBIO so far?
"The group sees CCBIO as an ideal platform for therapy and biomarker development. CCBIO has attracted clinical trials to our institution, where our laboratory has been heavily involved in the biomarker program, developing mass cytometry as a novel multiplexing technique for diagnostics and for therapy guidance in aggressive blood cancer." ••



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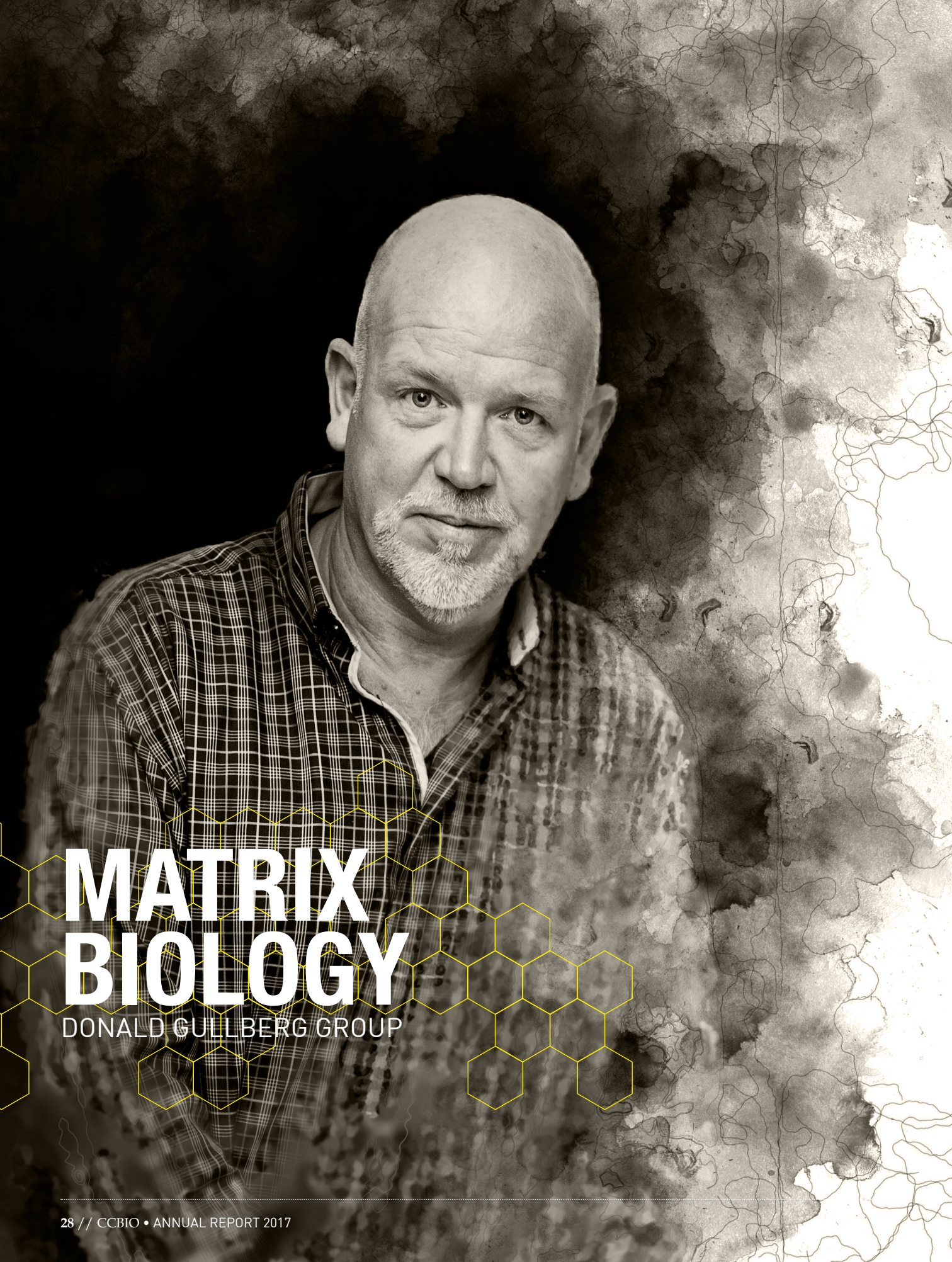


MATRIX BIOLOGY

DONALD GULLBERG GROUP

Research focus
The research is focused on work related to integrin alpha11 which is a collagen receptor with a number of features making it a key molecule in tissue fibrosis and tumor-stroma interactions. The group has performed detailed molecular studies of cell-collagen interactions. Developed animal models include a constitutive integrin alpha11 knockout mouse model, a transgenic alpha11 promoter reporter strain, and most recently a transgenic mouse strain overexpression of integrin alpha11.

Projects
The CCBIO projects deals with the role of integrin alpha11 in tumor stroma using:
• Tumor-fibroblast heterospheroids as a 3D model system to understand bidirectional communication between tumor cells and fibroblasts.
• Development of new animal models to: 1) block human integrin alpha11 function; 2) conditionally inactivate genes in an integrin alpha11-specific manner.
• In collaboration with Nanotools, the group has generated monoclonal antibodies to human alpha11 integrin which block integrin alpha11 function.
• In collaboration with the transgenic facility at Stanford, a transgenic mouse has been generated where Cre-recombinase is driven by 3kb of human integrin alpha11 promoter (ITGA11-Cre mouse v1.0). The long-term aim is to use these models to analyze the role of cancer associated fibroblasts in tumor stroma interactions.

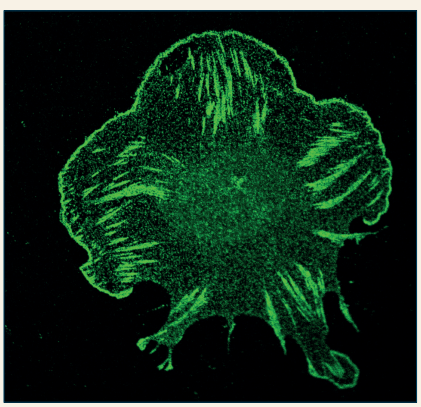
Important results
Novel animal models: The first mouse strain enabling conditional inactivation of genes in an integrin alpha11 promoter directed manner has been successfully generated. Characterization of ITGA11-Cre mouse v1.0 is ongoing.
Novel antibodies: Function blocking antibodies as well as antibodies suitable for biomarker studies are being characterized in functional assays as well as immunohistochemistry studies of tissues.

Future plans
In addition to ongoing work to characterize alpha11 antibodies and the Cre mouse strain, the group will epitope map alpha11 antibodies using mutant integrin alpha11 variants (with domain swapping and deletions). With regard to the Cre mouse strain they will generate the next generation ITGA11-Cre mouse strain (Itga11- Cre v.2.0) in which the Cre activity is not only restricted to the same tissues as alpha11 expression but also under temporal control. A construct coding for Cre-ERT2 and tdTomato will be introduced in the mouse Itga11 gene (unlike in the existing strain where the group use 3kB of the human ITGA11 gene). The intent is to use it to trace cells expressing alpha11. Another aim is to measure cell dynamics through the fluorescence signal in mice where genes involved in fibrosis or tumor development are conditionally inactivated.

Current challenges in the field
In basic integrin research, major questions concerns a better and more detailed understanding of molecular mechanism of integrin function. This is especially true after recent findings suggesting that collagen-binding integrins do not bind fibrillar forms of collagens in mature tissues in vivo, limiting their role to dynamic situations involving tissue remodeling.

In the field of tumor fibrosis the lack of good fibroblast and myofibroblast biomarkers to better monitor fibroblast heterogeneity in pathology is attracting major attention.

What has it meant for your group to be part of CCBIO so far?
"Being part of CCBIO has meant being part of an intellectually stimulating environment both during seminar series and the annual Solstrand symposia. It has offered an opportunity to establish open collaborations, which would not have been possible otherwise." ••



RESEARCH GROUP:

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Moses, Mussime, PhD student
Grønning, Mona, chief engineer
Lu, Ning, PhD, senior laboratory engineer
Mohamed, Fatima, master student

ORAL CANCER

ANNE CHRISTINE JOHANNESSEN GROUP

Research focus
To identify molecules of importance for oral cancer (OSCC) development, in order to identify patients at risk for developing oral cancer from premalignant lesions, and to reveal targets for more efficient, individualized therapy of oral cancer.

Projects
• Development and validation of a molecular diagnostic tool for early diagnostic and personalized treatment of oral cancer in Western Europe, North Africa and South-Central Asia. Recent findings point to the importance of oral cancer progression as a result of interactions between cancer cells and the neighboring tumor stroma including the immune system. The group's hypothesis is that a refined classification of oral cancers into subgroups with different prognosis is possible by combining epithelial biomarkers and the analysis of tumor stromal activation and immune response.
• Dissecting the role of miRNAs expressed by tumor associated fibroblasts for progression of oral squamous cell carcinoma, as potential biomarkers. Recent studies have shown the association of aberrant expression of microRNAs (miRNAs) in tumor-associated stroma with cancer progression.

Important results
Project 1: The results of this study suggest that minor cases of OSCC in both Norwegian and the Sudanese population are correlated with HPV infection, and that the activation of fibroblasts at the tumor front is correlated with more aggressive tumors in both Norwegian and Sudanese OSCC patients. Patients with high score FOXP3+ tumors (high infiltration with T reg cells) had a better overall survival (p= 0.04). A novel finding is the correlation between alterations in p53 in the tumor cells and activation of the tumor stroma in OSCC from the Sudanese population.
Project 2: The group has identified 12 differentially expressed miRNAs in oral cancer associated fibroblasts when compared with normal oral fibroblasts. They have successfully developed a chromogen based new method of combining miRNA in situ hybridization with protein immunohistochemistry in formalin fixed paraffin embedded tissues. Flexibility to choose either immunohistochemistry (IHC) or ISH in first step is an added advantage in the group's new method.

Future plans
Project 1: The results obtained so far used the manual method for quantification of the immunohistochemistry for different markers tested. The plan is to use digital quantification as well and to validate the results on other cohorts of patients with different demographical characteristics.
Project 2: The group has selected 4 miRNA from the 12 identified at project 2 and is currently using the combined ISH-IHC method on a cohort of Norwegian patients with OSCC in order to investigate their potential as prognostic biomarkers.

Current challenges in the field
Although new treatment modalities for OSCC have been tested, the prognosis and survival rate has not been improved significantly. Research has shown that OSCC is a very heterogeneous group of tumors, making it even more important to identify a panel of targets for more individualized therapy.

What has it meant for your group to be part of CCBIO so far?
"CCBIO has been an excellent forum to meet and discuss, through seminars and courses arranged by the research school and conferences. For me as a PI, this has also given me a broader research environment and possibilities for new collaboration." ••

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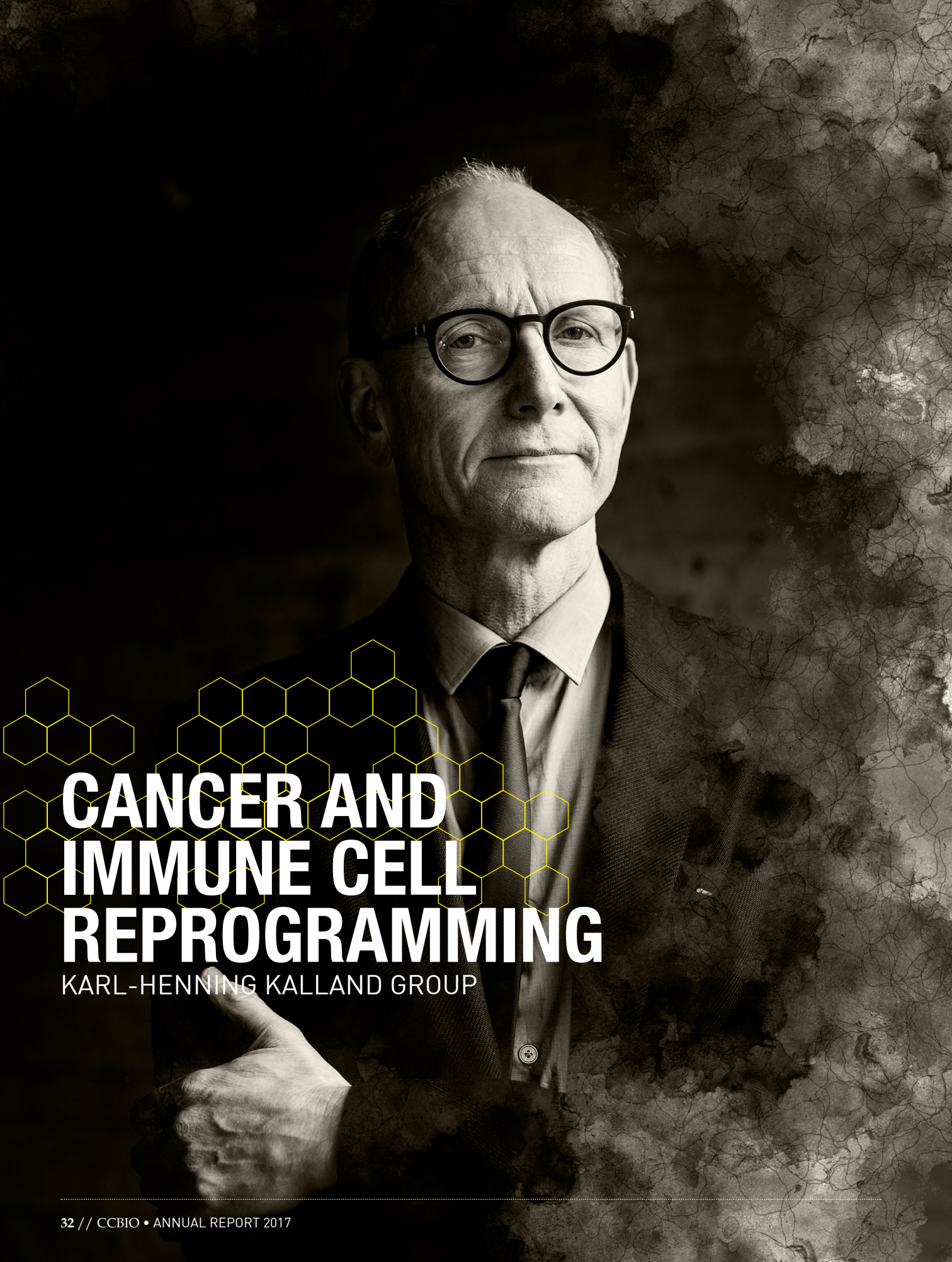


CANCER AND IMMUNE CELL REPROGRAMMING

KARL-HENNING KALLAND GROUP

Research focus
The current research focus of the Prostate Cancer Therapy Research Group is to improve ongoing cryoimmunotherapy (CryoIT) by molecular immunomodulation and development of a dendritic cell based booster vaccine.

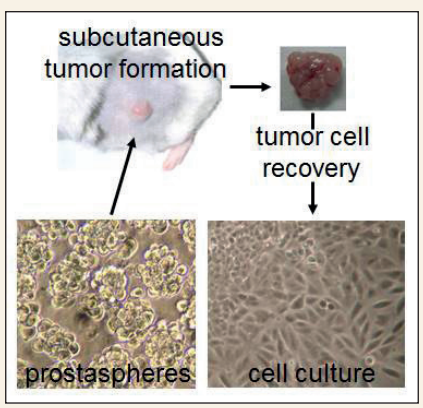
Projects
• Drug Discovery and Developmental Program. The group's newly developed model of stepwise prostate tumorigenesis was used in two different approaches in a drug discovery and development strategy. According to a repurposing strategy, a panel of more than 600 commercially available FDA-approved drugs was screened in an assay to detect compounds with the novel features of inhibition of WNT-β-catenin signaling pathway. Several candidate compounds were found and were extensively experimentally characterized using additional suitable methods.
• In a different drug discovery strategy, a large panel of compounds isolated from Chinese plants and herbs has been screened using a STAT3 activity reporter. Potential STAT3 inhibiting compounds have been found and characterization continues.
• Dendritic cell based cryoimmunotherapy (CryoIT). The ongoing autologous dendritic cell based CryoIT Phase I Clinical trial has by the end of 2017 treated 15 patients with metastatic castration resistant prostate cancer (mCRPC). Interim laboratory, radiological, clinical and research biobank patient data were plotted into a new WebCRF database locked September 15th. Analyses continue into 2018.

Important results
The identification of nitazoxanide as a compound that binds to the enzyme PAD2 followed by citrullination and degradation of β-catenin is a novel mechanism of modulation of β-catenin signaling and was published in Nature Chemical Biology. Additional experimental work on new compounds, molecular targets and molecular mechanisms of β-catenin regulation was published in PNAS and reviewed in Cell Cycle. The generation and examination of fluorescent and luminescent reporter systems of androgen receptor directed transcriptional regulation was published in PLoS ONE. An interim analysis of patients treated in the CryoIT Phase I clinical trial was conducted with encouraging results. In particular, ultradeep TCR-seq indicated that CryoIT was followed by several prevalent new T-cell clonotypes as a reflection of new immunity.

Future plans
The CryoIT clinical trial with advanced monitoring and research biobank expansion will continue. A booster strategy of CryoIT immunity will be prioritized if funding of applications will eventually be successful in 2018. The strategy includes development of a dendritic cell based booster vaccine and molecular enhancement of immunity and inhibition of immune tolerance with focus on β-catenin and STAT3 inhibition. Control of immunogenic cell death is one important integrated issue.

Current challenges in the field
The ability to turn tumor associated antigens into new, effective targets of the immune system on a personalized basis remains a critical challenge. There is a need to enhance anti-cancer immunity to sufficient therapeutic efficacy and at the same time to control induction of autoimmunity. Biomarker development to improve immunomonitoring is important.

What has it meant for your group to be part of CCBIO so far?
"It is a motivation to be part of CCBIO in order to meet the expectation that excellent science should be achieved. Both national and international scientific interactions have been stimulated. The international evaluation of the first period and the award of the second Centre of Excellence period strongly encourage ongoing and upcoming research." ••



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Bakke, Ragnhild Maukon

Technician:
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MECHANISMS OF TUMOR CELL PLASTICITY

JAMES LORENS GROUP

Research focus
The aim is to understand the molecular mechanisms of acquired drug resistance. Tumors are remarkably heterogeneous, the result of selective forces acting on genetically unstable tumor cells during cancer development and progression. Phenotypic plasticity, a feature of cancer spread and treatment resistance, endows tumor cells with astonishing functional flexibility that allows adaptation to different niches within the dynamic tumor microenvironment.

Projects
• Study of the role of the Axl receptor tyrosine kinase in the phenotypic plasticity of adult epithelial stem cells. Results show that Axl signaling is coopted during breast tumorigenesis, providing a rationale for its widespread expression in cancer.
• Axl is broadly associated with malignancy, drug resistance and poor patient survival, and further associated with evasion of anti-tumor immunity. Axl regulates both tumor cell plasticity and anti-tumor innate immunity in the tumor microenvironment.
• The vitamin K-antagonist warfarin, a popular anti-coagulant in clinical use, has anti-tumor activity attributed to the disruption of vitamin K-dependent post-translational modification of the Axl ligand, Gas6. Warfarin inhibits malignant traits and enhances anti-tumor immune responses. The group investigated the association between the warfarin use and cancer incidence in a large Norwegian population cohort. The results revealed a remarkable reduction in cancer incidence associated with warfarin use across tumor types.

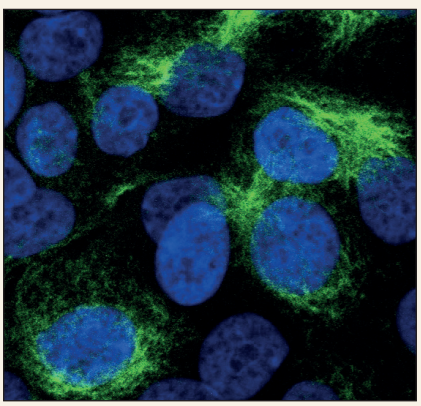
Important results
In Ludvig, et al. (2017) the group showed in collaboration with Rolf Brekken (Dallas) that Axl kinase inhibition blocked the aggressive traits of pancreatic cancer cells and enhanced the efficacy of gemcitabine in patient-derived xenografts and late-stage murine models by targeting the tumor-immune interface. Axl inhibition drove tumor cell differentiation and reversed gemcitabine resistance mechanisms, and potentiated an immune stimulatory microenvironment by targeting immune suppressive myeloid cell types.

In Haaland et al. (2017) the group reported that use of the anticoagulant warfarin was associated with a lower risk of new cancers in people over 50 years. This population-based cohort study using Norwegian national registry data comprised 1.25 million Norwegians. In the subgroup of people using warfarin for atrial fibrillation or atrial flutter, cancer risk was lower at any site and in all four common sites (lung, prostate, breast, and colon). Warfarin, used by millions of adults worldwide, may be associated with lower cancer incidence across a broad range of malignant neoplasms.

Future plans
The group has established state-of-the-art mass cytometry methodology to allow high dimensional measurement of phenotypic variation in the tumor microenvironment. They are studying how vitamin K-dependent post-translational modifications of Gas6 regulate Axl cell signaling, how Axl signaling supports phenotypic plasticity reprogramming and how this affects tumor-immune cell interactions. Based on mechanistic insights, the group will evaluate new biomarkers and immunotherapeutic combinations based on Axl targeting.

Current challenges in the field
In spite of the significant advances in new anti-cancer treatments that provide significant clinical responses, most patients still do not achieve long-lasting clinical benefit. Cancer cells invariably elude treatment through acquired drug resistance, reemerging as advanced, disseminated malignancy that is associated with increased mortality.

What has it meant for your group to be part of CCBIO so far?
"In addition to providing important financial support for our research program, CCBIO represents an impactful scientific environment and ideal training setting for young scientists. The array of prominent international adjunct professors and the quality of the CCBIO Annual Symposium have enriched the Bergen cancer research community." ••



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TRANSCAPILLARY EXCHANGE

ROLF REED GROUP

Research focus
The research focus is on the how the extracellular matrix participates in determining the properties of the tumors and how this in turn is reflected in growth and metastasis. Additional foci have been on how collagen binding integrins influence these properties and also how tumor hypoxia does the same.

Projects
Projects have focused on:
• The interaction between the collagen binding α11 integrin and integrin α11β1 to determine biophysical tumor properties, growth and metastasis
• Effect of hyperbaric oxygen treatment on tumor growth and properties as well as metastasis and metastatic profile
• Collaboration with the Akslen and Gullberg groups on the use of monoclonal antibodies against human α11 integrin as a biomarker for human cancer

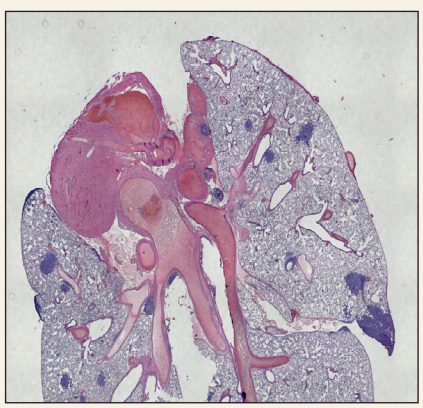
Important results
The long term project is on the in vivo interaction between collagen binding integrins, in particular α11β1 and the αVβ3 which is a non-collagen binding integrin, and which seems to take over the role of the collagen binding β1-integrins. The project investigates the properties of different tumor cell lines in mice with deletion of either one of these integrins. The studies demonstrate that both the matrix and the specific cell lines will affect tumor properties.

One study (published 2017) used four different cell lines that were exposed to normoxia or hypoxia alone or in combination with Transforming Growth Factor -β1 or Jagged-1 that are known to induce EMT, were investigated one by one. Importantly, it was found that one factor alone induced mesenchymal morphology in isolated breast cancer cells, but did not induce full EMT. Another study published in 2017 is an extension of a previous study which demonstrated that hyperbaric oxygen treatment (HBOT) attenuated tumor growth and shifted the phenotype from mesenchymal to epithelial (MET) in the DMBA-induced mammary tumor model. The new study investigated the effect of HBOT on tumor growth, angiogenesis, chemotherapy efficacy and metastasis in a triple negative (MDA-MB-231) and a triple positive (BT-474) breast cancer model in NOD/SCID female mice. HBOT significantly suppressed tumor growth in both the triple positive and negative tumors, and decreased proliferation, the number metastases and reduced expression of N-cadherin, Axl and collagen type I. The similar suppressive effect of HBOT on the two cell lines indicates that they share a common oxygen dependent anti-tumor mechanism. Notably, HBOT also reduced the number of metastatic lesions in the triple negative model.

Future plans
The group will continue to study the interaction between the matrix and cancer cells in determining the tumor's properties as well as growth and metastatic profile. They will also investigate the effect of hyperbaric oxygen further, and initiate the use of PdX models in their studies.

Current challenges in the field
The role of oxygen including hyperbaric oxygen is an important challenge, as well as collagen fiber network and its role in tumor biology.

What has it meant for your group to be part of CCBIO so far?
"CCBIO provides an expanded network and stimulating research environment for collaborations locally and through its overall network." ••



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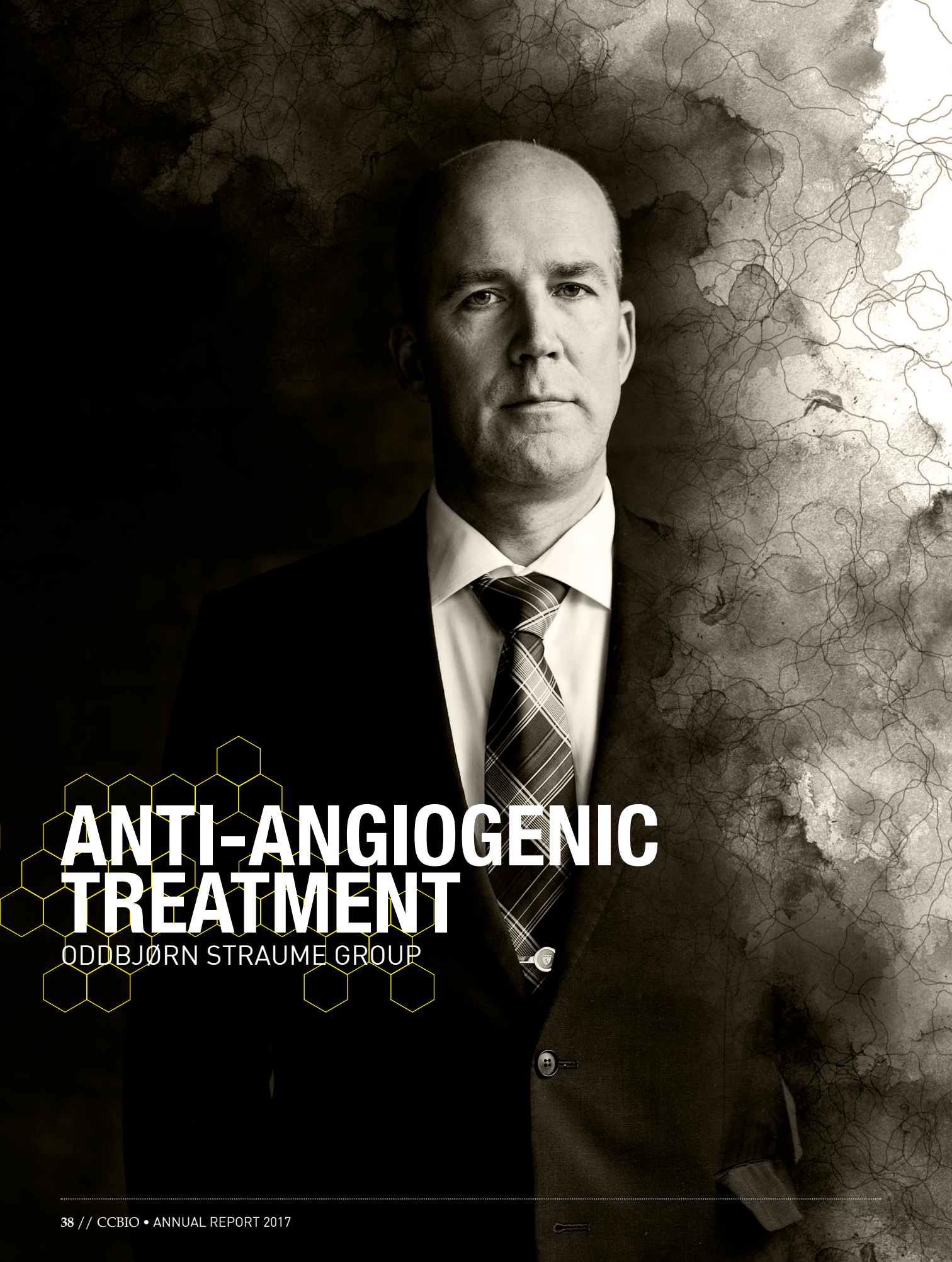


ANTI-ANGIOGENIC TREATMENT

ODDBJØRN STRAUME GROUP

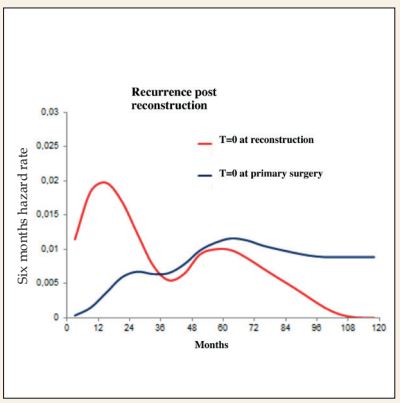
Research focus
The main research goal is to identify predictive biomarkers in clinical materials. The group studies population based patient series, clinical trial series as well as single cancer patients treated in the clinic.

Projects
• Clinical trial: A Phase Ib/II randomised open label study of BGB324 in combination with pembrolizumab or dabrafenib/trametinib compared to pembrolizumab or dabrafenib/trametinib alone, in patients with advanced non-resectable (Stage IIIc) or metastatic (Stage IV) melanoma. Main objective is to analyze safety and efficacy of BGB324 in combination with MAPK inhibitors and immunotherapy as well as to identify predictive markers of response.
• Clinical trial: A National, Multicenter, Interventional Study in Patients with Unresectable or Metastatic Melanoma (IPI4). The goal is to identify predictive value of VEGF related biomarkers in the trial.
• Clinical trial: Efficacy of bevacizumab monotherapy in treatment of metastatic melanoma and predictive value of angiogenic markers. The goal is to analyze predictive markers of response in liquid biopsies.
• Clinical trial: Predictive markers of response to sunitinib in treatment of metastatic renal cell carcinoma. The goal is to analyze predictive markers of response in liquid biopsies and biopsies.
• Research project: Importance of physical trauma on time to recurrence after primary treatment of breast cancer. Analyzing patient series as well as blood samples from patients undergoing different types of breast surgery as well as burn injury patients. The project is based on the hypothesis that dormant micrometastases can initiate tumor growth following a systemic burst of growth factors after surgery or trauma.
• Research project: The Role of the Epithelial-to-Mesenchymal Transition (EMT) and Cancer Stem Cell Traits in Breast Cancer Metastasis. Analyzing the role of activation of the EMT associated Axl receptor in initiation and progression of breast cancer.
• Research project: Targeting Cancer Stem Cells with Axl Receptor Inhibitors to Improve the Treatment of Cancer. Using different preclinical models to study efficacy of the Axl inhibitor BGB324 in cancer. In particular, the combinations of BGB324 with immune check point inhibitors are encouraging.

Important results
Selected results from the projects above:
1: Seventeen patients have received treatment in the trial as of Jan 2018. Four more regional centers have initiated inclusion of patients.
3: In melanoma patients treated with bevacizumab, strong expression of Activin A, Interleukin 1β and urokinase type Plasminogen activator receptor in metastases was significantly associated with objective response, as well as with markers of activated angiogenesis.
4: The group has found that IL6, IL6R and CRP are important biomarkers in renal cell carcinoma patients treated with sunitinib.
6: Warfarin, that has an Axl inhibitory role, is associated with reduced incidence of different cancers in a large registry based study of the Norwegian population.

Current challenges in the field
The lack of reliable and robust predictive biomarkers of response to treatment for cancer is a major challenge.

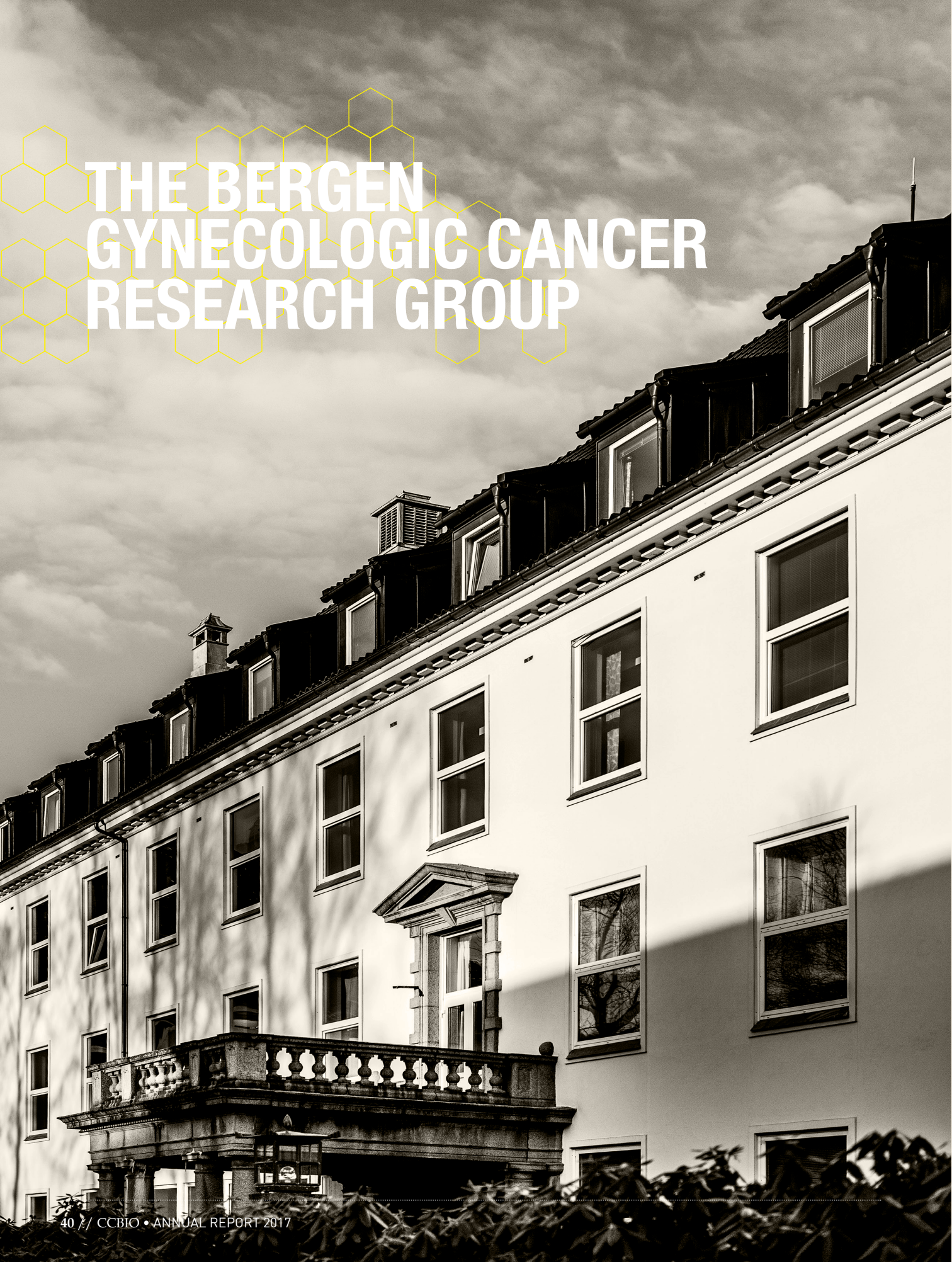
What has it meant for your group to be part of CCBIO so far?
"To be part of the CCBIO family opens up for the possibility to collaborate with different research groups with different approaches both nationally and internationally. This has been a major advantage for our projects and opens up many doors. Long term funding of research gives us the opportunity to initiate large and complex projects, such as clinical trials, and allows us to focus in depth." ••



RESEARCH GROUP:

Straume, Oddbjørn, MD, PhD, group leader
Schuster, Cornelia, postdoc, MD, PhD
Pilskog, Martin, PhD candidate, MD
Haaland, Gry, PhD candidate, MD
Davidsen, Kjersti, PhD candidate, MD
Dillekås, Hanna, PhD candidate, MD

THE BERGEN GYNECOLOGIC CANCER RESEARCH GROUP



Research focus
The Bergen Gynecologic Cancer Research Group focuses on identifying molecular alterations underlying initiation and development of gynecologic cancers.

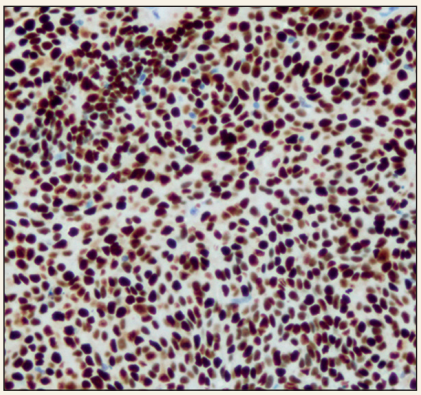
Projects
• To identify biomarkers for gynecologic cancers. The group has establishd the usefulness of Estrogen Receptor (ER), Progesterone Receptor (PR) and Androgen Receptor (AR) as biomarkers in endometrial cancer. The MOMATEC2 study (NCT02543710), a phase 4 implementation trial, is ongoing for validation of ER/PR status to stratify for lymphadenectomy in endometrial cancer.
• Molecular profiling of paired primary and metastatic endometrial cancer. Results were published in Nature Genetics in 2016 and is continued in collaboration with Professor Beroukhim, The Broad Institute, USA. For cervical cancer, genetic alterations linked to molecular subtypes of cervical cancer are studied in collaboration with Professor Ojesina, UAB, USA.
• Combining molecular biomarkers and genetic data with imaging parameters derived from PET-CT and/or MRI provides exciting information on tumor characteristics and potential new imaging-based preoperative biomarkers. Both imaging and molecular biomarkers are explored in endometrial cancer orthotopic mouse models, based on cell lines or patient-derived xenograft (PDX) models. These models are also used for drug testing and validation of predictive biomarkers.

Important results
The team identified PBK expression and preoperative imaging as promising biomarkers in early endometrial neoplasia. L1CAM was found to be a predictive marker for lymph node metastases in preoperative curettage specimens and plasma samples in endometrial cancers. The team found high expression of glucocorticoid receptors (GR) to significantly associate with markers of aggressive disease and poor survival, also in multivariate analysis. GR may represent a therapeutic target in the adjuvant therapy of poor prognosis early-stage as well as metastatic endometrial cancer. With a focus on identifying therapeutic targets in metastatic disease, the team found that loss of HER2 expression is common in metastatic endometrial cancer lesions. Assessment of HER2 levels in metastases may be important to define the potential benefit of anti-HER2 treatment.

Future plans
The research group will continue to explore genetic alterations linked to progression of endometrial cancer from primary tumor to metastasis and increase the focus on genomic alterations linked to cervical cancer. They will continue the MoMaTEC2 trial and collect Quality of Life (QOL) data during follow-up of endometrial cancer patients. They will also perform functional studies of identified driver genes, and study the complexity of hormones in endometrial cancer with a goal of exploring effects of drugs that are already approved for other cancers.

Current challenges in the field
With a tight link between endometrial cancer and obesity/high age, the incidence of endometrial cancer is expected to rise. Identifying specific patient populations that are likely to respond to therapy is therefore even more important.

What has it meant for your group to be part of CCBIO so far?
"CCBIO offers an excellent network of researchers in the field of cancer, and allows close collaborations between research groups with similar focus but different expertise. The CCBIO Seminars and the CCBIO Annual Symposium are great venues to interact and develop collaborations and future projects. The CCBIO Research School has been important in the training of PhD students in the group and has also provided teaching opportunities for senior researchers." ••



RESEARCH GROUP:

Senior staff:
Krakstad, Camilla, professor, MS, PhD, group leader
Haldorsen, Ingfrid, adjunct professor, MD, PhD
Trovik, Jone, professor, MD, PhD
Werner, Henrica, MD, PhD

Clinical staff:
Valen, Ellen, study nurse
Enge, Elisabeth, study nurse

Postdoctoral fellows/scientists:
Høivik, Erling, MS, PhD
Onyango, Therese Bredholt, MS, PhD
Elin Strand, MSc, PhD
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PhD candidates:
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Fonnes, Tina, VET
Halle, Mari Kyllesø, MS
Mauland, Karen, MD
Ytre-Hauge, Sigmund, MD
Edelvik, Kristine Fasmer
Åse, Hildegunn, MD
Dybvik, Julie, MD
Engerud, Hilde, MD

Technical support:
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Madissoo, Kadri, MS
Berg, Hege Fredriksen, MSc

Medical students:
Mjøs, Siv
Myrvold, Madeleine


ASSOCIATE
INVESTIGATORS

PRECISION MEDICINE IN OVARIAN CANCER

LINE BJØRGE

Research focus
The main research focus is ovarian cancer, and the aim is to translate data from comprehensive molecular profiling into clinical meaningful strategies to improve prevention and individualized patient care. The main focus for the translational research portfolio is biomarker studies, preclinical models and early as well as late phase clinical studies. Dr. Bjørge is the principal investigator for two projects funded by the European Commission and national coordinator for different international phase II and III studies on treatment of gynecological cancer. Together with Emmet McCormack, Bjørge has established the research group INOvA (Innovative Novel Ovarian cancer treatment Approaches).

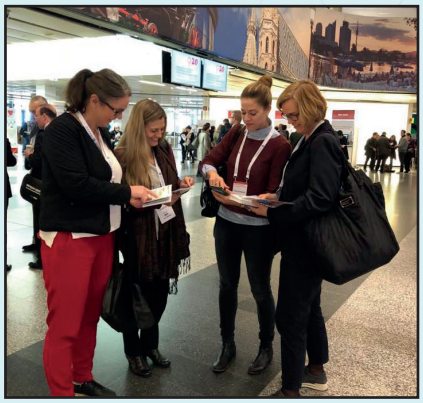
Projects
The following projects are ongoing:
• Female cancer prediction using cervical omics to individualize screening and prevention (FORECEE, https://forecee.eu)
• Prediction of platinum response in ovarian carcinomas (RESPONSE)
• Precision medicine in epithelial ovarian cancer – The role of tumor biology for surgical outcomes
• Image-Guided Surgery (IGS) and Personalised Postoperative Immunotherapy To Improving Cancer Outcome (ISPIC, http://www.ispic.eu)
• Bioprofiling in patients undergoing treatment with targeted therapeutics
• Development and validation of a molecular tool for more precise diagnosis and personalized treatment of oral and vulva carcinomas

Important results
The INOvA team has identified a theranostic platform for imaging-guided surgery in ovarian cancer and established a portfolio of different preclinical animal models for ovarian carcinoma. Further the groups have initiated its very first investigator initiated early phase clinical study entitled: IMPACT: A phase 0 non-randomized Window-of-Opportunity study of novel and repurposed therapeutic agents in women triaged to primary surgery for advanced epithelial ovarian cancer in stages IIIa - IV.

Future plans
Through the use of mass cytometry and omics analysis the INOvA team aims to establish an immunogram and identify debulking signatures for epithelial ovarian cancer, respectively. The preclinical animal model portfolio for ovarian cancer will be further expanded and used to explore image-guided-surgery and immunotherapeutic strategies. During fall 2018 the group's second investigator initiated clinical study will be initiated. It is named INFLUENCE: The influence of cytoreduction on patient-reported outcomes in patients with epithelial ovarian cancer.

Current challenges in the field
Based on the improved recognition of cellular and molecular diversity, a more refined personalized approach to research and clinical trials for ovarian cancer is needed. A roadmap for research priorities has been suggested, including development of better experimental models, characterization of the tumor microenvironment, better understanding of clonal diversity, recurrent disease, exceptional responders, and improved value of surgical cytoreduction. Furthermore, as progress is being made in prolonging the survival of ovarian cancer patients, recognizing how the disease itself, as well as the treatment, may interfere with the patients' overall wellbeing and quality of life is critical.

What has it meant for your group to be part of CCBIO so far?
"The CCBIO platform represents a strong scientific fundament for collaboration, education and training as well as economic support. New and fruitful collaborations have been established both with groups in Bergen and abroad. The education platforms instituted have represented fruitful structured training programs (research school, annual meetings, seminars, and bioinformatics group) for both junior and senior researchers. Funding of both positions and running cost have been important both for initiation of new project and maintenance of ongoing projects." ••



RESEARCH GROUP:

Bjørge, Line, professor, medical director, MD, PhD, MBA, group leader
Anandan, Shamundeeswari, MSc, early stage researcher, PhD candidate
Bischoff, Katharina, MD, PhD candicate
Torkildsen, Cecilie Fredvik, MD, PhD candidate
Enge, Elisabeth, study nurse
Kleinmanns, Katrin, MSc, early stage researcher, PhD candidate
Dongre, Harsh, MSc, PhD candidate


ASSOCIATE
INVESTIGATORS

TRANSLATIONAL MOLECULAR IMAGING IN CANCER

EMMET MCCORMACK

Research focus
Main motivation of the group is the development and effective translation of novel therapies and imaging strategies for the treatment of cancer, particularly cancers with limited therapeutic options. It is the group's belief that the current dogma of rushing novel pharmaceuticals through inappropriate preclinical models is one of the major reasons for their limited clinical penetration. This can only be solved through multidisciplinary development of preclinical surrogates, models and diagnostic tools that more accurately mimic clinical conditions. Subsequently, the development of patient derived xenograft models in haematological malignancies (in collaboration with Professors Øystein Bruserud and Bjørn Tore Gjertsen), gynecological cancers (in collaboration with Professors Line Bjørge and Camilla Krakstad) and pancreatic cancer (in collaboration with Professor Anders Molven and Dr. Dag Hoem) in Bergen has been performed, in addition to application of multimodal imaging for use in evaluation of novel therapies. The group now has multimodal imaging of over 40 personalized cancer models, spanning most cancer phenotypes in addition to lab-on-a-chip scaffolds for greater in vitro understanding of the bone marrow microenvironments.

Projects
• SonoCURE explores the application of Sonoporation (the transient formation of pores in cells by microbubbles activated by ultrasound) in the treatment of Pancreatic Ductal AdenoCarcinoma (PDAC). The application aims to preclinically elucidate, evaluate, and potentiate a new era of sonoporation theranostics for PDAC through application of innovative biomarker mining, organoid models and preclinical modelling.
• PreLIM focuses on the development of novel preclinical models of leukemia and lymphomas in the development of novel targeted and immune- therapies, and exploration of microenvironmental factors critical to disease development and emergence of resistant clones.
•Throug the InoVa project, the group is developing the application of image-guided surgery, whereby fluorescent dyes will target biomarkers on surgically amenable cancers to aid their greater resection.

Important results
The SonoCURE team have demonstrated the preclinical development and participated in the clinical application of sonoporation in a world's first clinical trial in pancreatic ductal adenocarcinoma. In this study, patients survived on average 17.6 months, compared with 8.9 months through the simple addition of sonoporation to a standard of care treatment protocol.

The PreLIM team contributed to the development of a novel combination of two small molecule inhibitors of JAK and Bcl-2, which synergised in AML.
InoVa purchased the first preclincal system for fluorescence-guided surgery of cancer. This equipment will aid resolution of malignant tissue from normal tissue and should aid the easier visualisation of metastasis, critical in the surgical resection of gynaecological cancers.

Future plans
Novel bubble delivery systems are being developed within the group which should permit the precise delivery of a drug payload through sonoporation. Furthermore, to aid swift clinical translation, they are developing a number of innovative organoid and immunocompetent patient derived xenograft models to accurately reflect patients pancreatic ductal adenocarcinoma, ovarian carcinoma, leukemia and lymphomas. Evolution of the image-guided surgery system into the treatment of dogs with sarcomas is anticipated in 2018, providing a novel strategy for veterinary oncology care and a unique opportunity to translate observations in companion animals to the clinic.

Current challenges in the field
Development of relevant preclinical models and imaging modalities that will impact the lives of our patients.

What has it meant for you to be part of CCBIO so far?
«Being a CCBIO affiliate has led to new collaborations and opportunities for research funding that otherwise would have been very difficult.» ••

RESEARCH GROUP:

Senior staff:
Mc Cormack, Emmet, professor, PhD, group leader
Kotopoulis, Spiros, senior researcher, PhD
Bredholt, Geir, researcher, PhD
Leitch, Calum, researcher, MSc
Fonnes, Tina, researcher, cand.med.vet.

Technical staff:
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Fosse, Vibeke, veterinarian, DVM
Han, Jianhua, staff engineer,MSc, MD
Popa, Mihaela Lucia, veterinarian, DVM
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Thodesen, Elisa Ulvøen, staff engineer, MSc
Xing, Zhe, staff engineer, PhD, DDS, MMed

Postdoctoral fellows:
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de Garibay, Gorka Ruiz, PhD

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Bergsjø, Louise Emblem, MSc
Bischof, Katharina, MD
Bjånes, Tormod Karlsen, MD
de Jalón, Elvira García, MSc
Dowling, Tara Helen, MSc
Engen, Caroline Benedicte Nitter, MSc
Haugse, Ragnhild, MSc
Kleinmanns, Katrin, MSc
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Shafiee, Sahba, MSc
Stigen, Endre, MSc

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Karlsen, Ida, BSc
Lam, Christina, BSc
Rozmus, Ezekiel Richard, BSc
Sundøy, Silje Maria, BSc


ASSOCIATE
INVESTIGATORS

HEALTH ECONOMICS

JAN ERIK ASKILDSEN AND JOHN CAIRNS

Research focus
Health economics at CCBIO is concerned with two major research problems: what is the cost-effectiveness of biomarkers, and how does the interplay between the diagnostic market and the pharmaceutical market affect incentives to invest in R&D for cancer biomarkers, termed the industrial organization of biomarkers. The Health Economics Research Group is located at the Department of Economics, University of Bergen, in close cooperation with the London School of Hygiene and Tropical Medicine (LSHTM) in the UK.

Projects
The primary project is in the form of a PhD being undertaken by Kelly Seo. The overall aim of this PhD is to inform the potential value of biomarkers throughout the process of technology development. To do this, a generic economic model will be developed integrating cost-effectiveness analysis and value of information analysis. The first stage is a systematic literature review on economic evaluations of predictive biomarkers in oncology. This will provide a systematic and critical review of the cost-effectiveness of predictive biomarkers and modeling approaches used in previous studies. As part of this wider review, an initial review of biomarkers and targeted therapies for metastatic colorectal cancer (mCRC) has been completed.

Another ongoing project (undertaken jointly with Beatriz Luis) is examining the impact of cancer biomarkers on health outcomes in Norway. It addresses two research questions: has the introduction of cancer biomarkers had a positive impact on health outcomes in the Norwegian population, and what is the difference in premature mortality in Norway between targeted therapies with and without companion diagnostics?

Important results
Cancer biomarkers for targeted therapies in mCRC improve the cost-effectiveness of targeted therapies. However, this does not ensure that the therapies themselves are cost-effective. While companion biomarkers reduce therapy costs, the savings are not sufficient enough to make these treatments cost-effective. The studies that evaluate biomarkers have often restricted attention to the cost of tests and do not always consider the characteristics of the test or the prevalence of the marker.

Current challenges in the field
A specific continuing challenge is to capture accurately the health benefits from adopting new health technologies. These arise in two areas in particular: the time to event analyses and the valuation of different health states which underlie the estimation of quality-adjusted life-years (QALYs). A broader challenge of increasing importance is how to decide which health technologies should be introduced in routine clinical practice. As clusters of new drugs arrive in close succession, the challenge is to make a timely determination of which should be adopted, particularly as treatment strategies become more stratified (possibly as a result of increased use of biomarkers). An excellent example of this is the treatment of non-small cell lung cancer.

What has it meant for your group to be part of CCBIO so far?
"Being part of CCBIO has facilitated greater focus on the economic evaluation of cancer therapies. It has also provided additional opportunities to challenge the assumptions underlying our economic analyses. It has been stimulating to teach health economics in CCBIO903 Cancer research: Ethical, economic and social aspects with CCBIO colleagues who are experts in the broader issues underlying cancer research." ••

RESEARCH GROUP:

Cairns, John, professor, associate investigator
Askildsen, Jan Erik, professor, associate investigator
Gabrielsen, Tommy Staahl, professor
Riise, Julie, associate professor
Seo, Mikyung Kelly, PhD candidate
Luís, Ana Beatriz Mateus D'Avó, PhD candidate


ASSOCIATE
INVESTIGATORS

BIOINFORMATICS

INGE JONASSEN

Research focus
The primary focus of the group, in collaboration with the Akslen group, is the development and application of computational deconvolution methods for decomposing transcriptome data from samples composed of a combination of tumor cells and the surrounding and supporting microenvironment. The research aims to decompose computationally the signal into that originating from the tumor cells and those originating from other tissues/cell types in the sample. This will be an enabling step towards studying the interactions between tumor cells and the environment and integrating them into the research along the continuum from diagnosis to treatment and outcome.

Projects
The group's first objective was to analyse several public benchmark transcriptome datasets (microarray and RNA-Seq) with a variety of deconvolution methods, test their performance and find out which of the mathematical assumptions reflect biological reality to a sufficient degree and can lead to more robust results. On a second level, they developed a new computational method that addresses several computational challenges and they show extensively the performance of the group's method relative to other state-of-the-art methods (manuscript under review) based on the benchmark data. The group's proposed approach on breast cancer data was further tested and biologically consistent results were found. In this framework, they also developed SelGenes, a tool for selecting marker genes (i.e. genes highly specific for a tissue/cell type) for the cell types included in heterogeneous samples (published in master thesis). The performance of the group's approach was tested both on the benchmark data and on cancer data and biologically consistent results were found. Another focus of the group is the development and application of systems biology integrative approaches. In collaboration with the Akslen group, they applied a subpathway enrichment analysis approach to reveal mechanisms that change between tumor samples with high and low Nestin expression, associated with the basal-like phenotype in breast cancer. Moreover, in collaboration with the Biosignal Lab (Professor Anastasios Bezerianos, University of Patras, Greece), the group developed a time-varying method for microRNA-mediated subpathway enrichment analysis. The tool was tested on interferon-gamma (IFN-g) stimulated melanoma cells.

Important results
One manuscript has been submitted in collaboration with the Akslen group on the development of a novel computational method for in silico deconvolution of complex gene expression data. Results on subpathway enrichment analysis in relation to Nestin expression in breast cancer subtypes was published by Krüger et al. (Sci Rep 2017).

Future plans
The group is working toward utilizing single cell mass cytometry data together and integrate this with transcriptional data in order to understand cells' signaling status and downstream effects on gene transcription. For this they have sought collaboration with systems biology groups to jointly develop a systems understanding of relevant signaling pathways and link this with therapy response in experimental model systems aiming to personalized systems medicine.

Current challenges in the field
Capitalizing on novel experimental approaches giving molecular biology data on different levels of resolution through innovative data analysis and modelling approaches, and to perform this in close collaboration with the domain experts to enable tight integration between our work and experimental follow-up and verification.

What has it meant for your group to be part of CCBIO so far?
«Being part of CCBIO has given us the possibility to work closely with other groups, including those at CCBIO, in a more long-term focused manner to develop novel methodologies and to test these on relevant data sets in the context of the center. Being part of the center, also gives us opportunities for collaborative research.» ••

RESEARCH GROUP:

Jonassen, Inge, professor, group leader
Dimitrakopoulou, Konstantina, postdoc
Kjørsvik, Øystein, master student


ASSOCIATE
INVESTIGATORS

GLOBAL HEALTH PRIORITIES

OLE FRITHJOF NORHEIM

Research focus
Norheim's team is interested in how cancer biomarkers can inform health care priority setting. Fair and good priority setting is needed, also in high-income countries. The gap between what is medically possible and what is sustainable for a health care system is increasing, and oncology is one of the main drivers. Yet, research in oncology may also contribute to solutions.

CCBIO's aim is to discover, validate and translate cancer biomarkers. This will make cancer medicine more personalized. What before were patient groups characterized by common patterns of their cancer will now be individual or small patient groups identified by biomarkers and other individual characteristics. Breast cancer is no longer just breast cancer, and priorities among subgroups will and should differ. This challenges our ethical thinking about treating people as equals.

Projects
The team is currently involved in projects addressing the two priority setting challenges in personalized cancer treatment:
• Investigating (PhD project) how new cancer biomarkers influence treatment recommendations for new and expensive cancer drugs. How will a biomarker influence treatment recommendations? In the project, patient age, another individual indicator of risk and expected benefit, is assessed on how it influence treatment recommendations. The team will examine how decisions are being influenced, and also how we think they should be influenced. These two are not always in harmony.
• Together with the ELSA group, economists and others associated with CCBIO, the team is also developing a joint project that will, among other things, investigate how the development from larger patient groups into smaller and more individualized patient groups better can be understood and addressed when prioritizing, approving and reimbursing new and expensive drugs.

Important results
Preliminary findings indicate that biomarkers now are used by policy-makers to single out subgroups where interventions are more cost-effective than for the average patient. There is also an opposite trend where use of biomarkers leads to more costly drugs for small patient groups.

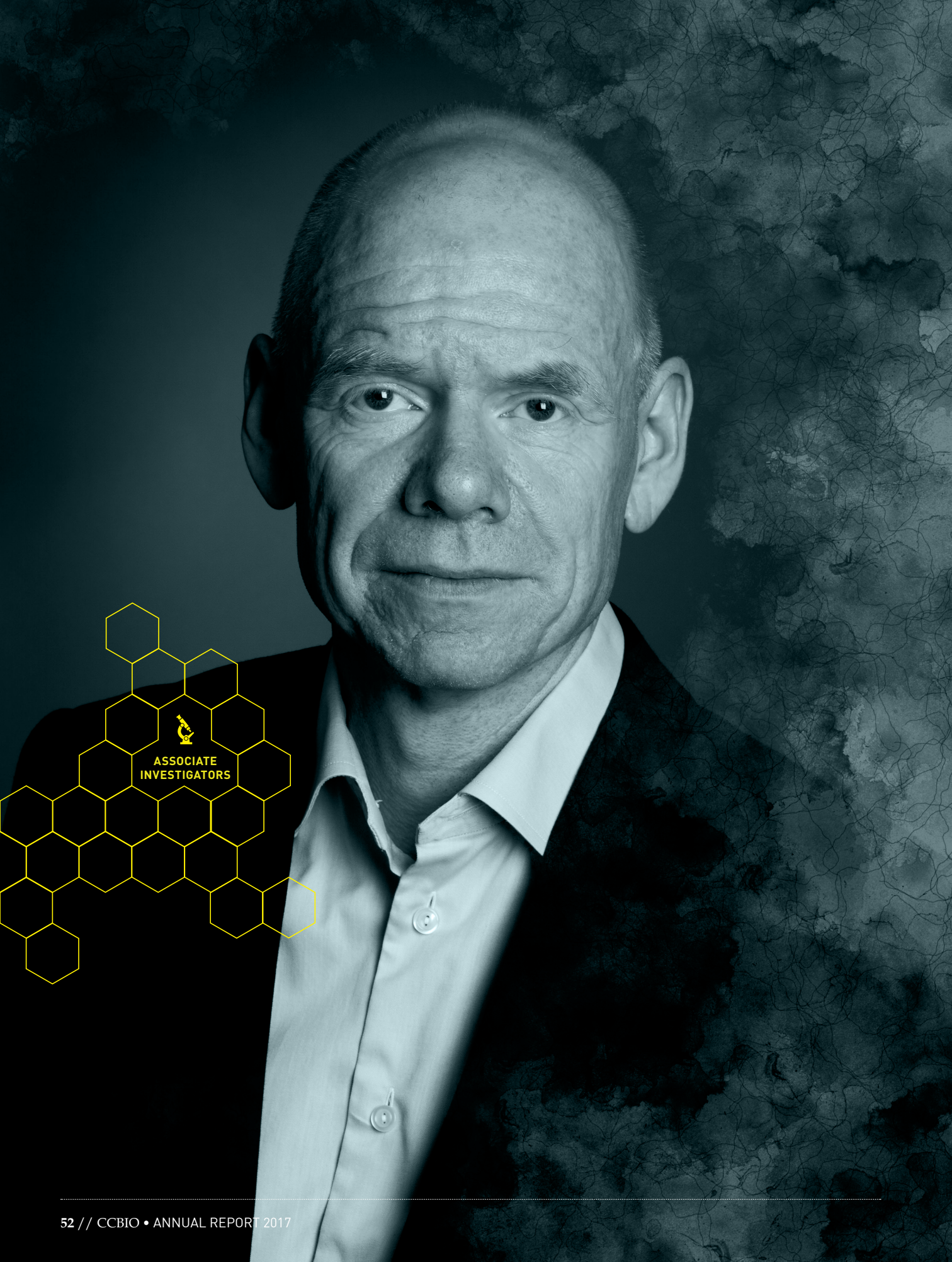
Future plans
The team will continue working on the PhD project, adding more theory of ethics and priority setting to the work, and thereby being able to provide some answers to pressing normative questions. They also work to establish collaboration and a good dialogue with CCBIO clinicians to better understand and integrate the clinical mindset into their work, and possibly seed some thoughts about priority setting into the clinical minds too.

Current challenges in the field
The increasing amount of new and expensive cancer drugs that are entering the marked is a challenge. Sometimes their effect is marginal and prices unreasonable. These drugs will impose a heavy burden on our publicly financed health care system. Hard work and tough decisions are required to make sure that increasingly scarce resources will continue to be distributed in a fair and cost-effective way.

What has it meant for your group to be part of CCBIO so far?
«Being part of CCBIO has given us the possibility to work on the very forefront of medical science, providing a unique opportunity to explore priority setting in this important field, both scientifically and publicly. In addition, we meet and collaborate with fantastic colleagues.» ••

RESEARCH GROUP:

Norheim, Ole Frithjof, professor, MD, PhD, group leader
Tranvåg, Eirik Joakim, PhD candidate, MD


ASSOCIATE
INVESTIGATORS

INTEGRATING ELSA INTO CCBIO

ROGER STRAND

Research focus
Strand's group perform research on the ethical, legal and societal aspects (ELSA) of CCBIO research, distinguishing between two interrelated goals: (1) A better understanding of the developments, expectations and imaginaries of personalized/precision cancer medicine, including its political economy and ethical and social issues; (2) A better integration of this understanding into practices of "responsible cancer research" in the sense of RRI (Responsible Research and Innovation).

Projects
The ELSA group of CCBIO is a small-scale operation that can be seen as one project. They interact and are tightly linked, however, to similar ongoing ELSA and RRI projects funded by the Research Council of Norway's (RCN) BIOTEK2021 program (NorZymeD, AquaFly, Res Publica) as well as Horizon 2020 (HEIRRI). They are furthermore developing a joint project on the opportunities and challenges of precision cancer medicine with a team of CCBIO ethicists, economists and biomedical researchers.

Important results
Strand's group builds insights and intellectual understanding (for peers) and ELSA awareness (within the consortium and its partners and audiences). A central insight is that the quality of a biomarker is a complex issue with scientific and technical but also clinical, economic, ethical and political dimensions. A biomarker may be well validated, informative and elegant from a scientific perspective and still fail because it does not make profit (or even threatens profit) or it is seen as destabilizing some patients' right to a specific treatment. Perhaps an important result is to open up the question "What is a good biomarker?" to include the social and political perspective, and ask if that perspective can be reverse-engineered into the search and design of biomarkers.

Future plans
The group aims to collaborate more with CCBIO ethicists and economists and develop one interdisciplinary humanities and social science team to study the opportunities and challenges of precision cancer medicine. They wish to deepen the collaboration with CCBIO cancer researchers to promote the integration of ELSA perspectives and RRI into practice. Furthermore, the group will continue their European and US collaborations on the more conceptual research into RRI and the coproduction of science, technology and society. Finally, they plan to take a more active and visible stand vis-à-vis the Norwegian society and public sphere.

Current challenges in the field
There is the challenge of practical relevance. Research in the field of Science and Technology Studies has produced thousands of pages of excellent empirical study and theoretical analysis of the challenges and opportunities of modern medicine and modern medical research. The latter 15 years we have been challenged also by policy to become relevant to practice and integrate our insights into the daily life of medical research – notably through policy concepts such as ELSA and RRI.

What has it meant for your group to be part of CCBIO so far?
"Francis Bacon said in his 1620 classic "The New Organon": "The men of experiment are like the ant, they only collect and use; the reasoners resemble spiders, who make cobwebs out of their own substance. But the bee takes a middle course: it gathers its material from the flowers of the garden and of the field, but transforms and digests it by a power of its own." Philosophers of science run the risk of resembling spiders. CCBIO gives us access to the flowers, and with it, the opportunity to engage in intellectual exchange in a truly interdisciplinary garden, ranging from the clinical to the preclinical, from medical science to ethics and economics. This is how we should see the CCBIO team in its entirety: A colorful, energetic beehive!" ••

RESEARCH GROUP:

Strand, Roger, professor, group leader
Blanchard, Anne, postdoc
Nygaard, Ina Hannestad, research assistant
Stenmarck, Mille Sofie, medical student
Huse, Karoline, medical student

// CAMILLA KRAKSTAD

Research focus
Identify molecular alterations underlying development and progression of gynecologic cancers.

Projects
• The MOMATEC2 study (NCT02543710) a phase 4 implementation trial, is validating ER/PR status as a biomarker for lymphadenectomy in endometrial cancer.
• To analyze complex genetic data from endometrial cancers (collaboration with CCBIO investigator Beroukhim, USA).
• To study genetic alterations linked to subtypes of cervical cancer (collaboration with Professor Ojesina, USA).
• To explore imaging and molecular biomarkers in endometrial cancer, including orthotopic mouse models, based on cell lines or patient-derived xenograft (PDX) models.

Important results
The team identified PBK expression and preoperative imaging as promising biomarkers in early endometrial neoplasia. L1CAM was found to be a predictive marker for lymph node metastases in preoperative curettage specimens and plasma samples in endometrial cancers.
The team found high expression of glucocorticoid receptors (GR) to significantly associate with markers of aggressive disease and poor survival, also in multivariate analysis. GR may represent a therapeutic target in the adjuvant therapy of poor prognosis early-stage as well as metastatic endometrial cancer.
With a focus on identifying therapeutic targets in metastatic disease, the team found that loss of HER2 expression is common in metastatic endometrial cancer lesions. Assessment of HER2 levels in metastases may be important to define the potential benefit of anti-HER2 treatment.

Future plans
The research group will continue to explore genetic alterations linked to progression of endometrial cancer from primary tumor to metastasis and increase the focus on genomic alterations linked to cervical cancer. Also, functional studies of identified driver genes will be performed.

Current challenges in the field
With a tight link between endometrial cancer and obesity, the incidence of endometrial cancer is expected to rise. Identifying specific patient populations that are likely to respond to therapy is therefore even more important.

What has it meant for you to be part of CCBIO so far?
"CCBIO offers an excellent network and allows close collaborations between research groups with similar focus but different expertise. The CCBIO seminars and the CCBIO annual symposium are great venues to interact and develop collaborations and future projects. The CCBIO research school has been important in the training of PhD students in the group and has also provided teaching opportunities for senior researchers." ••

// ELISABETH WIK

Research focus
To study prognostic and predictive biomarkers in breast cancer, with focus on integrating large-scale omics data and clinico-pathologic information, in particular describing biologic characteristics of breast cancer molecular subtypes.

Projects
• To study angiogenesis related alterations in subsets of breast cancer.
• To study dopaminergic compounds in breast cancer with a potential of repurposing in subsets of breast cancer patients.
• To map tumors of young breast cancer patients.
• To study improved computational diagnostics in breast cancer histopathology.

Important results
Studies on estrogen receptor in endometrial cancer has, along

with other results from the previous Salvesen group, contributed to change of clinical practice and diagnostic work-up for this tumor type at Haukeland University Hospital. Data on the histopathologic assessment of lymph nodes in breast cancer (PhD Sura Aziz) has resulted in change of routine practice for the histopathologic report on lymph node metastases in breast cancer.

Future plans
Independent projects will be established within the Akslen group. Along with follow-up plans for the projects above, the focus will be on characterization of young breast cancer patients. Novel methods for reading the tumor tissue, including computational assessment, will be explored, searching to improve existing diagnostic tools and disease classifications, also with the aim of including ELSA in our studies.

Current challenges in the field
Taking tumor biological complexity and heterogeneity into account in tissue based studies of cancer biomarkers and to integrate different levels of omics data in translational biomarker studies.

What has it meant for you to be part of CCBIO so far?
"Being part of the CCBIO community is a door-opener for research, and I have also learned a lot from teaching and organizing CCBIO activities. Networking with experts in various fields of cancer research has been valuable, and inclusion of the ELSA group in CCBIO has been of great importance." ••

// DANIELA ELENA COSTEA

Research focus
Understanding the role of epithelial-microenvironment interactions in carcinoma progression.

Projects
• Epithelial-mesenchymal interactions in oral and vulvar squamous cell carcinoma. The group is now investigating differences in energy metabolism and epithelial-mesenchymal interactions between HPV- and HPV+ cancer cells and surrounding fibroblasts. This project includes a CCBIO collaboration with Associate Investigator Line Bjørge.
• Exploring the use of electronic nose for diagnosis of head and neck premalignant and malignant lesions. Due to its low costs and simple logistics, this method holds the promise for being developed into a tool for disease screening in developing countries. We test an e-nose device developed by the Aenose Company, the Netherlands, in Sudan, a developing country where head and neck cancer (HNC) poses a major burden of disease.

Important results
Project 1: Preliminary results show that carcinoma cells induce a "reverse Warburg effect" in normal fibroblasts by promoting mitochondrial dysfunction and oxidative stress in different ways that fuel ATP production in cancer cells.
Project 2: A specific breath volatile organic compounds pattern for HNC Sudanese patients has been developed in the hospital settings of Sudan with 81% accuracy.

Future plans
Project 1: To develop specific vectors for clinical trials targeted towards the key molecules identified in this study to play a crucial role in epithelial-mesenchymal interactions.
Project 2: The use of electronic nose method is currently further tested on a larger scale for use as a screening tool for detection of HNC.

Current challenges in the field
As tumors with high mutation rates, HNC should respond better to novel pharmaceuticals, but the results of clinical trials are so far disappointing. This is, at least partly, due to inappropriate preclinical models that use rodent models as preclinical surrogates for human cancer. Therefore, the group directs its efforts to establish human 3D models for HNC and other types of carcinomas, and is using them for testing new methods for targeting epithelial-mesenchymal interactions for impairing tumor progression.

What has it meant for you to be part of CCBIO so far?
"The rapid pace of research activity and the broad range of seminars organized by CCBIO have stimulated our activity and promoted interaction with world-leading scientists. Our newly recruited master and PhD candidates have benefited tremendously by attending the courses organized by CCBIO's research school." ••

INTERNATIONAL FACULTY

CCBIO has a formalized international network based on employing high ranking researchers within various fields of cancer research in 10% adjunct professor and researcher positions. CCBIO's rationale with this network is to establish an array of experienced advisors on scientific projects, collaboration, networks, and research strategy, as well as to perform joint research in the forefront and facilitate the transfer of knowledge. Another important aim is to enable CCBIO's Research School to have research based courses on the highest level and to enable co-supervision and exchange of research- and postdoctoral fellows. By 2017, 13 highly ranked international affiliated investigators are employed in this network, and CCBIO has experienced good results in terms of fruitful collaboration and exchange of knowledge.

// FRÉDÉRIC AMANT

Frédéric Amant is currently professor at the KU Leuven, Belgium and University of Amsterdam, the Netherlands. Professor Amant co-founded the European Network for Individualized Treatment of Endometrial Cancer (ENITEC), a task force within the European Society of Gynecologic Oncology (ESGO). He also heads the International Network on Cancer, Infertility and Pregnancy (INCIP), also within ESGO, and is recognized as a world authority on cancer in pregnancy. Furthermore, he founded the Patient Derived Tumor Xenograft Platform (Trace) at KU Leuven and is a member of the European consortium on xenografts EurOPDX.

Professor Amant was involved in MOMATEC I, a prospective study on endometrial cancer combining serum and endometrial biopsy biomarkers and clinical data. This international collaborative study initiated in Bergen is a source of valuable new data focusing on predictive markers for lymph node involvement and survival. Today, his Amsterdam group supports the continuation of this collaboration in the frame work of MOMATEC II. The second Bergen initiated study tailors surgical treatment of endometrial cancer on the basis of biomarkers, and needs more international support. In addition, he is open to share the TRACE experience

and models with CCBIO, allowing the usage of excellent preclinical models to validate experiments. Eleven models of different tumor types are available and can be shared. In addition, through EurOPDX, more models are accessible. Together with CCBIO based Erica Werner he continues to further develop ENITEC which is the sole uterus focused research group worldwide and continues to grow. Here, collaborations will be updated and new proposals discussed.

// RAMEEN BEROUKHIM

Rameen Beroukhim is currently a physician in the Department of Medical Oncology at the Dana-Farber Cancer Institute, an associate physician in medical oncology at Brigham and Women's Hospital and an assistant professor of medicine at Harvard Medical School. Dr. Beroukhim co-chairs the International Cancer Genome Consortium effort to characterize structural alterations across 2800 cancer whole genomes. He is also a principal investigator of three multi-investigator R01 grants, a U24 grant, and of individual and multi-PI foundation- and industry-funded grants. Dr. Beroukhim's scientific focus is on the genomic features of oncogenesis and cancer progression in brain and other cancers, and the implications of these in identifying novel cancer dependencies, therapeutic strategies, and biomarkers.

The major focus of Dr. Beroukhim's longstanding collaboration with CCBIO has been the genomic characterization of endometrial cancer. Since collaborating on the first integrated genomic characterization of endometrial cancers, identifying chromosomal alterations and RNA signatures that determine prognosis, the teams have since followed up with multiple publications including the first study describing the genomic evolution of large numbers of endometrial cancers through metastasis. The Beroukhim lab highly appreciate CCBIO's collection of endometrial cancer tissue samples with deep clinical, radiologic, and molecular characterization, and hope to continue to leverage these resources for translational discovery. Current collaborations are focusing on generating more detailed descriptions of the endometrial cancer genome as it evolves through treatment and metastasis, integrating these data with radiologic and clinical data to build comprehensive radiogenomic profiles that inform how endometrial cancers develop and evolve, and using these data to interrogate novel treatment approaches in carefully selected endometrial cancer model systems.

//JEAN-CHRISTOPHE BOURDON

Dr. Jean-Christophe Bourdon is currently senior lecturer at the School of Medicine at Dundee University. He became co-director of the Inserm-European Associated Laboratory (Toulouse University, France) in 2006 and was awarded the prestigious fellowship from Breast Cancer Campaign in 2012. Dr. Bourdon's research group is internationally recognised to have pioneered and developed the p53 isoform research field, which has reformed and broadened the p53 field beyond cancer to premature aging and age-related degenerative diseases. Research interests are both in fundamental and translational research. Bourdon's lab aims to decipher the molecular mechanisms of cell fate decision mediated by the p53 isoforms in response to cell signals and treatment. In translational research, Bourdon's lab aim to establish the p53 isoforms as predictive biomarkers and to identify new therapeutic compounds targeting the p53 isoform pathways.

Dr Bourdon has a long lasting collaboration with Professor Bjørn Tore Gjertsen at CCBIO on the development of the p53 isoforms as biomarkers in AML and breast cancer. In addition, Dr Bourdon co-supervise with Professor Gjertsen a PhD project exploring the role of the p53 isoforms in the cell fate decision induced by the new anticancer and anti-metastatic inhibitor of Axl receptor kinase inhibitor developed at CCBIO (BGB324). In future collaborations, Bourdon would like to extend further the use of the p53 isoforms as predictive biomarkers to new compounds developed at CCBIO and to decipher the molecular mechanism of cell response to such treatment. Bourdon would like also to develop new diagnostic tools related to the p53 isoforms in partnership with CCBIO.

// ROLF A. BREKKEN

Professor Rolf A. Brekken is currently at the Department of Surgery at UT Southwestern where he joined as faculty in 2002 and was promoted to associate professor with tenure in 2009 and to professor in 2015. His laboratory is located in the Hamon Center for Therapeutic Oncology Research. Professor Brekken is the Effie Marie Cain Scholar in Angiogenesis Research and Deputy Director of the Hamon Center for Therapeutic Oncology Research. Two therapeutic antibodies Brekken helped develop have entered clinical testing in cancer patients and he recently co-founded a company, Tuevol Therapeutics, which is focused on the development of novel therapies for cancer. Professor Brekken's laboratory studies the tumor microenvironment. In particular his group is focused on three areas: 1) ECM signaling in tumors; 2) therapeutic immune reactivation; 3) how immune cells contribute to the metastatic cascade.

Professor Brekken has an active and longstanding collaboration with Professor Jim Lorens on the function of Axl in tumor progression. The collaboration is focused on Axl biology and the efficacy of Axl inhibition using small molecules and specific Axl mAbs. Brekken also collaborates with Dr. Nils Halberg and Professor Emmet McCormack to investigate the microenvironment of pancreatic cancer. Additionally, he has a joint project with Dr. Randy Watnick at Harvard, which developed through connections made at CCBIO and involves Professors Lars A. Akslen and Jim Lorens.

// HANI GABRA

After 5 years as clinical scientist and head of the ICRF Ovarian Cancer Cell and Molecular Genetics Laboratory in Edinburgh, Professor Hani Gabra took in 2003 up the position as Professor of Medical Oncology, Head of the Molecular Therapeutics Unit and Director of the Ovarian Cancer Action Research Centre at the Imperial College London. He continued in these roles until May 2017 when he took a new role as Chief Physician Scientist/Vice President and Head of the Clinical Discovery Unit at AstraZeneca in Cambridge. He continues in his chair at Imperial College with a reduced commitment.

Professor Gabra was the founding president of the European Translational Ovarian Cancer Network (EUTROC) until 2017, a consortium of 70 centers conducting translational studies and clinical trials in ovarian cancer. He led the Ovarian Cancer Section of the Scottish Gynaecological Cancer Trials Group (SCOTROC), has served on CRUK's CTAAC national clinical trials funding committee, and currently sits on the INCa French Translational Research Funding Committee. Professor Gabra's basic science research interests are in tumor-suppressor biology and cancer multiplatform molecular profiling and integrative OMICS. He has translational research interests in the molecular basis of ovarian cancer platinum resistance as well as all phases of clinical research in gynecological cancer.
In his new role at AstraZeneca, Professor Gabra is involved in new drug develop- ment particularly around ovarian cancer and also in novel approaches to trans- lational/clinical trial design. He hopes that there will be many opportunities for collaboration in this new role with CCBIO in gynaecological and other cancers.

// RITVA HELJASVAARA

Senior Researcher Ritva Heljasvaara joined in 1998 one of the world's leading extracellular matrix (ECM) and collagen research groups led by Professor Taina Pihlajaniemi at the University of Oulu, and is currently the co-director of the group. Together with five other teams at the University of Oulu, their research group forms the Finnish Centre of Excellence in Cell-Extracellular Matrix Research of Academy of Finland for 2012-2017. Dr. Heljasvaara is recognized for her expertise in ECM and tumor biology and for her work on experimental mouse tumor models. Her current research focuses on understanding the functions of the ECM components in skin, breast and hematologic malignancies.
In collaboration with Professor Donald

Gullberg, Dr. Heljasvaara has investigated the role of the fibroblast-specific integrin α11 in skin squamous cell carcinoma (SCC), by subjecting the Itga11 knockout mice to the chemical DMBA/TPA-induced skin carcinogenesis model. The key findings indicate that α11 is upregulated in skin tumor stroma and it has a supportive role in skin tumorigenesis with effects on carcinoma-associated fibroblast (CAF) differentiation, ECM organization and tumor stiffness. Besides scientific research, Dr. Heljasvaara has contributed in teaching at the Matrix Biology PhD course in June 2017, organized by CCBIO and the Bergen Biomedical Research School. In future collaboration with Professors Gullberg and Reed, the aim is to further clarify how α11 regulates fibroblast phenotype, collagen biosynthesis and tumor stiffness.

// MARK LABARGE

Mark LaBarge is currently professor at the Department of Population Sciences, and deputy director of the Center for Cancer and Aging at the City of Hope National Cancer Center, California. Professor LaBarge's principle interests are to understand the role of microenvironment in mammary stem cell fate decisions in the context of aging and breast cancer. The objective of his research is to generate a comprehensive understanding of the effects of aging on the human mammary gland and how the resulting processes may contribute to tumorigenesis. His team is actively engaged in developing strategies to delay the biological effects of aging in the breast as a means of cancer prevention.

Professor LaBarge has a collaboration with James Lorens which has taken shape in three main areas. First, the teams have been using high-dimensional single cell CyTOF-based analyses to quantify stereotypical phenotypic changes in human mammary epithelia with age. They find that the most significant changes that arise with age are in a core of signaling and cytoskeleton proteins in luminal cells. The same changes also are evident in young epithelial cells undergoing the earliest stages of malignant progression. Second, they reported in Integrative Biology (Ertsas et.al.) a novel method for studying microenvironment-driven signaling in single cells, which they are now using to understand how the perception of microenvironment changes with age and transformation. Finally, in work that includes also the labs of Nils Halberg, Lars A. Akslen, Rolf Brekken and Oddbjørn Straume, they are exploring the role of Axl signaling in regulating phenotypic transitions in mammary epithelia, and whether it is coopted during breast tumorigenesis.

// KLAUS PANTEL

Professor Pantel is currently director of the Institute of Tumor Biology at the University Medical Center Hamburg-Eppendorf. Professor Pantel has done pioneer work in the field of cancer micrometastasis, circulating tumor cells and circulating nucleic acids (ctDNA, microRNAs). He coordinates the European TRANSCAN group "CTC-SCAN", the European IMI consortium CANCER-ID (www.cancer-id.eu) on blood-based "Liquid Biopsies" and has established a clinical micrometastasis research network at the University Cancer Center Hamburg with a clear focus on diagnosis and treatment of solid tumors.

Professor Pantel's expertise is particularly on disseminating tumor cells as biomarker of treatment efficacy. This work provides new insights into the biology of early tumor cell dissemination in cancer patients with particular emphasis on the identification of the putative metastatic founder cells ("stem cells") and the regulation of cancer dormancy responsible for late relapses in breast cancer patients.

Professor Pantel has a broad collaboration with CCBIO, most recently in a prospective non-randomized phase I trial of metastatic castration resistant prostate cancer. Here, he collaborated among other with Liv Cecilie Vestrheim Thomsen, Waqas Azeem, Lars A. Akslen, Bjørn Tore Gjertsen and Karl Henning Kalland. The trial shows that dendritic cell based cryoimmunotherapy associates with clinical variables and changes in T-cell receptor expression. Professor Pantel is also co-organizer of the CCBIO Satellite Symposium on Liquid Biopsies which will take place the day before the CCBIO Annual Symposium, May 22nd 2018 at Solstrand outside of Bergen.

// THORSTEN SCHLOMM

Dr. Schlomm was until early 2018 a faculty member and scientific director of the Martini-Clinic, Prostate Cancer Center at the University Medical Center Hamburg-Eppendorf (UKE). Currently he has taken over the chairman position of the urology department at the university medical center Charité Berlin. Clinical validation of molecular markers are central topics of Dr. Schlomm's research. In 2003, he established a prostate cancer biobank at the UKE, now consisting of over 20 000 prostate cancer samples, ready to use for molecular diagnostics. Together with Guido Sauter´s group, Dr. Schlomm developed a prostate cancer TMA including over 17.000 fully annotated prostate cancers. Currently, he is expanding this platform towards other cancer entities in Berlin. At present, he is the clinical coordinator of the German ICGC (International Cancer Genome Consortium) and the TCGA (The Cancer Genome Atlas) prostate cancer genome sequencing projects.

Dr. Schlomm´s main collaboration partner of CCBIO is Prof. Karl-Henning Kalland. In 2017 Dr. Schlomm organized the Heinrich Warner Symposium, a biannual prostate cancer symposium in Hamburg, featuring international experts on prostate cancer biology, diagnosis and treatment. Dr. Kalland was among the invited speakers at the 2017 symposium. Together with Dr. Kallands group, Dr. Schlomm generated and tested several cancer biological hypotheses, was a consultant in grant applications to the Research Council of Norway and the Norwegian Cancer Society and is planning to collaborate in a immunotherapy based trial in 2018.

// THERESE SØRLIE

Therese Sørlie is currently head of the Department of Cancer Genetics, Institute for Cancer Research at Oslo University Hospital and adjunct professor at the University of Oslo, Medical Faculty. Sørlie's group investigates breast tumor initiation and progression; from the cell of origin in which the first oncogenic events take place, the specific pathways and processes that are deregulated in the further progression of the tumors, to the specific events that are essential for the transition from in situ to invasive cancer. The aim is to identify the cellular origins of breast tumors and the mechanisms behind tumor initiation and further development into the heterogeneous molecular subtypes.

The collaboration with CCBIO and its director Lars A. Akslen is rooted by a mutual interest in breast cancer and in particular in the importance of the tumor microenvironment for tumor progression. Tumor growth is influenced at all stages of development by the surrounding tissues, cells of the immune system, circulating particles and even the microbiome. Together they have started to investigate the role of immune cells in the pre-invasive stage of breast cancer, DCIS, in comparison with invasive breast cancer. The plan is to expand on this and explore the tumor-microenvironment interactions and their impact on risk for progression from DCIS to invasive breast cancer.

// JEAN PAUL THIERY

Professor Jean Paul Thiery is a well-known researcher within the field of cancer therapeutics. Until July 2015, he was professor and head of the Department of Biochemistry of the Yong Loo Lin School of Medicine at the National University of Singapore (NUS). He also held a research director position at IMCB A*STAR and has been director of research at the Center National de la Recherche Scientifique (CNRS), Paris. Later, from 1995 to 2003, he established and headed the Cell Biology Department of the Institut Curie. Professor Thiery has made seminal contributions in the fields of cell adhesion, cell migration, morphogenesis and cancer, publishing more than 450 peer-reviewed articles in different areas of the life sciences.

Professor Thiery is currently collaborating with Professor James Lorens to unravel mechanisms driving immune escape in solid tumors. He is exploring the role of epithelial mesenchymal transition in carcinoma in the formation of defective immunological synapse. Together with Professor Lorens and colleagues, Professor Thiery is conducting experiments to assess the role of Axl tyrosine kinase in driving resistance

of mesenchymal-like carcinoma cells to cytotoxic T lymphocyte lysis.

// RANDOLPH WATNICK

Dr. Watnick is currently assistant professor at the Department of Surgery, Harvard Medical School and research associate in the Vascular Biology Program at Boston Children's Hospital. Dr. Watnick's expertise is in tumor stromal interactions, regulators of metastasis and gene regulation in epithelial and mesenchymal cells. His research group studies the regulation of angiogenesis, proliferation and motility in both epithelial cells and fibroblasts. The team has identified a novel suppressor of metastasis, Prosaposin, which acts both locally and distally by stimulating the expression and activity of p53, which then stimulates the expression of Tsp-1. Significantly, Prosaposin also inhibits both primary tumor growth and metastasis when administered in a systemic fashion thus making it a potential therapeutic agent to stem the metastatic dissemination of human tumors. Dr. Watnick's group has also developed a therapeutic peptide derived from Prosaposin, which is now in Phase 1 clinical trials.

Dr. Watnick has a longstanding collaboration with Professor Akslen on several projects, which among other has made important findings related to the role of Notch1 in breast cancer initiation and progression. Their collaboration on the tumor microenvironment has led to important observations related to CD36, CD47 and Prosaposin expression in pancreatic cancer and their correlations to outcome and patient survival. Dr. Watnick will continue to work closely with the Akslen group. Also, this past year the Watnick lab began a collaboration with the laboratory of another affiliate of CCBIO, Dr. Rolf Brekken at the University of Texas Southwest Medical Center. The Watnick and Brekken labs are investigating the role of prosaposin in reshaping the immune landscape within the tumor microenvironment.

// ARNE ÖSTMAN

Professor Arne Östman is currently professor at the Karolinska Institute (KI). His research is focused on the biology of tumor microenvironment with special focus on tumor associated fibroblasts and their role in cancer progression. Professor Östman is also vice-coordinator of STRATCAN, a government funded initiative for development of excellent cancer research at KI (2010-).

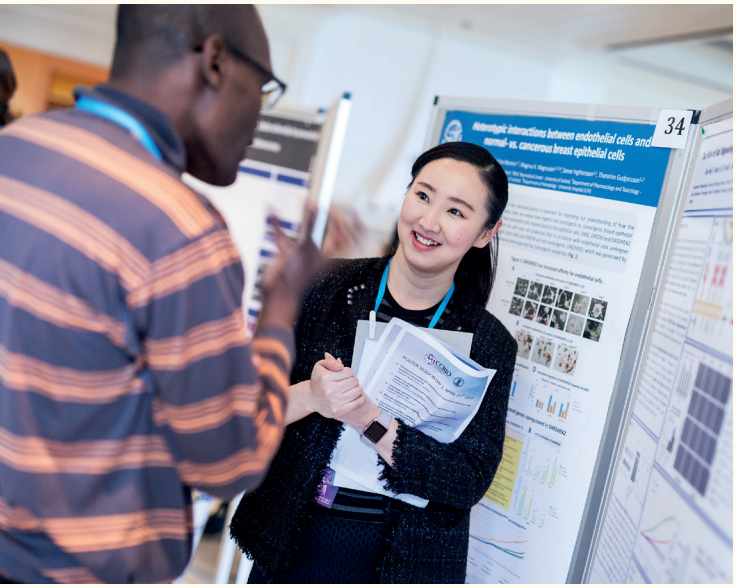
Since the Professor II appointment at UiB in 2015, Östman has obtained funding from Kreftforeningen which is used for a project on identification of novel tumor stroma-derived biomarkers in breast cancer. The project is performed in close collaboration with the Akslen group. This project is presently being expanded to a three-party format also involving researchers at the EMBL-sponsored FIMM institute in Helsinki. Östman is also developing other collaborative efforts with the Akslen group, including use of novel digital-image-analyses-based methods for characterization of breast cancer tumor vasculature. This project includes researchers at Uppsala University. Other CCBIO connections of Östman include an EU grant application together with Gullberg, and emerging collaborations with the Costea group on cancer-associated fibroblasts in oral cancer. Together with Akslen, Östman has acted as co-organizer of two well-attended workshops which have gathered Scandinavian tumor pathologists and cancer researchers. The two first meetings were held in Sotra, Bergen (2016) and Sigtuna, Sweden (2017) and a third meeting is planned for 2018 in Helsinki. Östman contributed with one chapter to the recent collection of reviews on tumor microenvironment edited by Akslen and Watnick.

Research School for Cancer Studies: Courses at CCBIO

The CCBIO Research School for Cancer Studies (RSCS) 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 Anne Christine Johannessen in collaboration with CCBIO's director.

In accordance with its aims, the RSCS is now well established as a scientifically stimulating and inclusive meeting place for junior researchers within various areas of cancer research and related ELSA fields with a common focus on translational studies of cancer biomarkers. PhD candidates and postdocs have an opportunity to meet each other and deliberate upon their research projects across the established research groups



and disciplines. CCBIO has successfully integrated the RSCS into its strategic activities like the CCBIO Annual Symposium, CCBIO Junior Scientist Symposia and CCBIO Seminars. In conjunction with lectures and seminars, CCBIO makes sure to use the opportunity for both young and senior researchers to have targeted meetings with the invited speakers where potential points of common interest are mapped out. In combination with CCBIO's strategy of inviting external speakers also for the other courses and its recruitment of an international network of adjunct positions, this ensures that the center's younger researchers have access to renowned national and international researchers from outside CCBIO.

In 2017, CCBIO held courses that run continuously, reflecting that they are integral parts of CCBIO's strategic activities, as well as the Extracellular Matrix course BMED904 and the new course on Cancer Genomics, CCBIO906. The other method specific courses will be repeated in 2018 and 2019 when CCBIO's next batch of PhDs and postdocs have been recruited.

CCBIO901 and CCBIO902 – Courses Integrated into CCBIO's Strategic Activities

CCBIO's Junior Scientist Symposium, where PhDs and postdocs organize their own seminars and present their results four times a year, forms the PhD Course CCBIO901. CCBIO's monthly seminars and the CCBIO Annual Symposium form the PhD course CCBIO902. Both are described in detail in separate chapters of this annual report.

CCBIO903 – Cancer Research: Ethical, Economic and Social Aspects

CCBIO903, held since 2015, is a 5 ECTS credits course which besides enrolling CCBIO PhD candidates, is also open to other PhD candidates and to students at the Medical Student Research Program. PhD candidates from medical fields of research from all over Norway can also attend. CCBIO903 is led by Roger Strand, Anne Blanchard (both UIB) and John Cairns (London School of Hygiene and Tropical Medicine; CCBIO-affiliated).

The course is highly interactive, and aims to address issues that cancer researchers and clinicians face every day, such as how to prioritise research questions or how to choose between treatments for a patient; involving both ethical, social and economic considerations. These issues have been strongly present in the media in recent years, adding further pressure on the researchers and clinicians to address these dilemmas. In this context, the objective of the course is to help participants to find ways to systematically reflect on the broader social and

ethical context of their own research, as well as to introduce them to methods of cost-benefit analysis of health measures and treatment options.

Some of the questions addressed during the course are:

- How can your research contribute to debates on what is good for society?
- Should everyone have access to the newest cancer therapy?
- How should we assess the cost-effectiveness of cancer bio markers?
- How can economic models help guide health care resource allocation?
- How do we make medical decisions when surrounded by risks, uncertainties and even ignorance?
- What might a 'good life' be for (future) cancer patients?
- What may the future hold for cancer research?

The next course will take place over two weeks in 2018, 29/01 – 02/02 and 19/02 – 22/02, and in addition to the core lectures, it will be structured around lectures and open discussions based on the edited volume: Cancer Biomarkers: Ethics, Economics and Society. 2017, Eds. A. Blanchard and R. Strand; Norway: Megaloceros Press. The course will be led by a diverse team of instructors that have co-authored chapters of the volume: John Cairns and Kelly Seo (CCBIO & London School of Hygiene and Tropical Medicine); Ole F. Norheim and Eirik Tranvåg (Dept of Global Public Health and Primary Care, UiB); Caroline Engen and Elisabeth Wik (CCBIO); and Roger Strand and Anne Blanchard (CCBIO & Centre for the Study of the Sciences and the Humanities, UiB).

The participants will be asked to write a term paper that include an analysis of the ethical, economic and social aspects of a specific field or topic, preferably related to their own PhD project. The candidates will also give an oral presentation during the course, based on their own term paper in order to receive feedback from the whole group and the lecturers.

CCBIO904 – Biomarkers and Tumor Biology in Clinical Practice

CCBIO904 was held for the first time in November 2015, and the next course will be April 23rd to 25th, 2018. Based on the 2015 course, 15-20 participating students are expected, and several other participants for individual lectures during the 3 days of the course. Oddbjørn Straume has the academic responsibility, and Reidun Kopperud is the course coordinator.

CCBIO904 covers aspects of tumor biology important for the understanding of why cancer develops and which mechanisms are important for tumor growth, metastases and morbidity in patients. It is a 4 ECTS credits course, primarily intended for PhD candidates who are affiliated with CCBIO, but is also open to other students, researchers and students attending the designated Medical Student Research Program. The course has special focus on tumor biological changes that may have or already have significance for personalized cancer treatment and clinical trial studies of new diagnostics and treatment. The course includes lectures, demonstrations, group work, curriculum and a written exam, and aims to give a broad understanding of all aspects of tumor biology based on updated knowledge. The participants will also gain deeper insight into how knowledge about tumor biological changes affects our strategies to customize assessment and treatment for this group of patients.

BMED904 – Matrix Biology

BMED904 is a well-established course from the Bergen Biomedical Research School (BBRS) that has been included into CCBIO's course portfolio. In June 2015, the course was arranged jointly with CCBIO's RSCS for the first time. BMED904 is a five day course, running every 2 years, that includes lectures from local researchers and a number of internationally well-known researchers within the field of matrix biology as well as practical laboratory training. In 2017, fifteen students signed up for the course and up to 70 attended individual lectures. Attending students were from Bergen, other cities in Norway and from Sweden. The course is organized and executed by Marion Kusche-Gullberg and Donald Gullberg.

The course focused on basic molecular mechanisms pertaining to the biological role of the extracellular matrix. Three of the lecture highlights were John Couchman (Copenhagen), Cathy Merry (Manchester, UK) and Kalle Sipilä (London, UK). In addition to attending lectures, the students read relevant articles, worked on articles group-wise and presented their articles for the rest of the group. All students also spent time in the Matrix Biology Lab, where microscopy of integrin-tagged cells as well as culture in 3D collagen matrices was demonstrated.

The course worked well, student evaluations were very positiv. The next course will be June, 2019, and will cover various aspects of extracellular matrix (ECM) biology, including the structure and function of the main classes of ECM molecules

and the composition of the ECM in different tissues and cellular receptors for ECM molecules and their signaling. A recurring theme will be the roles of the various ECM molecules and their functions in health and disease.

CCBIO905 – Methods in Cancer Biomarker Research

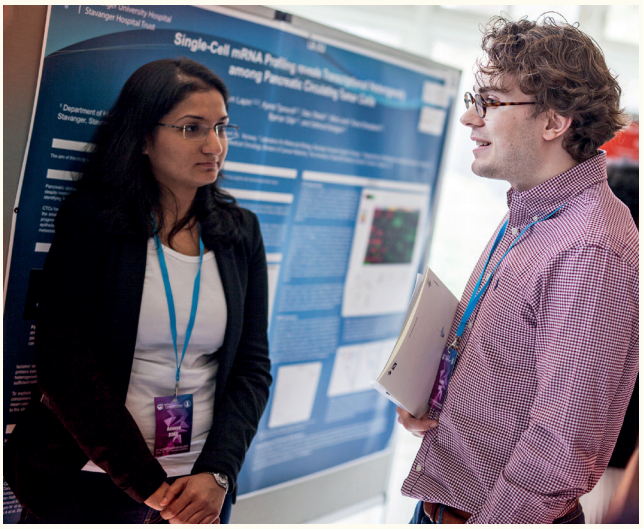
CCBIO905 was held for the first time in September 2015 as a three-day course geared towards students with an interest in methods relevant for basic and translational cancer biomarker research. This course will again be held August 27-29, 2018. Lars A. Akslen and Jim Lorens have the academic responsibility and Ingeborg Winge is the course coordinator. It is a 5 ECTS credits course, primarily intended for PhD candidates who are affiliated with CCBIO, but is also open to other students, researchers and students attending the designated Medical Student Research Program.

CCBIO905 presents a broad range of topics. In order to cover it all, the 2015 course had 15 thematic parts, including several methods ranging from basic techniques on nucleotides and proteins to more advanced approaches, as well as bioinformatics and biobanking supplemented by presentations on ethics and economics of cancer biomarkers. As an integral part of the course, the students are acquired to band together and prepare group presentations on important scientific papers

describing results from clinical trials that have led to approval of new cancer treatments. The presentations should address topics like the studies' background, drug mechanisms, the methods and impact of the biomarkers reported in terms of predictive power, and the trials' clinical results. The course concludes with a three-hour multiple-choice examination.

CCBIO906 – Cancer Genomics

CCBIO906 is a new course in the CCBIO Research School for Cancer Studies, first held November 1-3, 2017. Ola Myklebost has the academic responsibility, and Solveig Lund Witsø is coordinator. The next CCBIO906 course is planned for 2019. Eleven participants attended 3 full days with lectures by



experts of genomics from Bergen and Oslo, followed by group discussions.
The course provides broad understanding of aspects of cancer genome biology and their investigation by next generation sequencing (NGS) technologies, and applications as biomarkers for diagnostics and treatment. Methods for analyzing DNA variation and structure and RNA expression patterns are covered, as well as nuclear and chromatin structure, ethical and legal aspects, and hereditary predisposition. When completing the course, the candidates should be able to formulate problems, plan and carry out NGS analyses on samples from cancer patients. They should also be able to assess the expediency and application of different NGS methods in cancer diagnostics and research, and to know the contact points for NGS analysis and data storage and analysis in the Bergen area.

The aim is to give the candidate tools to evaluate how knowledge about genome aberrations can help in understanding tumor biological mechanisms and be applied to improved diagnosis, guide targeted treatment and follow up of cancer patients, as well as ethical and legal challenges when investigating patient genomes.

To pass the course, the candidate must be present all three days of the course, and pass an online written exam. This is a 3 ECTS credits course (50-60 hours student work time).

International Collaboration and Further Development of Courses

CCBIO has strong emphasis upon internationalization and most of the CCBIO groups have a research focus that is inherently international. In addition, CCBIO aims to move beyond the usual internationalization measures. Accordingly, CCBIO has received funding from the Research Council of Norway (RCN) and The Norwegian Centre for International Cooperation in Education (SIU)'s effort towards Partnerships for Excellent Education and Research (INTPART). This funding mechanism is geared towards forwarding a stronger integration of excellent research with excellent teaching, in

collaboration with international partners. CCBIO has now, through the INTPART funding, established a students' education and exchange program in a collaboration with the Boston based Harvard Medical School and Harvard Kennedy School. CCBIO Junior Investigator Elisabeth Wik and Randy Watnick, CCBIO-affiliated and associate professor at the Vascular Biology Program, Harvard Medical School, coordinate the program at the Bergen and Harvard sides, respectively. Akslen and Wik received in 2017 also support from the Olav Thon Foundation in the category "Support for student active research in medicine and/or natural sciences/ mathematics". The project is supported by a total of 1.5 million NOK over three years. The project includes student participation in research and is integrated with the ongoing INTPART project and the collaborations between the Centre for Cancer Biomarkers CCBIO at UiB and Harvard Medical School.

A two-day seminar in scientific writing December 13th and 14th 2017 was the kickoff of the CCBIO-INTPART program. The seminar met huge interest and was fully booked shortly after announcement. The auditorium, which takes 90, was full, and the organizers managed a long waiting list till the last minute. Master students, PhD students, postdocs and senior researchers attended, and gave great reviews after the seminar. The seminar covered topics such as organizing ideas, improving manuscript, clear writing, scientific story

telling, titles and abstracts, cover letter, common mistakes and making a manuscript memorable. Lecturers were Christine Møller, an experienced lecturer in medical and scientific writing and assistant editor of APMIS (Acta Pathologica Microbiologica et Immunologica Scandinavica), and Randy Watnick. Reviews after the course were excellent, and as the huge interest revealed a great need for knowledge in scientific writing, the course will be implemented as part of the CCBIO

Research School for Cancer Studies (RSCS) program.

A three-week PhD course on vascular biology with lecturers from the Vascular Biology Program, Harvard School of Medicine, will take place autumn 2018. Further, exchange programs for PhD and master students and other seminars on transferrable skills are in the planning. Courses that cannot be linked to the INTPART effort will experience improved access to resources through the freeing up of funds. The Thon funding also supports student's exchange to labs of collaborating researchers. The activities are being expanded in 2018, with inclusion of new courses and exchange activites.

The ELSA, ethics and economics associated research activities in CCBIO are also supported by the INTPART programme, through collaboration with the STS programme at Harvard Kennedy School as well as the Harvard T.H. Chan School of Public Health. The latter sustains a long-standing collaboration with Ole F. Norheim. Given that our own students and research candidates in the associated programmes are relatively few, we have not yet opted for separate, designated INTPART-funded courses. Rather, individual student and teacher exchange has proved to be extremely valuable. ••

RESEARCHER TRAINING

The centrally organized part of CCBIO's researcher training is the CCBIO Research School for Cancer Studies (RSCS). The RSCS is a scientifically stimulating and inclusive meeting place for junior researchers within various areas of cancer research with a common focus on translational studies of cancer biomarkers. It also serves as a bridge to CCBIO's ELSA efforts. Through RSCS and its embedment into CCBIO's other strategic activities (see chapter on RSCS), PhD candidates and postdocs get ample opportunity to meet each other and deliberate upon their research projects across the established groups. CCBIO strives to stimulate its PhDs and postdocs to independence and encourages the formation of subgroups where experienced postdocs provide guidance to younger researchers within their CCBIO research group.

Throughout 2017, CCBIO had a total of 56 PhD students, of which 64% were female and 36% were male. Well above half of the PhD students were of Norwegian origin and among the remainder, Africa and Asia were particularly well represented with about a third of all PhDs. CCBIO prides itself with being an international CoE.

Doctoral Defenses

In 2017, CCBIO graduated 12 doctoral candidates affiliated to CCBIO, from different groups and work ranging from basic to translational and clinical studies. Among these, students at other universities, such as NTNU (Trondheim, Norway) were supported by supervision from CCBIO.

JAN ROGER OLSEN: "Context dependent transcription factor regulation in normal and malignant cell differentiation". Supervisors: Professor Karl-Henning Kalland, Xisong Ke and Anne Margrete Øyan.

MARIA OMSLAND: "Investigation of the intercellular structure tunneling nanotube (TNT) in leukemia". Supervisors: Dr. Vibeke Andresen and Professor Bjørn Tore Gjertsen.

PUGAZENDHI MURUGAN ERUSAPPAN: "Molecular Aspects of Integrin α11 Function". Supervisors: Professors Donald Gullberg and Helge Wiig.

KAREN KLEPSLAND MAULAND: "Context-related biomarkers in endometrial cancer – a study with focus on obesity and genomic alterations". Supervisors: Dr. Henrica MJ Werner, Professor Helga B. Salvesen, Dr. Erling André Høivik and Professor Jone Trovik.

SURA AZIZ: "Biological and clinicopathologic markers in breast cancer. With focus on histologic features, markers of proliferation and angiogenesis". Supervisors: Professor Lars A. Akslen and Associate Professor Elisabeth Wik.

KRISTI KRÜGER: "Markers of angiogenesis and the basal-like phenotype of breast cancer". Supervisors: Professor Lars A. Akslen and Associate Professor Elisabeth Wik.

ANNA BERG: "Molecular alterations and diagnostic imaging in premalignant and malignant endometrial lesions for improved diagnosis and treatment". Supervisors: Professor Ingfrid Haldorsen, Professor Camilla Krakstad and Dr. Henrica MJ Werner.

STEFAN HINZ: "Mechanisms of AXL mediated cell plasticity and drug resistance". Supervisors: Professor James B. Lorens and PhD Gro Gausdal.

MARI KYLLESØ HALLE: "Molecular alterations suggesting new treatment strategies in uterine carcinomas". Supervisors: Professors Camilla Krakstad and Jone Trovik.

INGA REIGSTAD: "Investigation of different aspects of the tumor microenvironment as determinants of tumor development and progression". Supervisors: Professors Linda Stuhr and Rolf K. Reed.

MARIT VALLA: "Molecular subtypes of breast cancer: incidence and prognosis". Supervisors: Professor Anna M. Bofin, NTNU, Researcher Signe Opdahl, also NTNU, and Professor Lars A. Akslen, CCBIO. This was a collaboration project between CCBIO and NTNU.

GRY SANDVIK HAALAND: "Investigations of the cancer therapeutic and protective effects of warfarin-mediated inhibition of the receptor tyrosine kinase AXL". Supervisors: Professor James Lorens and MD PhD Oddbjørn Straume.

CCBIO
Bioinformatics Group

The CCBIO Bioinformatics Group (BIG) was established to facilitate work on bioinformatics analyses, and to increase cooperation in these matters across CCBIO research groups. Elisabeth Wik coordinates BIG. In 2017, in addition to taking part in the CBU workshops, a seminar on 'Basic R' took place. Also, CCBIO-BIG supported the 3-day workshop on networks analysis arranged by NORBIS (the National Research School in Bioinformatics, Biostatistics and Systems Biology).

Kjell Petersen and Charitra Kumar Mishra have represented ELIXIR/CBU in the support group. Elisabeth Wik was coordinator from CCBIO. Kjell Petersen has been the main responsible for running the CBU bioinformatics support monthly workshops, assisted by Chartira Kumar Mishra. CCBIO researchers attending these workshops are invited to suggest topic for a 'mini lecture' at the workshops, and have appreciated the possibility this collaboration with CBU has offered. The monthly workshops have covered topics like clustering analyses and gene set enrichment analyses, and have given additional support on programming in R and use of Bioconductor, in addition to offering assistance in other matters relating to computational analyses in research projects. This year, BIG teamed up with the CBU support team (Kjell Petersen, Charitra Kumar Mishra and Tomasz Furmanek) for a workshop on 'Basic R'. In addition, Konstantina Dimitrakopoulou (postdoc in Professor Inge Jonassen and Professor Lars A. Akslen's groups) contributed. Further, CCBIO supported the 3-days NORBIS workshop "Network Biology/Integromics Bioinformatics – Applications Towards Medicine", and contributed in the organizing committee. The workshop included hands-on sessions with experts in the field of analyses of protein interaction data (by application of Cytoscape) and integrative pathway analyses (by R/Bioconductor). Each CCBIO research group presented at the workshop got a minimum of one seat at the hands-on sessions (that were fully booked), aiming to disseminate knowledge to colleagues in the different groups after the workshop. Read more about these initiatives in the chapter Special Seminars and Meetings.

The need of BIG organized seminars and workshops seems to vary, and assessment of the estimated needs for bioinformatics support within CCBIO is done continuously, planning activities accordingly. Other bioinformatics oriented initiatives have also been taken within CCBIO this last year, like the Cancer Genomics course (CCBIO906). ••

CCBIO Junior Scientist Symposium

In 2017, CCBIO901, the CCBIO Junior Scientist Symposium (JUSS), was organized and chaired by researcher Erling A. Høivik and postdoctoral fellows Agnete Engelsen (spring semester) and Liv Cecilie Vestrheim Thomsen (autumn semester).

These seminars aim to let junior scientists organize and present their work in an environment of peers and give opportunity for the participants to get feedback across disciplines on what they are working on, as well as practising on asking relevant questions to presenters.

The aim throughout the seminar series is also to introduce researchers early in their career to tools and transferable skills they might need to further their career, such as presentation skills both in front of an audience and in writing, media handling and ethical considerations in the everyday working life.

During 2017, four half-day symposia were arranged. There were around 35 participants at each seminar, and the program included presentations from PhD candidates as well as from postdoctoral fellows and other researchers. In 2017 every symposium also included an inspirational lecture by a senior researcher such as professor Myklebost or researcher Gro Gausdal. The inspirational lectures provided insight in how different successful research careers can develop, and introduced novel and high-impact findings relevant for the early career participants.

The 15th CCBIO Junior Scientist Symposium was opened by CCBIO Director Lars A. Akslen. He presented an overview of the aims and history of the JUSS seminar series as well as encouraged the junior scientist to continue interacting in research communities, to be curious and to enjoy reading. This year, topics discussed were machine learning, superresolution imaging and genomic evolution in breast cancer. The seminar participants also learned about the national research school in bioinformatics, biostatistics and systems biology (NORBIS), philosophic reasoning on new health entities and identities resulting from the personalization of medicine and how to and why a media strategy ought to be part of their professional life.

Throughout the year, the high quality level of both the research presented and of how it was delivered, the enthusiasm of presenters and audience, and the conversations and fruitful discussions during the breaks were exceptional. ••

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM – February 23rd 2017

Auditorium B301, Haukeland University Hospital

Symposium Chairs: Agnete Engelsen and Erling Høivik

10.00-10.50: Inspirational lecture by Professor Ola Myklebost (K2): NoSarC – Norwegian Sarcoma Consortium (www.NoSarC.no), - Personalised treatment for orphan cancers

10.50-11.00: Coffee break

11.00-11.45: Caroline Benedicte Nitter Engen (K2): Personalised medicine and the evolution of new health entities and identities

11.45-12.45: Lunch (lunch included, please specify upon registration)

12.45-13.15: Hege Avsnes Dale/ Endy Spriet (Molecular Imaging Center (MIC)): Introduction to super-resolution imaging

13.15-13.20: Coffee break

13.20-13.40: Sigmund Ytre-Hauge (K2): MRI texture analysis in endometrial cancer

13.40-14.00: Hanna Dillekås (K2): Recurrence of breast cancer in relation to delayed reconstruction

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM – June 15th 2017

Auditorium D303, Haukeland University Hospital

Symposium Chairs: Agnete Engelsen and Erling Høivik

10.00-10.30: Gro Gausdal (BerGenBio ASA): BerGenBio: From bench to bedside: Developing first-in-class drugs to treat aggressive cancer

10.30-10.50: Coffee break

10.50-11.30: Liv Cecilie Vestrheim Thomsen & Jørn Skavland (K2): Cryoimmunotherapy in castration resistant prostate cancer - a phase 1 study with several novel aspects on treat ment and analysis

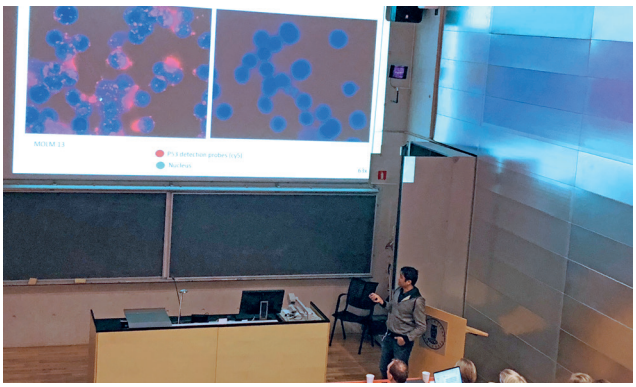
11.30-11.50: Christine Stansberg (NORBIS): NORBIS, the national research school in bioinfor matics, biostatistics and systems biology

11.50-13.00: Lunch (lunch included, please specify upon registration)

13.00-13.20 Emilia Signe Hugdahl (K1): Telomerase reverse transcriptase (TERT) promoter mutations in melanoma

13.20-13.40 Reidun Æsøy (K2) Iodinin analogues - potential novel anti-leukaemic drugs

13.40-14.00 Sandy Chen (IBM/ Uni. Auckland): Catching up to the times, the story of a conventional chemotherapeutic agent in the age of im mune and targeted-therapy



Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM – August 31st 2017

Auditorium 4, BBB-building, 10.00-14.00

Symposium Chairs: Erling Høivik and Liv Cecilie V. Thomsen

10.00-10.05: Startup; from the Chairs

10.05-10.45: Key presentation: Erlend Hodneland (Christian Michelsen Research AS): Machine learning in biomedical sciences

10.45-11.00: Coffee break

11.00-11.20: Tina Fonnes (K2): Loss of Asparaginase-like protein 1 is a marker for poor survival in endometrial carcinoma

11.20-11.40: Martha Rolland Jacobsen (K1): Analysis of biomarkers in a molecular diagnostic tool for oral squamous cell carcinoma

11.40-12.00: Stein-Erik Gullaksen (K2): Using mass cytometry for biomarker discovery in chronic myeloid leukemia treated with tyrosine kinase inhibitors

12.00-12.55: LUNCH (free lunch included, please specify upon registration)

12.55-13.40: Sura Aziz (K1): Predictive molecular biomarkers in breast cancer, current progress and future challenges

13.40-14.00: Hildegunn Aase (K1): Digital breast tomosynthesis, the future screening tool for breast cancer?

Centre for Cancer Biomarkers

SCIENTIFIC PROGRAM – November 23rd 2017

Auditorium 4, BBB-building, 10.00-14.00

Symposium Chairs: Erling Høivik and Liv Cecilie V. Thomsen

10.00-10.10: Startup; Input from the CCBIO Director Lars A. Akslen (K1)

10.10-10.55 Stian Knappskog (Key presentation, K2): Genomic evolution of breast cancer metastasis and relapse

10.55-11.15: Coffee break

11.15-11.35: Lalit Rane (K2): In situ mRNA detection by proximity ligation assay in myeloid leukemias

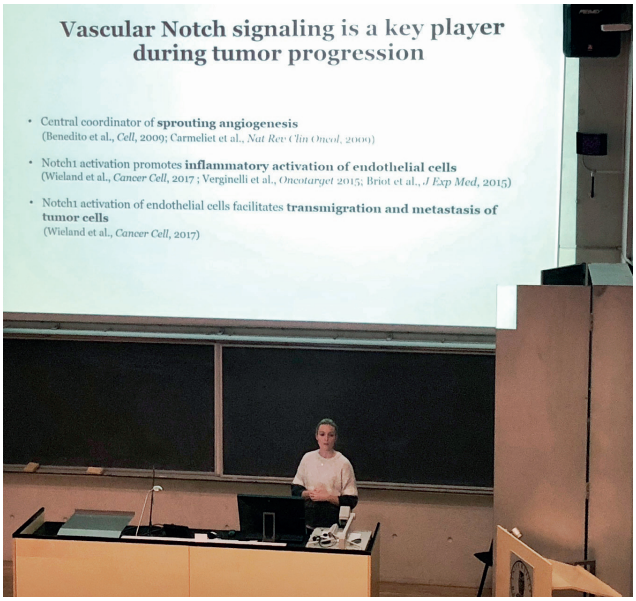
11.35-11.55: Ingvild L. Tangen (K2): Expression of L1CAM in preoperative blood samples detects LN metastases and poor outcomes in endometrial cancer

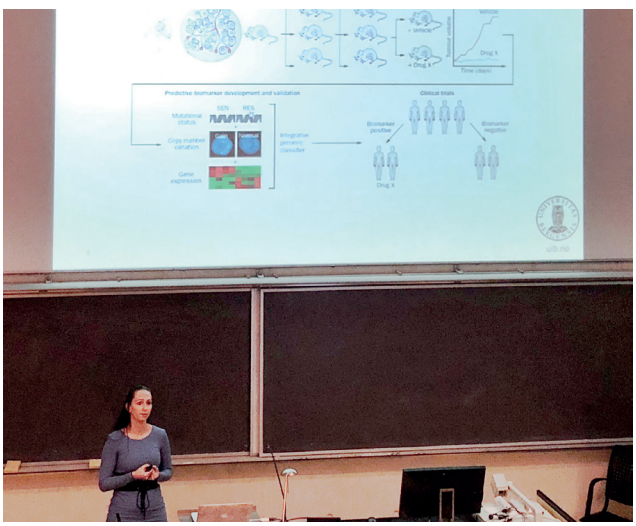
11.55-12.15 Reidun Jetne Edelmann (K1): Notch1/ Jagged1-defined tumor vessel phenotypes in human breast cancer

12.15-12.55 LUNCH (free lunch included, please specify upon registration)

12.55-13.40: Marion Solheim (UIB Communication): Young scientists and media coverage - a talk about responsibility, free PR and future funding

13.40-14.00 Tara Helen Dowling (K2): Exploring novel treatment approaches for acute myeloid leukemia and myelodysplastic syn dromes; by developing an innovative Ossicle xenograft mouse model





CCBIO Research Seminars

Whereas speakers in the first two years of the CCBIO seminars were mainly CCBIO principal investigators presenting their research, in 2017, as in 2016 and 2015, the seminars have focused almost exclusively on international speakers.

CCBIO's monthly research seminars are included into the master level course BMED380 and the PhD-level course CCBIO902, hence students and younger researchers are especially frequent participants. The seminars are however open to all students, researchers and staff. Information about the seminar speakers and abstracts are spread through web, email and poster, and we reach researchers beyond the CCBIO groups. We also get attendees from other research communities at the university and the hospital, as well as lower level students. The seminar series thus fulfills the aim of conveying relevant biomarker research to the local scientific community and students and younger researchers in particular, readying the ground for future recruitment.

Last, but not least, each seminar is followed by an informal pizza get-together that is an important catalyst for interaction on all levels. In most cases, targeted meetings with the speakers are arranged before or after the lectures so that CCBIOs researchers, in particular the younger ones, get the opportunity to discuss projects and collaboration with the invited lecturers. ••

CCBIO

Seminars in 2017

26.01.17
Norman J. Maitland, Department of Biology, University of York, UK. Title: Modelling of cell fate and differentiation using tissue-derived human prostate epithelial cells.

23.02.17
Øystein Bruserud, the Leukemia Research Group, Department of Clinical Science, University of Bergen, Norway. Title: Classification and prognostication of acute myeloid leukemia – the past, the present and the future.

16.03.17
Klas Wiman, the Department of Oncology-Pathology, Karolinska Institute, Sweden. Title: Targeting missense and nonsense mutant p53 in cancer – from molecular biology to the clinic.

11.05.17
Ulf Landegren, Department of Immunology, Genetics and Pathology, Uppsala University, Sweden. Title: Molecular tools for high performance analyses of proteins and nucleic acids.

15.06.17
Kalle Sipila, Centre for Stem Cells and Regenerative Medicine, King's College London, UK. Title: Integrative genomic and functional analysis of human primary oral SCC cells.

28.09.17
Nuno M. Coelho, Matrix Dynamics Group, University of Toronto. Title: DDR1 expression, collagen-dependent activation and signaling in cancer and tissue fibrosis.

26.10.17
Jan Jacob Schuringa, Department of Experimental Hematology, Cancer Research Centre Groningen, University Medical Centre Groningen, The Netherlands. Title: Towards identification and targeting of leukemic stem cells and (epi)genetically distinct subclones using humanized niche xenograft mouse models.

23.11.17
Satu Mustjoki, Hematology Research Unit Helsinki, Department of Clinical Chemistry and Hematology, University of Helsinki and Helsinki University Hospital Comprehensive Cancer Center, Finland. Title: Immunogenicity in hematological malignancies and immunological effects of targeted therapy.

CCBIO Special Seminars

Whenever CCBIO's PIs have separate symposia with interesting lecturers, senior researchers visiting outside of the annual symposium and the CCBIO seminars, or the opportunity arises to invite especially interesting lecturers, CCBIO encourages them to arrange talks under the umbrella of the CCBIO Special Seminars. In this way, the special seminars are integrated into CCBIO's seminar series, while at the same time making them stand out. The special seminars have typically been very well visited.

CCBIO Special Seminar 15.05.17, with invited speaker **Professor Bruce Baguley** from Auckland Cancer Research Centre, Medical Science, Faculty of Medical and Health Sciences at the University of Auckland, New Zealand. Title: "The vascular endothelial barrier: relevance to cancer therapy". The vascular and extravascular compartments are separated by vascular endothelial cells, which form a barrier that maintains distinct cellular and protein components. The increasing use of antibodies in cancer therapy raises the question of how therapeutic proteins cross this barrier. In this talk, Professor Baguley examined the possible role of Axl, Gas6 and other proteins in the control of vascular permeability. He also summarised clinical trials of a drug that was designed to disrupt this barrier.

CCBIO Special Seminar 08.06.17, with invited speaker **Martin Widschwendter,** professor in women's cancer, Head of the Department of Women's Cancer at University College London (UCL) and a Consultant Gynaecological Oncology Surgeon at University College London Hospital (UCLH). Title: "Epigenetics and Cancer Risk". Professor Widschwendter presented the FORECEE (Female cancer prediction using cervical omics to individualise screening and prevention) consortium, which has developed an exciting opportunity to utilise clinically abundant cervical cells in tandem with a multi-omics enabled (genome, epigenome, metagenome) analysis pipeline to understand an individual's risk of developing all female specific cancers and to direct a personalised screening and prevention strategy. The FORECEE project is aligned with the novel concept of "P4 Medicine" (predictive, preventive, personalised, and participatory): it aims to develop a risk prediction tool and translate its output into personalised recommendations for screening and prevention of female cancers.

CCBIO Special Seminar 03.11.17, with invited speaker **Rameen Beroukhim** of the Dana-Farber Cancer Institute/ Harvard Cancer Center, USA, and a CCBIO affiliated international investigator. Title: "Structural variations in the cancer genome". Dr. Beroukhim's talk concerned the somatic genetics of cancer, and identifying alterations in chromosomal structure (including copy-number gains and losses and loss of heterozygosity) that contribute to tumor growth, and how to characterize the biological effects of these alterations. His group aims to understand the biological basis of the various cancer subtypes to guide development of therapeutics, and to develop prognostic and predictive markers to guide the application of those therapeutics. Much of their effort focuses on developing computational methods with general applicability to the study of the somatic genetics of cancer. An example is the Genomic Identification of Significant Targets In Cancer (GISTIC) algorithm, a statistical technique that distinguishes chromosomal alterations that are likely to drive tumorigenesis from alterations that may result from random chance alone.

CCBIO Special Seminar 12.12.17, with invited speaker **Randolph Watnick** from the Department of Surgery, Harvard Medical School and the Vascular Biology Program at Boston Children's Hospital. Randolph Watnick is also a CCBIO affiliated international investigator.

Watnick presented research from his team showing that the tumor suppressor p53 is differentially regulated in progenitor-like mammary epithelial cells compared with differentiated mammary epithelial cells. This differential regulation of p53 activity was proved to be a function of its acetylation status, modulated by the deacetylase SIRT1. It was showed that the expression of SIRT1 in mammary epithelial progenitor-like cells is mediated by Notch1. When hypothesizing that Notch1-mediated regulation of tissue progenitor cells is recapitulated in tumor-initiating cells, the group investigated whether the Notch signaling pathway is critical to the tumor-initiating properties of mammary epithelial cells. Strikingly, high Notch1 expression also identifies functional cancer stem cells and Notch-mediated repression of SIRT1 regulates both tumor initiation and chemoresistance. Watnick concluded that the results demonstrate that a novel signaling axis, involving Notch1, SIRT1 and p53 functionally defines tumor-initiating epithelial cells as well as cancer stem cells. Watnick is also co-editor of the new CCBIO book **"Biomarkers of the Tumor Microenvironment - Basic Studies and Practical Applications"** together with Professor Akslen, and both were available after the seminar to discuss and sign the book. ••

CCBIO Meetings and Workshops

The 3rd International p53 isoforms workshop

CCBIO hosted the 3rd International p53 isoforms workshop, in Bergen June 18th -21st 2017. The organising committee consisted of JC Bourdon, Dundee, UK, Bjørn Tore Gjertsen, CCBIO, Norway, Antony Braithwaite, Dunedin, NZ, Bertrand Mollereau, ENS, Lyon, France, Varda Rotter, Weizmann Institute, Israel, Pierre Roux, CRBM, Montpellier, France, Olivier Terrier, Lyon, France.

The workshop was a great success, and we welcomed researchers from all corners of the world including the pioneers who contributed in discovery and crucial first investigations in the p53 field. The program reflected the great diversity of functions where p53 isoforms are involved. We were presented research on p53 isoforms in relation to cancer, immune regulation, p53-based therapy, tissue regeneration, pathogens, aging, degeneration and evolution. Inspiring keynotes were presented by Antony Braithwaite, Judith Campisi, Thomas Meyer, Curtis Harris, Mina Bissel, David Kaplan, Jean-Christophe Bourdon, and Sir David Lane. Local presenters Stian Knappskog and Bjørn Tore Gjertsen gave us an insight in p53 isoform expression in patient samples from colon cancer and acute myeloid leukemia, respectively. Different isoforms were suggested to predict disease outcome in these two diseases. The over 80 participants represented scientific levels from master students to professors, reflecting the continuous interest of p53 as a past, present, and future field of research. The intimate venue gave young scientist the opportunity to engage in discussions with the true legends in this field. During the conference we had two poster sessions, and 18 posters were presented. ••

THE 3RD INTERNATIONAL P53 ISOFORMS WORKSHOP

Day 1: Sunday June 18, 2017

16.00-16.15 Prof Lars A. Akslen: Opening and introduction

Session 1: p53 isoforms as biomarkers.

16.15-16.40 Prof Bjorn Tore Gjertsen: p53 beta and gamma isoforms in normal leukocytes and acute leukemia.

16.40-17.05 Dr Stian Knappskog: p53 isoforms as biomarkers in metastatic colon cancer.

17.05-17.30 Prof Kanaga Sabapathy: Functional analysis of p47 (D40p53), the amino-terminal truncated isoform of p53.

17.30-17.55 Dr Kelly Avery-Kiejda: Deciphering the complex role of D40p53 in breast cancer.

17.55-18.40 Keynote: Prof Antony Braithwaite: Functions of the D133p53 isoform in immune regulation.

19.00-21.00 Cocktails and poster session.

Day 2: Monday 19th June 2017

Session 2: TP53 mutation and p53 isoforms as biomarkers

08.25-08.50 Prof Moshe Oren: A comprehensive library of p53 variants elucidates patterns of evolutionary conservation and mutations in cancer.

08.50-09.05 Dr Elisabeth Maritschnegg: Examination of the presence and clinical significance of p53 prions in ovarian cancer.

09.05-09.30 Dr Oleg Laptenko: Biological activities of mutant p53 proteins resulting from an open reading frame shifts that demonstrate significant structural similarity to TAp53 beta and gamma isoforms.

09.30-09.45 Dr Sunali Mehta: A Study of TP53 RNA Splicing Illustrates Pitfalls of RNA-seq methodology.

09.45-10.00 Dr Brianna Morten: The difficulties of measuring the p53 isoforms at the gene and protein levels: A tale of caution.

10.00-10.25 Prof Michal Sharon: Post-translational regulation of p53 function through 20S proteasomemediated cleavage.

10.25-10.45 Coffee break

10.45-11.30 Keynote: Prof Judith Campisi: Control of cellular senescence aging and cancer by p53

11.30-11.55 Prof David Malkin: p53 'Epi' events in Li-Fraumeni Syndrome.

11.55-12.10 Dr Hind Hafsi: p53 isoforms as mutation targets in cancer: lessons from public databases.

12.10-12.25 Stephanie Schubert: TP53 beta variants in colorectal cancer predisposition.

12.25-12.50 Dr Pan Pantziarka: Drug Repurposing And Reducing Cancer Incidence in Li Fraumeni Syndrome.

12.50-14.20 Lunch break and poster session

Session 3: p53-based therapy.

14.20-14.45 Prof Klas Wiman: Novel cancer therapy by reactivation of missense and nonsense mutant p53.

14.45-15.00 Dr Naoise Synnott: Mutant p53 as A Therapeutic Target for the Treatment of TripleNegative Breast Cancer: Preclinical Investigation with the Anti-p53 Drug, APR246.

15.00-15.25 Prof Chandra Verma: p53 isoforms in drug discovery: modelling novel druggable interactions.

15.25-15.40 Dr Joanna Zawacka-Pankau: Pharmacological re-activation of p53 protein family members affects proliferation and migration of cancer cells with TP53 gene mutations.

15.40-16.05 Prof Varda Rotter: Re-activating mutant p53 into a wild type p53 by p53-small peptides.

16.05-16.25 Coffee break.

Session 4: How to control cell reprogramming and tissue regeneration? Lessons from the interaction infectious pathogens/ p53 isoforms.

16.25-17.10 Keynote: Prof Thomas Meyer: The enigmatic link between infection and the early onset of TP53 mutations in cancer.

17.10-17.35 Dr Roy Chowdhury: The Unfragmented Relation ship between Chlamydia and Mitochondria: A p53 Story.

17.35-18.00 Dr Olivier Terrier: Hijacking of p53 functions in human infections: each virus has its own way.

18.00-18.15 Dr Julia Dubois: Interplay between influenza viruses and the alternative splicing of TP53.

18.15-18.40 Sebastien Joruiz: Which p53 isoforms is the most important? Lesson from HPV.

Day 3: Tuesday 20th June 2017

Session 5: p53 isoform in cancer, ageing, reprogramming.

08.30-09.15 Keynote: Prof Curtis C. Harris: p53 Isoforms, Aging and Cancer

09.15-09.40 Prof Pierre Roux: The multiple roles of Δ 133p53 in cancer progression

09.40-09.55 Dr Marina Kazantseva: Elevated 133p53 in prostate tumors correlates with an immune suppressive signature and poorer outcome

09.55-10.40 Keynote: Prof Mina Bissel: The crucial roles of Laminins and p53 isoforms in tissue specificity and gene expression: a perfect tango of Dynamic Reciprocity in 3-D

10.40-11.00 Coffee break

Session 6 – effects of extra cellular matrix on p53

11.00-11.25 Dr Sun-Young Lee: Interplay between p53 isoforms and extracellular signaling in maintaining tissue-specific form and function

11.25-11.50 Prof Giannino Del Sal: Cell stiffness induced mechano-signaling in cancer: mutant p53 is at the crossroads

11.50-12.05 Dr Angelo Peschiaroli: Np63-mediated regulation of hyaluronic acid metabolism and signaling supports HNSCC tumorigenesis

12.05-12.30 Dr Patricia Muller: Mutant p53alpha isoform drives cancer cell engulfment activity, leading to cell-in-cell structures that associate with tumorigenesis and recurrence

12.30-14.00 Lunch break and poster session

Session 7 – Degeneration and regeneration

14.00-14.45 Keynote: Prof David Kaplan: The p53 family in neurodegeneration and stem cell aging

14.45-15.00 Dr Izumi Horikawa: 133p53 represses p53-inducible senescence genes and enhances the generation of human induced pluripotent stem cells

15.00-15.15 Dr Tania Slatter: Improving the prognosis from glioblastoma by targeting subtypes characterised by increased 133p53 or mutant p53

15.15-15.40 Prof Simone Di Giovanni: Regenerative transcriptional signalling networks for axonal regeneration and functional recovery: from p53 to epigenetic reprogramming

15.40-16.00 Coffee break

16.00-16.15 Dr Martin Fischer: Integrative analysis reveals common and distinct targets of the p53 gene regulatory network in the mouse and human genome

16.15-16.40 Prof Joaquin Maximilano Espinosa: Identification of a core p53 transcriptional program with highly distributed tumor suppressive activity

16.40-17.05 Dr Simon McDade: $\Delta Np63\gamma$ is both necessary and sufficient to activate SRC/AKT signalling axis and SNAI2-mediated EMT and invasion

17.05-17.30 Prof David Meek: The potential for regulating different forms of p53 by posttranslation modification

17.30-18.15 Keynote: Dr Jean-Christophe Bourdon: p53: a system of protein isoforms. How does it work?

18.15 Drinks and mingling

Day 4: Wednesday 21st June 2017

Session 8: p53 family isoform in cancer and evolution

08.30-09.15 Keynote: Prof Sir David Lane: The discovery of new p53 isoforms in Zebrafish

09.15-09.40 Prof Gerry Melino: The p53 family in cancer biology (p63 and microenvironment)

09.40-09.55 Dr Yari Ciribilli: p53 isoforms are differentially expressed in human melanomas

09.55-10.15 Coffee break

10.15-10.30 Dr Neda Slade: The expression of p53/p73 isoforms, NME and GLI in melanoma cell lines

10.30-10.45 Dr Yann Audic: Control of DeltaNp63alpha/ gamma ratio by the RNA binding protein Ptbp1 in Xenopus laevis development

10.45-11.10 Prof Bertrand Mollereau: p53 integrates the antagonism between autophagy and apoptosis in response to stress

11.10 Dr Jean-Christophe Bourdon: Conclusion

The Biomarkers & Bioinformatics in Clinical Trials and Clinical Studies Symposium

CCBIO, in collaboration with the regional health authorities Helse Vest, arranged in June 2017 a new type of symposium focusing on the methodology required to identify new biomarkers in patient materials. The Biomarkers & Bioinformatics in Clinical Trials and Clinical Studies Symposium, June 18th-19th 2017 at Solstrand Hotel, was aimed at researchers focusing on biomarker detection through use of patient material and advanced bioinformatics tools.

As the research background of the presenters as well as of the participants differed widely, the two days were filled with interesting lectures followed by enthusiastic discussions on a range of topics related to how novel and complex methods within bioinformatics, biostatistics and mathematics can help biomedical research move forward. Reflections on practical and ethical challenges of performing research involving patients and their biological tissues resonated well, and the conversations continued into the breaks. During the symposium the participants were introduced to many of the available infrastructures, tools and available contact points for practical help and networking, such as Biobank Haukeland, PubGene, CytBase, Elixir with the national services Norwegian e-Infrastructure for Life Sciences and Tjenester for Sensitive Data (TSD), and Centre for Digital Life Norway. Several of the attendees had brought posters presenting their ongoing projects, and utilized these as starting points for discussions with the experts.

Throughout the meeting, as well as during meals, presenters and participants kept up the lively conversations, recieving both challenges and help regarding ongoing projects. In the relaxing and beautiful surroundings of Solstrand, people used the time to get to know each other and possibly create a basis for new collaborations and concepts. ••

Scientific Program of the Biomarkers & Bioinformatics in Clinical Trials and Clinical Studies Symposium

Day 1, Sunday June 18, 2017

13.30-14.15 Arrival and registration
14.15-14.30 Sonia Gavasso: Welcome and introduction
14.30-15.15 Ola Myklebost: The role of bioinformatics and clinical trials in the discovery of biomarkers
15.15-15.40 Break
Session: Working with complex data
15.40-16.05 Leonardo Meza-Zepeda: Genomics: how to select the right approach to identify true biomarkers
16.05-16.30 Harald Barsnes: The key role of proteomics in biomarker discovery
16.30-16.55 Ellen Mosleth: Novel approach for extracting information from experiments with multiple input factors
16.55-17.15 Break
17.15-17.30 Morten Brun: Topological data analysis
17.30-17.50 Gonzalo Nido: Ultra-deep sequencing of mitochondrial DNA in single cells
17.50-18.10 Endre Anderssen: Integrated analysis of epigenomic and gene expression
19.30--→ Dinner - Enjoy a culinary experience at Solstrand Hotel & Bad with participants and presenters

Day 2, Monday June 19, 2017

Session: Clinical trials
09.00-09.30 Nina Jebsen: What are clinical trials?
09.30-09.50 Patient: Patient's view on clinical trials
09.50-10.10 Break
Session: Clinical trials for biomarker detection and evaluation - opportunities, benefits and challenges
10.10-10.30 Christian Vedeler: A clinician's view
10.30-10.50 Reidun Kopperud: A molecular biologist's view
10.50-11.10 Nello Blaser: The biostatistician's view
11.10-11.30 Roger Strand: The ethicist's view
11.30-12.30 Lunch
Session: Sample and data management
12.30-12.45 Ann Cathrine Kroksveen: Biobank Haukeland, the research biobank at Haukeland University Hospital
12.45-13.00 Randi Hovland: Pubgene for management and interpretation of genomic data
13.00-13.15 Stein-Erik Gullaksen: CytBASE
13.15-13.45 Eirik Thorsnes: Big data
13.45-14.10 Kjell Petersen: National services offered by Elixir Norway for non-sensitive and sensitive molecular Life Science data: NeLS and TSD
14.10-14.30 Break
Session: Clinical mass cytometry
14.30-14.50 Lucius Bader: A practical example: A cross-section al study for disease mechanisms in rheumatoid arthritis
14.50-15.10 Gerd Bringeland: Antibody monitoring in multiple sclerosis
15.10-15.30 Jørn Skavland: An analytical approach: Are there any biomarker relevant molecular changes out there?
15.30-15.45 Rune Kleppe: Centre for Digital Life Norway - Opportunities for multidisciplinary research and innovation.
15.45-15.55 Ellen Mosleth and Sonia Gavasso: Closing remarks

Workshop in Basic R

As part of CCBIO's strategy to strengthen the bioinformatic axis of the center, and to prepare the CCBIO scientists for the NORBIS/CCBIO 3-days seminar on networks biology, the CCBIO Bioinformatics Group (CCBIO-BIG) teamed up with the Computational Biology Unit (CBU) support team for a workshop on Basic R. Konstantina Dimitrakopoulou (postdoc in Prof. Inge Jonassen and Prof. Lars A. Akslen's groups) also contributed.

R is a programming language, widely applicable in biostatistics and bioinformatic analyses. R is also known as a valuable resource for data plotting. CCBIO finds that increased knowledge in bioinformatic analyses and relevant analysis tools is important to fully understand the different levels of high-throughput data used in cancer research.

Thirty CCBIOers gathered 16th and 17th of August to learn the basic steps of applying R in biostatistics and bioinformatic analyses. Kjell Petersen and colleagues gave massive amounts of input on basic R programming to the students. Additionally to learn some of the basic steps in R, an aim for the workshop was networking of CCBIOers who will be applying R as an analysis tool in biostatistics and bioinformatics.

Workshop: Network Biology/Integromics Bioinformatics – Applications Towards Medicine

NORBIS, in collaboration with CCBIO, DLN and CBU, hosted the "Network Biology/Integromics Bioinformatics – Applications Towards Medicine" workshop at Grand Hotel Terminus in Bergen, August 23rd-25th 2017. The event aimed at familiarizing researchers and students from interdisciplinary fields with concepts of the network science field, as well as presenting cutting edge research in network biology and medicine. The participants were introduced to graph theory and learned about biological networks; the key goal of the event was to exhibit the universality of principles underlying many complex systems like the internet, social networks and biological networks. The workshop included 10 international and 4 national speakers and 120 participants.

The highlight of the workshop was the lecture given by Professor Albert-László Barabási (Northeastern University and Harvard University, Boston, US), who presented the pioneering model he introduced in 1999 about the scale-free topology of many real networks - a model currently widely used in the study of biological networks. Barabási also displayed its application repertoire for the comprehension of

complex diseases. The workshop further featured presentations from other leading researchers in the field, including Alfonso Valencia (BSC, Barcelona), Benno Schwikowski (Institut Pasteur, Paris) and Christos Ouzounis (CERTH, Thessaloniki).

During the first two days, there were also hand-on sessions which aimed at introducing participants to popular software and tools used in the field, including Cytoscape and R packages from Bioconductor. There were many cutting edge lectures followed by enthusiastic discussions on the approaches, databases and methods that can assist researchers to navigate in the diverse omics data available and ways to integrate them in order to comprehend disease mechanisms, identify novel biomarkers and novel drug targets. Social networking sessions were also part of the program. The workshop closed with a memorable Horizon lecture, co-organized with the Faculty of Mathematics and Natural Sciences, by Professor Albert-László Barabási discussing the structure of many complex self-organized systems. ••

Scientific Program for the Network Biology/Integromics Bioinformatics workshop – Applications Towards Medicine

Wednesday 23 August

09:00 09:15 Inge Jonassen: Welcome
09:15 10:45 Konstantina Dimitrakopoulou: Introduction to biological networks
10:45 11:00 Coffee break
11:00 12:00 Christos Ouzounis: Developing computational biology: From comparative genomics to systems biomedicine
12:00 13:00 Lunch
13:00 14:30 Eileen Marie Hanna: Introduction to Cytoscape Note:hands-on tutorial, for all participants
14:30 14:45 Coffee break
14:45 16:45 Pablo Porras Millan: Protein interaction data (databases and analysis). Note: Cytoscape hands-on session, for selected participants

Thursday 24 August

09:00 09:55 João Pedro de Magalhães: Bioinformatics, systems biology and ageing: Navigating the new oceans of data to discover the Fountain of Youth
10:00 11:00 Albert-László Barabási: Network Medicine: From Cellular Networks to the Human Diseasome
11:00 11:15 Coffee break
11:15 12:15 Benno Schwikowski: LEAN discovery of hot spots in networks
12:15 13:15 Lunch
13:15 14:15 Leonidas Alexopoulos: Pathway-based approaches for early drug and biomarker discovery. Research and Industrial applications in osteoarthritis, liver cancer, non-alcoholic fat liver disease, multiple sclerosis, melanoma, chronic kidney disease, and liver toxicity.
14:15 15:15 Eivind Almaas: Differential co-expression network analysis: from pathways to disease
15:15 15:30 Coffee break
15:30 17:30 Aristidis Vrahatis: Integrative pathway analysis Note: R/Bioconductor hands-on session, for selected participants

19:00 DINNER at Kalfaret Brygghus

Friday 25 August

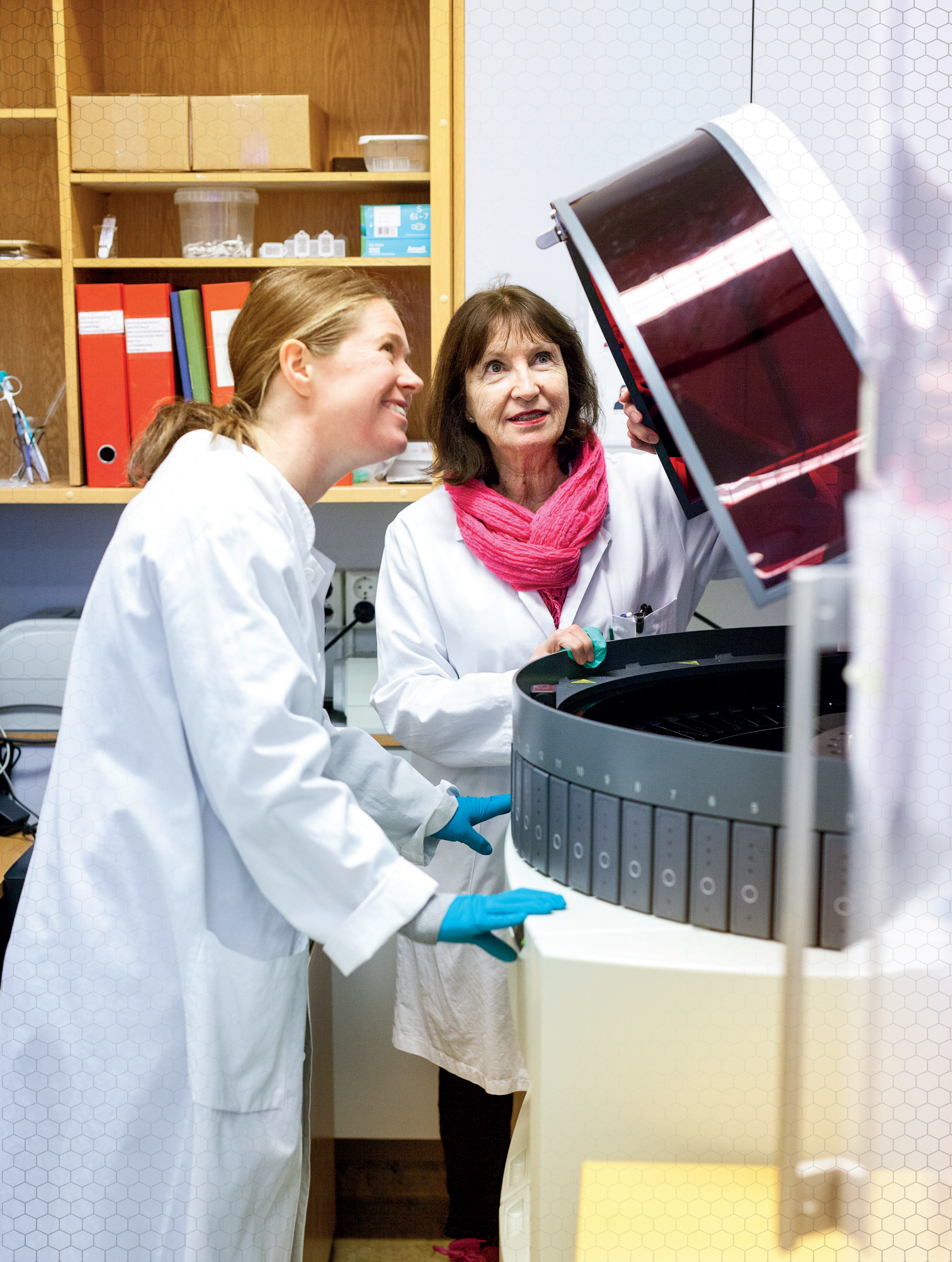
09:00 10:00 Alfonso Valencia: Networks based approaches for the study of epigenomics
10:00 11:00 Ruth Barshir: Using network approaches towards understanding tissuespecificity of hereditary diseases
11:00 11:15 Coffee break
11:15 12:15 Laura Furlong: DisGeNET discovery platform 5.0: Illuminating the study of human diseases
12:15 13:00 Lunch
13:00 13:45 Marc Vaudel: Networks as a roadmap for clinical data
13:45 13:55 Christine Stansberg: Closing remarks and NOR BIS announcements
14:00 14:30 Refreshments served before the Horizon lecture, Auditorium 1 in the UiB building for Natural Sciences
14:30 15:45 Albert-László Barabási, Horizon lecture: Network Science - From structure to control

International Workshop in Oral Pathology

CCBIO Junior Investigator Daniela Elena Costea is coordinating a project entitled 'Collaboration for education and research in oral pathology between Norway, Moldova, Belarus and Armenia'. UiB/CCBIO's Bergen Oral Cancer Research Group and Experimental Pathology Research Group received in 2016 3 million NOK in funding from SIU through the Eurasia program, to a collaboration project for education and research in oral pathology between Norway, Moldova, Belarus and Armenia. The project started off with a workshop in Bergen in 2016, and in September 2017, the project researchers and educators met at the State University of Medicine and Pharmacy «Nicolae Testemitanu», Chisinau, Moldova for a workshop in this program. At the workshop, the teaching curriculums for dental students and dental hygienists in Norway, Belarus, Armenia and the Republic of Moldova were first analyzed, and a 'blueprint'

of a harmonized curriculum was generated. The workshop was followed by a full day of lectures under the title 'Oral pathology awareness day' on the role of the specialist in oral pathology, diagnosis and prevention of oral cancer and lesions with malignant potential, autoimmune diseases with oral manifestations, Sjogren's syndrome, vesicular-bullous lesions, etc. This event emphasized the importance of studying oral pathology, a borderline discipline between pathology and oro-maxillofacial surgery, which often creates confusion to a dentist that did not receive teaching and training in oral pathology, such is the case of the dentists educated at the universities from Moldova, Belarus or Armenia. Knowledge on various oral pathology topics will enable these dentists also to take the right decision when he or she will encounter a patient with an oral mucous lesion and will increase the quality of the health care provided to the patients in these countries. In addition to the educational and scientific component, UiB/CCBIO and SIU also contribute with administrative and IT components and competence that are meant to help building up the appropriate administrative and IT platforms at the EURASIA collaborative countries necessary for the implementation of the project.

As a result of the discussions during the workshop, several activities have been initiated, such as students exchanges and visiting staff/researchers. An important activity in the project is also the developing of an online course in oral pathology (Professor Anne Christine Johannessen is responsible) and experimental research methods in oral pathology (Professor Daniela Elena Costea is responsible), in collaboration with the IT department at the University of Bergen. ••



2nd Scandinavian Seminar in Translational Pathology

CCBIO was co-organizer of the 2nd Scandinavian Seminar in Translational Pathology, "Next generation tissue based tumor pathology" which was arranged in Sigtuna, Sweden, 17-18 November 2017. Organisers were Patrick Micke, Uppsala, Johanna Mattsson, Uppsala, Lars A. Akslen, Bergen, Karin Jirström, Lund, Johan Botling, Uppsala, Fredrik Pontén, Uppsala and Arne Östman, Stockholm. The meeting focused on tissue based tumor research with the aim of creating a Scandinavian network consisting of scientifically dedicated pathologists and pre-clinical researchers with an interest in the prospects of next generation tissue profiling. Exciting data and developments in multiplex biomarker studies on tissue samples, novel mapping of the tumor microenvironment, tissue proteomics, and the application of artificial intelligence in pathology were presented, along with multiple organ-specific application projects. The extensive and impressive tissue and cell mapping efforts by the Human

Protein Atlas were also discussed. Around 80 participants were gathered at Sigtuna. The meeting in 2018 will be held in Helsinki. ••

Scientific program of the 2nd Scandinavian Seminar in Translational Pathology

Day 1, Friday 17th of November

09:30-09:45 Introduction by Lars A. Akslen
09:45-10:00 Patrick Micke: The Uppsala lung cancer project
10:00-10:15 Karin Jirström: Moving from retro spective to prospective cancer biomarker studies: The best is yet to come?
10:15-10:30 Arne Östman: Multi-marker profiling of tumor microenvironment for biomarker discovery
10:30-10:45 Per Henrik Edkvist: U-CAN
10:45-11:10 Break
11:10-11:25 Johan Botling: The future of molecular diagnostics
11:25-11:40 Lars A. Akslen: Tumor microenvironment markers across breast cancer subtypes
11:40-11:55 Cecilia Lindskog: The Human Protein Atlas: Spatial Proteomics in health and disease
11:55-12:10 Olli Carpén: Molecular response prediction in ovarial cancer
12:10-12:25 Christofer Juhlin: Omics in endocrine tumors
12:25-12:40 Carlos Fernández Moro: Typing of pancreaticobilary adenocarcinomas improves Diagnosis and Prognostic Stratification
12:40-12:55 Karin Leandersson: The immune landscape of breast cancer
13:00-13:55 Lunch
13:55-15:05 Short track: 14 x 5 min presentations
15:05-15:20 Break
15:20-16:10 Short track: 10 x 5 min presentations
16:10-16:35 Break
16:35-16:55 Mats Nilsson: Mapping tissue heterogeneity using in situ sequencing
16:55-17:15 Teijo Pellinen: mIHC-based phenotypic profiling of solid cancers
17:15-17:30 Fredrik Pontén: A New Pathology Atlas
17:30-17:40 Break
17:40-18:00 Guttorm Haraldsen: Inhibition of endothelial Notch signalling attenuates inflammation
18:00-18:20 Artur Mezheyeuski: Multispectral imaging for quantitative immune profiling in lung cancer patients
18:20-18:40 Anna Dimberg: Vascular abnormalization in glioblastoma
19:00-20:30 Dinner
20:30-22:00 Quiz
22:00-24:00 Celebration of the winners

Day 2, Saturday 18th of November

08:30-08:50 Anders Bergh: Tumor instructed normal tissue
08:50-09:10 Johan Hartman: Patient-derived organo typic cultures for therapy prediction
09:10-09:30 Johan Lundin: Artificial intelligence for tissue phenomics and molecular pathology
09:30-09:50 Martin Johansson: Molecular tumorigenesis of renal cancer
09:50-10:05 Break
10:05-10:25 Levent Akyurek: Cytoskeletal filamin regulates vascular remodelling in cancer
10:25-10:45 Richard Palmkvist: TAP1 down-regulation elicits immune escape and poor prognosis in colorectal cancer
10:45-11:05 Hans Brunnström: Diagnostic markers in lung cancer
11:05-11:20 Break
11:20-11:40 Caj Haglund: Search for novel biomarkers in colorectal cancer
11:40-12:00 Monica Nistér: Growth factors and brain tumors
12:00-12:20 T. Diaz de Ståhl: Brain tumor genomics
12:20-12:40 Anna Bofin: Challenges facing breast cancer diagnostics
12:40-13:00 Laszlo Szekely: DIY imaging and imageautomation tools in pathology
13:00-13:10 Arne Östman, Lars A. Akslen: Concluding remarks

Seminar in scientific writing

CCBIO hosted a two-day seminar in scientific writing December 13th and 14th. This was a seminar that came about through an exchange program between the University of Bergen and Harvard Medical School. More precisely, through an INTPART program CCBIO has received funding for from the Recearch Council of Norway (RCN) and the Norwegian Centre for International Cooperation in Education (SIU) to promote students' education and exchange in a collaboration between CCBIO and the Boston based Harvard Medical School and Harvard Kennedy School. Elisabeth Wik and Randy Watnick coordinate the program at the Bergen and Harvard sides, respectively. This two-day seminar in scientific writing was the kickoff of the CCBIO-INTPART program.

The seminar was fully booked shortly after announcement. The auditorium, which takes 90, was full, and the organizers managed a long waiting list until the last minute. The huge interest in this seminar, from students and researchers at both the Medical Faculty, Haukeland University Hospital and other university departments, reflects a need for quality courses addressing 'scientific writing'. Master students, PhD students, postdocs and senior researchers attended, and gave great

reviews after the seminar. The seminar covered topics such as organizing ideas, improving manuscript, clear writing, scientific storytelling, titles and abstracts, cover letter, common mistakes and making a manuscript memorable. Lecturers were Christine Møller, an experienced lecturer in medical and scientific writing and assistant editor of APMIS (Acta Pathologica Microbiologica et Immunologica Scandinavica), and Randy Watnick. A three-week PhD course on vascular biology with lecturers from the Vascular Biology Program, Harvard School of Medicine, will take place autumn 2018. Further, exchange programs for PhD and master students and other seminars on transferable skills are in the planning. ••

Scientific program
for the Scientific Writing Seminar
Wednesday 13th of December

Wednesday 13th of December

09:00–10:00 Organizing your ideas and improving your manuscript

10:00–10:15 Break

10:15–11:15 Clear Writing 1 + Nominalization exercise

11:15–11:30 Break

11:30–12:30 Clear Writing 2 + Deadwood exercise

12:30–13:15 Lunch

13:15–14:15 The Art of Scientific Story Telling 1: How to organize your results and message

14:15–14:30 Break

14:30–15:30 Punctuation + Comma exercise

Thursday 14th of December

09:00–10:00 Titles and abstracts

10:00–10:15 Break

10:15–11:15 The Art of Scientific Story Telling 2: Common mistakes and how to avoid them

11:15–12:00 What makes a manuscript memorable?

12:00–12:45 Lunch

12:45–13:15 Numbers exercise

13:15–13:45 The cover letter

13:45–14:00 Summing up

The 5th CCBIO Annual Symposium

19th-20th April, 2017, at Solstrand Hotel & Bad

More than 200 participated at the annual meeting, with lecturers from within CCBIO as well as visiting top researchers from Europe and the United States. Both junior and senior researchers met to be updated on the latest in their own field of research within cancer biomarkers, and at the same time enjoy the beautiful resort and surroundings of Solstrand.

This year's program covered various timely topics like EMT (epithelial-mesenchymal transition), tumor microenvironment, immune regulation and immune therapy, neural regulation of tumors, cell signaling, TP53, systems biology of tumors and drug screening, tumor hypoxia, PDX models, tumor imaging techniques and liquid biopsy. Several distinguished international and national speakers presented their data and views on current front-line concepts. The program also included a session for younger investigators, presenting data ranging from genomics studies to the ethics of cancer biomarkers. Towards the end, Jeanette Wood had a very thoughtful presentation on the roles and interplay of pharma, biotech, academia and funding bodies in drug discovery.

The release of the first CCBIO-based book was announced by Roger Strand: Cancer Biomarkers: Ethics, Economics, and Society (edited by Anne Blanchard and Roger Strand). The program also included an example of how the latest news from the research front might be less uplifting. Dr. Robert P. Gale of the University of California (Los Angeles) presented figures indicating that Next Generation Sequencing (NGS), a detailed mapping of genetic alterations of tumors, does not necessarily lead to improved treatment for most cancer patients.

The symposium also made room for two long poster sessions during which younger researchers could present their research. The 38 posters attracted much interest, and a jury selected 3 winners of best posters. ••

Centre for Cancer Biomarkers

5th CCBIO Symposium 2017

Solstrand, April 19-20, 2017 Bergen -Norway

Norwegian Centre of Excellence
The Research Council of Norway

SCIENTIFIC PROGRAM

Day 1: Wednesday April 19, 2017

09:00-10:00 Registration and Coffee

10:00-10:15 **Lars A. Akslen (Director of CCBIO):** Introduction to CCBIO Symposium 2017.

Chair: Jean Paul Thiery

10:15-11:00 **John Heymach:** EMT, immunomodulation and therapeutic resistance

11:00-11:45 **Angela Nieto**: The partial EMT and cell plasticity in fibrosis and cancer

11:45-12:30 **Robert Gale:** What precisely is precision oncology and will it work?

12:30-14:30 LUNCH AND POSTER SESSION I

Young Investigators
- Chair: Bjørn Tore Gjertsen

14:30-14.50 **Erling A. Høivik:** The genetic evolution of endometrial cancer metastasis

14:50-15:10 **Randi Hovland:** Liquid biopsy biomarkers in clinical trials

15:10-15:30 **Oddmund Nordgård:** Liquid biopsies in pancreatic cancer

15:30-15:50 **Thomas Arnesen:** N-terminal acetyl-transferases - novel cancer drug targets

15:50-16:10 **Eirik Tranvåg:** Biomarkers and potential impact on priority setting

16:10-16:40 COFFEE

16:40-16:50 **Roger Strand:** Book Presentation: "Cancer Biomarkers: Ethics, Economics, and Society"

Chair: Oddbjørn Straume

16:50-17:20 **Diane Bielenberg:** Expression of Neuropilins in the Epithelium and Endothelium are Biomarkers of Cancer Progression

17:20-17:50 **Kristin Taskén:** What's up with β adrenergic receptor signaling and prostate cancer?

Day 2: Thursday April 20, 2017

Chair: Donald Gullberg

09:00-09:45 **Carl Henrik Heldin**: Signaling via TGFb receptors: possible targets in tumor treatment

09:45-10:15 **Jean-Christoph Bourdon:** The cell response to anticancer drugs is defined by the p53 protein isoforms in mutant TP53 cells

10:15-10:45 **Krister Wennerberg**: Systems medicine methods for identification of stratified leukemia therapies and their predictive biomarkers

10:45-11:15 COFFEE

Chair: Karl-Henning Kalland

11:15-11:45 **Salem Chouaib:** Effect of hypoxic stress on the cytotoxic anti-tumor response

11:45-12:15 **Spiros Kotopoulis:** Targeting cells with ultrasound: from theory to reality

12:30-14:15 LUNCH AND POSTER SESSION II

Chair: Emmet McCormack

14:15-14.45 **Frederic Amant:** Patient derived xenografts as a preclinical model

14:45-15:15 **Janine Terra Erler:** ECM remodelling during cancer progression.

15:15-15:45 **Jeanette Wood:** Role of pharma, biotech, academia and funding bodies in drug discovery innovation

15:45-16:00 **Bjørn Tore Gjertsen (Co-Director of CCBIO):** Closing remarks.

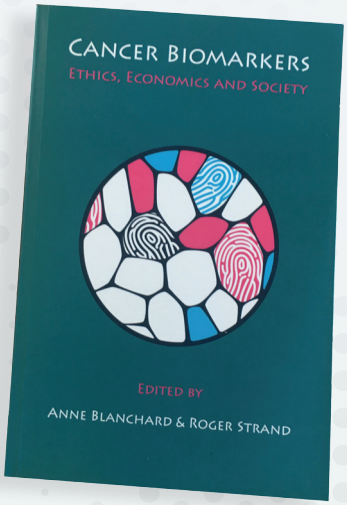
The 5th **Annual Symposium**

19th-20th April 2017
at Solstrand Hotel & Bad

Cancer Biomarkers: Ethics, Economics and Society

The Ethics, Economics and ELSA research groups of CCBIO are coordinating their research activities more than ever. In April 2017 they published their first joint book volume "Cancer Biomarkers: Ethics, Economics and Society". This was CCBIO's first book release. The foreword by Bruce Zetter, and preface by Lars A. Akslen, were followed by several chapters with contributions by CCBIO investigators and other experts.

A shared platform for CCBIO´s research in ethics, economics and ELSA topics has recently been established. A core element in the transformation of cancer medicine into precision medicine is that individuals rather than groups become the unit of analysis. By joining forces they will be able to understand better the implications and preconditions of this transformation in terms of ethical considerations, market mechanisms, scientific development and the political economy of cancer research.



Cancer care is undergoing a shift from a 'one-size-fits all' approach to more personalised medicine. One way of personalising cancer treatments is through biomarkers: molecules or biochemical changes found in the patient's tissues and body fluids.

This book reflects upon the promise of cancer biomarkers and asks questions such as: How may the complexity of cancer biology impede the robustness of biomarkers in the clinic? How should one draw the line between the various sub-groups of patients for personalised treatment? How can one evaluate the cost-effectiveness and fairness of personalised cancer treatments? By bringing together authors from the fields of science and technology studies, medical ethics and philosophy, health economics and oncology, the book aims to give a critical yet accessible overview of some of the key social, ethical and economic issues that surround cancer biomarkers.

CCBIO Director Lars A. Akslen comments about the book: "In this book, important topics surrounding the medical part of biomarker research are presented and discussed. Key questions are asked and reflected upon: What is a good (enough) biomarker? How should we prioritize in modern cancer treatment? Can biomarkers make a real difference? How can biomarkers change and improve the cost structure when using very expensive drugs and when only a few patients respond to the treatment? How can we deal with big data profiles for individual patients - such as patterns of genetic alterations or functional protein signatures? Hopefully, these thoughtful chapters can stimulate our reflections on how we design and perform biomarker research. On top of basic and clinical projects, we have realized that bringing in these additional topics have intensified our reflection on own activities. This goes to the core of the RRI-concept, i.e. to perform responsible research and innovation."

Bruce Zetter, Charles Nowiszewski Professor of Cancer Biology in the Department of Surgery, Harvard Medical School, comments: "The book should be required reading for oncologists, medical students, graduate students and especially for those who make policy decisions regarding the use and reimbursement of cancer biomarkers." ••

Biomarkers of the Tumor Microenvironment - Basic Studies and Practical Applications

CCBIO with editors Lars A. Akslen and Randolph S. Watnick published August 31, 2017, a new book through Springer Publishing, titled «Biomarkers of the Tumor Microenvironment - Basic Studies and Practical Applications». The book contains 22 chapters with more than 500 pages and multiple illustrations, with a general introduction to the topic (prologue) by Robert A. Weinberg. The foreword is written by Jean Paul Thiery. Several CCBIO investigators and affiliated professors have contributed.

This book reviews different aspects of the cancer microenvironment, and its regulation and importance for tumor progression. Practical applications, in terms of how biomarkers are increasingly included in therapy protocols, are also discussed.

The book covers basic model studies of novel biomarkers and treatment targets of the microenvironment, exploration and validation of different classes of biomarkers in human tumors, and challenges of clinical implementation and treatment trials. It has high-quality illustrations and colour images of tissue-based biomarkers.

Biomarkers of the Tumor Microenvironment: Basic Studies and Practical Applications is aimed at research pathologists in the cancer field, and also cancer researchers from other backgrounds, especially those using morphology techniques and models focusing on cross-talk between different cell types in tumors.

"The importance of the microenvironment for tumor progress is a rapidly expanding and very exciting field", say Lars A. Akslen and Randolph S. Watnick, the book editors. "How immune cells, vascular cells, fibroblasts and the matrix co-operate and coordinate with tumor cells to advance cancer growth and spread is increasingly recognized. How companion biomarkers related to the tumor microenvironment can be used in diagnostic and therapeutic work is therefore a key question. We are very excited that this book project has been finally realized, and we would like to thank all contributors for their important work," Akslen and Watnick conclude. ••

10 DISSEMINATION AND COMMUNICATION

Dissemination and Communication

CCBIO aims to communicate novel findings to the public in a timely and informative way. Our research can be viewed, read and listened to both in national mainstream media and publications with more specific audiences. We are also actively using our web pages, keeping them updated at all times and presenting big and small news stories from our research community.

Social media has grown to be a 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.

CCBIO offers schools a unique way of learning about cancer cells in the form of a play, or a highly entertaining presentation for other audiences. Since 2016, we have offered a choice between the play "Stop the cancer cell Gloria Glutton!" which is appropriate for children in the age of 4 to 13, or the lecture/stand-up routine "Christine the Cancer Cell – A sociopath in the body", suitable for youth and adults. Both are free of charge, and the creator and performer is Henriette Christie Ertsås, PhD Fellow at the Department of Biomedicine and CCBIO. During 2017, 7 shows were booked at schools and events, and proved to be a success both with the children and the teachers and parents.

Every year, CCBIO is present at the national Research Days Festival in Bergen, with an interactive stand where people and children in particular, can do a little research themselves. This is always very popular.

Example of facebook-entry. The CCBIO director and other CCBIO researchers are interviewed about cancer research.

Example of twitter entry. Short video with the CCBIO SAB Chairman Carl-Henrik Heldin, sharing 5 tips on how to become a successful cancer researcher, filmed at the CCBIO Annual Symposium 2017.

CCBIO in the Media

In 2017, CCBIO had a total of 54 mass media appearances. Links to each news story can be found at www.ccbio.no, submenu CCBIO in the media.

28.11.17 – NATIONAL FOUNDATION OF CANCER RESEARCH (USA)
«Parasite Killer Too Found to be Effective Cancer Treatment Candidate» – Karl-Henning Kalland

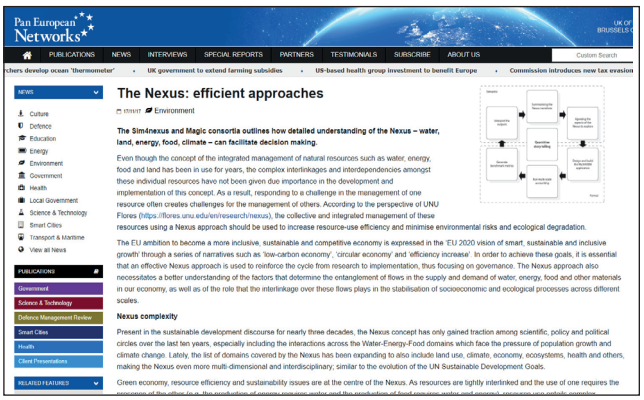
23.11.17 – THE AUSTRALIAN HOSPITAL HEALTHCARE BULLETIN
«Gut instinct: tapeworm drug fights prostate cancer»
– Karl-Henning Kalland

20.11.17 – SCIENCENORDIC
«Tapeworm drug fights prostate cancer»
– Karl-Henning Kalland

17.11.17 – COLORECTAL CANCER CANADA
«Tapeworm Medicine Stops Prostate, Colon Cancer Cells from Growing, New Study Finds» – Karl-Henning Kalland

17.11.17 – PROSTATE CANCER NEWS TODAY
«Tapeworm Medicine Stops Prostate, Colon Cancer Cells from Growing, New Study Finds» – Karl-Henning Kalland

17.11.17 – PAN EUROPEAN NETWORKS
«The Nexus: efficient approaches» – Roger Strand



17.11.17 – DOTEMIRATES
«Existing parasite drug may fight prostate, colon cancer»
– Karl-Henning Kalland

16.11.17 – EUROPEAN PHARMACEUTICAL REVIEW
«Tapeworm drug fights prostate cancer»
– Karl-Henning Kalland

15.11.17 – EUREKALERT!
«Tapeworm drug fights prostate cancer»
– Karl-Henning Kalland

14.11.17 – ALPHAGALILEO
«Tapeworm drug fights Prostate Cancer»
– Karl-Henning Kalland

09.11.17 – AFTENPOSTEN
«Mye brukt hjertemedisin beskytter mot kreft»
– Gry Sandvik Haaland

09.11.17 – BERGENS TIDENDE
«Mye brukt hjertemedisin beskytter mot kreft»
– Gry Sandvik Haaland

23.10.17 – THE ASCO POST
«Axl Inhibitor BGB324 in Combination With Trametinib Plus Dabrafenib or Pembrolizumab in Advanced Melanoma»
– Oddbjørn Straume

18.10.17 – 4-TRADERS
«BerGenBio: announces strong recruitment and encouraging safety profile for AXL Inhibitor BGB324 in a melanoma study at 9th World Congress of Melanoma»
– Oddbjørn Straume

18.10.17 – NEWSWEB OSLO BØRS (OSLO STOCK EXCHANGE)
«BerGenBio announces strong recruitment and encouraging safety profile for AXL Inhibitor BGB324 in a melanoma study at 9th World Congress of Melanoma»
– Oddbjørn Straume

17.10.17 – ALPHAGALILEO
«More than 700 experts on biochemistry and molecular biology take part in the first edition of the FEBS3+ Congress»
– Roger Strand

12.10.17 – HEGNAR.NO
«BerGenBio skal holde presentasjon i Australia»
– Oddbjørn Straume

12.10.17 – NEWSWEB OSLO BØRS (OSLO STOCK EXCHANGE)
«Clinical Study with BGB324, BerGenBio's Selective First-in-Class AXL Inhibitor, to be Presented at the 9th World Congress of Melanoma» – Oddbjørn Straume

10.10.17 – NORDIC LIFE SCIENCE NEWS
«Bergen – Pushing bioinformatics further»
– Inge Jonassen

02.10.17 – HAUGESUND AVIS
«Jeg hørte om alle det gikk bra med, og trodde det skulle virke også på meg» – Oddbjørn Straume

14.09.17 – DEN NORSKE TANNLEGEFORENINGS TIDENDE
«Biomarkører - fremtidens verktøy i kreftbehandlingen?»
– Daniela E. Costea

04.09.17 – FORSKERFORUM
«Immunforsvarets frontliner» – Agnete Engelsen


Feltrapport | Hvordan arbeider forskere, og hva finner de ut? Feltrapport er Forskerforums faste reportasje fra forskningsmiljøer.

Immunforsvarets frontliner

I prinsippet kan immunsystemet vårt ta knekken på kreft. Men kreftcellene tyr til kamuflasje for å sleppe unna.

TEKST: KIERSTIN GJENGEDAL | FOTO: GUSSE TORGØE

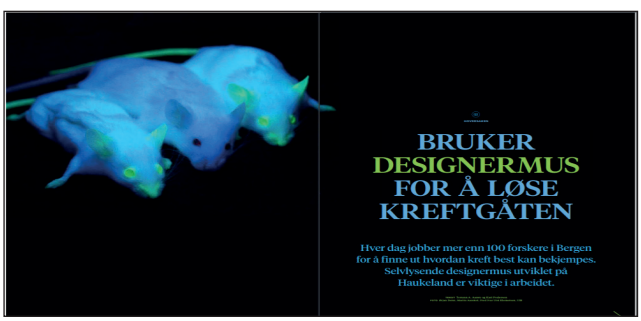
GUSTAVE ROUSSY

– Gustave Roussy-instituttet er grunnlagt på samspelet mellom forsking, pasientbehandling og undervising. Det er ein stor styrke, seier Agnete Engelsen.

30.07.17 – VG
«Fars gener bidrar til at mor får svangerskapsforgiftning» – Liv Cecilie Vestrheim Thomsen

22.07.17 – BERGENS TIDENDE MAGASINET
«Bruker designermus for å løse kreftgåten»
– Lars A. Akslen, Bjørn Tore Gjertsen, Oddbjørn Straume, Line Bjørge, Monica Hellesøy and Stein Erik Gullaksen


– Kreftforskning er som å samle inn mange biter, og så forsøke å sette dem sammen og se h


BRUKER DESIGNERMUS FOR Å LØSE KREFTGÅTEN

Hver dag jobber mer enn 100 forskere i Bergen for å finne ut hvordan kreft best kan bekjempes. Selvlysende designermus utviklet på Haukeland er viktige i arbeidet.

16.07.17 – KHRONO
«Ny forskingsdirektør i Helse Bergen»
– Bjørn Tore Gjertsen

13.07.17 – PÅ HØYDEN
«Gjertsen ny forskingsdirektør i Helse Bergen»
– Bjørn Tore Gjertsen

09.07.17 – FIRDAPOSTEN
«Vert ny forskingsdirektør ved Helse Bergen»
– Bjørn Tore Gjertsen


Firdaposten

Prøv oss! 5 kr for 5 veker

Skriv sjølv | Nettavisen + | Kjøp billettar | Gamle bilde | FREDAG 9. FEBRUAR 2018 | Bli abonnent! | Meny

LOKALNYTT HELSEVESEN HELSE

Vert ny forskingsdirektør ved Helse Bergen

Ny leiar: Bjørn Tore Gjertsen tek over som forskingsdirektør ved Helse Bergen frå 01. november. Foto: Kathrine Sunde, Haukeland Universitetssjukehus

Av Andreas Hopen

09. juli 2017, kl. 12:24

DEL Lokale nyheiter - 5 kr for 5 veker

Bjørn Tore Gjertsen frå Florø tek over som forskingsdirektør ved Helse Bergen på Haukeland universitetssjukehus. 50-åringen jobbar no som overlege ved Seksjon for forsking og innovasjon (Seksjon for blodsjukdommar), og han er professor i hematologi og prosjektleiar ved Centre of Cancer Biomakers ved universitet i Bergen. Gjertsen tek over den nye jobben 01. november 2017.

ANNONSE

Annonsen er lukket av Google

Slutt å se denne annonsen | Annonsevalg

09.07.17 – HELSE BERGEN NETTAVIS
«Bjørn Tore Gjertsen er ny forskingsdirektør»
– Bjørn Tore Gjertsen

06.07.17 – PÅ HØYDEN
«Eg er blitt betre på small talk»
– Anne Christine Johannessen

29.06.17 – IFINNMARK
«Nå kommer varmen – men husk at huden ikke glemmer solskader» – Oddbjørn Straume

27.06.17 – PÅ HØYDEN
«Forskningsrådet deler ut én milliard» – Inge Jonassen

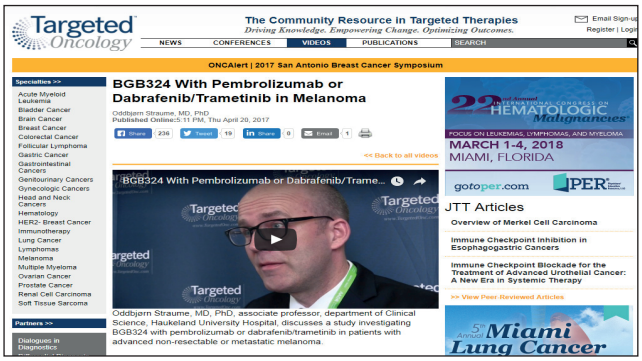
22.06.17 – ABC NYHETER
«Intens sommersoling kan gi føflekkreft»
– Oddbjørn Straume

06.06.17 – TIDSSKRIFTET, DEN NORSKE LEGEFORENING
«Proliferasjonsmarkører ved brystkreft» – Gøril Knutsvik

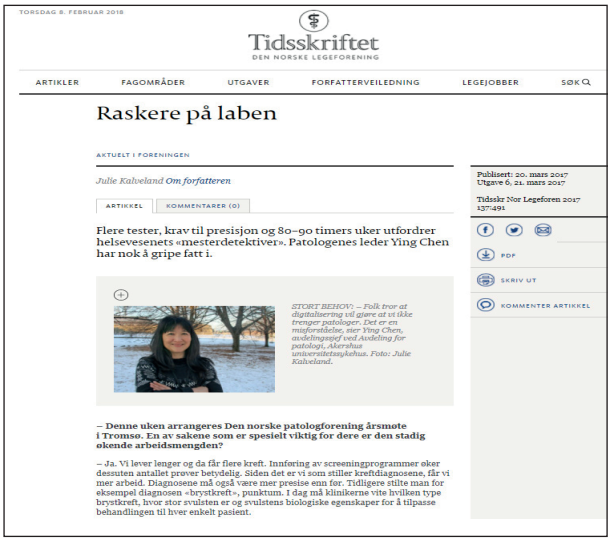
22.05.17 – OSLO BØRS NEWSWEB
«BerGenBio Announces Start of Randomised Phase I/II Trial Assessing Selective AXL Inhibitor BGB324 in Combination with Current Therapies in Melanoma» – Oddbjørn Straume

18.05.17 – NRK RADIO, EKKO
«Kreft i fremtiden» – radio interview with Roger Strand and Lars A. Akslen

20.04.17 – TARGETED ONCOLOGY
«BGB324 With Pembrolizumab or Dabrafenib/Trametinib in Melanoma» – video interview with Oddbjørn Straume



20.03.17 – TIDSSKRIFTET, DEN NORSKE LEGEFORENING
«Raskere på laben» – Ying Chen



12.03.17 – FIRDA PLUSS
«Proffdansar tok spranget til kreftforsking»
– Amalie Svanøe

12.03.17 – BERGENSAVISEN PLUSS
«Proffdanser tok spranget til kreftforskning»
– Amalie Svanøe

12.03.17 – BERGENSAVISEN
«Danseren ble forsker» – Amalie Svanøe

08.03.17 – BERGENS TIDENDE
«Nå vil Bergenbio på børs»
– James Lorens and Oddbjørn Straume

05.03.17 – FIRDAPOSTEN
«Dansaren Amalie er blitt til forskaren Amalie»
– Amalie Svanøe

01.03.17 – PÅ HØYDEN
«Den ubehagelige forskningen har vært det svake punktet i SFF-porteføljen» – Roger Strand

27.02.17 – DAGENS MEDISIN
«Sikret finansiering» – Oddbjørn Straume

25.02.17 – ØSTLANDSPOSTEN
«Blir kreftforsker i USA» – Maria Omsland

20.02.17 – TIDSSKRIFTET, DEN NORSKE LEGEFORENING
«Hva er ansvarlig kreftforskning»
– Roger Strand and Lars A. Akslen


TORSDAG 8. FEBRUAR 2018

Tidsskriftet
DEN NORSKE LEGEFORENING

ARTIKLER FAGOMRÅDER UTGAVER FORFATTERVEILEDNING LEGEJOBBER SØK

Hva er ansvarlig kreftforskning?

KRONIKK | ONKOLOGI

Roger Strand, Lars A. Akslen Om forfatterne

ARTIKKEL LITTERATUR KOMMENTARER (2) ENGLISH

Nye muligheter innen kreftbehandling gir bedre helse, men også risiko for økte kostnader og flere prioriteringsdilemmaer. Kritisk diskusjon av kreftforskningens egne fremtidsforestillinger kan bidra til en mer ansvarlig forsknings- og helsepolitikk. Rammeverk for ansvarlig forskning og innovasjon gir nyttige begreper for en slik diskusjon.

Illustrasjon: Grjan Jensen/Dagerpop

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PDF
SKRIV UT
KOMMENTER ARTIKKEL

20.02.17 – UIB NEWS
«Alt skal klaffe» – James Lorens (interview regarding the mention in the Norwegian Prime Minister's New Year's Address)


INNOVASJON

Biokjemi ble suksessbedrift

Historien om selskapet BerGenBio er historien om en forsker som etter 10 år i USA vet hva som må til for å gjøre forskning om til medisin. Det er også historien om hvordan en baker en kake.

PÅ LABEN: I BerGenBio er de i gang med å prøve ut en ny kreftmedisin på pasienter. Foto: Ingvild Pastervell Mellen

09.02.17 – DAGENS MEDISIN
«Helsefolk» – Agnete Engelsen

03.02.17 – KK (KVINNER OG KLÆR)
«Norge er i verdenstoppen når det gjelder dødelighet av føflekkreft» – Lars A. Akslen


MENY kk

FØFLEKKKREFT: Personer med lys hud som ikke blir særlig brun ved soling er særlig utsatt for føflekkreft. Dette bør du være obs på! Foto: Shutterstock / Albina Glisic

Føflekk

- Norge er i verdenstoppen når det gjelder dødelighet av føflekkreft

... Og noen er mer utsatt enn andre, og de bør være ekstra påpasselige med solvanene sine. Dette må du være obs på!

Stine Tunstrøm | Journalist

03.02.17 – KVINNHERINGEN
«Revolusjonerande utvikling»
– Oddbjørn Straume

12.01.17 – UNIFORUM
«Får 10 millionar kroner til Parkinson-forsking frå Olav Thon Stiftelsen» – Lars A. Akslen and Elisabeth Wik

12.01.17 – UNIVERSITAS
«Knut Mørken og Are Raklev vant pris for fremragende undervisning» – Lars A. Akslen and Elisabeth Wik

12.01.17 – NTB INFO
«Olav Thon Stiftelsen: Her er prisvinnerne for 2017»
– Lars A. Akslen and Elisabeth Wik


NTB info Hjem Følg innhold Våre kunder Om tjenesten Bli kunde

OLAV THON STIFTELSEN

Olav Thon Stiftelsen: – Her er prisvinnerne for 2017

12.1.2017 10:10 | Olav Thon Gruppen

Del

Olav Thon Stiftelsen deler årlig ut priser til personer og forskningsprosjekter som har utmerket seg spesielt innen sine fagområder i Norge og i utlandet.

Olav Thon (t.v.) og rektor ved Universitetet i Oslo, Ole Petter Ottersen, under kunngjøringen av prisvinnerne for 2017. Foto må krediteres med: Yngve Vogt/UiO

13.01.17 – PÅ HØYDEN
«Tre Olav Thon-tildelinger til UiB»
– Lars A. Akslen and Elisabeth Wik

FACTS AND FIGURES 2017

104 54

The 104 scientific publications and 54 mass media stories in 2017 shows that CCBIO emphasizes dissemination of its research results.

PERFORMANCE INDICATORS

	2013	2014	2015	2016	2017	TOTAL
PUBLICATIONS	76	71	77	85	94	403
COMPLETED PHDS	5	6	3	10	12	36
EXTERNAL FUNDING MNOK	7,2	21,9	22,5	36,0	34,0	122
MEDIA APPEARENCES	39	11	32	31	54	167

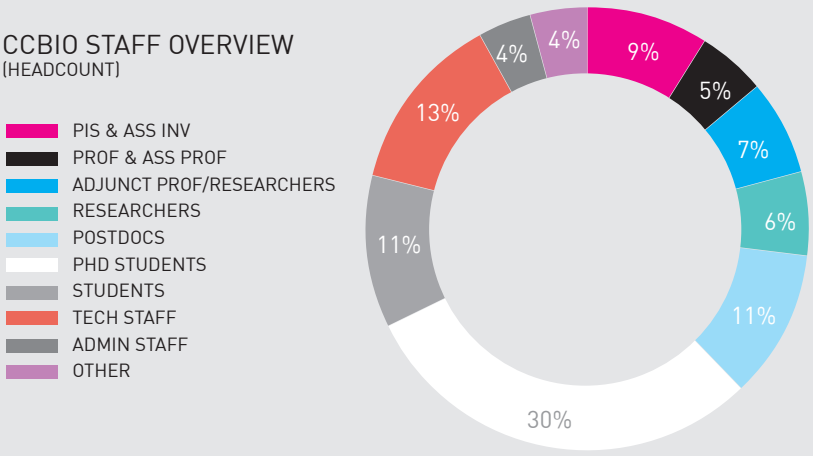
The table illustrates CCBIO's performance for 2013-2017. The scientific production is high and rising, as the first round of CoE financed PhDs and postdocs conclude their projects. The influx of external funding is very good and numbers illustrate external funds consumed for the respective year.

GENDER DISTRIBUTION
(HEADCOUNT)

TOTAL: 211 PERSONS

In general, of the 211 persons involved in CCBIO, the gender distribution is female dominated with 66 %. This also reflects the gender distribution for PhD students and postdocs with 65 % females and 35 % males in both groups. This tendency shifts among professors and associate professors, where the balance is 41 % female and 59 % male. However, recruitment of excellent female staff to enlarge CCBIO's group of investigators has considerably lowered the male dominance in this group. By attaining a more balanced gender distribution in its top tire, CCBIO aims to put all available talent to its best use. Hence, gender balance can be achieved without compromising on excellence.

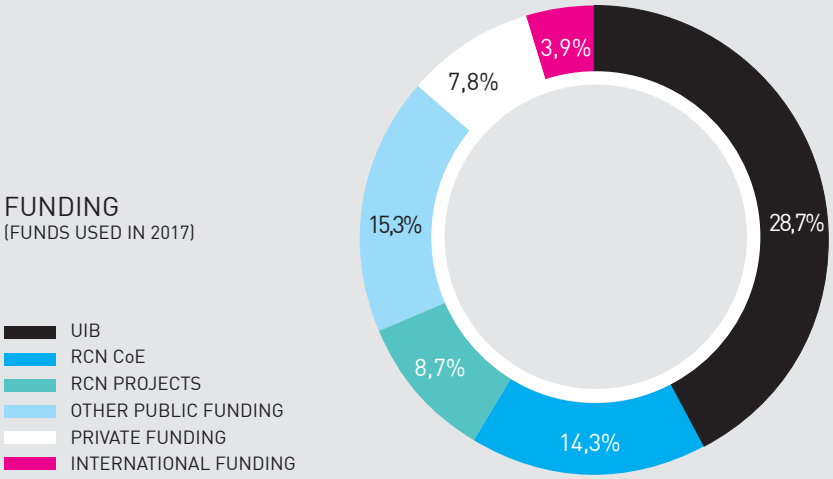
CCBIO STAFF OVERVIEW
(HEADCOUNT)



TOTAL: 211 PERSONS

CCBIO has a quite balanced composition of junior and senior researchers. In the second financing term, CCBIO aims to increase the amount of CoE-financed postdoctoral positions to be more in accordance with the RCN's policy of a 1-to-1 relation between PhDs and postdocs. This will improve the chance of recruiting future excellent researchers, and thereby increase the chance of high impact publications and major breakthroughs originating from CCBIO's recruitment positions and increase the level of excellence. Recruitment of investigators, several female, is an important effort to ensure continuation of high impact projects after 2023, in addition to improve the gender balance within the CCBIO investigator group. CCBIO's international network of 13 adjunct professors and researchers ensures excellent access to high-level collaboration, advice and tuition for CCBIO's researchers, younger researchers and PhDs respectively. The majority of CCBIO's staff has Norwegian origin (62 %) and an equal amount originates from African and Asian countries (19 %) and other Western countries (19 %).

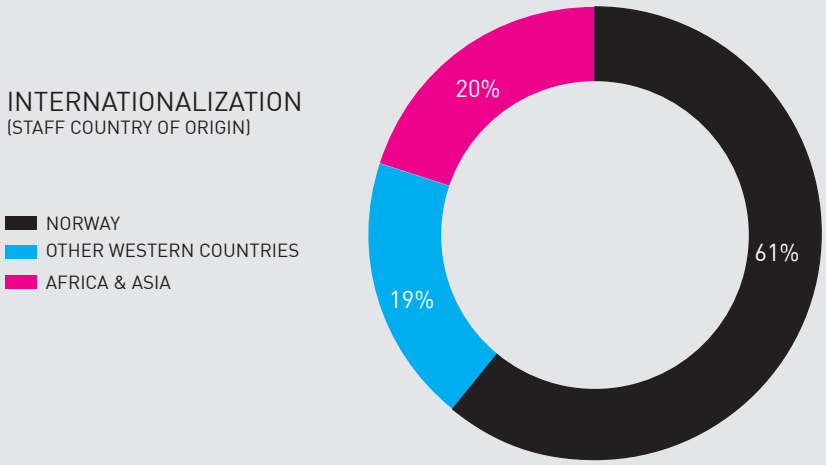
FUNDING
(FUNDS USED IN 2017)



TOTAL = 78,8 MILL NOK

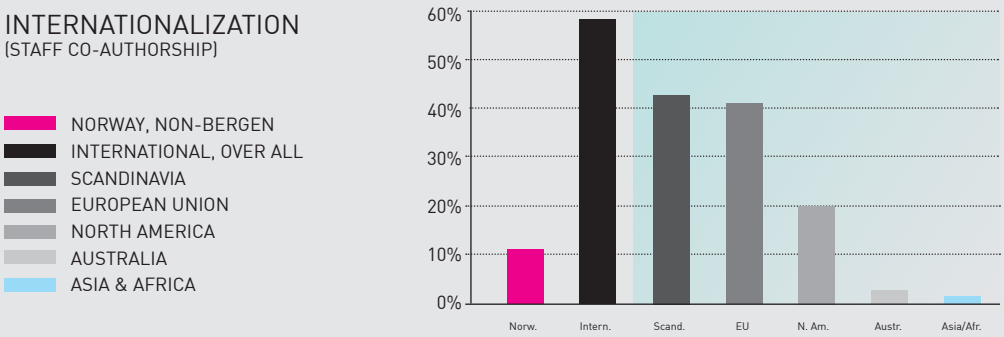
Total funds used in 2017 were 78.8 MNOK, of which 55.3% is the RCN CoE funding and own funding from UiB, which is a slight increase from 2016. The external funding is 34.8 MNOK. This is almost three times the budgeted amount and illustrates a high success rate with public and private funding agencies. We expect to see a further increase in external funds used as CCBIO moves into the second term because of CCBIO's resource intensive research, while at the same time ensuring that funding is used to the best possible effect.

INTERNATIONALIZATION
(STAFF COUNTRY OF ORIGIN)



CCBIO is an international institution where 39 % of its staff are foreign nationalities. Among PhDs and postdocs, 45 % and 42 % respectively originate from outside of Norway. Among CCBIO's senior researchers 39% are foreign nationalities due to CCBIO's recruitment of a predominantly international network of top tire researchers to adjunct positions. CCBIO's large international research network has generated a large amount of scientific publications. Here 58 % of co-authors are from international institutions. International co-authorship has stronger prevalence than co-authorship by researchers from other Norwegian universities (11% of publications). Subdividing the international co-authorships into regions demonstrates that CCBIO collaborates with institutions from most major world regions. Many of CCBIO's international publications have co-authors from more than one region, showing true multilateral collaboration across world regions.

INTERNATIONALIZATION
(STAFF CO-AUTHORSHIP)



Complete list of personnel at CCBIO

Name	Position	Academic title	Group
Aasebø, Elise	PhD student	MS, PhD	Gjertsen
Aass, Håvard Hoel	Senior Executive Officer	MA	Administration
Ahmed, Israa	PhD student	DDS	Johannessen
Akslen, Lars A.	Professor, Director, Principal Investigator	MD, PhD	Akslen
Alam, Jahedul	PhD student	MS	Gullberg
Ali, Hassan	PhD student	DDS	Johannessen
Amant, Frédéric	Adjunct Professor	MD, PhD	CCBIO
Andresen, Vibeke	Researcher	MS, PhD	Gjertsen
Arnes, Jarle	Senior Consultant	MD, PhD	Akslen
Askeland, Cecilie	PhD student	MD	Akslen
Askildsen, Jan Erik	Professor, Associate Investigator	MA, PhD	Askildsen
Azeem, Waqas	PhD student	MS	Kalland
Aziz, Sura Muhammed	PhD student	MD	Akslen
Bachmann, Ingeborg M.	Professor	MD, PhD	Akslen
Bakke, Ragnhild Maukon	Student		Kalland
Bedringaas, Siv Lise	Chief Engineer	MS	Gjertsen
Bentsen, Pål Tore	PhD student	MS	Gjertsen
Berg, Anna	PhD student	MD	Gyn-Cancer
Berge, Sissel Vik	Chief Engineer		Lorens
Beroukhim, Rameen	Adjunct Researcher	MD, PhD	CCBIO
Birkeland, Eivind Salmorin	Student	MS	Johannessen
Birkeland, Even	Postdoc	MS, PhD	Akslen
Bischof, Katharina	PhD student	MD	Gjertsen
Bjørge, Line	Professor, Associate Investigator	MD, PhD	Gjertsen
Blanchard, Anne	Postdoc	MA, PhD	Strand
Bougnaud, Sébastien	Postdoc	MS, PhD	Lorens
Bourdon, Jean-Christophe	Adjunct Researcher	MS., PhD	CCBIO
Breines, Ragna	Administrative Leader	Siv.Ing, PhD	Administration
Brekken, Rolf	Adjunct Professor	MD, PhD	CCBIO
Brohdal, Tore Andre	Student		Reed
Brodal, Hans Petter	Staff Engineer	MS	Gjertsen
Børretzen, Astrid	Senior Consultant	MD	Akslen
Cairns, John	Adjunct Professor, Associate Investigator	MA, PhD	Cairns
Chen, Ying	PhD student	MD	Akslen
Costea, Daniela Elena	Professor, Junior Investigator	DDS, PhD	Johannessen
Davidsen, Kjersti	PhD student	MD	Lorens/Straume
Dillekås, Hanna	PhD student	MD	Straume
Dimitrakopoulou, Konstantina	Postdoc	MS, PhD	Jonassen
D'Mello, Stacey Ann	Researcher		Lorens
Dongre, Harsh	PhD student		Johannessen

Name	Position	Academic title	Group
Dowling, Tara Helen	PhD student	MS	Gjertsen
Dybvik, Julie	PhD student	MD	Gyn-Cancer
Dyrkolbotn, Kjetil	Higher Executive Officer	MA	Administration
Edelmann, Reidun Jetne	Postdoc	MD, PhD	Akslen
Edvardsen, Britt	Chief Engineer		Gyn-Cancer
Eldevik Fasmer, Kristine	PhD student		Gyn-Cancer
Enge, Elisabeth	Study Nurse		Gyn-Cancer
Engelsen, Agnete	Postdoc	MS, PhD	Lorens
Engen, Caroline Benedicte	PhD student	MD	Gjertsen
Engerud, Hilde	PhD student	MD	Gyn-Cancer
Ertsås, Henriette	PhD student	MS	Lorens
Erusappan, Pugazendhi	PhD student	MS	Gullberg
Eskender, Mariamawit	Student		Akslen
Fagerholt, Oda Helen Eck	Student		Gjertsen
Finne, Kenneth	Postdoc	MS, PhD	Akslen
Fonnes, Tina	PhD student	DVM	Gyn-Cancer
Forthun, Rakel Brendsdal	Researcher	MS, PhD	Gjertsen
Fredriksen Berg, Hege	Staff Engineer	MS	Gyn-Cancer
Freds, Larry	PhD student	MS	Gullberg
Furriol, Jessica	Postdoc	MS, PhD	Akslen
Gabra, Hani	Adjunct Professor	MD, PhD	CCBIO
Gabrielsen, Tommy Staahl	Professor	MA, PhD	Askildsen
Gafaar, Nuha	PhD student	DDS	Johannessen
Gavasso, Sonia	Researcher	MS, PhD	Gjertsen
Gjertsen, Bjørn Tore	Professor, Co-Director (Feb 2016-), PI	MD, PhD	Gjertsen
Grønning, Mona	Chief Engineer		Gullberg
Gullaksen, Stein Erik	PhD student	MS	Gjertsen
Gullberg, Donald	Professor, Principal Investigator	MS, PhD	Gullberg
Ha, Trung Quang	PhD student	MD, MS	Gjertsen
Haaland, Gry	PhD student	MD	Lorens/Straume
Hajjar, Ehsan	PhD student	MS	Gjertsen
Haldorsen, Ingfrid Salvesen	Professor	MD, PhD	Gyn-Cancer
Halle, Mari Kyllesø	PhD student	MS	Gyn-Cancer
Hallseth, Gerd Lillian	Chief Engineer		Akslen
Halvorsen, Ole Johan	Professor	MD, PhD	Akslen
Hassan, Ali	Student	DDS	Johannessen
Heljasvaara, Ritva	Adjunct Researcher	MS, PhD	CCBIO
Hellesøy, Monica	Researcher	MS, PhD	Gjertsen
Hinz, Stefan	PhD student	MS	Lorens
Hjelle, Sigrun Margrethe	Postdoc	MS, PhD	Gjertsen
Hoang, Hua My	Staff Engineer		Kalland
Hove, Elisabeth	Senior Executive Officer		Administration
Hua, Yaping	PhD student	MS	Kalland
Hugdahl, Emilia	PhD student	MD	Akslen
Huse, Karoline	Student		Strand
Høgås, Mildrid Bønes	Senior Executive Officer		Administration
Høivik, Erling André	Postdoc	MS, PhD	Gyn-Cancer
Jacobsen, Martha Rolland	Student		Johannessen
Jebsen, Nina Louise	Postdoc	MD, PhD	Gjertsen
Johannessen, Anne Christine	Professor, Principal Investigator	DDS, PhD	Johannessen
Jonassen, Inge	Professor, Associate Investigator	MS, PhD	Jonassen
Kalland, Karl-Henning	Professor, Principal Investigator	MD, PhD	Kalland
Kalvenes, Mai Britt	Senior Engineer	MS, PhD	Akslen
Kang, Jing	Staff Engineer	MD	Lorens
Ke, Xisong	Researcher	MS, PhD	Kalland
Kjølle, Silje	PhD student	MS	Akslen
Kjørsvik, Øystein	Student		Jonassen
Klingen, Tor Audun	PhD student	MD	Akslen
Knutsvik, Gøril	Researcher	MD, PhD	Akslen
Konstantinova, Victoria	Student	DDS, MA	Johannessen
Kopperud, Reidun	Senior Engineer	MS, PhD	Gjertsen
Krakstad, Camilla	Associate Professor, Junior Investigator	MS, PhD	Gyn-Cancer
Krüger, Kristi	PhD student	MD	Akslen
Kusche-Gullberg, Marion	Professor	MS, PhD	Gullberg
Labarge, Mark	Adjunct Professor	MS, PhD	CCBIO
Ladstein, Rita Grude	Associate Professor	MD, PhD	Akslen
Leitch, Calum	PhD student	MS	Gjertsen
Lie, Maria Kolnes	PhD student	MS	Lorens
Litlabø, Hanne Bjelland	Student		Akslen
Litlekalsøy, Jorunn	Chief Engineer		Johannessen
Lorens, James B.	Professor, Principal Investigator	MS, PhD	Lorens
Lu, Ning	Senior Engineer	MS, PhD	Gullberg
Luís, Ana Beatriz Mateus D'Avó	PhD student	MA	Askildsen
Løken, Geir Olav	Administrative Leader	MA	Administration
Madissoo, Kadri	Staff Engineer	MS	Gyn-Cancer
Mannelqvist, Monica	Senior Engineer	MS, PhD	Akslen
Marvyin, Kristo	Student		Kalland
Mauland, Karen Klepsland	PhD student	MD	Gyn-Cancer
Mc Cormack, Emmet	Professor, Associate Investigator	MS, PhD	Gjertsen
Mjøs, Siv	Student		Gyn-Cancer
Mohamed, Fatima	Student		Gullberg
Moses, Musime	PhD student	MS	Gullberg
Myrvold, Madeleine	Student		Gyn-Cancer
Nalwoga, Hawa	Researcher	MD, PhD	Akslen
Nazar, Mohammad	PhD student	DDS	Johannessen
Neppelberg, Evelyn	Associate Professor	DDS, PhD	Johannessen
Nguyen, Rebecca	Laboratory apprentice		Gjertsen
Nginamau, Elisabeth Sivy	Researcher	MD, PhD	Johannessen

New staff member in the CCBIO administration

Ragna Breines, born 1980, holds a PhD in molecular biology from the Arctic University of Norway (UiT). She is currently CCBIO's administrative leader and part of the CCBIO management team while Geir Olav Løken is on leave. Ragna has the overall responsibility for the administrative aspects of CCBIO's activities across the six UiB departments. In addition, she interacts with collaborators nationally and internationally. Ragna has previously held various administrative positions at the Medical Faculty, UiT. The last four years she has been project coordinator for network projects and for an international summer school at the Geophysical Institute, UiB.

List of personnel continues

Name	Position	Academic title	Group
Norheim, Ole Frithjof	Professor, Associate Investigator	MD, PhD	Norheim
Nygaard, Ina Hannestad	Research Assistant		Strand
Olsen, Jan Roger	PhD student	MS	Kalland
Omsland, Maria	PhD student	MS	Gjertsen
Onyango, Therese Bredholt	Postdoc	MS, PhD	Gyn-Cancer
Pantel, Klaus	Adjunct Professor	MD, PhD	CCBIO
Pilskog, Martin	PhD student	MD	Straume/Akslen
Puntervoll, Hanne Eknes	Senior Engineer	MS, PhD	Akslen
Qu, Yi	Postdoc	MS, PhD	Kalland
Rajthala, Saroj	PhD student	MS	Johannessen
Ramnefjell, Maria	PhD student	MD	Akslen
Rane, Lalit Shirish	Postdoc	MS, PhD	Gjertsen
Reed, Rolf K.	Professor, Principal Investigator	MD, PhD	Reed
Reigstad, Inga	PhD student	MD, PhD	Reed
Riise, Julie	Associate Professor	MA, PhD	Askildsen
Sabir, Misbah	Staff Engineer	MS	Gjertsen
Salvesen, Gerd Signe	Staff Engineer		Reed
Sandnes, Dagny Ann	Staff Engineer		Johannessen
Sapkota, Dipak	Postdoc	DDS, PhD	Johannessen
Scarlett, Samantha	Research Coordinator	MS	Gjertsen
Schlomm, Thorsten	Adjunct Professor	MD, PhD	CCBIO
Schmid, Caroline	Postdoc	MS, PhD	Reed
Schuster, Cornelia	PhD student	MD, PhD	Straume
Seo, Mikyung Kelly	PhD student	MA	Cairns
Shafiee, Sahba	PhD student	MS	Gjertsen
Skavland, Jørn	Postdoc	MS, PhD	Gjertsen
Skogstrand, Trude	Postdoc	MS, PhD	Reed
Smeland, Hilde Ytre-Hauge	PhD student	MS, PhD	Reed
Solheim, Marion	Advisor		Administration
Stefansson, Ingunn	Associate Professor	MD, PhD	Akslen
Stenmarck, Mille Sofie	Student		Strand
Stigen, Endre	Staff Engineer		Lorens
Strand, Elin	Postdoc	MS, PhD	Gyn-Cancer
Strand, Roger	Professor, Associate Investigator	MS, PhD	Strand
Straume, Oddbjørn	Professor, Principal Investigator	MD, PhD	Straume
Stuhr, Linda	Professor	MS, PhD	Reed
Suleiman, Salwa	Researcher	DDS, PhD	Johannessen
Sulen, André	PhD student	MS, PhD	Gjertsen
Svanøe, Amalie	Student		Akslen
Svendsen, Henrik Løvendahl	Senior Consultant	MS, MD	Akslen
Sørlie, Therese	Adjunct Professor	MD, PhD	CCBIO
Tangen, Ingvild Løberg	PhD student	MS, PhD	Gyn-Cancer
Thiery, Jean Paul	Adjunct Professor	MD, PhD	CCBIO
Tislevoll, Benedicte Sjo	Student		Gjertsen
Tranvåg, Eirik Joakim	PhD student	MD	Norheim
Trovik, Jone	Professor	MD, PhD	Gyn-Cancer
Tveiterås, Maria	Staff Engineer		Reed
Valen, Ellen	Study Nurse		Gyn-Cancer
Vidhammer, Eli Synnøve	Senior Executive Officer		Administration
Vesterheim, Liv Cecilie	Postdoc	MD, PhD	Gjertsen
Watnick, Randolph	Adjunct Researcher	MD, PhD	CCBIO
Werner, Henrica Maria Johanna	Postdoc	MD, PhD	Gyn-Cancer
Wik, Elisabeth	Postdoc, Junior Investigator	MD, PhD	Akslen
Winge Ingeborg	Senior Engineer	PhD	Akslen
Ytre-Hauge, Sigmund	PhD student	MD	Gyn-Cancer
Øijordsbakken, Gunnvor	Chief Engineer		Johannessen
Östman, Arne	Adjunct Professor	MD, PhD	CCBIO
Øyan, Anne Margrethe	Researcher	MS, PhD	Kalland
Åse, Hildegunn	PhD student	MD	Gyn-Cancer

CCBIO LIST OF PUBLICATIONS

CCBIO - List of Publications

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

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